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

FORM 10-Q

(Mark One)

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

For the quarterly period ended March 31, 2022

OR

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

For the transition period from _____ to _____

Commission File Number: 001-38473

Evelo Biosciences, Inc.
(Exact name of registrant as specified in its charter)

Delaware	**46-5594527**
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)
620 Memorial Drive Cambridge, Massachusetts	**02139**
(Address of principal executive offices)	(Zip Code)

(617) 577-0300
(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, $0.001 par value per share	**EVLO**	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 May 9, 2022, the registrant had 53,659,859 shares of common stock, $0.001 par value per share, outstanding.

FORWARD-LOOKING STATEMENTS

This Quarterly Report on Form 10-Q contains forward-looking statements, including within the meaning of 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 fact contained in this Quarterly Report on Form 10-Q are “forward-looking statements” for purposes of this Quarterly Report on Form 10-Q. These statements involve known and unknown risks, uncertainties, assumptions 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 terminology such as “anticipate,” “believe,” “could,” “estimate,” “expect,” “intend,” “may,” “plan,” “potential,” "target," “predict,” “project,” "contemplate," “should,” “will,” “would,” "continue" or the negative or plural of those terms or other similar expressions.

Forward-looking statements may include, but are not limited to, statements about:

- our status as a development-stage company and our expectation to incur losses in the future;
- our ability to continue as a going concern, our future capital needs and our need to raise additional funds;
- our estimates regarding our expenses including research and development costs, future revenues and anticipated future capital requirements;
- our future results of operations, financial position, business strategy and prospective products;
- our ability to build a pipeline of product candidates and develop and commercialize drugs;
- our ability to develop therapeutic interventions;
- plans and objectives of management for future operations and the future results of anticipated products;
- our ability to enroll patients and volunteers in clinical trials, timely and successfully complete those trials and receive necessary regulatory approvals;
- timing and plans for clinical trials and product candidate approvals;
- the timing, progress, receipt and release of data from our ongoing and planned clinical trials and the potential use of those candidates to treat various indications;
- our ability to establish our own manufacturing facilities and to receive or manufacture sufficient quantities of our product candidates;
- our expectations regarding the potential safety, efficacy or clinical utility of our product candidates;
- the impact of the COVID-19 pandemic on our operations, including our preclinical studies and clinical trials, and the continuity of our business;
- our ability to protect and enforce our intellectual property rights;
- federal, state and foreign regulatory requirements, including regulation of our product candidates by the U.S. Food and Drug Administration (the "FDA");
- the likelihood of regulatory filings and approvals;
- our ability to obtain and retain key executives and attract and retain qualified personnel;
- activities related to strategic collaborations and anticipated revenue therefrom;
- our ability to successfully manage our growth; and
- developments relating to our competitors and our industry.

The forward-looking statements in this Quarterly Report on Form 10-Q are only predictions. We have based these forward-looking statements 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. Forward-looking statements are inherently subject to risks, uncertainties and assumptions, some of which cannot be predicted or quantified and some of which are beyond our control. Risks, uncertainties and assumptions that may cause actual results to differ materially from current expectations include, among other things, those set forth below in “Summary Risk Factors,” in Part I, Item 2. “Management’s Discussion and Analysis of Financial Condition and Results of Operations,” in Part II, Item 1A. “Risk Factors” and for the reasons described elsewhere in this Quarterly Report on Form 10-Q. Any forward-looking statement in this Quarterly Report on Form 10-Q reflects our current view with respect to future events, speaks only as of the date of this Quarterly Report on Form 10-Q, and is subject to these and other risks, uncertainties and assumptions. Given these uncertainties, you should not rely on these forward-looking statements as predictions of future events. Although we believe that the expectations reflected in the

forward-looking statements are reasonable, our information may be incomplete or limited and we cannot guarantee future results. 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 law, we do not plan, and assume no obligation, to update or revise these forward-looking statements for any reason, even if new information becomes available in the future. We qualify all of our forward-looking statements by these cautionary statements.

This Quarterly Report on Form 10-Q may also contain estimates, projections and other information concerning our industry, our business and the markets for certain drugs and consumer products, including data regarding the estimated size of those markets, their projected growth rates and the incidence of certain medical conditions. Information that is based on estimates, forecasts, projections or similar methodologies is inherently subject to uncertainties and actual events or circumstances may differ materially from events and circumstances reflected in this information. Unless otherwise expressly stated, we obtained these industry, business, market and other data from reports, research surveys, studies and similar data prepared by third parties, industry, medical and general publications, government data and similar sources, and we have not independently verified the data from third party sources. In some cases, we do not expressly refer to the sources from which these data are derived.

In this Quarterly Report on Form 10-Q, unless otherwise stated or as the context otherwise requires, references to the "Company," “Evelo,” “we,” “us,” “our” and similar references refer to Evelo Biosciences, Inc. and our wholly owned subsidiaries. This Quarterly Report on Form 10-Q also contains references to our trademarks and to trademarks belonging to other entities. Solely for convenience, trademarks and trade names referred to, including logos, artwork and other visual displays, may appear without the ® or TM symbols, but such references are not intended to indicate, in any way, that their respective owners will not assert, to the fullest extent under applicable law, their rights thereto. We do not intend any use or display of other companies’ trade names or trademarks to imply a relationship with, or endorsement or sponsorship of us by, any other companies.

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. Principal risks and uncertainties affecting our business include the following:

- We are a development-stage company and have incurred significant losses since our inception. We expect to incur losses for the foreseeable future and may never achieve or maintain profitability. Moreover, our limited operating history may make it difficult to evaluate the success of our business to date and to assess our future viability.
- We have identified conditions and events that raise substantial doubt about our ability to continue as a going concern. We will need additional funding in order to complete development of our product candidates and commercialize our products, if approved. If we are unable to raise capital when needed, we will be forced to delay, reduce or discontinue our product development programs or commercialization efforts.
- Our product candidates are based on targeting SINTAX™, the small intestinal axis, which is an unproven approach to therapeutic intervention.
- We are dependent on the success of our product candidates. If the product candidates do not successfully complete clinical development or receive regulatory approval, our business may be harmed.
- The regulatory approval process is lengthy, expensive and uncertain with respect to outcome. We may be unable to obtain regulatory approval for our product candidates under applicable regulatory requirements of the United States and/or internationally. The denial or delay of any such approval would delay commercialization of our product candidates and adversely impact our ability to generate revenue, our business and our results of operations.
- We rely, and will continue to rely, on third parties to conduct the clinical trials for our product candidates, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such trials.
- We do not have our own manufacturing capabilities and rely, and will continue to rely, on third parties to produce clinical supplies and, if approved, commercial supplies of our product candidates. This reliance on third parties increases the risk that we will not have sufficient quantities of our product candidates or such quantities at an acceptable cost, which could delay, prevent or impair our development or commercialization efforts.
- If we are unable to establish our own sales, marketing and distribution capabilities, or to enter into agreements with third parties to sell and market our product candidates, we may not be successful in commercializing our product candidates if and when they are approved, and we may not be able to generate any revenue.
- 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 revenue.
- We face substantial competition, which may result in others discovering, developing or commercializing drugs before or more successfully than we do.
- Our product candidates may cause undesirable side effects or have other properties that could delay or prevent their regulatory approval, cause us to suspend or discontinue clinical trials, limit the commercial profile of an approved label or result in significant negative consequences following marketing approval, if any.
- If we are unable to adequately protect our proprietary technology, or obtain and maintain issued patents which are sufficient to protect our product candidates, other companies could compete against us more directly, which would have a material adverse impact on our business, results of operations, financial condition and prospects.
- The COVID-19 pandemic has adversely impacted, and may continue to adversely impact, our business, including our preclinical studies and clinical trials, results of operations and financial condition.

Evelo Biosciences, Inc.
Form 10-Q for the Quarterly Period Ended March 31, 2022

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PART I—FINANCIAL INFORMATION

Item 1. Financial Statements.

Evelo Biosciences, Inc.
Condensed Consolidated Balance Sheets
(In thousands, except per share and share amounts)
(Unaudited)

	March 31, 2022	December 31, 2021
Assets		
Current assets:		
Cash and cash equivalents	$ 39,631	$ 68,441
Prepaid expenses and other current assets	3,494	2,585
Total current assets	43,125	71,026
Property and equipment, net	6,126	6,622
Right of use asset - operating lease	8,419	8,910
Other assets	1,155	1,313
Total assets	$ 58,825	$ 87,871
Liabilities and stockholders' (deficit) equity		
Current liabilities:		
Debt, current portion	$ 1,844	$ —
Accounts payable	1,760	1,601
Accrued expenses	9,876	13,068
Operating lease liability, current portion	2,027	1,951
Other current liabilities	665	742
Total current liabilities	16,172	17,362
Noncurrent liabilities:		
Debt, net of current portion	44,772	46,557
Operating lease liability, net of current portion	7,183	7,785
Deferred revenue	7,500	7,500
Total liabilities	75,627	79,204
Commitments and contingencies (Note 10)		
Stockholder's (deficit) equity:		
Preferred stock, $0.001 par value; 10,000,000 shares authorized; no shares issued or outstanding as of March 31, 2022 and December 31, 2021, respectively	—	—
Common stock, $0.001 par value; 200,000,000 shares authorized; 53,648,189 and 53,576,454 shares issued and outstanding as of March 31, 2022 and December 31, 2021, respectively	54	54
Additional paid-in capital	427,700	423,308
Accumulated deficit	(444,556)	(414,695)
Total stockholders' (deficit) equity	(16,802)	8,667
Total liabilities and stockholders' (deficit) equity	$ 58,825	$ 87,871

See accompanying notes to unaudited condensed consolidated financial statements.

Evelo Biosciences, Inc.
Condensed Consolidated Statements of Operations
(In thousands, except share and per share data)
(Unaudited)

	Three Months Ended March 31,	
	2022	**2021**
Operating expenses:		
Research and development	$ 19,321	$ 21,508
General and administrative	9,417	5,963
Total operating expenses	28,738	27,471
Loss from operations	(28,738)	(27,471)
Other (expense) income:		
Interest expense, net	(1,027)	(765)
Other miscellaneous income, net	20	162
Total other expense, net	(1,007)	(603)
Loss before income taxes	(29,745)	(28,074)
Income tax expense	(116)	(122)
Net loss	$ (29,861)	$ (28,196)
Net loss per share attributable to common stockholders, basic and diluted	$ (0.56)	$ (0.55)
Weighted-average number of common shares outstanding, basic and diluted	53,619,635	51,343,923

See accompanying notes to unaudited condensed consolidated financial statements.

Evelo Biosciences, Inc.
Condensed Consolidated Statements of Stockholders' (Deficit) Equity
(In thousands, except share amounts)
(Unaudited)

	Three Months Ended March 31, 2022				
	Common Stock		Additional Paid-In Capital	Accumulated Deficit	Total
	Shares	Amount			
Balance - December 31, 2021	53,576,454	$ 54	$ 423,308	$ (414,695)	$ 8,667
Issuance of common stock under Employee Stock Purchase Plan	36,329	—	129	—	129
Vesting of restricted common stock	35,406	—	—	—	—
Stock-based compensation expense	—	—	4,275	—	4,275
Fees associated with public offering of common stock	—	—	(12)	—	(12)
Net loss	—	—	—	(29,861)	(29,861)
Balance - March 31, 2022	53,648,189	$ 54	$ 427,700	$ (444,556)	$ (16,802)

(Unaudited)

	Three Months Ended March 31, 2021				
	Common Stock		Additional Paid-In Capital	Accumulated Deficit	Total
	Shares	Amount			
Balance - December 31, 2020	47,470,119	$ 47	$ 322,957	$ (292,519)	$ 30,485
Issuance of common stock, net	5,814,734	6	81,955	—	81,961
Issuance of common stock under Employee Stock Purchase Plan	27,587	—	90	—	90
Exercise of stock options	45,299	—	235	—	235
Stock-based compensation expense	—	—	3,264	—	3,264
Net loss	—	—	—	(28,196)	(28,196)
Balance - March 31, 2021	53,357,739	$ 53	$ 408,501	$ (320,715)	$ 87,839

See accompanying notes to unaudited condensed consolidated financial statements.

Evelo Biosciences, Inc.
Condensed Consolidated Statements of Cash Flows
(In thousands)
(Unaudited)

	Three Months Ended March 31,	
	2022	**2021**
Operating activities		
Net loss	$ (29,861)	$ (28,196)
Adjustments to reconcile net loss to net cash used in operating activities:		
Stock-based compensation expense	4,275	3,264
Depreciation expense	517	536
Non-cash interest expense	59	124
Non-cash lease expense	491	445
Loss on disposal of property and equipment	232	—
Changes in operating assets and liabilities:		
Prepaid expenses and other current assets	(1,011)	46
Accounts receivable	—	(7,500)
Accounts payable	159	(1,062)
Accrued expenses and other current liabilities	(3,267)	(981)
Operating lease liabilities	(526)	(458)
Deferred revenue	—	7,500
Other liabilities	—	2
Net cash used in operating activities	(28,932)	(26,280)
Investing activities		
Purchases of property and equipment	(153)	(314)
Net cash used in investing activities	(153)	(314)
Financing activities		
Proceeds from issuance of common stock, net of issuance cost	—	82,003
Proceeds from the issuance of common stock under employee stock purchase plan and exercise of stock options	129	325
Fees associated with public offering of common stock	(12)	—
Net cash provided by financing activities	117	82,328
Net (decrease) increase in cash, cash equivalents and restricted cash	(28,968)	55,734
Cash, cash equivalents and restricted cash – beginning of period	69,754	70,420
Cash, cash equivalents and restricted cash – end of period	$ 40,786	$ 126,154
Supplemental disclosure of cash flow information		
Cash paid for interest	$ 973	$ 649
Cash paid for taxes	$ 393	$ —
Noncash investing and financing activities		
Public offering costs in accrued expenses	$ —	$ 42
Property and equipment additions included in accrued expenses	$ 27	$ 171

See accompanying notes to the unaudited condensed consolidated financial statements.

EVELO BIOSCIENCES, INC.

NOTES TO CONDENSED CONSOLIDATED FINANCIAL STATEMENTS (UNAUDITED)

1. Organization and Basis of Presentation

Evelo Biosciences, Inc. ("Evelo," "we," "our," "us" or the "Company") is a biotechnology company incorporated in Delaware on May 6, 2014. We are discovering and developing a new class of orally delivered investigational medicines that are intended to act on cells in the small intestine to produce therapeutic effects throughout the body. We are advancing these investigational medicines with the aim of treating a broad range of immune mediated diseases, with an initial focus on inflammatory diseases and oncology. Our headquarters is located in Cambridge, Massachusetts.

Since inception, we have devoted substantially all of our efforts to research and development and raising capital. We have not generated any product or license revenue related to our primary business purpose to date. We are subject to a number of risks similar to those of other development stage companies, including a dependence on key individuals, the need to develop commercially viable products, the competition from other companies, many of whom are larger and better capitalized, and the need to obtain adequate additional financing to fund the development of our products.

We have incurred operating losses since inception and we expect such losses and negative operating cash flows to continue for the foreseeable future. As of March 31, 2022, we held cash, cash equivalents and restricted cash of $40.8 million and have an accumulated deficit of $444.6 million. Since inception, we have financed operations primarily with the proceeds from the issuance of common stock combined with proceeds from previous sales of convertible preferred stock to equity investors, and from debt financing.

In accordance with the Financial Accounting Standards Board (“FASB”) Accounting Standards Update (“ASU”) 2014-15, *Disclosure of Uncertainties about an Entity’s Ability to Continue as a Going Concern (Subtopic 205-40)*, we evaluated whether there are conditions and events, considered in the aggregate, that raise substantial doubt about our ability to continue as a going concern within one year after the date that these unaudited condensed consolidated financial statements are issued. The transition to profitability is dependent upon the successful development, approval and commercialization of our products and product candidates, and the achievement of a level of revenues adequate to support our cost structure. Based on our current operating plan, we believe that our cash and cash equivalents balance as of March 31, 2022 will not be sufficient to fund operations and capital expenditures for at least the twelve months following the filing of this Quarterly Report on Form 10-Q, and we will need to obtain additional funding. We intend to pursue strategic partnerships and collaborations, or obtain additional funding through available financing sources which include additional public offerings of common stock and the private financing of debt or equity. Management’s belief with respect to our ability to fund operations is based on estimates that are subject to risks and uncertainties. If actual results are different from management’s estimates, we may need to seek additional funding sooner than would otherwise be expected. There can be no assurance that we will be able to obtain additional funding on acceptable terms, if at all. If we are unable to obtain sufficient funding, we may be required to delay our development efforts, limit activities and reduce research and development costs, which could adversely affect our business prospects. Because of the uncertainty in securing additional funding and the insufficient amount of cash and cash equivalent resources as of March 31, 2022, management concluded that substantial doubt exists with respect to our ability to continue as a going concern within one year after the date that these unaudited condensed consolidated financial statements are issued.

The accompanying unaudited condensed consolidated financial statements were prepared in accordance with accounting principles generally accepted in the United States of America (“U.S. GAAP”). Any reference in these notes to applicable guidance is meant to refer to the authoritative United States generally accepted accounting principles as found in the Accounting Standard Codification (“ASC”) and ASUs of the FASB. Certain information and footnote disclosures normally included in financial statements prepared in accordance with U.S. GAAP were condensed or omitted from this report, as is permitted by such rules and regulations. Accordingly, these financial statements should be read in conjunction with our Annual Report on Form 10-K for the year ended December 31, 2021 and the related notes thereto. These unaudited condensed consolidated financial statements are prepared on the same basis as the audited financial statements. In the opinion of our management, the accompanying unaudited condensed consolidated financial statements contain all adjustments which are necessary to present fairly our financial position as of March 31, 2022, the results of our operations and stockholders' equity for the three months ended March 31, 2022 and 2021. Such adjustments are of a normal and recurring nature. The results for the three months ended March 31, 2022 are not necessarily indicative of the results for the year ending December 31, 2022, or for any future period.

2. Summary of Significant Accounting Policies

Use of Estimates

The preparation of the unaudited condensed consolidated financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the amounts reported in the consolidated financial statements and accompanying notes. Significant estimates and assumptions reflected in these unaudited condensed consolidated financial statements include, but are not limited to, estimates related to the application of *Revenue from Contracts with Customers (Topic 606)* ("ASC 606") to our collaboration agreement with Meddist Company Limited (" ALJ"), the accrual of research and development expenses, the expected future lives of property and equipment and the valuation of stock-based awards. We base our estimates on historical experience and market-specific or other relevant assumptions that we believe to be reasonable under the circumstances. Actual results could differ from those estimates.

Principles of Consolidation

The unaudited condensed consolidated financial statements include the accounts of our business and our wholly owned and controlled subsidiaries. All intercompany transactions and balances have been eliminated in consolidation.

Subsequent Event Considerations

We consider events or transactions that occur after the balance sheet date but prior to the issuance of the unaudited condensed consolidated financial statements to identify matters that require additional disclosure or that may significantly affect currently reported financial condition such as our judgments related to estimates. Subsequent events were evaluated as required. Those events determined to be sufficiently material are described in Note 17 - Subsequent Events.

Emerging Growth Company Status

We are an “emerging growth company” as defined in the Jumpstart Our Business Startups Act of 2012 (the "JOBS Act"), and we may take advantage of reduced reporting requirements that are otherwise applicable to public companies until we are no longer an emerging growth company. Section 107 of the JOBS Act provides that an emerging growth company can take advantage of the extended transition period afforded by the JOBS Act for the implementation of new or revised accounting standards. We elected to use the extended transition period for complying with new or revised accounting standards and, as a result of this election, our unaudited condensed consolidated financial statements may not be comparable to companies that comply with public company effective dates. We may take advantage of these exemptions up until the last day of the fiscal year following the fifth anniversary of our IPO or such earlier time that we no longer are an emerging growth company. We would cease to be an emerging growth company if we have more than $1.07 billion in annual revenue, have more than $700.0 million in market value of our stock held by non-affiliates (and have been a public company for at least 12 months and have filed one annual report on Form 10-K), or have issued more than $1.0 billion of non-convertible debt securities over a three-year period.

Concentrations of Credit Risk and Off-Balance Sheet Risk

Financial instruments that potentially expose us to concentrations of credit risk primarily consist of cash and cash equivalents. We place our cash and cash equivalents primarily in two custodian accounts at accredited financial institutions. Such deposits have and will continue to exceed federally insured limits.

As of March 31, 2022 and December 31, 2021, we have no off-balance sheet risk such as foreign exchange contracts, option contracts, derivatives or other foreign hedging arrangements.

Comprehensive Loss

Comprehensive loss consists of net loss and changes in equity during a period arising from transactions and other equity and circumstances, of which we have none. Our comprehensive loss equals our net loss for all periods presented.

Cash, Cash Equivalents and Restricted Cash

Cash equivalents are comprised of highly liquid investments that are readily convertible into cash with original maturities of three months or less, comprised of cash held in banks and amounts held in money market funds. Cash equivalents are stated at cost, which approximates market value. Our restricted cash consists of restricted cash in connection with building leases for our office and laboratory premises and deposits held in relation to our credit card facility. As of March 31, 2022 and December 31, 2021 we had $1.2 million and $1.3 million, respectively, in noncurrent restricted cash included within other assets in the unaudited condensed consolidated balance sheets.

The following reconciles cash, cash equivalents and restricted cash as of March 31, 2022 and December 31, 2021, as presented on our statements of cash flows to the related balance sheet accounts (in thousands):

	March 31, 2022	December 31, 2021
Cash and cash equivalents:		
Cash	$ 5,224	$ 1,452
Money market funds	34,407	66,989
Total cash and cash equivalents	39,631	68,441
Restricted cash	1,155	1,313
Cash, cash equivalents and restricted cash	$ 40,786	$ 69,754

Fair Value of Financial Instruments

FASB ASC 820, *Fair Value Measurement* (“ASC 820”) establishes a fair value hierarchy for instruments measured at fair value that distinguishes between assumptions based on market data (observable inputs) and our own assumptions (unobservable inputs). As a basis for considering market participant assumptions in fair value measurements, ASC 820 establishes a three-tier fair value hierarchy that distinguishes between the following:

- Level 1 inputs are quoted prices (unadjusted) in active markets for identical assets or liabilities;
- Level 2 inputs are inputs other than quoted prices included within Level 1 that are observable for the asset or liability, either directly or indirectly; and
- Level 3 inputs are unobservable inputs that reflect our own assumptions about the assumptions market participants would use in pricing the asset or liability.

To the extent that the valuation is based on models or inputs that are less observable or unobservable in the market, the determination of fair value requires more judgment. Accordingly, the degree of judgment we exercised in determining fair value is greatest for instruments categorized in Level 3.

Property and Equipment

Property and equipment consists of computer hardware and software, furniture and fixtures, office equipment, research and lab equipment and leasehold improvement recorded at cost. Property and equipment is depreciated using the straight-line method over the estimated useful lives of the assets.

A summary of the estimated useful lives of our property and equipment is as follows:

Computer hardware	3 to 5 years
Computer software	3 years
Furniture and fixtures	7 years
Research and laboratory equipment (used/new)	3 to 5 years
Leasehold improvements	Lesser of asset life or remaining life of lease

Assets acquired and not placed in service are recorded to construction-in-process and are not depreciated. Assets are recorded according to classification and depreciated upon placement in service. Repairs and maintenance costs are expensed as incurred.

We periodically evaluate property and equipment for impairment whenever events or changes in circumstances indicate that a potential impairment may have occurred. We neither identified nor recorded any material impairment charges during the periods presented.

Income Taxes

We record deferred tax assets and liabilities for the expected future tax consequences of temporary differences between the financial statement carrying amounts and the tax bases of assets and liabilities and for loss and credit carryforwards using enacted tax rates expected to be in effect in the years in which the differences reverse. We account for interest and penalties related to uncertain tax positions as part of our provision for income taxes. A valuation allowance is provided to reduce the net deferred tax assets to the amount that will more likely than not be realized. We have incurred net losses since inception and, in recognition of the uncertainty in the realization of favorable tax attributes in future tax returns, we recorded a full valuation allowance against our otherwise recognizable net deferred tax assets.

Revenue Recognition

We recognize revenue under the Financial Accounting Standards Board guidance of ASC 606. Since inception, we have entered into one contract subject to ASC 606, however, as discussed in Note 3 - ALJ Commercialization and License Agreement, all revenue pursuant to this arrangement has been deferred.

Collaboration Agreements

We analyze our collaboration arrangements under the Financial Accounting Standards Board guidance of *Collaborative Arrangements (Topic 808)* ("ASC 808"). To the extent an arrangement falls within the scope of ASC 808, we assess whether aspects of the arrangement between us and our collaboration partner are within the scope of other accounting guidance, including ASC 606.

Deferred Revenue

We record a contract liability as deferred revenue on our unaudited condensed consolidated balance sheets when we receive payment but have not yet satisfied our related performance obligations specified in the sales or other contract. Revenue is recognized from deferred revenue in the period in which our obligations under the agreement are fulfilled or are proportionately recognized in the proportional amount of fulfillment. See Note 3 - ALJ Commercialization and License Agreement.

Research and Development Costs

Research and development costs are expensed in the period incurred. Research and development expenses consist of both internal and external costs associated with the development of our product candidates, such as payroll, consulting and manufacturing costs associated with the development of our product candidates. Costs for certain development activities, such as clinical trials and manufacturing development activities, are recognized based on an evaluation of the progress to completion of specific tasks using data such as patient enrollment, clinical site activations, and information provided to us by our vendors on their actual costs incurred or level of effort expended. Payments for these activities are based on the terms of the individual arrangements, which may differ from the pattern of costs incurred, and are reflected on the unaudited condensed consolidated balance sheets as prepaid or accrued research and development expenses.

Nonrefundable advance payments for goods or services to be received in the future for use in research and development activities are deferred and capitalized. The capitalized amounts are expensed as the related goods are delivered or the services are performed.

We have and may continue to acquire the rights to develop and commercialize new product candidates from third parties. The upfront payments to acquire any license, product or rights, as well as any future milestone payments, are immediately recognized as research and development expense provided that there is no alternative future use of the rights in other research and development projects. Any milestone payments made for Intellectual Property after regulatory approval, or that have alternative future use, are capitalized and amortized.

Stock-Based Compensation

We record stock-based compensation for equity awards granted to employees and directors based on the grant date fair value of awards issued. The expense is recorded over the requisite service period, which is the vesting period, on a straight-line basis. We account for stock-based compensation arrangements with non-employees based upon the fair value of the consideration received or the equity instruments issued, whichever amount is more reliably measurable. We use the Black-Scholes option-pricing model to determine the fair value of option grants. We record forfeitures as they occur.

Segments

We have one operating segment. Our chief operating decision maker, our Chief Executive Officer, manages our operations on a consolidated basis for the purposes of allocating resources.

Net Loss per Share

Basic net loss per share is calculated by dividing the net loss by the weighted-average number of shares of common stock outstanding during the period. For purposes of the dilutive net loss per share applicable to common stockholders calculation, stock options, common stock from Employee Stock Purchase Plan, convertible debt, warrants to purchase common shares and unvested restricted stock are considered to be common stock equivalents but are excluded from the calculation of diluted net loss per share applicable to common stockholders, as their effect would be anti-dilutive; therefore, basic and diluted net loss per share applicable to common stockholders were the same for all periods presented.

Recently Adopted Accounting Pronouncements

Debt with Conversion and Other Options

On August 5, 2020, the FASB issued ASU No. 2020-06, *Debt—Debt with Conversion and Other Options (Subtopic 470-20) and Derivatives and Hedging—Contracts in Entity's Own Equity (Subtopic 815-40): Accounting for Convertible Instruments and Contracts in an Entity's Own Equity* ("ASU-2020-06"), which simplifies the accounting for certain financial instruments with characteristics of liabilities and equity, including convertible instruments and contracts on an entity's own equity. The guidance simplifies the evaluation of whether a contract in the issuer's own equity can be classified in equity or an embedded feature qualifies for the derivative scope exception. We adopted the guidance for the year beginning January 1, 2022, The adoption has no impact on our consolidated financial statements and related disclosures.

Codification Improvements

In October 2020, the FASB issued ASU No. 2020-10 - *Codification Improvements*. The amendments improve the codification by having all disclosure-related guidance available in the disclosure sections of the codification and also includes various other minor amendments. We adopted the guidance for the year beginning January 1, 2022, with no impact on our consolidated financial statements and related disclosures.

Accounting Pronouncements Issued and Not Adopted

Financial Instruments - Credit Losses

In June 2016, the FASB issued ASU No. 2016-13, *Financial Instruments—Credit Losses (Topic 326)—Measurement of Credit Losses on Financial Instruments*, which was subsequently updated (together "ASU 2016-13"). The provisions of ASU 2016-13 modify the impairment model to utilize an expected loss methodology in place of the currently used incurred loss methodology, and require a consideration of a broader range of reasonable and supportable information to inform credit loss estimates. ASU 2016-13 is effective for us on January 1, 2023, with early adoption permitted. We are currently evaluating the potential impact that this standard may have on our financial position and results of operations, as well as the timing of our adoption of this standard.

3. ALJ Commercialization and License Agreement

In March 2021, we entered into a commercialization and license agreement ("ALJ Agreement") with ALJ. Pursuant to the ALJ Agreement, we granted to ALJ an exclusive, non-transferable, sublicensable license to our product candidate EDP1815. In consideration for the rights granted under the ALJ Agreement, ALJ was obligated to pay a one-time, non-refundable upfront fee of $7.5 million. The parties will also share the future operating profits and losses for certain products in certain territories equally (50:50) as well as certain development, regulatory and commercialization costs. We have concluded that the delivery of the license to ALJ shall be accounted for under ASC 606. The development, regulatory and commercialization activities within the territories shall be accounted for under ASC 808.

We have recognized no revenue under the ALJ Agreement to date as we have yet to undertake any of our performance obligations within the agreement. The $7.5 million upfront fee was recorded as deferred revenue as a non-current liability in the accompanying unaudited condensed consolidated balance sheets as the performance obligation is not expected to be completed within the next twelve months.

We anticipate payments under the cost-sharing or profit and loss sharing arrangements will be classified in the statement of operations consistent with the guidance of ASC 808. To date, we have neither received nor incurred any such payments.

4. Leases

In January 2018, we entered into an operating sublease arrangement for approximately 40,765 square feet of office and research and development space at 620 Memorial Drive, Cambridge, MA 02139, extending through September 2025. The lease requires a security deposit which we fulfilled with a standing letter of credit secured by restricted cash on deposit.

For the three months ended March 31, 2022 and 2021, we recorded rent expense of $0.8 million and $0.7 million, respectively.

The minimum aggregate lease commitments as of March 31, 2022 are as follows (in thousands):

Remainder of 2022	$	2,049
2023		3,154
2024		3,249
2025		2,492
Total minimum lease payments		10,944
Less: imputed interest		(1,734)
Total operating lease liability	$	9,210
Operating cash flows used for operating leases	$	760
Weighted-average remaining lease term		3.5 years
Weighted-average discount rate		9.5 %

5. Fair Value Measurements

The following presents the fair value hierarchy for financial assets measured at fair value on a recurring basis as of March 31, 2022 (in thousands):

	Total	Level 1
Assets:		
Money market funds included in cash and cash equivalents	$ 34,407	$ 34,407
Total	$ 34,407	$ 34,407

The following presents the fair value hierarchy for financial assets measured at fair value on a recurring basis as of December 31, 2021 (in thousands):

	Total	Level 1
Assets:		
Money market funds included in cash and cash equivalents	$ 66,989	$ 66,989
Total	$ 66,989	$ 66,989

As of March 31, 2022 and December 31, 2021, our financial assets measured at fair value consist entirely of assets measured at Level 1. There were no financial liabilities measured at fair value.

6. Property and Equipment, Net

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

	March 31, 2022	December 31, 2021
Lab equipment	$ 9,609	$ 9,689
Leasehold improvements	2,157	2,157
Furniture and fixtures	818	809
Computers and software	261	259
Office equipment	38	21
Construction-in-process	1,394	1,321
	14,277	14,256
Less: accumulated depreciation	(8,151)	(7,634)
Property and equipment, net	$ 6,126	$ 6,622

We recognized $0.5 million and $0.5 million of depreciation expense for the three months ended March 31, 2022 and 2021, respectively.

7. Accrued Expenses

Accrued expenses consist of the following (in thousands):

	March 31, 2022	December 31, 2021
Accrued external research and development expenses	$ 4,291	$ 4,895
Accrued payroll and related expenses	3,528	6,412
Accrued professional fees	1,282	1,013
Accrued other expenses	775	748
Total accrued expenses	$ 9,876	$ 13,068

8. Loan and Security Agreements

In July 2019, we entered into a loan and security agreement with K2 HealthVentures LLC and others (collectively, "K2HV"), under which K2HV agreed to extend term loans of up to $45.0 million in three tranches. The initial tranche of $20.0 million was funded in July 2019. The second tranche of $10.0 million was funded in July 2020. The availability of the third tranche of $15.0 million expired in January 2021. The facility was amended in June 2021 (the "Amended Credit Facility"), to supersede the expired $15.0 million third tranche commitment with a new $15.0 million fourth tranche commitment, which we drew down in June 2021. The Amended Credit Facility resulted in a debt extinguishment for accounting purposes and we recorded a loss on the extinguishment of debt of $3.2 million in the quarterly period ended June 30, 2021, equaling the difference between the fair value for reacquisition of the new debt and the carrying amount of the existing debt.

In connection with the Amended Credit Facility, we issued to K2 HealthVentures Equity Trust LLC, an affiliate of K2HV, a warrant to purchase up to 139,770 shares of our common stock. In addition, K2HV has the option, exercisable at any time, to convert up to $5.0 million of principal outstanding into up to 375,940 shares of our common stock. See Note 11 - Stockholders' Equity.

Interest on the outstanding loan balance accrues at a variable annual rate equal to the greater of (i) 8.65% and (ii) the prime rate plus 3.15%. Terms are for interest-only payments on a monthly basis through February 2023. Thereafter, terms provide for equal monthly payments of principal plus interest until the loans mature in August 2024 whereupon the remaining balance is due and payable. Pursuant to the Amended Credit Facility, we elected to adjust the repayment schedule such that commencing on March 1, 2023, we will make consecutive equal monthly payments of principal and accrued and unpaid interest based on a notional thirty month repayment period. The loan maturity date remains August 1, 2024 and any outstanding principal and unpaid interest is due at maturity. Upon final payment or prepayment of the loans, we will pay a final payment equal to 4.8% of the aggregate original principal amount of the loans borrowed.

Borrowings under the Amended Credit Facility are collateralized by substantially all our tangible personal property along with our equity interests in our subsidiaries. The Amended Credit Facility contains customary representations, warranties and covenants. As of March 31, 2022, we were in compliance with all such covenants.

The minimum future loan payments under the Amended Credit Facility as of March 31, 2022 are as follows (in thousands):

Remainder of 2022	$	2,974
2023		17,404
2024		34,770
Total minimum payments		55,148
Less: amounts representing interest and discount		(8,532)
Total debt	$	46,616

Interest expense was approximately $1.0 million and $0.8 million for the three months ended March 31, 2022 and 2021, respectively.

9. In-License Agreements

Mayo Foundation for Medical Education and Research

In August 2017, we and the Mayo Clinic entered into a license agreement which was subsequently amended. Under the agreement, the Mayo Clinic granted us (i) an exclusive, worldwide, sublicensable license under the Mayo Clinic's rights to certain intellectual property and microbial strains and (ii) a non-exclusive, worldwide, sublicensable license to certain related know-how to develop and commercialize certain microbial strains and licensed products incorporating such strains. As consideration, we paid a nonrefundable upfront fee of $0.3 million and are obligated to pay annual license maintenance fees. The nonrefundable upfront fees were expensed to research and development expense in 2017. Annual maintenance fees are expensed as incurred over the term of the agreement. We may owe the Mayo Clinic milestone payments upon the achievement of certain milestones up to a maximum of $59.1 million in the aggregate, as well as royalties on net sales of licensed products in low single-digit percentages. As of March 31, 2022, we incurred milestone payments since inception of approximately $0.3 million and no amounts are currently due.

University of Chicago

In March 2016, we and the University of Chicago entered into a patent license agreement ("2016 University of Chicago Agreement"). Under the agreement, the University of Chicago granted us (i) an exclusive, royalty-bearing and sublicensable license to certain patent rights related to the administration of microbes to treat cancer and (ii) a non-exclusive, royalty-bearing, sublicensable license to access technical information for the development and commercialization of microbial products to treat cancer in combination with checkpoint inhibitors. As consideration, we paid a nonrefundable upfront fee of less than $0.5 million and are obligated to pay annual license maintenance fees. Nonrefundable upfront fees were expensed to research and development expense in 2016. Annual maintenance fees are expensed as incurred over the term of the agreement. We may owe the University of Chicago milestone payments totaling an aggregate of approximately $60.9 million upon the achievement of certain milestones, as well as royalties on net sales of licensed products ranging from low to high single-digit percentages. As of March 31, 2022, we incurred milestone payments since inception of approximately $0.4 million and no amounts are currently due.

10. Commitments and Contingencies

Collaboration Agreement with Sacco S.r.l.

In July 2019, we entered into an agreement with Sacco S.r.l. ("Sacco") pursuant to which Sacco will manufacture and supply single strain, non-genetically modified microbes intended for oral delivery or oral use in pharmaceutical products exclusively for us for a period of five years. Sacco may terminate the agreement if the provision of manufacturing services has been, or is scheduled to be, inactive for a period of six consecutive months. We agreed to pay Sacco an aggregate of €3.0 million, consisting of payments of €0.6 million annually during the exclusivity period. We incurred annual exclusivity fees since inception of approximately €1.8 million, and no amounts are currently due. We currently have an additional contractual arrangement for manufacturing in place with an affiliate of Sacco that will require us to spend an aggregate minimum amount of €1.5 million annually during each of 2022, 2023 and 2024 and €0.9 million on or before March 1, 2025.

Litigation and Other Proceedings

We may periodically become subject to legal proceedings and claims arising in connection with on-going business activities, including claims or disputes related to patents issued to us or that are pending. We are not a party to any material litigation and have established no contingency reserves for any litigation liability.

On February 12, 2021, the European Patent Office issued a Communication of a Notice of Opposition for European patent EP 3223834 held by us. In July 2021, we filed our reply to the Notice of Opposition. In January 2022, the European Patent Office issued a preliminary opinion and a summons to oral proceedings. The deadline for final written submissions is in July 2022 and the date for the oral proceedings is in September 2022. We are currently evaluating our available options and deciding next steps with respect to this matter. The patent at issue does not relate to any of our current product candidates, and receipt of this communication and/or any subsequent proceeding is not expected to affect any of our current development plans.

11. Stockholders' (Deficit) Equity

2019 Shelf Registration

In June 2019, we filed a Registration Statement on Form S-3 ("2019 Shelf Registration") with the Securities and Exchange Commission ("SEC") for the registration and offering of common stock, preferred stock, debt securities, warrants and/or units or any combination thereof in the aggregate amount of up to $200.0 million for a period of up to three years from the date of effectiveness. We simultaneously entered into an "at-the-market" sales agreement ("ATM") providing for the offering, issuance and sale for up to $50.0 million of common stock under the 2019 Shelf Registration. During the three months ended March 31, 2022, we issued no shares of common stock under the ATM. During the year ended December 31, 2021, we issued 139,734 common shares under the ATM with offering prices ranging between $12.54 and $13.17 per share for gross proceeds of $1.8 million and net proceeds of $1.7 million.

February 2, 2021 Offering

In February 2021, we sold 5,175,000 shares of common stock in an underwritten public offering under our 2019 Shelf Registration at a price of $15.00 per share, which included the underwriters' exercise of its option to purchase 675,000 shares, for gross proceeds of $77.6 million and net proceeds of $72.7 million.

ALJ Health Care Private Placement

In January 2021, we entered into a stock purchase agreement with ALJ Health Care & Life Science Company Limited ("ALJ Health") pursuant to which, on February 2, 2021, ALJ Health purchased 500,000 shares of common stock in a private placement for $15.00 per share, equal to the public offering price per share at which common stock was sold to the public as referred above. The placement generated proceeds of $7.5 million. The shares were not registered under the Securities Act of 1933, as amended.

2021 Shelf Registration

In August 2021, we filed a Registration Statement on Form S-3 ("2021 Shelf Registration") with the SEC for the registration and offering of common stock, preferred stock, debt securities, warrants and/or units or any combination thereof in the aggregate amount of up to $200.0 million for a period of up to three years from the date of effectiveness. During the three months ended March 31, 2022, we issued no shares of common stock under the 2021 Shelf Registration. No shares of common stock registered under the 2021 Shelf Registration were sold in the year ended December 31, 2021.

Warrants

In connection with our Amended Credit Facility (see Note 8 - Loan and Security Agreements), we issued K2 HealthVentures Equity Trust LLC a warrant to purchase up to 139,770 shares of our common stock with an exercise price of $13.30 per share, expiring in June 2031. The warrant holder has the option to exercise the purchase on a cashless basis. In addition, the warrant holder has the option, exercisable at any time, to convert up to $5.0 million of outstanding loan principal into up to 375,940 shares of common stock at a price of $13.30 per share.

12. Stock-Based Compensation

2021 Inducement Plan

In May, 2021, our board of directors adopted the Evelo Biosciences, Inc. 2021 Employment Inducement Award Plan (the “Inducement Award Plan”) without stockholder approval pursuant to Rule 5635(c)(4) of the Nasdaq Stock Market LLC listing rules (“Rule 5635(c)(4)”). In accordance with Rule 5635(c)(4), cash and equity-based incentive awards under the Inducement Award Plan may only be made to a newly-hired employee who was not previously a member of our board of directors, or to an employee who is rehired following a bona fide period of non-employment by us, as a material inducement to the employee’s entering into employment with us. An aggregate of 1,250,000 shares of our common stock were reserved for issuance under the Inducement Award Plan.

The exercise price of stock options granted under the Inducement Award Plan will not be less than the fair market value of a share of our common stock on the grant date. Other terms of awards, including vesting requirements, are determined by our board of directors and are subject to the provisions of the Inducement Award Plan. Stock options granted to employees generally vest over a four-year period, but may be granted with different vesting terms. Certain options may provide for accelerated vesting in the event of a change in control. Stock options granted under the Inducement Award Plan expire no later than 10 years from the date of grant. As of March 31, 2022, stock option awards covering up to 800,000 shares of our common stock were issued under the Inducement Award Plan, none of which were exercised or canceled. As of March 31, 2022, restricted stock unit (“RSU”) awards covering up to 4,545 shares of our common stock were granted under the Inducement Award Plan, none of which have vested or forfeited. As of March 31, 2022, 445,455 shares of common stock are available for future grant under the Inducement Award Plan.

2018 Incentive Award Plan

In April 2018, our board of directors adopted, and our stockholders approved, the 2018 Incentive Award Plan (the "2018 Plan"), effective in May 2018, under which we may grant cash and equity-based incentive awards to our employees, officers, directors, consultants and advisors. The 2018 Plan initially allowed us to grant awards for up to 1,344,692 shares of common stock plus that number of shares of common stock subject to awards outstanding under the 2015 Plan (as defined below) that expire, lapse, terminate or are exchanged for cash, surrendered, repurchased, canceled prior to exercise or forfeited following the effective date of the 2018 Plan. Each year starting with 2019 and ending in and including 2028, the number of shares available for grants of awards under the 2018 Plan will be increased automatically on January 1 by a number of shares of common stock equal to the lesser of 4% of the shares of common stock outstanding on the final day of the preceding calendar year or the number of shares determined by our board of directors. Accordingly, on January 1, 2022, 2021, 2020 and 2019, the number of shares authorized for issuance under the 2018 Plan was increased by 2,143,058, 1,898,805, 1,286,824 and 1,273,031 shares, respectively.

The exercise price of stock options granted under the 2018 Plan shall be no less than the fair market value of a share of our common stock on the grant date. Other terms of awards, including vesting requirements, are determined by the board of directors and are subject to the provisions of the 2018 Plan. Stock options granted to employees generally vest over a four-year period, but may be granted with different vesting terms. Certain options provide for accelerated vesting in the event of a change in control. Awards granted to non-employee consultants generally vest monthly over a period of one to four years. Stock options granted under the 2018 Plan expire no later than 10 years from the date of grant. As of March 31, 2022, stock options awards covering up to 8,824,136 shares of our common stock were issued under the 2018 Plan, of which 43,247 shares were exercised and 1,328,684 shares were canceled. As of March 31, 2022, 824,123 shares of common stock are available for future grant under the 2018 Plan.

2015 Stock Incentive Plan

We previously granted equity awards under the 2015 Stock Incentive Plan (the "2015 Plan"), which originally provided for grant of incentive stock options, non-qualified stock options, RSAs and other stock-based awards to our employees, officers, directors, consultants and advisors. Following the effectiveness of the 2018 Plan, we ceased making grants under the 2015 Plan. The 2015 Plan continues to govern the terms and conditions of the outstanding awards granted under it.

The terms of equity award agreements made under the 2015 Plan, including vesting requirements, were determined by the board of directors and are subject to the provisions of the 2015 Plan. Stock options granted to employees generally vest over a four-year period but may be granted with different vesting terms. A limited number of awards contain performance-based vesting criteria and for such awards that are deemed probable of vesting, we record expense in the period in which such determination is made through any remaining estimated vesting period. Certain options provide for accelerated vesting in the event of a change in control. Awards granted to non-employee consultants generally vest monthly over a period of one to four years. Stock options issued under the 2015 Plan expire no later than 10 years from the date of grant.

Under the 2015 Plan, we were authorized to grant equity awards up to an aggregate of 5,417,044 shares of common stock. As of March 31, 2022, an aggregate of 5,758,518 options and other equity awards were granted under the 2015 Plan, of which 1,471,337 were exercised, 1,299,392 were canceled and 18,468 were repurchased as of March 31, 2022. A total of 113,006 shares previously reserved under the 2015 Plan that had not been exercised or were otherwise subject to outstanding exercise awards were no longer authorized as of May 8, 2018.

Stock-Based Compensation Expense

Stock-based compensation expense recorded in our unaudited condensed consolidated statements of operations consists of the following (in thousands):

	Three Months Ended March 31,	
	2022	**2021**
Research and development	2,036	1,823
General and administrative	$ 2,239	$ 1,441
Total stock-based compensation expense	4,275	$ 3,264

Stock Options

A summary of our stock option activity is as follows:

	Shares	**Weighted-Average Exercise Price**
Options outstanding as of December 31, 2021	9,713,182	$ 9.32
Granted	1,746,005	$ 5.03
Exercised	—	$ —
Canceled	(219,185)	$ 10.10
Options outstanding as of March 31, 2022	11,240,002	$ 8.65
Exercisable as of March 31, 2022	5,577,736	$ 7.13

The weighted-average fair value of options granted during the three months ended March 31, 2022 and 2021 was $3.77 and $12.07, respectively.

As of March 31, 2022, total unrecognized stock-based compensation expense relating to unvested stock options was $35.9 million, expected to be recognized over a weighted average period of 2.82 years.

Restricted Stock Units

We issue restricted stock units ("RSU") under the 2018 Plan and the 2021 Inducement Award Plan. Typically, each award of RSUs vests as to 25% on the first anniversary of the grant date, and either monthly thereafter or annually over three additional years. A summary of RSU activity is as follows:

	Shares	Weighted-Average Grant Date Fair Value
Unvested as of December 31, 2021	320,209	$ 9.04
Granted	108,375	$ 5.05
Vested	(35,406)	$ 15.44
Forfeited	(26,867)	$ 8.75
Unvested as of March 31, 2022	366,311	$ 7.26

Stock-based compensation expense related to RSUs was $0.4 million and $0.2 million for the three months ended March 31, 2022 and 2021, respectively.

2018 Employee Stock Purchase Plan

In April 2018, our board of directors adopted and our stockholders approved the 2018 Employee Stock Purchase Plan (“ESPP”), which became effective in May 2018. Under the terms of the ESPP, the number of shares of common stock that may be issued under the ESPP automatically increases on the first day of each calendar year, beginning in 2020 and ending in and including 2028, by an amount equal to the lesser of (i) 1% of the number of shares of our common stock outstanding on the last day of the applicable preceding calendar year and (ii) an amount determined by our board of directors. Accordingly, on January 1, 2022 and 2021, the number of shares authorized by our board of directors for issuance under the ESPP was increased by 535,765 and 474,701 shares, respectively. There were no additional share increases for the years 2020 and 2019.

A total of 36,329 shares and 27,587 shares were purchased under the ESPP during the three months ended March 31, 2022 and 2021, respectively. Compensation expense related to our ESPP for the three months ended March 31, 2022 and 2021 was not material.

As of March 31, 2022 and December 31, 2021, a total of 1,235,532 shares and 736,096 shares of common stock were reserved for issuance under the ESPP.

13. Income Taxes

For the three months ended March 31, 2022 and 2021 we recorded a tax provision of $0.1 million and $0.1 million respectively, primarily related to our wholly owned UK subsidiary.

As of March 31, 2022 and December 31, 2021, the balance in accrued expenses in the unaudited condensed consolidated balance sheets for deferred employer payroll taxes pursuant to the CARES Act was $0.2 million each.

14. Net Loss Per Share

Basic and diluted net loss per common share is determined by dividing net loss attributable to common stockholders by the weighted-average common shares outstanding during the period, as follows (net loss in thousands):

	Three Months Ended March 31,	
	2022	2021
Numerator		
Net loss	$ (29,861)	(28,196)
Denominator		
Weighted average shares outstanding used in computing net loss per share	53,619,635	51,343,923
Net loss per share, basic and diluted	$ (0.56)	$ (0.55)

We compute diluted net loss per common share by giving consideration to all potentially dilutive common shares, except where the effect of including such securities would be antidilutive. We have reported net losses since inception and, as such, have determined that all potentially dilutive common shares are anti-dilutive. Basic and diluted net loss per share of common stock were the same for all periods presented as the impact of all potentially dilutive securities outstanding was anti-dilutive.

The following table presents securities excluded from the computation of diluted weighted-average shares outstanding for the periods presented, as they are anti-dilutive:

	Three Months Ended March 31,	
	2022	2021
Unvested common stock from early exercise of options	—	18,386
Stock options to purchase common stock	11,240,002	8,290,500
Warrant	139,770	—
RSUs	366,311	385,250
Convertible debt (as-converted to common stock)	375,940	—
Common stock offering from ESPP	26,588	7,786
Total securities excluded	12,148,611	8,701,922

15. Related Party Transactions

We receive clinical advisory services from Weatherden Ltd. (“Weatherden”) under agreements that were entered into during 2017 and 2018. Duncan McHale, our Chief Medical Officer, is a part owner of Weatherden. During the three months ended March 31, 2022 and 2021, we paid Weatherden $0.1 million or less, respectively. As of March 31, 2022 and December 31, 2021, the amounts owed to Weatherden under the supply of service agreement were approximately $0.1 million or less, respectively.

In September 2019, we entered into a consulting agreement with David Epstein (the "Consulting Agreement"), our Chairman of the Board, for strategic advisory and other consulting services. The Consulting Agreement was amended in October 2020 and again in April 2021, and now has a term that is scheduled to end on June 30, 2022 unless earlier terminated pursuant to its terms. In accordance with the initial terms of the Consulting Agreement, Mr. Epstein was granted an option to purchase 75,000 shares of common stock, vesting in 36 equal monthly installments and subject to his continued provision of consulting services on the applicable vesting dates. Under the Consulting Agreement as amended in October 2020, Mr. Epstein was also entitled to receive (i) an annual equity award on each anniversary of the effective date of the Consulting Agreement in the form of an option to purchase shares of common stock having a grant date fair market value of approximately $0.2 million as determined by the Board in its discretion based on customary option pricing methodologies, vesting in 12 equal monthly installments and subject to his continued provision of consulting services on the applicable vesting date, and (ii) an aggregate annual cash consulting fee of $0.3 million. In the event the Consulting Agreement is renewed for a term of less than one year, the equity award and the number of shares of common stock shall be adjusted proportionately to the length of the renewal term. In October 2020, in connection with the commencement of his second year of service as a consultant, Mr. Epstein was granted an option to purchase 44,743 shares of common stock, vesting in nine equal monthly installments and subject to his continued provision of consulting services on the vesting dates. Under the Consulting Agreement as amended in April 2021 and effective on June 30, 2021, Mr. Epstein is entitled to receive

RSUs having an aggregate grant date fair value of approximately $0.5 million, as determined by our board of directors in its discretion based on a 10-day trailing average of the closing price of our common stock, as his sole compensation for his consulting services. The RSUs vest in 12 substantially equal monthly installments such that the RSUs shall be fully vested on June 30, 2022, subject to Mr. Epstein's continued provision of consulting services on the applicable vesting date. All of the foregoing options and restricted stock units were or are subject to accelerated vesting under change in control provisions.

16. Defined Contribution Plan

We provide benefits under certain retirement benefit plans. Our most significant defined contribution plan is in the United States, which is administered through a third-party administrator. Under the U.S. defined contribution plan, employees may elect to defer up to 85.0% of their compensation per year (subject to a maximum limit prescribed by federal tax law) and we match a portion of such employee contributions. For each of the three months ended March 31, 2022 and 2021, our matching contribution expense was $0.2 million.

17. Subsequent Events

On May 11, 2022, we notified the University of Chicago of our intent to terminate the 2016 University of Chicago Agreement, which we initially entered into in March 2016. None of our current or anticipated product candidates will be affected by the termination of licenses contained therein. The termination will be effective on July 11, 2022.

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 condensed consolidated financial statements and related notes appearing elsewhere in this Quarterly Report on Form 10-Q and with our Annual Report on Form 10-K for the year ended December 31, 2021 (the "2021 Annual Report"), including the audited consolidated financial statements and notes thereto contained in our 2021 Annual Report. Some of the information contained in this discussion and analysis or set forth elsewhere in this Quarterly Report on Form 10-Q, including information with respect to our plans and strategy for our business, includes forward looking statements that involve risks and uncertainties. As a result of many factors, including those factors set forth in Part II, Item 1A. "Risk Factors" of this Quarterly Report on Form 10-Q, our actual results could differ materially from the results described, in or implied, by these forward-looking statements. In this Quarterly Report on Form 10-Q, unless otherwise stated or as the context otherwise requires, references to "Evelo," "Evelo Biosciences," the "Company," "we," "us," "our" and similar references refer to Evelo Biosciences, Inc. and its consolidated subsidiaries.

Overview

We are discovering and developing a new class of orally delivered investigational medicines that are intended to act on cells in the small intestine to produce therapeutic effects throughout the body. The target cells in the small intestine play a central role in governing human immune, metabolic and neurologic systems. We refer to this biology as the small intestinal axis, or SINTAX™. We have built a platform to discover and develop novel oral medicines which target the small intestinal axis. By harnessing the small intestinal axis, we have the potential to transform healthcare via medicines that have the potential to be effective, safe, convenient and affordable and to thereby treat patients at all stages of diseases and to treat patients globally.

Our first product candidates are orally delivered pharmaceutical preparations of naturally occurring, specific single strains of microbes or microbial extracellular vesicles. In preclinical models, our product candidates engaged immune cells in the small intestine and drove changes in systemic biology without any observed systemic exposure. We have observed in clinical trials and preclinical studies that our approach led to modulated immune responses throughout the body by acting on the small intestinal axis. Our most advanced product candidate, EDP1815, is being developed for the treatment of inflammatory diseases. Additional product candidates include EDP2939 which is in development for the treatment of inflammatory diseases.

Clinical Programs

EDP1815

EDP1815 is an investigational oral biologic being developed for the treatment of inflammatory diseases. It is a single strain of *Prevotella histicola* isolated from a human donor and selected for its specific pharmacology.

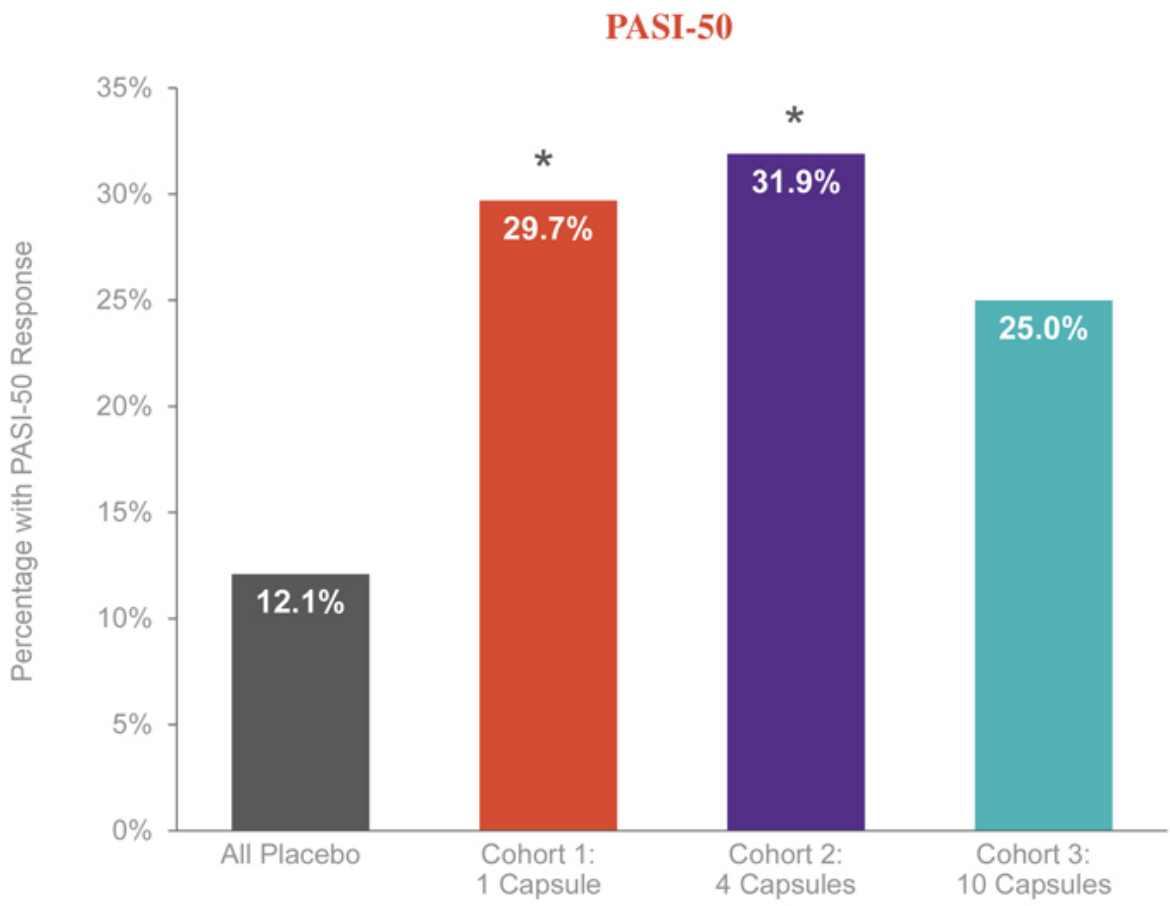
Psoriasis and atopic dermatitis

Phase 2 clinical trial in psoriasis

In September 2021, we announced positive data from our Phase 2 trial of EDP1815 in psoriasis. This multicenter, randomized, double-blind, placebo-controlled, dose-ranging Phase 2 trial was evaluated three doses of an enteric coated capsule formulation of EDP1815 in adult patients with mild and moderate psoriasis. The trial included a treatment phase (Part A) and an off treatment, follow-up phase (Part B). In Part A of the trial, 249 patients were randomized in a 1:1:1 ratio to one of three parallel cohorts: 1 capsule, 4 capsules or 10 capsules. They were then randomized in a 2:1 ratio to active or placebo prior to the start of dosing. Trial medication was taken once daily for 16 weeks, and all patients were followed for 4 weeks after treatment completion to week 20. Psoriasis Area and Severity Index (“PASI”) scores were assessed by both mean changes from baseline and responder rates. The primary endpoint was the mean percentage change in PASI scores between treatment and placebo at 16 weeks. Secondary endpoints included the proportion of study patients who achieved at least a 50% improvement in PASI from baseline at the week 16 timepoint (a "PASI-50" response), and other clinical measures of disease such as Physicians Global Assessment ("PGA"), Body Surface Area ("BSA"), PGA x BSA, Psoriasis Symptom Inventory ("PSI"), and Dermatology Life Quality Index ("DLQI").

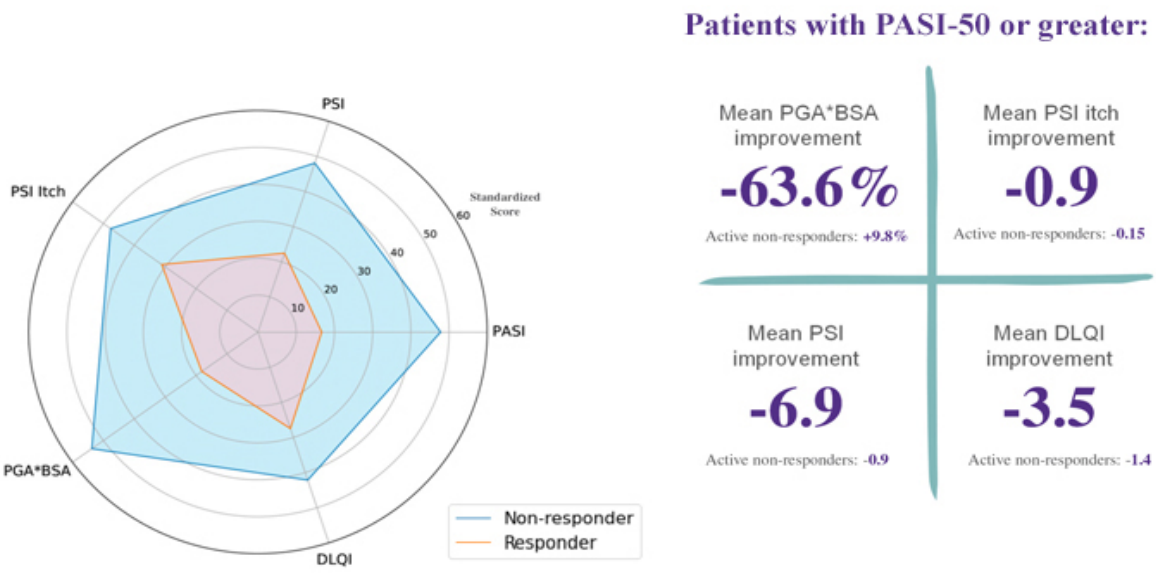
The primary endpoint, the difference in mean percentage change in PASI scores from baseline at week 16 between treatment and placebo, was prespecified as a Bayesian analysis. The Bayesian approach provides an estimate of the probability that EDP1815 was superior to placebo. The 16-week primary endpoint gave probabilities that EDP1815 is superior to placebo ranging from 80% to 90% across the prespecified analyses and cohorts.

The responder endpoint analysis evaluated the proportion of patients who achieved a PASI-50 (a meaningful clinical response) or greater reduction in PASI score at week 16. As shown in the figure below, 25% to 32% of patients across the three EDP1815 treated cohorts achieved a PASI-50 or greater reduction at week 16 compared to 12% on placebo. In cohorts 1 and 2, this difference in response rate was statistically significant ($p < 0.05$). Cohort 3 was not statistically significant, but directionally similar (25% vs. 12%). The pooled PASI-50 response across all three EDP1815 cohorts, an exploratory analysis, was 29% vs. 12% for placebo and was also statistically significant with a p-value of 0.027. An increase in the number of capsules of EDP1815 did not lead to a dose response.



* $p<0.05$.
PASI-50 responses at week 16. Statistically significant p-value (<0.05) for 2 of the 3 dose cohorts, and for all 3 cohorts when pooled.

Additionally, several patients on EDP1815 achieved a PASI-75 response or better at week 16. For individuals who had a PASI-50 response or better, consistent improvements in patient reported outcomes such as DLQI and PSI were observed as seen in the figure below.



Responders in active cohort demonstrated improvements across multiple secondary endpoints. A "responder" was defined as an active patient who achieved PASI-50 or greater.

EDP1815 was observed to be well tolerated in Part A (treatment phase) of the Phase 2 trial. The safety data were comparable to placebo. Adverse events ("AEs") classified as “gastrointestinal” were comparable between active and placebo groups, with no meaningful differences in rates of diarrhea, abdominal pain, nausea, or vomiting. There were no drug related serious adverse events.

All patients in Part A of the Phase 2 trial had the option to enter Part B (extended follow-up phase, off-treatment) of the trial. The objective of Part B was to assess durability of treatment response and incidence of rebound (for example, increase in PASI score to 125% of baseline value or above, or onset of new pustular erythrodermic psoriasis within 3 months) following cessation of dosing. All patients who elected to enroll in in Part B were assessed during follow-up visits at weeks 24 and 28. Only patients who had achieved a PASI-50 or greater at week 16 were also evaluated at week 40. Patients were not permitted to start other psoriasis treatments or trials during Part B.

In February 2022, we announced data from Part B of the Phase 2 trial in psoriasis, which included durable and deeper clinical responses. Eighty-three patients who had received EDP1815 in Part A entered Part B. Thirty of these 83 patients had achieved a PASI-50 or greater reduction at week 16 in Part A. Eighteen of the 30 patients remained at PASI-50 or greater at the end of Part B. Ten of the 30 patients had achieved a PASI-75 or greater at the end of Part A and 5 remained at PASI-75 or greater at the end of Part B. These durable results were achieved without any new psoriasis medication being used during this time. Nineteen of the 83 patients had achieved clear skin (PGA 0) or nearly clear skin (PGA 1) at the end of Part A and of these, 9 remained at PGA 0/1 at the end of Part B.

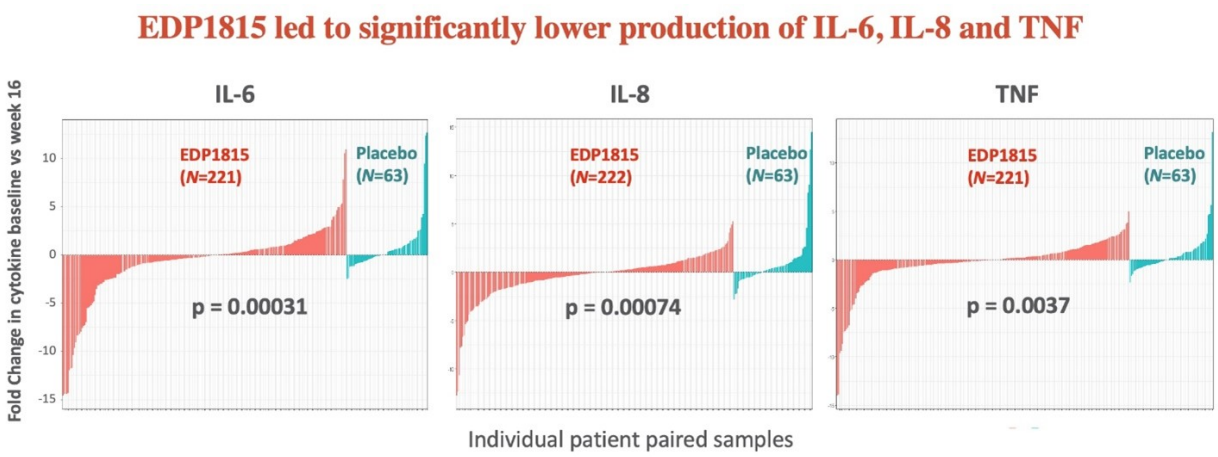
Of the 30 patients who had reached a PASI-50 at the end of Part A and entered Part B, 10 had already achieved a PASI-75 response at week 16 in Part A. Of the remaining 20 patients, 9 achieved a PASI-75 or greater response during the post-treatment period. These data, combined with the durability data, suggest that longer dosing could lead to further deepening of the responses in some patients.

There were no drug related adverse events in Part B of the Phase 2 trial, with the additional finding of no flare or rebound following cessation of dosing (which are seen with some other therapies for psoriasis).

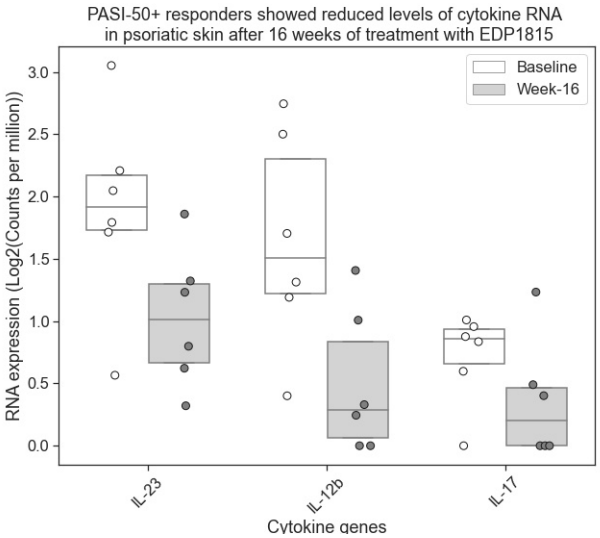
In February 2022, we also announced the results of immunological biomarker analyses from Part A of the Phase 2 trial in psoriasis. We had previously reported reductions in inflammatory cytokines in a Phase 1b trial of EDP1815 in mild and moderate psoriasis, and these data were replicated in the Phase 2 psoriasis trial, with high statistical significance.

Blood samples were taken from patients at baseline and after 16 weeks of dosing with EDP1815 or placebo. Samples from 96 of the trial patients, including all patients with a PASI-50 or greater response and all patients who worsened by 50% or more, were analyzed. The figures below show the changes in pro-inflammatory cytokines interleukin 6 (IL-6), interleukin 8 (IL-8) and tumor necrosis factor (TNF). Each vertical bar represents the fold change up or down from 0 in *ex vivo* stimulated cytokine production between the baseline and week 16 samples from a patient. Three different stimuli were used on each sample and the results from all three stimuli are presented together in the figures, giving the aggregate N (sample) numbers shown in the figures.

Treatment with EDP1815 led to a statistically significant reduction in the release of cytokines compared to placebo: IL-6 (p=0.0003), IL-8 (p=0.0007), and TNF (p=0.0037). The effect observed for EDP1815 may be clearly seen by the deep tail of reduced cytokine production on the left of the distribution for each cytokine, which was absent in the placebo groups. There was no worsening compared to placebo on the right of the distributions, resulting in the overall significant difference between EDP1815 and placebo.



In addition, skin biopsies of active lesions were taken from a subset of patients in the trial. Six of the patients who received EDP1815 and achieved at least a PASI-50 response from baseline at week 16 had paired biopsies. RNA-seq analysis of these biopsies showed reductions in transcript levels for psoriasis-relevant cytokines interleukin 23 (IL-23), interleukin 12b (IL-12b), and interleukin 17 (IL-17) in these lesions between baseline and week 16. The box plot below shows the median and interquartile ranges, as well as individual values of the cytokine expression levels in the skin, at baseline and week 16. These data suggest that EDP1815 reduced inflammation in the skin by modulating multiple proinflammatory cytokines.



We believe these data support the biology of the SINTAX and the development of a new potential class of medicine that is designed to act locally in the small intestine to affect inflammation throughout the body. In the Phase 2 trial, there was no observed exposure of EDP1815 outside the gut.

Based on these data, we currently intend to advance EDP1815 towards registration trials in psoriasis, following the completion of meetings with health authorities.

Pediatric Investigation Plan for EDP1815 in Psoriasis

In February 2022, the European Medicines Agency ("EMA") agreed to our Pediatric Investigation Plan ("PIP") for EDP1815 in psoriasis, in accordance with Regulation (EC) No 1901/2006 of the European Parliament and of the Council. The EMA agreement allows Evelo to include patients aged 12–17 years old in Phase 3 trials, and requires us to conduct a single clinical trial in patients 2–5 years old and 6–11 years old after the adult Marketing Authorization Application ("MAA") has been submitted, and to develop a pediatric formulation suitable for administration to patients 2–11 years old. Furthermore, the EMA confirmed that juvenile toxicity studies are not required for EDP1815 and granted us a waiver from studying EDP1815 in patients less than 2 years old.

Phase 1b and Phase 2 clinical trials in atopic dermatitis

In 2021, we reported preliminary clinical data from two cohorts of patients with mild and moderate atopic dermatitis in a Phase 1b randomized, placebo-controlled, dose-escalating safety and tolerability trial of EDP1815. The primary endpoint was safety and tolerability. In the first readout, we reported positive clinical data in a cohort of patients with mild and moderate atopic dermatitis (n=24), randomized 2:1 to receive EDP1815 in capsules (8.0 x 10^{11} total cells) or placebo for 56 days. This was the same concentration of EDP1815 that was used as one of the doses in our Phase 2 trial in psoriasis. In the first Phase 1b trial cohort of patients with atopic dermatitis, EDP1815 was well-tolerated with no treatment-related adverse events of moderate or severe intensity, and no serious adverse events. Secondary endpoints included a range of established markers of clinical efficacy in atopic dermatitis, such as Eczema Area and Severity Index (“EASI”), the Investigator’s Global Assessment times body surface area (“IGA* BSA”), and the SCORing Atopic Dermatitis (“SCORAD”) scores.

Clinical Measure	Treatment Difference between EDP1815 and Placebo Percentage Change at Day 56 *
EASI	52% (p=0.062)
IGA*BSA	65% (p=0.022)
SCORAD	35% (p=0.068)

* Least Squares Mean Percentage Change From Baseline. Note that the Phase 1b trial was not powered to detect statistically significant outcomes on efficacy endpoints: p-values presented are nominal values presented for illustrative purposes only.

The preliminary data showed consistent improvements in percentage change from baseline compared to placebo for all three clinical scores: EASI, IGA*BSA, and SCORAD. In January 2022, in connection with locking the database for the Phase 1b trial, we further analyzed these preliminary data and the methodology used to report the SCORAD results from the first cohort of atopic dermatitis patients in the Phase 1b trial described above. In the course of such review, we determined that the initial calculation of the SCORAD values was incorrect and we recalculated the SCORAD values. The correct SCORAD values are shown in the above table. The p-value change in SCORAD does not alter our prior determination that the SCORAD secondary endpoint showed consistent improvement in percentage change from baseline compared to placebo. In addition, 7 out of 16 (44%) patients treated with EDP1815 achieved an outcome of a 50% improvement from baseline in EASI score (an "EASI-50" response) by Day 70, compared with 0% in the placebo group, showing sustained improvement in those patients responding to EDP1815. In addition to physician-reported clinical outcomes, patient-reported outcomes were also assessed. Treatment with EDP1815 resulted in clinically meaningful improvement in DLQI and Patient-Oriented Eczema Measure ("POEM"). These patient-reported outcomes capture the important impact of the disease on patients, including the domains of itch and sleep, both of which saw improvements in patients receiving EDP1815 in the trial. All five measures of itch within the Pruritus-Numerical Rating Scale ("Pruritus-NRS"), SCORAD, POEM, and DLQI showed greater improvements in the treated group at Day 56 compared with placebo. We believe these results provide further evidence that modulating SINTAX has the potential to drive significant clinical benefit without the need for systemic exposure.

We reported data from a second cohort in the Phase 1b trial of 24 patients with moderate atopic dermatitis who were randomized in a 2:1 ratio, with 16 receiving a higher per capsule concentration formulation of EDP1815 (6.4×10^{11} total cells) and 8 receiving a matching placebo once daily for eight weeks. The higher concentration capsules given to the second cohort of atopic dermatitis patients were produced using a different manufacturing process from that used to produce the capsules given to the first cohort of atopic dermatitis patients. The primary objective was to assess the safety and tolerability of the higher per capsule concentration formulation of EDP1815 after eight weeks of dosing. The secondary objective was to assess the clinical improvement in patients with moderate atopic dermatitis. All the patients used an emollient twice daily for at least seven consecutive days immediately prior to day 1 and continued to use the background emollient treatment twice daily throughout the trial. In this second cohort, EDP1815 was shown to be well-tolerated with no treatment-related adverse events of moderate or severe intensity and no serious adverse events through eight weeks of dosing. An initial improvement in mean percent change in EASI was observed at day 15 compared to placebo; however, the population mean change decreased over the remainder of the dosing period, and there was no overall difference from placebo at the end of the dosing period. Given the difference in clinical effects observed between the two cohorts in the Phase 1b trial, which were dosed with EDP1815 produced using different manufacturing processes, we are evaluating drug substance produced using both manufacturing processes in our Phase 2 atopic dermatitis trial described below.

In February 2022, we began dosing patients in a Phase 2 trial of EDP1815 in atopic dermatitis. The primary objective of this multicenter, randomized, double-blind, placebo-controlled Phase 2 trial is to evaluate the efficacy and safety of EDP1815 in the treatment of atopic dermatitis when dosed for 16 weeks, compared to placebo. The trial is enrolling patients with mild, moderate, and severe atopic dermatitis and will evaluate EDP1815 drug substance produced using two different manufacturing processes. The primary endpoint is the proportion of patients who achieve an EASI-50 response at week 16. Secondary endpoints include several physician-reported outcomes, such as IGA and BSA, along with patient-reported outcomes such as DLQI, itch using the daily Pruritus-NRS, and POEM. Patients will be randomized into one of up to four cohorts. Each cohort will include approximately 100 patients randomized in a 3:1 ratio (75 to EDP1815 and 25 to placebo) for a total of up to 400 patients. Cohort 1 will explore a daily dose of 1.6×10^{11} total cells of EDP1815 or matching placebo administered as two capsules once daily. Cohorts 2 and 3 will explore a daily dose of 6.4×10^{11} total cells of EDP1815 or matching placebo administered as two capsules once daily or one capsule twice daily, respectively. The different dosages of drug (1.6×10^{11} total cells and 6.4×10^{11} total cells) are prepared from two different manufacturing processes. Cohorts 1, 2 and 3 were previously included as part of the initial trial protocol. In April 2022, we announced that, subject to allowance by regulatory authorities to proceed under the revised protocol, we intend to add a fourth cohort to this Phase 2 trial. Patients in this fourth cohort, if enrolled, would receive one capsule of EDP1815 (8.0×10^{10} total cells) designed to provide a faster release profile once daily or placebo. All patients will have the opportunity to join an open label extension trial once they complete 16 weeks of dosing. Patients in the open label extension trial will receive EDP1815 for a further 36 weeks. We anticipate that data from the first 3 cohorts of the Phase 2 atopic dermatitis trial will be available in the first quarter of 2023 and that data from the additional fourth cohort, if enrolled, will be available in the second quarter of 2023.

COVID-19

In March 2022, the Independent Data Monitoring Committee for the TACTIC-E clinical trial of EDP1815 for the treatment of hospitalized COVID-19 patients met for a scheduled review of data. No adverse signal was noted in the EDP1815 arm. However, we have concluded that the progressive mildness of the COVID-19 pandemic makes yielding a meaningful outcome for EDP1815 in TACTIC-E unlikely. Therefore, no further patients will be recruited. The trial will report results once all the data have been collected. The TACTIC-E clinical trial was a Phase 2/3 randomized trial, sponsored by Cambridge University Hospitals NHS Foundation Trust. The trial was investigating the safety and efficacy of certain experimental therapies in the prevention and treatment of life-threatening complications associated with COVID-19 in hospitalized individuals at early stages of the disease.

Scintigraphy Studies

We continue to evaluate different formulations of EDP1815 with the goal of providing optimum delivery of the drug substance in the small intestine. An on-going Phase 1 single center clinical trial in healthy human volunteers is assessing the release characteristics of capsules of EDP1815 by gamma scintigraphy imaging. In March 2022, results from the Phase 1 trial showed that a capsule with an improved release profile was able to deliver EDP1815 higher up in the small intestine. In 17 of the human volunteers studied, 15 (or 88%) showed that EDP1815 released in the jejunum, the upper part of the small intestine. Preclinical data have shown that the higher that EDP1815 is released in the small intestine, the greater the observed effect. We intend to evaluate this faster release capsule in patients in one or more suitable clinical trials including, subject to allowance by regulatory authorities, in our Phase 2 trial of EDP1815 in atopic dermatitis.

We currently intend to evaluate EDP1815 in additional inflammatory disease indications. Potential indications include psoriatic arthritis, asthma, axial spondylarthritis and rheumatoid arthritis.

EDP1867

EDP1867 is a non-live pharmaceutical preparation of a single strain of *Veillonella parvula*, isolated from the ileum of a human donor. It is made non-live by gamma-irradiation in the manufacturing process, making it unable to colonize or persist in the gut, a central feature of SINTAX medicines.

In April 2022, we announced that data from our Phase 1b clinical trial of EDP1867 in patients with atopic dermatitis (n=52, with 40 participants who had at least one dose of EDP1867) suggested EDP1867 was well-tolerated in both healthy volunteers and patients with moderate atopic dermatitis across all doses tested. No clear evidence of clinical benefit was observed in the small set of patients (n=15) with atopic dermatitis who received the lower dose of EDP1867 and provided analyzable data at week 8. Additionally, we announced our intention to place the EDP1867 program on hold to focus our efforts on our lead inflammation programs EDP1815 and EDP2939.

EDP2939

EDP2939 is an oral biologic consisting of extracellular vesicles ("EV") that we are investigating and developing for the potential treatment of inflammatory diseases. In May 2021, we presented preclinical data for EDP2939 at the American Association of Immunologists Meeting. In the preclinical mechanism of action study, mice undergoing a delayed-type hypersensitivity (DTH) reaction against keyhole limpet hemagglutinin (KLH) were treated with EDP2939, EDP2939 in combination with different blocking antibodies, or with placebo. These data suggest that the pharmacological activity of EDP2939 may require the stimulation of the TLR2 receptor and IL-10 receptor signaling, in addition to lymphocyte homing from the systemic circulation to the intestinal lymphoid tissue. *In-vitro*, EDP2939 induced TLR2-dependent release of IL-10. Biodistribution studies with fluorescently labelled EDP2939 showed that it was not detected outside the gastrointestinal tract. We also did not observe any adverse safety or tolerability issues in these preclinical studies. We believe these data suggest that treatment with EDP2939 could result in broad-based resolution of inflammation and the establishment of immune homeostasis. EDP2939 is the first EV product candidate we have nominated in our inflammation program. We anticipate initiation of clinical development in the third quarter of 2022, and expect data from a cohort of patients with psoriasis in the second half of 2023.

EDP1908

In December 2020, we announced EDP1908 as our lead candidate in oncology following presentation of preclinical data at the Society for Immunotherapy for Cancer meeting in November 2020. Preclinical data presented showed that orally administered EDP1908, an EV, resulted in superior tumor growth control versus the parent microbial strain or anti-PD-1 therapy, with an observed dose-dependent reduction in tumor growth.

Collaborations

In March 2021, we announced a strategic collaboration to develop and commercialize our lead inflammation product candidate, EDP1815, in the Middle East, Turkey, and Africa with Meddist Company Limited ("ALJ"), a company focused on accelerating access to affordable modern medical care while addressing unmet medical needs in developing markets around the world.

Together, we and ALJ will work to address the significant disparity in access to medical care in the fastest-growing populations and growth economies of the developing world. Africa’s population is projected to reach 1.7 billion by 2030 and 2.5 billion by 2050.

Under the terms of the agreement, we received an upfront payment from ALJ. We will be primarily responsible for the development and manufacturing of EDP1815 worldwide, whilst ALJ will be primarily responsible for development, regulatory submissions and commercialization activities in the agreed-upon regions. ALJ and we will participate in a 50:50 profit share arrangement. See the notes, including Note 3 - Summary of Significant Accounting Policies, to our unaudited condensed consolidated financial statements in this Quarterly Report on Form 10-Q for additional information regarding the commercialization and license agreement with ALJ.

Financing

Since our incorporation in 2014, we have devoted substantially all of our resources to developing our clinical and preclinical candidates, building our intellectual property portfolio and process development and manufacturing function, business planning, raising capital and providing general and administrative support for these operations. To date, we have financed our operations primarily with proceeds from sales of common and convertible preferred stock to our equity investors and borrowings under loan and security agreements with financial institutions.

We are a development stage company and have not generated any revenue. All of our product candidates are in clinical or preclinical development. Our ability to generate product revenue sufficient to achieve profitability will depend heavily on the successful development and eventual commercialization of one or more of our product candidates. Since our inception, we have incurred significant operating losses and we continue to incur significant research and development and other expenses related to our operations. For the three months ended March 31, 2022, our net loss was $29.9 million. As of March 31, 2022, we had an accumulated deficit of $444.6 million. We do not expect to generate revenue from sales of any products for the foreseeable future, if at all.

We expect that our expenses will increase substantially in connection with our ongoing activities, particularly as we:

- continue the ongoing clinical trials for EDP1815;
- initiate additional clinical trials for EDP1815;
- initiate clinical trials for EDP2939;
- initiate or advance the clinical development of any additional product candidates;
- conduct research and continue preclinical development of potential product candidates;
- make strategic investments in manufacturing capabilities, including potentially planning and building our own manufacturing facility;
- maintain our current intellectual property portfolio and opportunistically acquire complementary intellectual property;
- increase employees and employee-related expenses including salaries, benefits, travel and stock-based compensation expense; and
- seek to obtain regulatory approvals for our product candidates.

In addition, if we obtain marketing approval for any of our product candidates, we expect to incur significant commercialization expenses related to product manufacturing, marketing, sales and distribution.

As a result, we will need additional financing to support our continuing operations. Until such time as we can generate significant revenue from product sales, if ever, we expect to finance our operations through a combination of public or private equity or debt financings or other sources, which may include collaborations with third parties. Adequate additional financing may not be available to us on acceptable terms, or at all. Additionally, our ability to raise capital may be impacted by global macroeconomic conditions including as a result of international political conflict, supply chain issues and rising inflation. Our inability to raise capital as and when needed would have a negative impact on our financial condition and our ability to pursue our business strategy. We will need to generate significant revenue to achieve profitability, and we may never do so.

Because of the numerous risks and uncertainties associated with drug development, we are unable to predict the timing or amount of increased expenses or when or if we will be able to achieve or maintain profitability. Even if we are able to generate revenue from product sales, we may not become profitable. If we fail to become profitable or are unable to sustain profitability on a continuing basis, we may be unable to continue our operations at planned levels and be forced to reduce or terminate our operations.

Debt Financing

In June 2021, we amended our loan and security agreement with K2 HealthVentures LLC and others. The aggregate principal borrowings available under the amended agreement are $45.0 million, all of which we have drawn down to date. See “—Liquidity and Capital Resources" and Note 8 - Loan and Security Agreements to our unaudited condensed consolidated financial statements in this Quarterly Report on Form 10-Q for additional information regarding our debt facility.

Equity Financing

In June 2019, we filed a Registration Statement on Form S-3 (the "2019 Shelf Registration") with the Securities and Exchange Commission (the "SEC") for the registration of common stock, preferred stock, debt securities, warrants and/or units or any combination thereof in the aggregate amount of up to $200.0 million for a period of up to three years from the date of effectiveness. We simultaneously entered into an “at-the-market” offering sales agreement with Cowen and Company, LLC (the "ATM") providing for the offering, issuance and sale of up to $50.0 million of common stock under the 2019 Shelf Registration. During the three months ended March 31, 2022, we issued no shares of common stock under the ATM and no other securities under the 2019 Shelf Registration.

In August 2021, we filed a Registration Statement on Form S-3 (the “2021 Shelf Registration”) with the SEC for the registration of common stock, preferred stock, debt securities, warrants and/or units or any combination thereof in the aggregate amount of up to $200.0 million for a period of up to three years from the date of effectiveness. During the three months ended March 31, 2022, we issued no securities under the 2021 Shelf Registration.

See “—Liquidity and Capital Resources" and Note 11 - Stockholders' Equity to our unaudited condensed consolidated financial statements in this Quarterly Report on Form 10-Q for additional information regarding our equity financing.

Impact of COVID-19

On March 11, 2020, the World Health Organization (WHO) declared the COVID-19 outbreak a pandemic. The outbreak has resulted in governments around the world implementing stringent measures to help control the spread of the virus, including quarantines, “shelter in place” and “stay at home” orders, travel restrictions, business closures and curtailments, and school closures.

The prolonged COVID-19 pandemic has had, and for an extended period of time is expected to have, negative impacts on our operations and supply chain. Our ability to continue to operate without any significant negative impacts will, in part, depend on our ability to protect our employees and our supply chain. We have endeavored to follow recommended actions of government and health authorities to protect our employees with particular measures in place for those working in our laboratories, such as staggered work shifts and flexible schedules, and telecommuting for office workers. We continue working with our CMOs to minimize delays and disruptions to scheduled manufacturing batch runs for our product candidates and to ensure conformity to product specifications.

The COVID-19 pandemic has impacted and continues to impact our enrollment of new patients into, and the retention of existing patients in, our ongoing clinical trials, due primarily to lower patient participation. The pandemic likely will continue to impact enrollment and retention of patients in new and existing clinical trials. We continue to recruit individuals in line with the local and national guidelines of the clinical research sites. We are keeping in close contact with our CROs and clinical sites to provide support and guidance to ensure the safety of the patients in our clinical trials. We have prioritized our drug supply operations to secure the re-supply of patients currently enrolled in our clinical trials.

The extent to which the COVID-19 pandemic impacts our business and finances will depend on future developments, which are highly uncertain and cannot be predicted with confidence, such as the duration of the pandemic, travel restrictions and social distancing in the United States, the United Kingdom and other countries, business closures or business disruptions and the effectiveness of actions taken in the United States, the United Kingdom and other countries to contain and treat the disease. See “Risk Factors — The COVID-19 pandemic has adversely impacted and may continue to adversely impact our business, including our preclinical studies and clinical trials and finances” in Part II, Item 1A of this Quarterly Report on Form 10-Q.

Financial Operations Overview

Revenue

We have not generated any revenue since our inception and do not expect to generate any revenue from the sale of products in the near future, if at all. As discussed in Note 3 - ALJ Commercialization and License Agreement to our unaudited condensed consolidated financial statements included elsewhere in this Quarterly Report on Form 10-Q, we have entered into a collaboration agreement that will result in the recognition of $7.5 million of revenue upon regulatory approval of EDP1815 in certain designated markets. If our development efforts for our current product candidates or additional product candidates that we may develop in the future are successful and result in marketing approval or if we enter into collaboration or license agreements with third parties, we may generate revenue in the future from a combination of product sales or payments from such collaboration or license agreements.

Operating Expenses

Our operating expenses since inception have consisted primarily of research and development activities and general and administrative costs.

Research and Development Expenses

Research and development expenses consist primarily of costs incurred for our research activities, including our discovery efforts and the development of our product candidates, which include:

- expenses incurred under agreements with third parties, including investigative sites, external laboratories and CROs that conduct research, preclinical activities and clinical trials on our behalf;
- manufacturing process-development costs as well as technology transfer and other expenses incurred with CMOs that manufacture drug substance and drug product for use in our preclinical activities and any current or future clinical trials;
- salaries, benefits and other related costs, including stock-based compensation expense, for personnel in our research and development functions;
- expenses to acquire technologies to be used in research and development;
- costs of outside consultants, including their fees, stock-based compensation and related travel expenses;
- the cost of laboratory supplies and acquiring, developing and manufacturing preclinical study and clinical trial materials;
- costs related to compliance with regulatory requirements; and
- facility-related expenses, which include depreciation costs and allocated expenses for rent and maintenance of facilities and other operating costs.

We expense research and development costs as incurred. We recognize external development costs based on an evaluation of the progress to completion of specific tasks using information provided to us by our vendors and our clinical investigative sites. 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 financial statements as prepaid or accrued research and development expenses. Nonrefundable advance payments for goods or services to be received in the future for use in research and development activities are deferred and capitalized when there is no alternative future use for the research and development. The capitalized amounts are expensed as the related goods are delivered or the services are performed.

Our primary focus of research and development since inception has been building a platform to enable us to develop medicines based on an understanding that cells in the small intestine play a central role in governing the immune, metabolic and neurological systems, and to show potential clinical utility. Our platform and program expenses consist principally of costs such as preclinical research, clinical and preclinical manufacturing activity costs, clinical development costs, licensing expenses as well as an allocation of certain indirect costs, facility costs and depreciation expense. We do not allocate personnel costs, which primarily include salaries, discretionary bonus and stock-based compensation costs, as such costs are separately classified as research and development personnel costs.

Research and development activities are central to our business model. Product candidates in later stages of clinical development generally have higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of later-stage clinical trials. We expect that our research and development expenses will continue to increase in the foreseeable future as we continue to implement our business strategy and our ongoing clinical trials for our product candidates including EDP1815, initiate additional clinical trials including for EDP1815 and EDP2939, discover and develop additional product candidates, seek regulatory approvals for any products that successfully complete clinical trials, continue to source or potentially build manufacturing capabilities, hire additional research and development personnel and expand into additional therapeutic areas.

At this time, we cannot reasonably estimate or know the nature, timing and estimated costs of the efforts that will be necessary to complete the development of, and obtain regulatory approval for, any of our product candidates. We are also unable to predict when, if ever, material net cash inflows will commence from sales or licensing of our product candidates. This is due to the numerous risks and uncertainties associated with drug development, including the uncertainty of:

- our ability to add and retain key research and development personnel;
- our ability to successfully develop, obtain regulatory approval for, and then successfully commercialize our product candidates;
- our successful enrollment and completion of clinical trials;
- any delays in clinical trials as a result of the COVID-19 pandemic;
- the costs associated with the development of our current product candidates and/or any additional product candidates we identify in-house or acquire through collaborations;
- our ability to discover, develop and utilize biomarkers to demonstrate target engagement, pathway engagement and the impact on disease progression of our product candidates;
- our ability to establish an appropriate safety profile with IND-enabling toxicology studies;
- our ability to establish and maintain agreements with CMOs and other entities for clinical trial supply and future commercial supply, if our product candidates are approved;
- the terms and timing of any collaboration, license or other arrangement, including the terms and timing of any milestone payments thereunder;
- our ability to obtain and maintain patent, trade secret and other intellectual property protection and regulatory exclusivity for our product candidates if and when approved;
- our receipt of marketing approvals from applicable regulatory authorities;
- our ability to commercialize products, if and when approved, whether alone or in collaboration with others; and
- the continued acceptable safety profiles of product candidates following approval.

A change in any of these variables with respect to the development of any of our product candidates would significantly change the costs, timing and viability associated with the development of that product candidate. We expect our research and development expenses to increase at least over the next several years as we continue to implement our business strategy, advance our current programs, expand our research and development efforts, seek regulatory approvals for any product candidates that successfully complete clinical trials, identify and develop additional product candidates and incur expenses associated with hiring additional personnel to support our research and development efforts.

General and Administrative Expenses

General and administrative expenses consist primarily of salaries, benefits and other related costs, including stock-based compensation, for personnel in our executive, finance, corporate, business development and administrative functions. General and administrative expenses also include legal fees relating to patent and corporate matters; other professional fees for accounting, auditing, tax and administrative consulting services; insurance costs; administrative travel expenses; and facility-related expenses, which include depreciation costs and allocated expenses for rent, maintenance of facilities and other operating costs.

We anticipate that our general and administrative expenses will increase in the future as we increase our headcount to support the expected growth in our research and development activities and the potential commercialization of our product candidates. We also expect to continue to incur increased expenses associated with being a public company, including increased costs of accounting, audit, legal, regulatory and tax-related services associated with maintaining compliance with exchange listing and SEC requirements, director and officer insurance costs and investor and public relations costs.

Interest Expense, Net

Interest expense, net primarily consists of interest expense incurred on our debt offset by interest earned on our cash and cash equivalents. During the three months ended March 31, 2022 and 2021, interest expense, net consisted primarily of interest at the stated rate on borrowings under our loan and security agreements, amortization of deferred financing costs and interest expense related to the accretion of debt discount offset by interest earned on institutional money market instruments.

Other Miscellaneous Income, Net

Other miscellaneous income, net for the three months ended March 31, 2022 and 2021 primarily consists of government grants related to our operations in the United Kingdom and foreign currency exchange losses.

Income Taxes

Income tax expense for the three months ended March 31, 2022 and 2021 reflects the provision for income taxes at our wholly owned UK subsidiary.

Since our inception in 2014, we recorded no U.S. federal or state income tax benefits for the net losses we incurred or for our earned research and development tax credits, due to our uncertainty of realizing a benefit from those items.

Results of Operations

Comparison of the Three Months Ended March 31, 2022 and 2021

Our statement of operations for the three months ended March 31, 2022 compared to the three months ended March 31, 2021 is as follows (in thousands):

	Three Months Ended March 31,		
	2022	2021	Change
Operating expenses:			
Research and development	$ 19,321	$ 21,508	$ (2,187)
General and administrative	9,417	5,963	3,454
Total operating expenses	28,738	27,471	1,267
Loss from operations	(28,738)	(27,471)	(1,267)
Other (expense) income:			
Interest expense, net	(1,027)	(765)	(262)
Other miscellaneous income, net	20	162	(142)
Total other expense, net	(1,007)	(603)	(404)
Loss before income taxes	(29,745)	(28,074)	(1,671)
Income tax expense	(116)	(122)	6
Net loss	$ (29,861)	$ (28,196)	$ (1,665)

Net Loss

Net loss for the three months ended March 31, 2022 was $29.9 million, compared to $28.2 million for the three months ended March 31, 2021. The additional current year net loss of $1.7 million was the result of increases in our general and administrative expenses and total other expense, net, of $3.5 million and $0.4 million, respectively, partially offset by a $2.2 million decrease of research and development expenses.

Research and Development Expenses

Our research and development expenses for the three months ended March 31, 2022 compared to the three months ended March 31, 2021 are as follows (in thousands):

	Three Months Ended March 31,		
	2022	2021	Change
Inflammation programs	$ 7,000	$ 10,690	$ (3,690)
Oncology programs	84	916	(832)
Personnel costs	6,543	5,165	1,378
Stock-based compensation	2,036	1,823	213
Platform expenses	3,658	2,914	744
Total research and development expenses	$ 19,321	$ 21,508	$ (2,187)

Research and development expenses were $19.3 million for the three months ended March 31, 2022, compared to $21.5 million for the three months ended March 31, 2021. The overall decrease of $2.2 million was driven by the completion of the first EDP1815 Phase 2 clinical trial in psoriasis and the closeout of the EDP1503 program. The $4.5 million decrease in expenditures for those programs were partially offset by the ramp up of the EDP1815 Phase 2 clinical trial in atopic dermatitis and the EDP2939 program. In addition, there were higher personnel costs of $1.4 million and stock-based compensation costs of $0.2 million due to increases in the clinical development and technical operations headcount to support clinical program activities. Lastly, there was a $0.7 million increase in investment for our platform expenses to support our early stage and preclinical candidates. Overall, we expect that our research and development expenses will increase in the foreseeable future as we continue our clinical trials for our product candidates including EDP1815, initiate new clinical trials for our product candidates including EDP1815 and EDP2939, expand into additional therapeutic areas, continue discovery and development efforts for additional product candidates, hire additional research and development personnel and seek to increase manufacturing capabilities.

General and Administrative Expenses

Our general and administrative expenses for the three months ended March 31, 2022 compared to the three months ended March 31, 2021 are as follows (in thousands):

	Three Months Ended March 31,		
	2022	2021	Change
Personnel costs	$ 3,730	$ 2,112	$ 1,618
Stock-based compensation	2,239	1,441	798
Professional fees	2,257	1,524	733
Facility costs, office expense and other	1,191	886	305
Total general and administrative expenses	$ 9,417	$ 5,963	$ 3,454

General and administrative expenses were $9.4 million for the three months ended March 31, 2022, compared to $6.0 million for the three months ended March 31, 2021. The increase of $3.5 million was primarily driven by $1.6 million related to increases in pre-commercial and other general and administrative function headcount and related higher stock-based compensation expense of $0.8 million. Additionally, professional fees increased by $0.7 million and cost increases of $0.3 million related to a return of our employees to the office and increased travel.

Total Other Expense, Net

Total other expense, net for the three months ended March 31, 2022 was $1.0 million compared to $0.6 million for the three months ended March 31, 2021. The $0.4 million increase in other expense was primarily driven by a $0.3 million increase in interest expense resulting from higher outstanding principal balances on our debt facility and a $0.1 million decrease in other miscellaneous income.

Liquidity and Capital Resources

We have incurred losses and have generated negative operating cash flows since our inception, and anticipate that we will continue to incur losses for at least the next several years. As of December 31, 2021, we had an accumulated deficit of $414.7 million and have incurred an additional net loss of approximately $29.9 million for the three months ended March 31, 2022. To date, we have financed our operations primarily with proceeds from public and private offerings of our common stock, sales of our convertible preferred stock to our equity investors and borrowings under our debt facilities. From inception through March 31, 2022, we have received gross proceeds of $434.9 million from equity and debt transactions, including a net $45.0 million borrowed under our debt facilities. As of March 31, 2022, we had cash and cash equivalents of $39.6 million and an accumulated deficit of $444.6 million.

During the three months ended March 31, 2022, we sold no securities under the 2019 Shelf Registration including no sales of shares of our common stock pursuant to the ATM. During the three months ended March 31, 2022, we sold no securities under the 2021 Shelf Registration. In July 2019, we entered into a loan and security agreement (as amended prior to June 16, 2021, the "2019 Credit Facility") with K2 HealthVentures LLC and others (collectively, "K2HV"), providing for up to $45.0 million of current and future potential debt financing. In July 2019, we borrowed $20.0 million, representing the first tranche under the 2019 Credit Facility. In July 2020, we drew down the second tranche of $10.0 million under the 2019 Credit Facility. The availability of the third tranche of $15.0 million under the 2019 Credit Facility expired in January 2021.

On June 16, 2021 (the "Amended Credit Facility Effective Date"), we further amended the 2019 Credit Facility (as so amended, the “Amended Credit Facility”), pursuant to which (i) the existing $15.0 million third tranche commitment was replaced and superseded with a new $15.0 million fourth tranche commitment, which we drew down on June 16, 2021, (ii) K2HV may convert up to $5.0 million of outstanding principal of the Loans (as defined in the Amended Credit Facility) into shares of our common stock, (iii) the interest-only period is extended through February 28, 2023, with the first amortization payment on March 1, 2023, (iv) an election was included allowing us to adjust the amortization schedule to be based on a 30-month repayment period, and upon final payment or prepayment of the loans we must pay a final payment equal to 4.8% of the aggregate original principal amount of the loans borrowed which we elected on December 22, 2021, and (v) at our election, we may prepay the loans, subject to a prepayment fee of 2% of the amount prepaid if such prepayment occurs no later than the 18-month anniversary of the Amended Credit Facility Effective Date, or if the prepayment occurs after the 18-month anniversary of the Amended Credit Facility Effective Date but prior to the maturity date, 1% of the amount prepaid. All of the other terms and conditions of the 2019 Credit Facility remain unchanged and in full force and effect under the Amended Credit Facility.

As of March 31, 2022, our principal source of liquidity is cash and cash equivalents, which totaled approximately $39.6 million. Based on our current operating plan, our existing cash and cash equivalents as of March 31, 2022 will be sufficient to enable us to fund operating expenses and capital expenditure requirements into the third quarter of 2022. We base these estimates on assumptions that may prove to be wrong, and we may use our available capital resources sooner than we currently expect.

Based on our current operating plan, we believe we do not have sufficient cash and cash equivalents on hand to support current operations for at least one year from the date of issuance of the financial statements appearing within this Quarterly Report on Form 10-Q. To finance our operations beyond that point, we will need to raise additional capital. There can be no assurance that we will be able to obtain additional funding on acceptable terms, if at all. We have concluded that this circumstance raises substantial doubt about our ability to continue as a going concern for at least one year from the date of the issuance of our unaudited condensed consolidated financial statements for the period ended March 31, 2022. As such, we plan to seek to raise capital from time to time through future equity financings, debt financings or partnerships to fund our future operations and remain as a going concern. 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. See Note 1 - Organization of the notes to our unaudited condensed consolidated financial statements in this Quarterly Report on Form 10-Q for additional information on our assessment.

Until such time as we can generate revenue from product sales, if ever, we expect to finance our cash needs through a combination of equity offerings, debt financings and potential collaborations, license and development agreements.

Cash Flows

Our total cash, cash equivalents and restricted cash decreased by $29.0 million during the three months ended March 31, 2022 to $40.8 million. Our statements of cash flows for the three months ended March 31, 2022 compared to the three months ended March 31, 2021 are summarized as follows (in thousands):

	Three Months Ended March 31,	
	2022	2021
Cash used in operating activities	$ (28,932)	$ (26,280)
Cash used in investing activities	(153)	(314)
Cash provided by financing activities	117	82,328
Net (decrease) increase in cash, cash equivalents and restricted cash	$ (28,968)	$ 55,734

Operating Activities

Net cash used in operating activities for the three months ended March 31, 2022 was $28.9 million, driven primarily by our net loss of $29.9 million. This was partially offset by non-cash charges consisting of stock-based compensation expense of $4.3 million, depreciation expense of $0.5 million, non-cash lease expense of $0.5 million, and non-cash interest expense of $0.1 million. The change in operating assets and liabilities account for $4.6 million of cash used in operations.

Net cash used in operating activities for the three months ended March 31, 2021 was $26.3 million driven primarily by our net loss of $28.2 million. This was partially offset by non-cash charges consisting of stock-based compensation expense of $3.3 million, depreciation expense of $0.5 million, non-cash lease expense of $0.4 million, and non-cash interest expense of $0.1 million. The change in operating assets and liabilities account for $2.5 million of cash used in operations.

Investing Activities

Net cash used in investing activities for the three months ended March 31, 2022 was $0.2 million, consisting of the purchase of capital equipment.

Net cash used in investing activities for the three months ended March 31, 2021 was $0.3 million, consisting of the purchase of capital equipment.

Financing Activities

Net cash provided by financing activities for the three months ended March 31, 2022 was $0.1 million, consisting of net proceeds from the exercise of stock options.

Net cash provided by financing activities for the three months ended March 31, 2021 was $82.3 million, consisting of $82.3 million in proceeds from the issuance of common stock, net of issuance cost.

Recent Accounting Pronouncements

For a discussion of recently adopted or issued accounting pronouncements please refer to Note 2 - Summary of Significant Accounting Policies of our unaudited condensed consolidated financial statements included elsewhere in this Quarterly Report on Form 10-Q.

Critical Accounting Policies and Use of Estimates

Our management's discussion and analysis of financial condition and results of operations is based on our unaudited condensed consolidated financial statements, which have been prepared in accordance with U.S. GAAP. The preparation of these unaudited condensed consolidated financial statements requires us to make estimates and judgments that affect the reported amounts. Changes in estimates are reflected in reported results for the period in which they become known. Actual results may differ materially from these estimates under different assumptions or conditions.

Except as described in Part I, Item 4 - Controls and Procedures and Note 2 - Summary of Significant Accounting Policies, there were no material changes to our critical accounting policies in the three months ended March 31, 2022 from those described in "Management's Discussion and Analysis of Financial Condition and Results of Operations," included in our 2021 Annual Report.

Item 3. Quantitative and Qualitative Disclosures About Market Risk.

We are a smaller reporting company, as defined by Rule 12b-2 of the Exchange Act and are not required to provide this information.

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 our principal financial officer, evaluated, as of the end of the period covered by this Quarterly Report on Form 10-Q, the effectiveness of our disclosure controls and procedures, as defined under 13a-15(e) and 15d-15(e) under the Exchange Act. The term “disclosure controls and procedures,” as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act, means controls and other procedures of a company that are designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act are recorded, processed, summarized and reported within the time periods specified in the SEC’s rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by us in the reports that we file or submit under the Exchange Act is accumulated and communicated to our management, including our principal executive officer and principal financial officer, as appropriate, to allow timely decisions regarding required disclosure. Following such evaluation, due solely to the material weakness previously disclosed in our Annual Report on Form 10-K for the period ended December 31, 2021 and further described below, the principal executive officer and principal financial officer have concluded that our disclosure controls and procedures were not effective as of March 31, 2022.

Previously Reported Material Weakness

A material weakness is a deficiency, or a combination of deficiencies, in internal control over financial reporting, such that there is a reasonable possibility that a material misstatement of our annual or interim financial statements will not be prevented or detected on a timely basis. As previously disclosed in our Annual Report on Form 10-K for the year ended December 31, 2021, we identified a material weakness in our internal control over financial reporting in connection with the preparation of our financial statements as of and for the year ended December 31, 2021. Specifically, the review of certain financial transactions and preparation and review of account reconciliations was not performed using a sufficient level of precision and accuracy. This material weakness resulted from an insufficient complement of resources with an appropriate level of accounting knowledge, experience, or training. No material financial statement misstatements were identified in relation to this material weakness in our internal control over financial reporting. Based on additional procedures and post-closing review, management concluded that the condensed consolidated financial statements included in this Quarterly Report on Form 10-Q present fairly, in all material respects, our financial position, results of operations, and cash flows for the periods presented, in conformity with accounting principles generally accepted in the United States.

Remediation Plan

Our management, under the supervision of our principal executive officer and principal financial officer, previously adopted and has been implementing a plan to remediate the material weakness and continues to take steps that we believe will address the underlying causes of the material weakness. Those actions primarily include hiring additional accounting and finance personnel with technical accounting and financial reporting experience and enhancing our internal review procedures during the financial statement close process. During the preparation of this Quarterly Report on Form 10-Q, our management implemented certain additional substantive and analytical review procedures intended to ensure that information required to be disclosed by us in our periodic reports is recorded, processed, summarized, and reported within the time periods specified in the SEC’s rules and forms.

Changes in Internal Control over Financial Reporting

Except for the remediation efforts described above taken to address the previously disclosed material weakness, there was no change in our internal control over financial reporting, as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act, that occurred during our most recent fiscal quarter that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

PART II—OTHER INFORMATION

Item 1. Legal Proceedings.

From time to time, we may be involved in claims and proceedings arising in the course of our business. The outcome of any such claim or proceeding, regardless of the merits, is inherently uncertain. We are not subject to any material legal proceedings.

On February 12, 2021, the European Patent Office issued a Communication of a Notice of Opposition for European patent EP 3223834, which is held by us. In July 2021, we filed our reply to the Notice of Opposition. In January 2022, the European Patent Office issued a preliminary opinion and a summons to oral proceedings. The deadline for final written submissions is in July 2022 and the date for the oral proceedings is in September 2022. We are currently evaluating the options available to us with respect to this matter. The patent at issue does not relate to any of our current product candidates, and receipt of this communication and/or any subsequent proceeding is not expected to affect any of our current development plans.

Item 1A. Risk Factors.

Investing in our common stock involves a high degree of risk. You should carefully consider the risks described below, as well as the other information in this Quarterly Report on Form 10-Q, including our unaudited condensed consolidated financial statements and the related notes and Part I, Item 2. "Management's Discussion and Analysis of Results of Operations and Financial Condition" and in our Annual Report on Form 10-K filed with the SEC on March 24, 2022, including our consolidated financial statements and the related notes thereto, before deciding whether to invest in our common stock. The occurrence of any of the events or developments described below could harm our business, financial condition, results of operations and growth prospects. In such an event, the market price of our common stock could decline, and you may lose all or part of your investment.

Risks Related to Our Financial Position and Need for Additional Capital

We are a development-stage company and have incurred significant losses since our inception. We expect to incur losses for the foreseeable future and may never achieve or maintain profitability.

Since inception, we have incurred significant operating losses. Our net loss was $29.9 million and $28.2 million for the three months ended March 31, 2022 and 2021, respectively. As of March 31, 2022, we had an accumulated deficit of $444.6 million. As noted below, we have identified conditions and events that raise substantial doubt about our ability to continue as a going concern. Through March 31, 2022, we have financed our operations through proceeds from equity offerings of our common stock, private placements of our preferred stock and borrowings under loan and security agreements. We have devoted substantially all of our financial resources and efforts to developing our platform, identifying potential product candidates and conducting preclinical and clinical trials. We are in the early stages of developing our product candidates, and we have not completed the development of any product candidate. We expect to continue to incur significant expenses and operating losses for the foreseeable future. We anticipate that our expenses will increase substantially as we:

- seek to initiate additional and larger clinical trials of our product candidates;
- seek to enhance our platform and discover and develop additional product candidates;
- seek regulatory approvals for any product candidates that successfully complete clinical trials;
- seek to establish a sales, marketing and distribution infrastructure and scale-up manufacturing capabilities to commercialize any products for which we may obtain regulatory approval;
- maintain, expand and protect our intellectual property portfolio; and
- add clinical, scientific, operational, financial and management information systems and personnel, including personnel to support our product development and potential future commercialization efforts and to support our operations as a public company.

In addition, we anticipate that our expenses will increase substantially if we experience any delays or encounter any issues with any of the above, including but not limited to failed studies, complex results, safety issues or other regulatory challenges.

To become and remain profitable, we must succeed in developing and eventually commercializing products that generate significant revenue. This will require us to be successful in a range of challenging activities, including completing preclinical testing and clinical trials of our product candidates, discovering additional product candidates, obtaining regulatory approval for these product candidates and manufacturing, marketing and selling any products for which we may obtain regulatory approval. We are only in the preliminary stages of most of these activities. We may never succeed in these activities and, even if we do, may never generate revenue that is significant enough to achieve profitability.

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

Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would depress our value and could impair our ability to raise capital, expand our business, maintain our research and development efforts, diversify our product offerings or even continue our operations.

We will need additional funding in order to complete development of our product candidates and commercialize our products, if approved. If we are unable to raise capital when needed, we could be forced to delay, reduce or discontinue our product development programs or commercialization efforts.

We expect our expenses to increase in connection with our ongoing activities, particularly as we conduct clinical trials, build manufacturing capacity and expand into additional therapeutic areas.

We expect that our existing cash and cash equivalents as of March 31, 2022 will enable us to fund our planned operating expenses and capital expenditure requirements into the third quarter of 2022. We have based this estimate on assumptions that may prove to be wrong, and we could use our capital resources sooner than we currently expect. Our future capital requirements will depend on many factors, including:

- the progress and results of any ongoing and future clinical trials;
- the cost of manufacturing clinical supplies of our product candidates, including EDP1815 and EDP2939;
- the scope, progress, results and costs of preclinical development, laboratory testing and clinical trials for any other future product candidates;
- the costs, timing and outcome of regulatory review of our product candidates;
- the costs and timing of future commercialization activities, including manufacturing, marketing, sales and distribution for any of our product candidates for which we receive marketing approval;
- the revenue, if any, received from commercial sales of our product candidates for which we receive marketing approval;
- the costs and timing of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending any intellectual property-related claims;
- the effect of competing technological and market developments; and
- the extent to which we acquire or invest in businesses, products and technologies, including entering into licensing or collaboration arrangements for product candidates.

Any additional fundraising efforts may divert our management from their day-to-day activities, which may adversely affect our ability to develop and commercialize our product candidates. In addition, we cannot guarantee that future financing will be available in sufficient amounts or on terms acceptable to us, if at all. Additionally, market volatility resulting from the COVID-19 pandemic or other factors could also adversely impact our ability to access capital as and when needed. Moreover, the terms of any financing may adversely affect the holdings or the rights of our stockholders and the issuance of additional securities by us, whether equity or debt, or the possibility of such issuance, may cause the market price of our shares to decline. The sale of additional equity, including any shares subject to warrants that we have previously issued or may in the future issue, or of convertible securities, would dilute all of our stockholders. The occurrence of additional indebtedness could result in increased fixed payment obligations and we may be required to agree to certain restrictive covenants such as limitations on our ability to

incur additional debt, limitations on our ability to acquire, sell or license intellectual property rights and other operating restrictions that could adversely impact our ability to conduct our business. We could also be required to seek funds through arrangements with collaborators or others at an earlier stage than otherwise would be desirable and we may be required to relinquish rights to some of our technologies or product candidates or otherwise agree to terms unfavorable to us, any of which may have a material adverse effect on our business, operating results and prospects.

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 product development programs or the commercialization of any product candidates or cease our operations. In addition, we may be unable to make milestone and royalty payments due under our intellectual property license agreements or other payments under our agreements with contract research organizations ("CROs") and academic research collaborators, or expand our operations or otherwise capitalize on our business opportunities, as desired, which could materially affect our business, financial condition and results of operations.

Our limited operating history may make it difficult to evaluate the success of our business to date and to assess our future viability.

Since our inception in 2014, we have devoted substantially all of our resources to identifying and developing our product candidates, building our intellectual property portfolio, process development and manufacturing function, planning our business, raising capital and providing general and administrative support for these operations. All of our product candidates are in clinical or preclinical development. We have not yet demonstrated our ability to successfully complete a Phase 3 or other pivotal clinical trial, obtain regulatory approvals to commercialize a product, manufacture a commercial scale product, or arrange for a third party to do so on our behalf, or conduct sales and marketing activities necessary for successful product commercialization. Additionally, we expect our financial condition and operating results to continue to fluctuate significantly from quarter to quarter and year to year due to a variety of factors, many of which are beyond our control. Consequently, any predictions about our future success or viability may not be as accurate as they could be if we had a longer operating history.

We have identified conditions and events that raise substantial doubt about our ability to continue as a going concern.

We will be forced to delay or reduce the scope of our development programs, reduce our research and development costs and/or limit or cease our operations if we are unable to obtain additional funding to support our current operating plan. We have identified conditions and events that raise substantial doubt about our ability to continue as a going concern. As of March 31, 2022, we had $39.6 million in cash and cash equivalents. Based on our available cash resources, we believe we do not have sufficient cash and cash equivalents on hand to support current operations for at least one year from the date of issuance of the financial statements appearing within this Quarterly Report on Form 10-Q. This condition raises substantial doubt about our ability to continue as a going concern for at least one year from the date that our financial statements for the quarter ended March 31, 2022 were issued. Nevertheless, our financial statements do not include any adjustments that might result from the outcome of this uncertainty. 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 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. However, 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 commercialization efforts.

The terms of our loan and security agreements place restrictions on our operating and financial flexibility. If we raise additional capital through debt financing, the terms of any new debt could further restrict our ability to operate our business.

Our loan and security agreement dated July 19, 2019 (as amended prior to June 16, 2021, the "2019 Credit Facility") with K2 Health Ventures ("K2HV") for $45.0 million was secured by a lien covering substantially all of our personal property, excluding intellectual property. Contemporaneous with the closing of the first tranche of funding under the facility, we repaid the entire $15.0 million loan balance outstanding under our prior loan and security agreement with Pacific Western Bank.

On June 16, 2021 (the "Amended Credit Facility Effective Date"), we further amended the 2019 Credit Facility (as so amended, the "Amended Credit Facility"), pursuant to which (i) the existing $15.0 million third tranche commitment was replaced and superseded with a new $15.0 million fourth tranche commitment, which we drew down on June 16, 2021, (ii) K2HV may convert up to $5.0 million of outstanding principal of the Loans (as defined in the Amended Credit Facility) into shares of our common stock, (iii) the interest-only period is extended through February 28, 2023, with the first amortization payment on March 1, 2023, (iv) includes an election to adjust the amortization schedule to be based on a 30-month repayment period, and upon final payment or prepayment of the loans and we must pay a final payment equal to 4.8% of the aggregate original principal amount of the loans borrowed which we elected on December 22, 2021, and (v) at our election, we may prepay the loans, subject to a prepayment fee of 2% of the amount prepaid if such prepayment occurs no later than the 18-month anniversary of the Amended Credit Facility Effective Date, or if the prepayment occurs after the 18-month anniversary of the Amended Credit Facility Effective Date but prior to the maturity date, 1% of the amount prepaid. All of the other terms and conditions of the Amended Credit Facility remain unchanged and in full force and effect.

As of March 31, 2022, the outstanding principal balance under the Amended Credit Facility was $45.0 million. The Amended Credit Facility contains customary representations, warranties, affirmative and negative covenants and events of default applicable to us and our subsidiaries.

If we default under the Amended Credit Facility, K2HV may accelerate all of our repayment obligations and exercise all of their rights and remedies under the Amended Credit Facility and applicable law, potentially requiring us to renegotiate our agreement on terms less favorable to us or to immediately cease operations. Further, if we are liquidated, the lenders' rights to repayment would be senior to the rights of the holders of our common stock to receive any proceeds from the liquidation. K2HV could declare a default upon the occurrence of any event, among others, that they interpret as a material adverse effect or a change of control as delineated under the Amended Credit Facility, payment defaults, or breaches of covenants thereby requiring us to repay the loan immediately or to attempt to reverse the declaration of default through negotiation or litigation. Any declaration by K2HV of an event of default would significantly harm our business and prospects and could cause the price of our common stock to decline. If we raise any additional debt financing, the terms of such additional debt could further restrict our operating and financial flexibility.

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

We are early in our development efforts and may not be successful in our efforts to use our platform to build a pipeline of product candidates and develop marketable drugs.

We are using our technology platform to harness the small intestinal axis, with an initial focus on developing therapies in immunology, specifically inflammatory diseases, and also oncology. While we believe our preclinical studies and clinical trials to date have validated our platform to a degree, we are at an early stage of development and our platform has not yet, and may never lead to, approvable or marketable products. We are developing these product candidates and additional product candidates that we intend to use to treat broader immunological diseases, respiratory diseases, neuro-inflammation and degeneration, liver diseases, type I diabetes, food allergy, neurobehavior, cardiovascular disease and diseases of metabolism. We may have problems applying our technologies to these other areas, and our new product candidates may not demonstrate a comparable ability in treating disease as our initial product candidates. Even if we are successful in identifying additional product candidates, they may not be suitable for clinical development as a result of our inability to manufacture more complex oral biologics, limited efficacy, unacceptable safety profiles or other characteristics that indicate that they are unlikely to be products that will receive marketing approval and achieve market acceptance. The success of our product candidates will depend on several factors, including the following:

- completion of preclinical studies and clinical trials with positive results;
- receipt of marketing approvals from applicable regulatory authorities;
- obtaining and maintaining patent and trade secret protection and regulatory exclusivity for our product candidates;
- making arrangements with CMOs, or establishing our own commercial manufacturing capabilities;
- launching commercial sales of our products, if and when approved, whether alone or in collaboration with others;

- entering into new collaborations throughout the development process as appropriate, from preclinical studies through to commercialization;
- acceptance of our products, if and when approved, by patients, the medical community and third-party payors;
- effectively competing with other therapies;
- obtaining and maintaining coverage and adequate reimbursement by third-party payors, including government payors, for our products, if approved;
- protecting our rights in our intellectual property portfolio;
- operating without infringing or violating the valid and enforceable patents or other intellectual property of third parties;
- maintaining an acceptable safety profile of the products following approval; and
- maintaining and growing an organization of scientists and business people who can develop and commercialize our products and technology.

If we do not successfully develop and commercialize product candidates based upon our technical approach, we will not be able to obtain product revenue in future periods, which likely would result in significant harm to our financial position and adversely affect our stock price.

Our product candidates are designed to act on cells in the small intestine to produce systemic therapeutic effects with limited systemic exposure. This biological interaction between the small intestine and the rest of the body may not function in humans the way we have observed in mice and our drugs may not reproduce the systemic effects we have seen in preclinical and early clinical data.

We believe our product candidates, including EDP1815 and EDP2939 have the potential to work by modulating systemic responses via interactions with cells in the small intestine. Dosing to achieve sufficient exposure may require an inconvenient dosing regimen. Even with a successful formulation and appropriate delivery profile to achieve proper exposure of our microbes or extracellular vesicles to the small intestine, we may not get sufficient or even any activity at the site of disease. This may be because our understanding of the mechanisms of the small intestine do not work in humans the way we believe they do. Despite there being strong academic literature to support the concept and our observations in preclinical studies in mice and early clinical trials in humans, these principles and the ability to use pharmaceutical preparations derived from single strains of microbes to modulate the immune system and other systems have not yet been proven in humans.

Our product candidates are an unproven approach to therapeutic intervention.

All of our product candidates are based on targeting SINTAX. We have not, nor to our knowledge has any other company, received regulatory approval for an oral therapeutic based on this approach. We cannot be certain that our approach will lead to the development of approvable or marketable products. In addition, our product candidates may have different safety profiles and efficacy in various indications. Finally, the FDA or other regulatory agencies may lack experience in evaluating the safety and efficacy of products based on singe strains of microbes, which could result in a longer than expected regulatory review process, increase our expected development costs and delay or prevent commercialization of our product candidates.

Our platform relies on third parties for biological materials to expand our microbial library.

Our platform relies on third parties for biological materials, including human samples containing bacteria, to expand our microbial library. Some biological materials have not always met our expectations or requirements, and any disruption in the supply of these biological materials could materially adversely affect our business and ability to build our pipeline of product candidates. For example, if any supplied biological materials are contaminated, we would not be able to use such biological materials. Although we have quality control processes and screening procedures, biological materials are susceptible to damage and contamination. Improper storage of these materials, by us or any third-party suppliers, may require us to destroy some or all of our raw materials or products.

Even if our product candidates do not cause off target adverse events, there may be immunotoxicity associated with the fundamental pharmacology of our product candidates.

Our product candidates, including EDP1815 and EDP2939 are designed to work by modulating the immune system. While we have observed limited systemic exposure in preclinical and clinical studies, the pharmacological immune

effects we aim to induce are systemic. Systemic immunomodulation from taking our product candidates could lead to immunotoxicity in patients, which may cause us or regulatory authorities to delay, limit or suspend clinical development. Other immunomodulatory agents have shown immunotoxicity. This includes immune suppressive agents, such as HUMIRA or REMICADE, which have shown an increased risk of infection or, in rare instances, certain types of blood cancer. In the case of immune activating agents, such as YERVOY, induction of adverse auto-immune events has been observed in some patients. Immunotoxicity in one program could cause regulators to view these adverse events as a class effect of our product candidates which may impact the timing of the development of our pipeline of potential product candidates. Even if the adverse events are manageable, the profile of the drug may be such that it limits or diminishes the possible number of patients who could receive our therapy.

Our product candidates may cause undesirable side effects or have other properties that could delay or prevent their regulatory approval, limit the commercial profile of an approved label or result in significant negative consequences following marketing approval, if any.

Undesirable side effects caused by our product candidates could cause us 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 comparable foreign regulatory authorities. Results of our clinical trials could reveal a high and unacceptable severity and prevalence of side effects or unexpected characteristics. For example, some of our product candidates may consist of live biological material that may remain viable in humans, which carries a risk of causing infections in patients. Some infections may require treatment with antibiotics to eliminate the bacteria. All our product candidates are screened for antibiotic sensitivity but it is possible that if antibiotic therapy does not eliminate the live biological material, a resistant version of our strain could emerge. These events, while unlikely, could cause a delay in our clinical development and/or could increase the regulatory standards for the entire class of our product candidates. In an instance where the infection risk of taking our product candidates is high, this may cause the benefit risk profile of therapy to be non-competitive in the market and may lead to discontinuation of development of the product candidate.

In addition, it is possible that infections from our product candidates could be rare and not frequently observed in our clinical trials. In larger post marketing authorization trials, however, data could show that the infection risk, while small, does exist. If unacceptable side effects arise in the development of our product candidates, we, the FDA or comparable foreign regulatory authorities, the IRBs at the institutions in which our clinical trials are conducted, or the data safety monitors could suspend or terminate our clinical trials, or the FDA or comparable foreign regulatory authorities could order us to cease clinical trials or deny approval of our product candidates for any or all targeted indications. Treatment-related side effects could also affect patient recruitment or the ability of enrolled patients to complete the trial or could result in potential product liability claims. In addition, these side effects may not be appropriately recognized or managed by the treating medical staff. We expect to have to train medical personnel using our product candidates to understand the side effect profiles for our clinical trials and upon any commercialization of any of our product candidates. Inadequate training in recognizing or managing the potential side effects of our product candidates could result in patient injury or death. Any of these occurrences may harm our business, financial condition and prospects significantly.

If any of our product candidates receives marketing approval, and we or others later identify undesirable side effects caused by such products, a number of potentially significant negative consequences could result, including:

- regulatory authorities may withdraw their approval of the product;
- we may be required to recall a product or change the way such product is administered to patients;
- additional restrictions may be imposed on the marketing of the particular product or the manufacturing processes for the product or any component thereof;
- we may be required to conduct post-marketing studies or clinical trials;
- regulatory authorities may require the addition of labeling statements, such as a ‘"black box" warning or a contraindication;
- we may be required to implement a risk evaluation and mitigation strategy or create a medication guide outlining the risks of such side effects for distribution to patients or similar risk management measures;
- we could be sued and held liable for harm caused to patients;
- the product may become less competitive; and
- our reputation may suffer.

Any of the foregoing events could prevent us from achieving or maintaining market acceptance of a particular product candidate, if approved, and result in the loss of significant revenues to us, which would materially and adversely affect our results of operations and business.

Companies with microbiome products or differing microbial products may produce negative clinical data which will adversely affect public perception of our product candidates, and may negatively impact regulatory approval of, or demand for, our potential products.

Our product candidates are pharmaceutical compositions of commensal microbes or derivatives thereof. While we believe our approach is distinct from microbiome therapies, negative data from clinical trials using microbiome-based therapies (*e.g.*, fecal transplant) and other microbial therapies could negatively impact the perception of the therapeutic use of microbial-based products. This could negatively impact our ability to enroll patients in clinical trials. The clinical and commercial success of our potential products will depend in part on the public and clinical communities' acceptance of the use of therapeutic microbes. Moreover, our success depends upon physicians prescribing, and their patients being willing to receive, treatments that involve the use of product candidates we may develop in lieu of, or in addition to, existing treatments with which they are already familiar and for which greater clinical data may be available.

Adverse events in our preclinical studies or clinical trials, or those of our competitors or of academic researchers utilizing therapeutic microbes, even if not ultimately attributable to our product candidates, and the resulting publicity, could result in increased governmental regulation, unfavorable public perception, increased volatility in our stock price, potential regulatory delays in the testing or approval of our potential product candidates, stricter labeling requirements for our product candidates that are approved, if any, and a decrease in demand for any such products.

Catastrophic loss of our master cell banks could significantly impair our ability to manufacture our product candidates.

Our product candidates require that we manufacture from master cell banks ("MCBs") our microbial strains. There is a possibility of a catastrophic failure or destruction of our MCBs. This could make it impossible for us to continue to manufacture a specific product candidate or product. Recreating and re-certifying our MCBs is possible but not certain and could put at risk the supply of our product candidates for preclinical studies or clinical trials or any products, if approved, to our customers.

Clinical drug development involves a lengthy and expensive process, with an uncertain outcome. We may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of our product candidates.

All of our product candidates are currently in clinical or preclinical development. It is impossible to predict when or if any of our product candidates will prove effective and safe in humans or will receive regulatory approval, and the risk of failure through the product development process is high. Before obtaining marketing approval from regulatory authorities for the sale of any product candidate, we must complete preclinical development and then conduct extensive clinical trials to demonstrate the safety and efficacy of our product candidates in humans. Clinical testing is expensive, difficult to design and implement, can take many years to complete and is uncertain as to outcome. A failed clinical trial can occur at any stage of testing. The outcome of preclinical testing and early clinical trials may not be predictive of the success of later clinical trials, and interim results of a clinical trial do not necessarily predict final results. For example, in certain of our clinical trials, investigational drug products are being delivered in a capsule for targeted release in the small intestine. This formulation has not previously been clinically tested, nor are we able to dose mice with a capsule for targeted release in the small intestine. Our ongoing clinical trials will be the first time this formulation is tested, and we cannot assure you that the results of this formulation will be consistent with the observations from our preclinical studies. A number of companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in advanced clinical trials due to adverse safety profiles or lack of efficacy, notwithstanding promising results in earlier trials, and we cannot be certain that we will not face similar setbacks.

The results from earlier clinical trials of product candidates may not predict the results that will be obtained in subsequent subjects or in subsequent human clinical trials of that product candidate. There can be no assurance that any trial will ultimately be successful or support further clinical advancement of any given product candidate.

In addition, we cannot be certain as to the type and number of clinical trials the FDA or similar foreign regulatory authorities will require us to conduct before we may successfully gain approval, referred to as licensure with respect to biological products in the United States, to market any of our product candidates. Requirements for us to conduct more clinical trials than we anticipate for a given product candidate could cause us to incur significant development costs, delay or prevent the commercialization of our products or otherwise adversely affect our business.

We may experience numerous unforeseen events during, or as a result of, clinical trials that could delay or prevent our ability to receive marketing approval or commercialize our product candidates, including:

- regulators, IRBs or ethics committees may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- we may experience delays in reaching, or fail to reach, agreement on acceptable clinical trial contracts or clinical trial protocols with prospective trial sites;
- clinical trials of our product candidates may demonstrate undesirable side effects or produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional clinical trials or abandon product development programs;
- the number of patients required for clinical trials of our product candidates may be larger than we anticipate, enrollment in these clinical trials may be lower or slower than we anticipate, or patients may drop out of these clinical trials at a higher rate than we anticipate;
- our CROs, CMOs and other third-party contractors may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all;
- we may have to, or regulators or IRBs may require that we or our investigators, suspend or terminate clinical trials of our product candidates for various reasons, including noncompliance with regulatory requirements or a finding that the patients are being exposed to unacceptable health risks;
- the cost of clinical trials of our product candidates may be greater than we anticipate;
- the supply or quality of our product candidates or other materials necessary to conduct clinical trials of our product candidates may be insufficient or inadequate;
- regulators may revise the requirements for approving our product candidates, or such requirements may not be as we anticipate; and
- regarding trials managed by any future collaborators, our collaborators may face any of the above issues, and may conduct clinical trials in ways they view as advantageous to them but potentially suboptimal for us.

If we are required to conduct additional clinical trials or other testing of our product candidates beyond those that we currently contemplate, if we are unable to successfully complete clinical trials of our product candidates or other testing, if the results of these trials or tests are not positive or are only modestly positive, or if there are safety concerns, we may:

- be delayed in obtaining marketing approval for our product candidates;
- lose the support of any future collaborators, requiring us to bear more of the burden of developing certain microbial strains;
- not obtain marketing approval at all;
- obtain marketing approval in some countries and not in others;
- obtain approval for indications or patient populations that are not as broad as we intend or desire;
- obtain approval with labeling that includes significant use or distribution restrictions or safety warnings;
- be subject to additional post-marketing testing requirements; or
- have the product removed from the market after obtaining marketing approval.

In addition, disruptions caused by the COVID-19 pandemic may increase the likelihood that we encounter such difficulties or delays in initiating, enrolling, conducting or completing our planned and ongoing clinical trials.

We could also encounter delays if a clinical trial is suspended or terminated by us, by the IRBs of the institutions in which such trials are being conducted, by a data safety monitoring board or ethics committee for such trial or by the FDA or comparable foreign regulatory authorities. Such authorities may impose such a suspension or termination 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 comparable foreign

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 drug, or changes in governmental regulations or administrative actions. For example, in September 2021 the FDA placed the IND for the Phase 2 atopic dermatitis trial of EDP1815 on clinical hold and requested that we amend our protocol to account for risks to patients that require their current atopic dermatitis medications be discontinued, the manner in which safety data is collected, and defined study halting criteria. The FDA subsequently lifted the clinical hold.

Further, conducting clinical trials in foreign countries, as we have in the past and may continue to do for our product candidates, presents additional risks that may delay completion of our clinical trials. These risks include the failure of enrolled patients in foreign countries to adhere to the clinical protocol as a result of differences in healthcare services or cultural customs, managing additional administrative burdens associated with foreign regulatory schemes, as well as political and economic risks relevant to such foreign countries.

Our product development costs will increase if we experience delays in clinical testing or in obtaining marketing approvals. We do not know whether any of our preclinical studies or clinical trials will begin as planned, will need to be restructured or will be completed on schedule, or at all. Significant preclinical or clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize our product candidates or allow our competitors to bring products to market before we do, potentially impairing our ability to successfully commercialize our product candidates and harming our business and results of operations.

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 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 ("CTA") to be submitted in each member state to both the competent national health authority and an independent ethics committee the CTR introduces a centralized process and only requires the submission of a single application to all member states concerned. 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 study development may proceed. The CTR entails a three-year transition period. The extent to which ongoing and new clinical trials will be governed by the CTR varies. For clinical trials whose CTA was made under the Clinical Trials Directive before January 31, 2022, the Clinical Trials Directive will continue to apply on a transitional basis for three years. Additionally, sponsors may still choose to submit a CTA under either the Clinical Trials Directive or the CTR until January 31, 2023 and, if authorized, those will be governed by the Clinical Trials Directive until January 31, 2025. By that date, all ongoing trials 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 development plans.

It is currently unclear to what extent the 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 MHRA, launched an eight-week consultation on reframing the UK legislation for clinical trials. The consultation closed on March 14, 2022 and aims to streamline clinical trial approvals, enable innovation, enhance clinical trials transparency, enable greater risk proportionality and promote patient and public involvement in clinical trials. The outcome of the consultation will be closely watched and will determine whether the UK chooses to align with the regulation or diverge from it to maintain regulatory flexibility. A decision by the UK not to closely align its regulations with the new approach that will be adopted in the EU may have an effect on the cost of conducting clinical trials in the UK as opposed to other countries and/or make it harder to seek a marketing authorization in the EU for our product candidates on the basis of clinical trials conducted in the UK.

If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies governing clinical trials, our development plans may be impacted.

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

We may not be able to initiate or continue clinical trials for our product candidates if we are unable to locate and enroll a sufficient number of eligible patients to participate in these trials as required by the FDA or similar regulatory authorities outside the United States. For example, we are developing certain product candidates, such as EDP1815, to treat inflammatory diseases including psoriasis and atopic dermatitis. There are a limited number of patients from which to draw for clinical trials concerning any given indication.

Patient enrollment is also affected by other factors including:

- the severity of the disease under investigation;
- the patient eligibility criteria for the trial in question;
- the perceived risks and benefits of the product candidate under study;
- the availability of other treatments for the disease under investigation;
- the existence of competing clinical trials;
- the efforts to facilitate timely enrollment in clinical trials;
- our payments for conducting clinical trials;
- the patient referral practices of physicians;
- the ability to monitor patients adequately during and after treatment; and
- the proximity and availability of clinical trial sites for prospective patients.

Our inability to enroll a sufficient number of patients or volunteers for our clinical trials would result in significant delays and could require us to abandon one or more clinical trials altogether. Enrollment delays in our clinical trials may result in increased development costs for our product candidates, which would cause the value of our company to decline and limit our ability to obtain additional financing.

The COVID-19 pandemic has adversely impacted and may continue to adversely impact our business, including our preclinical studies and clinical trials, and finances.

The ongoing pandemic caused by the novel coronavirus disease, COVID-19, and government measures taken in response have had and continue to have a significant impact, both direct and indirect, on businesses and commerce, as worker shortages have occurred, supply chains have been disrupted, facilities and production have been suspended, and demand for certain goods and services, such as medical services and supplies, has spiked, while demand for other goods and services, such as travel, has fallen. In response to the spread of COVID-19, we have adopted and continue to employ several flexible business practices, including telecommuting and staggered work shifts in our laboratories, to protect our employees while continuing business operations. In addition, due to the COVID-19 pandemic, enrollment of new patients into, and the retention of existing patients in, our clinical trials have been and may in the future be impacted due primarily to lower patient participation. As a result of the COVID-19 pandemic, we may continue to experience disruptions and face new disruptions that could severely impact our business, preclinical studies and clinical trials and finances, including:

- delays in receiving approval from local regulatory authorities to initiate our planned clinical trials;
- delays or difficulties in enrolling patients in our clinical trials;
- delays or difficulties in clinical site initiation, including difficulties in recruiting clinical site investigators and clinical site staff;
- delays in clinical sites receiving the supplies and materials needed to conduct our clinical trials, including interruptions in global shipping that may affect the transport of clinical trial materials;
- changes in local regulations as part of a response to the COVID-19 pandemic which may require us to change the ways in which our clinical trials are conducted, which may result in unexpected costs, or to discontinue such clinical trials altogether;
- diversion of healthcare resources away from the conduct of clinical trials, including the diversion of hospitals serving as our clinical trial sites and hospital staff supporting the conduct of our clinical trials;
- interruptions of key clinical trial activities, such as clinical trial site data monitoring, due to limitations on travel imposed or recommended by governments, employers and others or interruption of clinical trial subject visits and study procedures (such as skin biopsies that are deemed non-essential activities), which may impact the integrity of subject data and clinical trials endpoints;

- risk that patients enrolled in our clinical trials will contract COVID-19 while the clinical trial is ongoing, which could impact the results of the clinical trial, including by increasing the number of observed adverse events;
- interruptions or delays in the operations of the FDA and similar regulatory authorities, which may impact review and approval timelines;
- interruptions of, or delays in, receiving supplies of our product candidates from our CMOs due to staffing shortages, production slowdowns or stoppages and disruptions in delivery systems;
- limitations on employee resources that would otherwise be focused on the conduct of our preclinical studies and clinical trials, including because of sickness of employees or their families or the desire of employees to avoid contact with large groups of people;
- refusal of the FDA or similar foreign regulatory authorities to accept data from clinical trials in affected geographies;
- impacts from prolonged remote work arrangements, such as increased cybersecurity risks and strains on our business continuity plans; and
- delays or difficulties with securities offerings due to disruptions and uncertainties in securities markets.

The COVID-19 pandemic continues to evolve. The extent to which the outbreak impacts our business, preclinical studies and clinical trials will depend on future developments which are highly uncertain and cannot be predicted with confidence, such as the varying geographic spread and severity of the disease and its variants, the duration of the pandemic, travel restrictions and social distancing in the United States and other countries, business closures or business disruptions and the effectiveness of actions taken in the United States and other countries to contain and treat the disease. While the potential economic impact brought by and the duration of the COVID-19 pandemic may be difficult to assess or predict, the widespread pandemic has resulted in, and may continue to result in, significant disruption of global financial markets reducing our ability to access capital, which could in the future negatively affect our liquidity. In addition, recessions and market corrections resulting from the COVID-19 pandemic have and could continue to detrimentally impact our business.

We have conducted and may continue to conduct clinical trials for our product candidates in sites outside the United States, and the FDA may not accept data from trials conducted in foreign locations.

We have conducted and may continue to conduct clinical trials outside the United States for our product candidates. The acceptance of study data from clinical trials conducted outside the U.S. or another jurisdiction by the FDA or comparable foreign regulatory authority may be subject to certain conditions or may not be accepted at all. In cases where data from foreign clinical trials are intended to serve as the sole basis for marketing approval in the U.S., the FDA will generally not approve the application on the basis of foreign data alone, unless: (i) the data are applicable to the U.S. population and U.S. medical practice; (ii) the trials were performed by clinical investigators of recognized competence and pursuant to GCP regulations; and (iii) the data may be considered valid without the need for an on-site inspection by the FDA, or if the FDA considers such inspection to be necessary, the FDA is able to validate the data through an on-site inspection or other appropriate means. In addition, even where the foreign study data are not intended to serve as the sole basis for approval, the FDA will not accept the data as support for an application for marketing approval unless the study is well-designed and well-conducted in accordance with GCP requirements and the FDA is able to validate the data from the study through an onsite inspection, if deemed necessary. Many foreign regulatory authorities have similar approval requirements. In addition, such foreign trials would be subject to the applicable local laws of the foreign jurisdictions where the trials are conducted. There can be no assurance that the FDA or any comparable foreign regulatory authority will accept data from trials conducted outside of the U.S. or the applicable jurisdiction. If the FDA or any comparable foreign regulatory authority does not accept such data, it would result in the need for additional trials, which could be costly and time-consuming, and which may result in current or future product candidates that we may develop not receiving approval for commercialization in the applicable jurisdiction or at all.

Interim, "topline" 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 topline 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 topline or preliminary results that we report may differ from future results of the same trials, or different conclusions or considerations may qualify such results once additional data have been received and fully evaluated. Topline data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. For example, we previously disclosed certain SCORAD figures from a Phase 1b clinical trial that, upon further review and analysis, required modification in subsequent disclosure. As a result, topline and other preliminary data should be viewed with caution until the final data are available and have been fully analyzed.

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. Adverse differences between topline, 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 we are not able to obtain, or if there are delays in obtaining, required regulatory approvals, we will not be able to commercialize our product candidates or will not be able to do so as soon as anticipated, and our ability to generate revenue will be materially impaired.

Our product candidates and the activities associated with their development and commercialization, including their design, testing, manufacture, safety, efficacy, recordkeeping, labeling, storage, approval, advertising, promotion, sale and distribution, are subject to comprehensive regulation and requirements by the FDA and other regulatory agencies in the United States, by legislative bodies in the EU and EU member states and by other regulatory authorities outside the United States. Failure to obtain marketing approval for a product candidate in any jurisdiction will prevent us from commercializing the product candidate in that jurisdiction and may affect our plans for commercialization in other jurisdictions as well. We have not received approval to market any of our product candidates from regulatory authorities in any jurisdiction. We have only limited experience in filing and supporting the applications necessary to gain marketing approvals and we expect to rely on third parties to assist us in this process.

Securing marketing approval requires the submission of extensive preclinical and clinical data and supporting information to regulatory authorities for each therapeutic indication to establish the product candidate's safety and efficacy to such regulatory authorities' satisfaction. Securing marketing approval also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities by, the regulatory authorities. Our product candidates may not be effective, may be only moderately effective or may prove to have undesirable or unintended side effects, toxicities or other characteristics that may preclude our obtaining marketing approval or prevent or limit commercial use.

The process of obtaining marketing approvals, both in the United States and abroad, is expensive and may take many years. The scope and amount of clinical data required to obtain marketing approvals can vary substantially from jurisdiction to jurisdiction, and it may be difficult to predict whether a particular regulatory body will require additional or different clinical trials than those conducted by a sponsor, especially for novel product candidates such as our product candidates. The FDA or other foreign regulatory authorities may delay, limit, or deny the approval of our product candidates for many reasons, including:

- our inability to demonstrate that the clinical benefits of our product candidates outweigh any safety or other perceived risks;
- the regulatory authority's disagreement with the interpretation of data from nonclinical or clinical studies;
- the regulatory agency's requirement that we conduct additional preclinical studies and clinical trials;
- changes in marketing approval policies during the development period;
- changes in or the enactment of additional statutes or regulations, or changes in regulatory review process for each submitted product application; or

- the regulatory authority's failure to approve the manufacturing processes or third-party manufacturers with which we contract.

Regulatory authorities have substantial discretion in the approval process and may refuse to accept a marketing application as deficient. In addition, varying interpretations of the data obtained from preclinical and clinical testing could delay, limit or prevent marketing approval of a product candidate. Any marketing approval we ultimately obtain may be limited or subject to restrictions or post-approval commitments that render the approved product not commercially viable. Of the large number of drugs in development, only a small percentage successfully complete the FDA or other regulatory approval processes and are commercialized.

Furthermore, our product candidates may not receive marketing approval even if they achieve their specified endpoints in clinical trials. Clinical data are often susceptible to varying interpretations, and many companies that have believed that their products performed satisfactorily in clinical trials have nonetheless failed to obtain FDA or the applicable foreign regulatory agency approval for their products. The FDA or foreign regulatory authorities may disagree with our trial design and our interpretation of data from nonclinical and clinical studies. Upon the review of data from any pivotal trial, the FDA or applicable foreign regulatory agency may request that the sponsor conduct additional analyses of the data and, if it believes the data are not satisfactory, could advise the sponsor to delay filing a marketing application.

Even if we eventually complete clinical testing and receive approval of a BLA or foreign marketing authorization for one of our product candidates, the FDA or applicable foreign regulatory agency may grant approval contingent on the performance of costly additional clinical trials which may be required after approval. The FDA or the applicable foreign regulatory agency may also approve our products for a more limited indication and/or a narrower patient population than we originally request, and the FDA or applicable foreign regulatory agency may not approve the labeling that we believe is necessary or desirable for the successful commercialization of our products. Any delay in obtaining, or inability to obtain, applicable regulatory approval would delay or prevent commercialization of our product candidates and would materially adversely impact our business and prospects.

The development of SINTAX medicines and their interactions with cells in the small intestine is an emerging field, and it is possible that the FDA or other regulatory authorities or bodies could issue regulations or new policies in the future affecting our product candidates.

If we experience delays in obtaining approval or if we fail to obtain approval of our product candidates, the commercial prospects for our product candidates may be harmed and our ability to generate revenues will be materially impaired.

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

Because we have limited financial and managerial resources, we intend to focus on developing product candidates for multiple initial indications that we identify as most likely to succeed in terms of both regulatory approval and commercialization. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications that may prove to have greater commercial potential. 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 product development programs and product candidates for specific indications may not yield any commercially viable products. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing or other royalty arrangements, in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate.

A fast track designation by the FDA may not actually lead to a faster development or regulatory review or approval process.

We may seek fast track designation for some of our product candidates. If a drug or biologic is intended for the treatment of a serious or life-threatening condition and nonclinical or clinical data demonstrate the potential to address unmet medical needs for this condition, the drug or biologic sponsor may apply for FDA fast track designation. Fast track designation provides increased opportunities for sponsor meetings with the FDA during preclinical and clinical development in addition to the potential for rolling review once a marketing application is filed. The FDA has broad discretion whether or not to grant this designation, and even if we believe a particular product candidate is eligible for this designation, we cannot assure you that the FDA would decide to grant it. Even if we do receive fast track designation, we may not experience a faster development process, review or approval compared to conventional FDA procedures. Fast track designation does not assure ultimate approval by the FDA. The FDA may withdraw fast track designation if it believes that the designation is no longer supported by data from our product development program. Additionally, similar considerations and concerns exist with respect to the pursuit of expedited regulatory approval pathways in jurisdictions outside of the U.S.

A breakthrough therapy designation by the FDA for our product candidates may not lead to a faster development or regulatory review or approval process, and it does not increase the likelihood that our product candidates will receive marketing approval.

We may seek a breakthrough therapy designation for our product candidates. A breakthrough therapy is defined as a drug or biologic that is intended to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the drug or biologic may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints. For drugs that have been designated as breakthrough therapies, interaction and communication between the FDA and the sponsor can help to identify the most efficient path for clinical development. Drugs designated as breakthrough therapies by the FDA receive all the Fast Track program features, including eligibility for rolling review of BLA submissions.

Designation as a breakthrough therapy is within the discretion of the FDA. Accordingly, even if we believe one of our product candidates meets the criteria for designation as a breakthrough therapy, the FDA may disagree and instead determine not to make such designation. In any event, the receipt of a breakthrough therapy designation for a product candidate may not result in a faster development process, review or approval compared to conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, even if one or more of our product candidates qualify as breakthrough therapies, the FDA may later decide that the products no longer meet the conditions for qualification and rescind the designation. Additionally, similar considerations and concerns exist with respect to the pursuit of expedited regulatory approval pathways in jurisdictions outside of the U.S.

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 comparable foreign regulatory authorities to review and/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 and comparable 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 and comparable foreign regulatory authorities' ability to perform routine functions. Average review times at the FDA and comparable 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 resulting staff changes, may also slow the time necessary for new drugs and biologics to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years including for 35 days beginning on December 22, 2018, 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, in March 2020, the FDA announced its intention to postpone most inspections of foreign manufacturing facilities, and on March 18, 2020, the FDA temporarily postponed routine surveillance inspections of domestic manufacturing facilities. Subsequently, in July 2020, the FDA resumed certain

on-site inspections of domestic manufacturing facilities subject to a risk-based prioritization system. The FDA utilized this risk-based assessment system to assist in determining when and where it was safest to conduct prioritized domestic inspections. Additionally, on April 15, 2021, the FDA began conducting voluntary remote interactive evaluations of certain drug manufacturing facilities and clinical research sites, among other facilities, in circumstances where the FDA determines that such remote evaluation would be appropriate based on mission needs and travel limitations. In July 2021, the FDA resumed standard inspectional operations of domestic facilities. Since that time, 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 the evolving COVID-19 pandemic. Regulatory authorities outside the United States have adopted similar restrictions or other policy measures in response to the COVID-19 pandemic. If a prolonged government shutdown occurs, or if global health concerns continue to 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.

Risks Related to our Dependence on Third Parties and Manufacturing

We rely, and expect to continue to rely, on third parties to conduct our clinical trials, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such trials.

We rely, and expect to continue to rely, on third parties, such as CROs, clinical data management organizations, medical institutions, clinical investigators and potential pharmaceutical partners, to conduct and manage our clinical trials.

Our reliance on these third parties for research and development activities will reduce our control over these activities but does not relieve us of our responsibilities. For example, we remain responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols for the trial. Moreover, the FDA requires us to comply with regulatory standards, commonly referred to as good clinical practices, for conducting, recording and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the rights, safety and welfare of patients are protected. Other countries' regulatory agencies also have requirements for clinical trials with which we must comply. We also may be required in certain instances to register ongoing clinical trials and post the results of completed clinical trials on government-sponsored databases such as *ClinicalTrials.gov* or similar foreign databases within specified timeframes. Failure to do so can result in fines, adverse publicity and civil and criminal sanctions.

Furthermore, these third parties may also have relationships with other entities, some of which may be our competitors. If these third parties do not successfully carry out their contractual duties, do not meet expected deadlines, experience work stoppages, terminate their agreements with us or need to be replaced, or do not conduct our clinical trials in accordance with regulatory requirements or our stated protocols, we may need to enter into new arrangements with alternative third parties, which could be difficult, costly or impossible, and our clinical trials may be extended, delayed or terminated or may need to be repeated. If any of the foregoing occur, we may not be able to obtain, or may be delayed in obtaining, marketing approvals for our product candidates and may not be able, or may be delayed in our efforts, to successfully commercialize our product candidates.

We also expect to rely on other third parties to store and distribute drug product required by our clinical trials. Any performance failure on the part of our distributors could delay clinical development or marketing approval of our product candidates or commercialization of our products, thereby producing additional losses and depriving us of potential product revenue.

We rely on third parties for the manufacture of our product candidates for preclinical and clinical testing and expect to continue to do so for the foreseeable future. This reliance on third parties increases the risk that we will not have sufficient quantities of our product candidates or that such quantities may not be available at an acceptable cost, which could delay, prevent or impair our development or commercialization efforts.

We rely, and expect to continue to rely, on third parties for the manufacture of our product candidates for preclinical and clinical testing, as well as for commercial manufacture, if any, of our product candidates receive marketing approval. Reliance on third parties for the manufacture of our product candidates increases the risk that we will not have sufficient quantities of our product candidates on a timely basis or at all, or that such quantities will be available at an acceptable cost or quality, which could delay, prevent or impair our development or commercialization efforts.

We may be unable to establish agreements with third-party manufacturers on acceptable terms or at all. Even if we are able to establish agreements with third-party manufacturers, reliance on third-party manufacturers entails additional risks, including:

- failure of third-party manufacturers to comply with regulatory requirements and maintain quality assurance;
- breach of manufacturing agreements by the third-party manufacturers;
- failure to manufacture our product according to our specifications;
- failure to manufacture our product according to our schedule or at all;
- misappropriation or disclosure of our proprietary information, including our trade secrets and know-how; and
- termination or non-renewal of agreements by third-party manufacturers at times that are costly or inconvenient for us.

Third-party manufacturers may not be able to comply with cGMP regulations or similar regulatory requirements outside the United States. Our failure, or the failure of our third-party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including clinical holds, fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocations, seizures or recalls of product candidates or products, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our products. Some of the contract manufacturers we rely on to produce our product candidates have never produced an FDA-approved therapeutic. If our contract manufacturers are unable to comply with cGMP or similar foreign regulations or if the FDA or foreign regulatory authorities do not approve their facility upon a pre-approval inspection, our product candidates may not be approved or may be delayed in obtaining approval. In addition, there are a limited number of manufacturers that operate under cGMP or similar foreign regulations that might be capable of manufacturing our products. Therefore, our product candidates and any future product candidates that we may develop may compete with other products for access to manufacturing facilities. Any failure to gain access to these limited manufacturing facilities could severely impact the clinical development, marketing approval and commercialization of our product candidates.

Any performance failure on the part of our existing or future manufacturers could delay clinical development or marketing approval. We do not currently have arrangements in place for redundant sources of all clinical supplies for both drug substance and drug product. If our current contract manufacturers cannot perform as agreed, we may be required to replace such manufacturers and we may be unable to replace them on a timely basis or at all. Our current and anticipated future dependence upon others for the manufacture of our product candidates or products could delay, prevent or impair our development and commercialization efforts. Moreover, as a result of the COVID-19 pandemic, third-party manufacturers may be affected, which could disrupt their activities and, as a result, we could face difficulties and delays in the manufacture of our product candidates, which may negatively affect our preclinical and clinical development activities.

We have no experience manufacturing our product candidates at commercial scale, and if we decide to establish our own manufacturing facility, we cannot assure you that we can manufacture our product candidates in compliance with regulations at a cost or in quantities necessary to make them commercially viable.

We may establish one or more manufacturing facilities for our product candidates for production at a commercial scale. We have no experience in commercial-scale manufacturing of our product candidates. We may develop our manufacturing capacity in part by expanding our current facility or building additional facilities. These activities would require substantial additional funds and we would need to hire and train a significant number of qualified employees to staff these facilities. We may not be able to develop commercial-scale manufacturing facilities that are adequate to produce materials for additional later-stage clinical trials or commercial use.

The equipment and facilities employed in the manufacture of pharmaceuticals are subject to stringent qualification requirements by regulatory agencies, including validation of facility, equipment, systems, processes and analytics. We may be subject to lengthy delays and expense in conducting validation clinical trials, if we can meet the requirements at all.

Risks Related to Commercialization of Our Product Candidates and Other Legal Compliance Matters

Even if any of our product candidates receives marketing approval, it may fail to achieve the degree of market acceptance by physicians, patients, hospitals, third-party payors and others in the medical community necessary for commercial success.

If any of our product candidates receives marketing approval, it may nonetheless fail to gain sufficient market acceptance by physicians, patients, third-party payors and others in the medical community. For example, current psoriasis treatment involves the use of steroids and biologics that are well established in the medical community, and physicians may continue to rely on these treatments. If our product candidates receive approval but do not achieve an adequate level of acceptance, we may not generate significant product revenue and we may not become profitable. The degree of market acceptance of our approved product candidates, if any, will depend on a number of factors, including:

- their efficacy, safety and other potential advantages compared to alternative treatments;
- the clinical indications for which our products are approved;
- our ability to offer them for sale at competitive prices;
- their 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 availability of third-party coverage and adequate reimbursement for our product candidates;
- the prevalence and severity of their side effects and their overall safety profiles;
- any restrictions on the use of our products together with other medications;
- interactions of our products with other medicines patients are taking; and
- the inability of certain types of patients to take our product.

We currently have no sales organization. If we are unable to establish effective sales, marketing and distribution capabilities or we enter into agreements with third parties with such capabilities, we may not be successful in commercializing our product candidates if and when they are approved.

We do not have a sales or marketing infrastructure and have no experience in the sale, marketing or distribution of our product candidates. To achieve commercial success for any product for which we obtain marketing approval, we will need to establish a sales and marketing organization or make arrangements with third parties to perform sales and marketing functions, and we may not be successful in doing so.

In the future, we expect to build a focused sales and marketing infrastructure to market or promote our product candidates in the United States and potentially elsewhere, if and when they are approved. There are risks involved with establishing our own sales, marketing and distribution capabilities. For example, recruiting and training a sales

force is expensive and time consuming and could delay any product launch. If the commercial launch of a 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 products on our own include:

- our inability to recruit, train and retain an adequate number of effective sales and marketing personnel;
- the inability of sales personnel to obtain access to or educate physicians on the benefits of our 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;
- unforeseen costs and expenses associated with creating an independent sales and marketing organization; and
- the inability to obtain sufficient coverage and reimbursement from third-party payors and governmental agencies.

Outside the United States, we may rely on third parties to sell, market and distribute our product candidates. We may not be successful in entering into arrangements with such third parties or may be unable to do so on terms that are favorable to us. In addition, our product revenue and our profitability, if any, may be lower if we rely on third parties for these functions than if we were to market, sell and distribute any products that we develop ourselves. We likely will have little control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our products effectively. If we do not establish sales, marketing and distribution capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing our product candidates.

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

The development and commercialization of new drug and biologic products is highly competitive and is characterized by rapid and substantial technological development and product innovations. We face competition with respect to our current product candidates and will face competition with respect to product candidates that we may seek to develop or commercialize in the future, including from major pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies worldwide. We are aware of a number of large pharmaceutical and biotechnology companies, including AbbVie Inc., Agenus Inc., AstraZeneca plc, Bristol Myers Squibb Company, F. Hoffmann-La Roche A.G., Gilead Sciences, Inc., Incyte Corporation, Johnson & Johnson, Merck and Company, Inc., Novartis International A.G., Pfizer Inc. and Regeneron Pharmaceuticals, Inc., as well as smaller, early-stage companies, that are pursuing the development of products, including microbial-based therapeutics, in some instances, for disease indications we are targeting. Some of these competitive products and therapies are or may be based on scientific approaches that are the same as or similar to our approach, and others are or may be based on entirely different approaches. Potential competitors also include academic institutions, government agencies and other public and private research organizations.

Many of the companies and organizations against which we are competing or against which we may compete in the future have significantly greater financial resources, established presence in the market and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and reimbursement and marketing approved products than we do. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors.

These and other third parties also compete with us in recruiting and retaining qualified scientific, sales and marketing and management personnel, 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 more effective, have fewer or less severe side effects, are more convenient or are less expensive than any products that we may develop. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours, which could delay us from obtaining FDA or other regulatory approval to market our product candidates and result in our competitors establishing a strong market position before we are able to enter the market, especially for any competitor developing a microbial-based therapeutic which will

likely share our same regulatory approval requirements. For more information, please see "Risk Factors - Our product candidates for which we intend to seek approval as biologic products may face competition sooner than anticipated, which may delay us from marketing our product candidates." In addition, our ability to compete may be affected in many cases by insurers or other third-party payors seeking to encourage the use of generic or biosimilar products.

Even if we are able to commercialize any product candidates, the products may become subject to unfavorable pricing regulations or third-party coverage and reimbursement policies, any of which could harm our business.

Our ability to commercialize any product candidates successfully will depend, in part, on the extent to which coverage and reimbursement for these products and related treatments will be available from government health administration authorities, private health insurers and other organizations. Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and impact reimbursement levels.

Obtaining and maintaining adequate reimbursement for our products may be difficult. We cannot be certain if and when we will obtain coverage and an adequate level of reimbursement for our products by third-party payors. A primary trend in the U.S. healthcare industry and elsewhere is cost containment. Government authorities and third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. Increasingly, third-party payors require that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for drugs. In addition, reimbursement rates from private health insurance companies vary depending on the insurance company, the insurance plan and other factors. We may also be required to conduct expensive pharmacoeconomic studies to justify coverage and reimbursement or the level of reimbursement relative to other therapies. If coverage and reimbursement are not available or reimbursement is available only to limited levels, we may not be able to successfully commercialize any product candidate for which we obtain marketing approval, and the royalties resulting from the sales of those products may also be adversely impacted.

There may be significant delays in obtaining reimbursement for newly approved drugs, and coverage may be more limited than the purposes for which the drug is approved by the FDA or similar regulatory authorities outside the United States. Moreover, eligibility for reimbursement does not imply that a drug will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution. Interim reimbursement levels for new drugs, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Reimbursement rates may vary according to the use of the drug and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost drugs and may be incorporated into existing payments for other services. Net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. Our inability to promptly obtain coverage and adequate reimbursement rates from both government-funded and private payors for any approved products that we develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize products and our overall financial condition.

The regulations that govern marketing approvals, pricing, coverage and reimbursement for new drug products vary widely from country to country. Current and future legislation may significantly change the approval requirements in ways that could involve additional costs and cause delays in obtaining approvals. Some countries require approval of the sale price of a drug before it can be reimbursed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. In some foreign markets, prescription drug pricing remains subject to continuing governmental control, including possible price reductions even after initial approval is granted. As a result, we might obtain marketing approval for a product in a particular country but then be subject to price regulations that delay our commercial launch of the product, possibly for lengthy time periods, thereby negatively impacting the revenues we are able to generate from the sale of the product in that country. Adverse pricing limitations may hinder our ability to recoup our investment in one or more product candidates, even if our product candidates obtain marketing approval. There can be no assurance that our product candidates, if they are approved for sale in the United States or in other countries, will be considered medically necessary or cost-effective for a specific indication, or that reimbursement coverage or an adequate level of reimbursement will be available.

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

We face an inherent risk of product liability exposure related to the testing of our product candidates in clinical trials and will face an even greater risk if we commercially sell any products that we develop. If we cannot successfully defend ourselves against claims that our product candidates or products caused injuries, we will incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- regulatory investigations, product recalls or withdrawals, or labeling, marketing or promotional restrictions;
- decreased demand for any product candidates or products that we may develop;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial patients;
- significant costs to defend the related litigation;
- substantial monetary awards to trial participants or patients;
- loss of revenue;
- reduced resources of our management to pursue our business strategy; and
- the inability to commercialize any products that we may develop.

Our current product liability insurance coverage and any product liability insurance coverage that we acquire in the future may not be adequate to cover all liabilities that we may incur. We may need to increase our insurance coverage as we expand our clinical trials or if we commence commercialization of our product candidates. Insurance coverage is increasingly expensive. We may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise.

Our product candidates for which we intend to seek approval as biologic products may face competition sooner than anticipated, which may delay us from marketing our product candidates.

Even if we are successful in achieving regulatory approval to commercialize a product candidate faster than our competitors, we may face competition from biosimilars. The Biologics Price Competition and Innovation Act (“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 12 years from the date on which the reference product was first licensed. During this 12-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 their product.

We believe that any of our product candidates approved as a biological product under a BLA should qualify for the 12-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 generic 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. Moreover, the extent to which a biosimilar, once approved, will be substituted for any one of our reference products in a way that is similar to traditional generic substitution for non-biological products is not yet clear, and will depend on a number of marketplace and regulatory factors that are still developing.

In the EU, the European Commission has granted marketing authorizations for biosimilars pursuant to a set of general and product class-specific guidelines for biosimilar approvals issued over the past few years. In the EU, upon receiving marketing authorization, new innovative products generally receive eight years of data exclusivity and an additional two years of market exclusivity. If granted, data exclusivity prevents regulatory authorities in the EU from referencing the innovator's data to assess a biosimilar application. During the additional two-year period of market exclusivity, a biosimilar marketing authorization can be submitted, and the innovator's data may be referenced, but no biosimilar product can be marketed until 10 years have elapsed from the initial authorization of the reference product in the EU. The overall 10-year of market exclusivity period may be extended to a maximum of 11 years if, during the first eight of those 10 years, the marketing authorization holder obtains an approval for one or more new therapeutic indications that bring significant clinical benefits compared with existing therapies. In addition,

companies may be developing biosimilars in other countries that could compete with our products. If competitors are able to obtain marketing approval for biosimilars referencing our products, our products may become subject to competition from such biosimilars, with the attendant competitive pressure and consequences.

Failure to obtain marketing approval in international jurisdictions would prevent our product candidates from being marketed abroad.

In order to market and sell our product candidates in the EU and many other jurisdictions, we or our collaborators must obtain separate marketing authorizations and comply with numerous and varying regulatory requirements. The approval procedure varies among countries and can involve additional testing. The time required to obtain approval in foreign countries may differ substantially from that required to obtain FDA or other applicable regulatory approval. Clinical trials conducted in one country may not be accepted by regulatory authorities in other countries. The regulatory approval process outside the United States generally includes all of the risks associated with obtaining FDA approval. In addition, in many countries outside the United States, it is required that the product be approved for reimbursement before the product can be approved for sale in that country. We or our collaborators may not obtain approvals for our product candidates from regulatory authorities outside the United States on a timely basis, if at all. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one regulatory authority outside the United States does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA. However, a failure or delay in obtaining regulatory approval in one country may have a negative effect on the regulatory process in others. We may not be able to file for marketing approvals and may not receive necessary approvals to commercialize our products in any market.

Additionally, 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. A proposal for revision of several legislative instruments related to medicinal products (potentially revising the duration of regulatory exclusivity, eligibility for expedited pathways, etc.) is expected to be adopted by the European Commission by the end of 2022. The proposed revisions, once they are agreed and adopted by the European Parliament and European Council (not expected before the end of 2024), may have a significant impact on the pharmaceutical industry in the long term.

Any product candidate for which we obtain marketing approval could be subject to post-marketing restrictions or withdrawal from the market, and we may be subject to penalties if we fail to comply with regulatory requirements or if we experience unanticipated problems with our products, when and if any of them are approved.

Any product candidate for which we obtain marketing approval, along with the manufacturing processes, post-approval clinical data, labeling, advertising and promotional activities for such product, will be subject to the continual requirements of and review by the FDA and other regulatory authorities. These requirements include submissions of safety and other post-marketing information and reports, registration and listing requirements, cGMP and similar requirements relating to manufacturing, quality control, quality assurance and corresponding maintenance of records and documents, requirements regarding the distribution of samples to physicians and recordkeeping. We and our contract manufacturers will also be subject to continual review and periodic inspections to assess compliance with cGMP and similar requirements. Accordingly, we and others with whom we work must continue to expend time, money and effort in all areas of regulatory compliance, including manufacturing, production and quality control.

Even if marketing approval of a product candidate is granted, the approval may be subject to limitations on the indicated uses for which the product may be marketed or to specific conditions of approval, including a requirement to implement a risk evaluation and mitigation strategy, which could include requirements for a medication guide, communication plan or restricted distribution system. If any of our product candidates receives marketing approval, the accompanying label may limit the approved use of our drug, which could limit sales of the product.

The FDA and foreign regulatory authorities may also impose requirements for costly post-marketing studies or clinical trials and surveillance to monitor the safety or efficacy of our approved products. The FDA and foreign regulatory authorities closely regulate the post-approval marketing and promotion of drugs and biologics to ensure they are marketed only for the approved indications and in accordance with the provisions of the approved labeling. The FDA and foreign regulatory authorities impose stringent restrictions on manufacturers' communications regarding off-label use, and if we market our products outside of their approved indications, we may be subject to enforcement action for off-label marketing. Violations of the FDA's or foreign regulatory authorities' restrictions

relating to the promotion of prescription drugs may also lead to investigations alleging violations of federal, state, local or foreign health care fraud and abuse laws, as well as consumer protection laws.

In addition, if a regulatory agency or we later discover previously unknown problems with our products, such as adverse events of unanticipated severity or frequency, problems with manufacturers or manufacturing processes, or failure to comply with regulatory requirements, the regulatory agency may impose restrictions on the products or us, including requiring withdrawal of the product from the market. Any failure to comply with applicable regulatory requirements may yield various problematic results, including:

- litigation involving patients taking our products;
- restrictions on such products, manufacturers or manufacturing processes;
- restrictions on the labeling or marketing of a product;
- restrictions on product distribution or use;
- requirements to conduct post-marketing studies or clinical trials;
- warning letters;
- withdrawal of products from the market;
- suspension or termination of ongoing clinical trials;
- refusal to approve pending applications or supplements to approved applications that we submit;
- recall of products;
- fines, restitution or disgorgement of profits or revenues;
- suspension or withdrawal of marketing approvals;
- damage to relationships with potential collaborators;
- unfavorable press coverage and damage to our reputation;
- refusal to permit the import or export of our products;
- product seizure or detention;
- injunctions; or
- imposition of civil or criminal penalties.

Noncompliance with similar EU requirements regarding safety monitoring or pharmacovigilance can also result in significant financial penalties. Similarly, failure to comply with U.S. and foreign regulatory requirements regarding the development of products for pediatric populations and the protection of personal health information can also lead to significant penalties and sanctions.

Any government investigation of alleged violations of law could require us to expend significant time and resources in response and could generate negative publicity. In addition, the FDA's and foreign regulatory authorities' regulations, policies or guidance may change and new or additional statutes or government regulations may be enacted that could prevent or delay regulatory approval of our product candidates or further restrict or regulate post-approval activities. Any failure to comply with ongoing regulatory requirements may significantly and adversely affect our ability to commercialize and generate revenues. If regulatory sanctions are applied or if regulatory approval is withheld or withdrawn, the value of our company and our operating results will be adversely affected.

Our relationships with customers, physicians and third-party payors will be subject to applicable anti-kickback, fraud and abuse and other healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, exclusion from governmental healthcare programs, contractual damages, reputational harm and diminished profits and future earnings.

Healthcare providers, physicians and third-party payors will play a primary role in the recommendation and prescription of any product candidates for which we may obtain marketing approval. Our future arrangements with third-party payors, physicians and customers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may restrict the business or financial arrangements and relationships through which we market, sell and distribute any products for which we obtain marketing approval. Restrictions under applicable federal, state and foreign healthcare laws and regulations include the following:

- the federal Anti-Kickback Statute prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made under a federal healthcare program, such as Medicare and Medicaid; a person or entity does not need to have actual knowledge of the statute or specific intent to violate the statute to have committed a violation;
- the false claims and civil monetary penalties laws, including the federal False Claims Act, which, among other things, impose criminal and civil penalties, including through civil whistleblower or qui tam actions, against individuals or entities for knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false 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 or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government. 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 federal False Claims Act;
- the federal Health Insurance Portability and Accountability Act of 1996 imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters; similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of these statutes or specific intent to violate them to have committed a violation;
- the federal Physician Payment Sunshine Act requires applicable manufacturers of covered drugs to report 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), teaching hospitals and ownership and investment interests held by physicians and their immediate family members. Manufacturers are required to submit reports to the government by the 90th day of each calendar year; and
- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, may apply to our business practices, including but not limited to: research, distribution, sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers. State laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government and may require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers, pricing information or marketing expenditures.

The risk of our being found in violation of these laws and regulations is increased by the fact that many of them have not been fully interpreted by the regulatory authorities or the courts, and their provisions are open to a variety of interpretations. Any action against us for violation of these laws and regulations, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management's attention from the operation of our business. The shifting compliance environment and the need to build and maintain a robust system to comply with multiple jurisdictions with different compliance and reporting requirements increases the possibility that a healthcare company may violate one or more of the requirements.

Efforts to ensure that our business arrangements with third parties do and will comply with applicable healthcare laws and regulations involves substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental laws and regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, imprisonment, exclusion from government funded healthcare programs such as Medicare and Medicaid and the curtailment or restructuring of our operations.

Recently enacted and future legislation may increase the difficulty and cost for us to obtain marketing approval for and commercialize our product candidates and affect the prices we may obtain.

In the United States and some foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and affect our ability to profitably sell any product candidates for which we obtain marketing approval.

In the United States, the Patient Protection and Affordable Care Act ("ACA") was intended to broaden access to health insurance, reduce or constrain the growth of healthcare spending, enhance remedies against fraud and abuse, add new transparency requirements for the healthcare and health insurance industries, impose new taxes and fees on the health industry and impose additional health policy reforms.

Among the provisions of the ACA that are of importance to our potential product candidates are the following:

- establishment of a new pathway for approval of lower cost biosimilars to compete with biologic products, such as those we are developing;
- an annual, nondeductible fee payable by any entity that manufactures or imports specified branded prescription drugs and biologic agents;
- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program;
- a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 70% point-of-sale discounts off negotiated prices;
- extension of manufacturers' Medicaid rebate liability;
- expansion of eligibility criteria for Medicaid programs;
- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;
- a new requirement to annually report drug samples that manufacturers and distributors provide to physicians; and
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities and conduct comparative clinical effectiveness research, along with funding for such research.

Since its enactment, there have been judicial, executive and Congressional 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 initiating 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. It is unclear how healthcare reform measures enacted by Congress or implemented by the Biden administration, if any, will impact our business.

In addition, other legislative changes have been proposed and adopted since the ACA was enacted. In August 2011, the Budget Control Act of 2011, among other things, included aggregate reductions of Medicare payments to providers of 2% per fiscal year, which went into effect on April 1, 2013 and, due to subsequent legislative amendments, will remain in effect through 2030, with the exception of a temporary suspension from May 1, 2020 through March 31, 2022 and a 1% reduction from April 1, 2022 through June 30, 2022, unless additional Congressional action is taken. On January 2, 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, reduced Medicare payments to several providers, including hospitals, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. Further, in March 2021, the American Rescue Plan Act of 2021 was signed into law, which, among other things, eliminated the statutory cap on drug manufacturers' Medicaid Drug Rebate Program rebate liability effective January 1, 2024. Under current law enacted as part of the ACA, drug manufacturers' Medicaid Drug Rebate Program rebate liability is capped at 100% of the average manufacturer price for a covered outpatient drug. These new laws may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for our products.

We expect that other healthcare reform measures that may be adopted in the future may result in additional reductions in Medicare and other healthcare funding, in more rigorous coverage criteria, in new payment methodologies and in additional downward pressure on the price that we receive for any approved product. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our product candidates, if approved.

Moreover, there has recently been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products. Individual states in the United States have become increasingly active in

implementing regulations designed to contain pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures. 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, if approved, or put pressure on our product pricing, which could negatively affect our business, results of operations, financial condition and prospects.

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 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.

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 be subject to enforcement action and we may not achieve or sustain profitability.

We may be subject to the U.K. Bribery Act 2010 (the "Bribery Act"), the U.S. Foreign Corrupt Practices Act of 1977, as amended (the "FCPA"), and other anti-corruption laws, as well as export control laws, import and customs laws, trade and economic sanctions laws and other laws governing our operations.

Our operations may be subject to anti-corruption laws, including the Bribery Act, the FCPA, the U.S. domestic bribery statute contained in 18 U.S.C. §201, the U.S. Travel Act and other anti-corruption laws that apply in countries where we do business. The Bribery Act, the FCPA and these other laws generally prohibit us, our employees and our intermediaries from authorizing, promising, offering or providing, directly or indirectly, improper or prohibited payments or anything else of value to government officials or other persons to obtain or retain business or gain some other business advantage. Under the Bribery Act, we may also be liable for failing to prevent a person associated with us from committing a bribery offense. We and our partners may operate in jurisdictions that pose a high risk of potential Bribery Act or FCPA violations, and we may participate in collaborations and relationships with third parties whose corrupt or illegal activities could potentially subject us to liability under the Bribery Act, FCPA or local anti-corruption laws, even if we do not explicitly authorize or have actual knowledge of such activities. In addition, we cannot predict the nature, scope or effect of future regulatory requirements to which our international operations might be subject or the manner in which existing laws might be administered or interpreted.

We may also be subject to other laws and regulations from time to time governing our international operations, including regulations administered by the governments of the United States, the United Kingdom or elsewhere and authorities in the European Union or elsewhere, including applicable export control regulations, economic sanctions and embargoes on certain countries and persons, anti-money laundering laws, import and customs requirements and currency exchange regulations, collectively referred to as the Trade Control laws.

There is no assurance that we will be completely effective in ensuring our compliance with all applicable anti-corruption laws, including the Bribery Act, the FCPA or other legal requirements, including Trade Control laws. If we are not in compliance with the Bribery Act, the FCPA and other anti-corruption laws or Trade Control laws, we may be subject to criminal and civil penalties, disgorgement and other sanctions and remedial measures and legal expenses, which could have an adverse impact on our business, financial condition, results of operations and liquidity. Likewise, any investigation of any potential violations of the Bribery Act, the FCPA, other anti-corruption laws or Trade Control laws by the United Kingdom, United States or other authorities could also have an adverse impact on our reputation, our business, results of operations and financial condition.

We may be subject to various laws relating to foreign investment and the export of certain technologies, and our failure to comply with these laws or adequately monitor the compliance of our suppliers and others with which we do business with could subject us to substantial fines, penalties and injunctions, the imposition of which on us could have a material adverse effect on the success of our business.

We may be subject to U.S. laws that regulate foreign investments in U.S. businesses and access by foreign persons to technology developed and produced in the United States. These laws include section 721 of the Defense Production Act of 1950, as amended by the Foreign Investment Risk Review Modernization Act of 2018, and the regulations at 31 C.F.R. Parts 800 and 801, as amended, administered by the Committee on Foreign Investment in the United States, and the Export Control Reform Act of 2018, which is being implemented in part through Commerce Department rule-making to impose new export control restrictions on "emerging and foundational technologies" yet to be fully identified. Application of these laws, including as they are implemented through regulations being developed, may negatively impact our business in various ways, including by:

- restricting our access to capital and markets;
- limiting the collaborations we may pursue;
- regulating the export our products, services, and technology from the United States and abroad; increasing our costs and the time necessary to obtain required authorizations and to ensure compliance; and
- threatening monetary fines and other penalties for non-compliance.

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

In some countries, particularly the EU member states, the pricing of prescription drugs is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. In addition, there can be considerable pressure by governments and other stakeholders on prices and reimbursement levels, including as part of cost containment measures. Political, economic and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after coverage and reimbursement have been obtained. Reference pricing used by various EU member states, and parallel distribution or arbitrage between low-priced and high-priced member states, can further reduce prices. To obtain reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of our product candidate to other available therapies. If coverage and reimbursement of our products are unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be harmed, possibly materially.

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

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

Although we maintain workers' compensation insurance to cover us for costs and expenses that we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against all potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with our storage or disposal of biological, hazardous or radioactive materials.

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

Risks Related to Our Intellectual Property

If we are unable to adequately protect our proprietary technology, or obtain and maintain issued patents which are sufficient to protect our product candidates, others could compete against us more directly, which would have a material adverse impact on our business, results of operations, financial condition and prospects.

Our success depends in large part on our ability to obtain and maintain patent and other intellectual property protection in the United States and other countries with respect to our proprietary technology and products. We seek to protect our proprietary position by filing patent applications in the United States and abroad related to our novel technologies and product candidates. We also rely on trade secrets to protect aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection.

The patent prosecution process is expensive and time-consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost, in a timely manner or in all jurisdictions. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. It is possible that defects of form in the preparation or filing of our patents or patent applications may exist or may arise in the future, such as, with respect to proper priority claims, inventorship, claim scope or patent term adjustments. If there are material defects in the form or preparation of our patents or patent applications, such patents or applications may be invalid and unenforceable. Moreover, our competitors may independently develop equivalent knowledge, methods and know-how. Any of these outcomes could impair our ability to prevent competition from third parties, which may have an adverse impact on our business, financial condition and operating results.

Pursuant to our current and future license agreements with third parties, in some circumstances we may not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the patents, covering technology that we license from third parties. We may also require the cooperation of our licensors to enforce any licensed patent rights, and such cooperation may not be provided or may be deficient. Therefore, these patents and applications may not be prosecuted and enforced in a manner consistent with the best interests of our business.

Although we have numerous patent applications pending, we cannot provide any assurances that any of our pending patent applications will mature into issued patents and, if they do, that such patents or our current patents will include claims with a scope sufficient to protect our product candidates or otherwise provide any competitive advantage. For example, we are pursuing claims to compositions of certain bacterial populations. Any claims that are issued may provide coverage for such compositions and/or their use. However, such claims would not prevent a third party from commercializing alternative compositions that do not include the bacterial populations claimed in pending applications, potential applications or patents that have issued or may issue. There can be no assurance that any such alternative composition will not be equally effective. These and other factors may provide opportunities for our competitors to design around our patents, should they issue.

Moreover, other parties have developed or may develop technologies that may be related or competitive to our approach, and may have filed or may file patent applications and may have received or may receive patents that may overlap or conflict with our patent applications, either by claiming similar methods or by claiming subject matter that could dominate our patent position. In addition, the standards that the United States Patent and Trademark Office ("USPTO") and other jurisdictions use to grant patents are not always applied predictably or uniformly and can change. Similarly, the ultimate degree of protection that will be afforded to biotechnology inventions, including ours, in the United States and other jurisdictions remains uncertain and is dependent upon the scope of the protection decided upon by patent offices, courts and lawmakers.

Publications of discoveries in the scientific literature often lag behind actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until eighteen months after filing, or in some cases not at all. Therefore, we cannot know with certainty whether we were the first to make the inventions claimed in any issued patents or pending patent applications, or that we were the first to file for patent protection of such inventions, nor can we know whether those from whom we may license patents were the first to make the inventions claimed or were the first to file. For these and other reasons, the issuance, scope, validity, enforceability and commercial value of our patent rights are subject to a level of uncertainty. Our pending and future patent applications may not result in patents being issued which protect our technology or products, in whole or in part, or which effectively prevent others from commercializing competitive technologies and products. Changes in the patent

laws and/or interpretation of the patent laws in the United States and other countries may diminish the value of our patents or narrow the scope of our patent protection.

We may be subject to a third-party pre-issuance submission of prior art to the USPTO or become involved in derivation, reexamination, inter partes review, ex partes reexamination, post-grant review or interference proceedings challenging our patent rights or the patent rights of others. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate, our patent rights, allow third parties to commercialize our technology or products and compete directly with us without payment to us, or result in our inability to manufacture or commercialize products without infringing third-party patent rights. For example, in February 2021, the European Patent Office informed us of a notice of opposition by a third party for a patent issued to us. In July 2021, we filed a reply to the notice of opposition. The patent at issue does not relate to our current product candidates.

Any limitation on the protection of the subject technology could hinder our ability to develop and commercialize applicable product candidates.

In addition, if the breadth or strength of protection provided by our patents and patent applications is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates. Furthermore, an adverse decision in an interference proceeding can result in a third party receiving the patent right sought by us, which in turn could affect our ability to develop, market or otherwise commercialize our product candidates. The issuance, scope, validity, enforceability and commercial value of our patents are subject to a level of uncertainty.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain, involves complex legal and factual questions and has in recent years been the subject of much litigation. Due to legal standards relating to patentability, validity, enforceability and claim scope of patents covering biotechnological and pharmaceutical inventions, our ability to obtain, maintain and enforce patents is uncertain and involves complex legal and factual questions. Even if issued, a patent's validity, inventorship, ownership or enforceability is not conclusive. Accordingly, rights under any existing patent or any patents we might obtain or license may not cover our product candidates, or may not provide us with sufficient protection for our product candidates to afford a commercial advantage against competitive products or processes, including those from branded and generic pharmaceutical companies.

The degree of future protection for our proprietary rights is uncertain, and we cannot ensure that:

- any of our pending patent applications, if issued, will include claims having a scope sufficient to protect our product candidates or any other products or product candidates;
- any of our pending patent applications will issue as patents;
- we will be able to successfully commercialize our product candidates, if approved, before our relevant patents expire;
- we were the first to make the inventions covered by any existing patent and pending patent applications;
- we were the first to file patent applications for these inventions;
- others will not develop similar or alternative technologies that do not infringe or design around our patents;
- others will not use pre-existing technology to effectively compete against us;
- any of our patents, if issued, will be found to ultimately be valid and enforceable;
- third parties will not compete with us in jurisdictions where we do not pursue and obtain patent protection;
- we will be able to obtain and/or maintain necessary or useful licenses on reasonable terms or at all;
- any patents issued to us will provide a basis for an exclusive market for our commercially viable products, will provide us with any competitive advantages or will not be challenged by third parties;
- we will develop additional proprietary technologies or product candidates that are separately patentable; or
- our commercial activities or products will not infringe upon the patents or proprietary rights of others.

Any litigation to enforce or defend our patent rights, even if we were to prevail, could be costly and time-consuming and would divert the attention of our management and key personnel from our business operations. We may not prevail in any lawsuits that we initiate, and the damages or other remedies awarded even if we were to prevail may not be commercially meaningful. Even if we are successful, domestic or foreign litigation, or USPTO or foreign

patent office proceedings, may result in substantial costs and distraction to our management. We may not be able, alone or with our licensors or potential collaborators, to prevent misappropriation of our proprietary rights, particularly in countries where the laws may not protect such rights as fully as in the United States. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation or other proceedings, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation or other proceedings. In addition, during the course of this kind of litigation or proceedings, there could be public announcements of the results of hearings, motions or other interim proceedings or developments or public access to related documents. If investors perceive these results to be negative, the market price for our common stock could be significantly harmed.

If we fail to comply with our obligations in the agreements under which we may license intellectual property rights from third parties or otherwise experience disruptions to our business relationships with our licensors, we could lose rights that are important to our business.

We have entered into, and may be required to enter into in the future, intellectual property license agreements that are important to our business. These license agreements may impose various diligence, milestone payment, royalty and other obligations on us. For example, we have entered into an exclusive license agreement with the Mayo Clinic pursuant to which we are required to use efforts to engage in various development and commercialization activities with respect to licensed products, and we are required to satisfy specified milestone and royalty payment obligations. If we fail to comply with any obligations under our agreements with licensors, we may be subject to termination of the license agreement in whole or in part or increased financial obligations to our licensors, in which case our ability to develop or commercialize products covered by the license agreement will be impaired. Further, we may need to outsource and rely on third parties for many aspects of the clinical development, sales and marketing of our products covered under our current and future license agreements. Delay or failure by these third parties could adversely affect the continuation of our license agreements with our licensors.

In addition, disputes may arise regarding intellectual property subject to a license agreement, including:

- the scope of rights granted under the license agreement and other interpretation-related issues;
- the extent to which our technology and processes infringe intellectual property of the licensor that is not subject to the licensing agreement; and
- our diligence obligations under the license agreement and what activities satisfy those obligations.

If disputes over intellectual property that we have licensed prevent or impair our ability to maintain our current licensing arrangements on acceptable terms, we may be unable to successfully develop and commercialize the affected product candidates.

The intellectual property which we have licensed from the Mayo Clinic was 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. industry. Compliance with such regulations may limit our exclusive rights, subject us to expenditure of resources with respect to reporting requirements and limit our ability to contract with non-U.S. manufacturers.

We have licensed certain intellectual property from the Mayo Clinic. The agreement indicates that the rights licensed to us are subject to the obligations to and the rights of the U.S. government, including those set forth in the Bayh-Dole Act of 1980. As a result, the U.S. government may have certain rights to intellectual property embodied in our current or future therapeutics based on the licensed intellectual property. These U.S. government rights in certain inventions developed under a government-funded program include a non-exclusive, non-transferable, irrevocable worldwide license to use inventions for any governmental purpose. In addition, the U.S. government has the right to require us to grant exclusive, partially exclusive or nonexclusive licenses to any of these inventions to a third party if it determines that: (i) adequate steps have not been taken to commercialize the invention; (ii) government action is necessary to meet public health or safety needs; or (iii) government action is necessary to meet requirements for public use under federal regulations, also referred to as "march-in rights." While the U.S. government has sparingly used, and to our knowledge never successfully exercised, such march-in rights, any exercise of the march-in rights by the U.S. government could harm our competitive position, business, financial condition, results of operations and prospects. If the U.S. government exercises such march-in rights, we may receive compensation that is deemed reasonable by the U.S. government in its sole discretion, which may be less than what we might be able to obtain in

the open market. Intellectual property generated under a government funded program is also subject to certain reporting requirements, compliance with which may require us to expend substantial resources.

In addition, the U.S. government requires that any therapeutics embodying any invention generated through the use of U.S. government funding be manufactured substantially in the United States. The manufacturing preference requirement can be waived if the owner of the intellectual property can show that reasonable but unsuccessful efforts have been made to grant licenses on similar terms to potential licensees that would be likely to manufacture substantially in the United States or that under the circumstances domestic manufacture is not commercially feasible. This preference for U.S. manufacturers may limit our ability to contract with non-U.S. therapeutic manufacturers for therapeutics covered by such intellectual property.

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

In addition to seeking patents for some of our technology and product candidates, we also rely on trade secrets, including unpatented know-how, technology and other proprietary information, to maintain our competitive position. We seek to protect these trade secrets, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to them, such as our employees, corporate collaborators, outside scientific collaborators, contract manufacturers, consultants, advisors and other third parties. We also seek to enter into confidentiality and invention or patent assignment agreements with our employees, advisors and consultants. Despite these efforts, any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. Our trade secrets may also be obtained by third parties by other means, such as breaches of our physical or computer security systems. 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. Moreover, if any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent them or those to whom they communicate from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor, our competitive position would be harmed.

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

As is the case with other biotechnology companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biotechnology industry involves both technological and legal complexity, and is therefore costly, time-consuming and inherently uncertain. Patent reform legislation in the United States, including the Leahy-Smith America Invents Act (the" Leahy-Smith Act"), signed into law on September 16, 2011, could increase those uncertainties and costs. The Leahy-Smith Act included a number of significant changes to U.S. patent law. These changes included provisions that affect the way patent applications are prosecuted, redefine prior art and provide more efficient and cost-effective avenues for competitors to challenge the validity of patents. In addition, the Leahy-Smith Act transformed the U.S. patent system into a “first to file” system. The first-to-file provisions became effective on March 16, 2013. The Leahy-Smith Act and its implementation could make it more difficult to obtain patent protection for our inventions and increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could harm our business, results of operations and financial condition.

In addition, recent United States Supreme Court rulings have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations. From time to time, the U.S. Supreme Court, other federal courts, the United States Congress or the USPTO, may change the standards of patentability and any such changes could have a negative impact on our business. 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.

The U.S. Supreme Court has ruled on several patent cases in recent years, either narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations. For example, in *Association for Molecular Pathology v. Myriad Genetics, Inc.*, the Supreme Court held that claims to isolated genomic DNA are not patentable, but claims to complementary DNA, or cDNA, molecules, which are not genomic sequences, may be patent eligible because they are not a natural product. The effect of the decision on

patents for other isolated natural products is uncertain. Our current product candidates include natural products. Therefore, this decision and its interpretation by the courts and the USPTO may impact prosecution, defense and enforcement of our patent portfolio. Depending on future actions by the U.S. Congress, the U.S. courts, the USPTO and the relevant law-making bodies in other countries, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future.

In addition to increasing uncertainty with regard to our ability to obtain future patents, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on these and other decisions by the U.S. Congress, the federal courts and the USPTO, the laws and regulations governing patents could change or be interpreted in unpredictable ways that would weaken our ability to obtain new patents or to enforce any patents that may issue to us in the future. In addition, these events may adversely affect our ability to defend any patents that may issue in procedures in the USPTO or in courts.

Furthermore, Europe's planned Unified Patent Court may in particular present uncertainties for our ability to protect and enforce our patent rights against competitors in Europe. While that new court is being implemented to provide more certainty and efficiency to patent enforcement throughout Europe, it will also provide our competitors with a new forum to use to centrally revoke our European patents. It will be several years before we will understand the scope of patent rights that will be recognized and the strength of patent remedies that will be provided by that court. We will have the right to opt our patents out of that system over the first seven years of the court, but doing so may preclude us from realizing the benefits of the new unified court.

Third parties may initiate legal proceedings alleging that we are infringing their intellectual property rights, the outcome of which would be uncertain and could have a material adverse effect on the success of our business.

Our commercial success depends upon our ability, and the ability of our collaborators, to develop, manufacture, market and sell our product candidates and use our proprietary technologies without infringing the proprietary rights of third parties. There is considerable intellectual property litigation in the biotechnology and pharmaceutical industries. While no such litigation has been brought against us and we have not been held by any court to have infringed a third party's intellectual property rights, we cannot guarantee that our technology, products or use of our products do not infringe third-party patents.

Numerous patents and pending applications are owned by third parties in the fields in which we are developing product candidates, both in the United States and elsewhere. It is also possible that we have failed to identify relevant third-party patents or applications. For example, applications filed before November 29, 2000 and certain applications filed after that date that will not be filed outside the United States remain confidential until patents issue. Moreover, it is difficult for industry participants, including us, to identify all third-party patent rights that may be relevant to our product candidates and technologies because patent searching is imperfect due to differences in terminology among patents, incomplete databases and the difficulty in assessing the meaning of patent claims. We may fail to identify relevant patents or patent applications or may identify pending patent applications of potential interest but incorrectly predict the likelihood that such patent applications may issue with claims of relevance to our technology. In addition, we may be unaware of one or more issued patents that would be infringed by the manufacture, sale or use of a current or future product candidate, or we may incorrectly conclude that a third-party patent is invalid, unenforceable or not infringed by our activities. Additionally, pending patent applications that have been published can, subject to certain limitations, be later amended in a manner that could cover our technologies, our products or the use of our products. We are aware of several pending patent applications containing one or more claims that could be construed to cover some of our product candidates or technology, should those claims issue in their original form or in the form presently being pursued.

The biotechnology and pharmaceutical industries are characterized by extensive litigation regarding patents and other intellectual property rights. Other parties may allege that our product candidates or the use of our technologies infringe patent claims or other intellectual property rights held by them, or that we are employing their proprietary technology without authorization. We may become party to, or threatened with, future adversarial proceedings or litigation regarding intellectual property rights with respect to our products and technology, including interference or derivation proceedings before the USPTO and similar bodies in other countries. Third parties may assert infringement claims against us based on existing intellectual property rights and intellectual property rights that may be granted in the future. If we were to challenge the validity of an issued U.S. patent in court, such as an issued U.S. patent of potential relevance to some of our product candidates or methods of use, we would need to

overcome a statutory presumption of validity that attaches to every U.S. patent. This means that in order to prevail, we would have to present clear and convincing evidence as to the invalidity of the patent's claims. There is no assurance that a court would find in our favor on questions of infringement or validity.

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

Even if we are successful in proceedings defending our intellectual property, we may incur substantial costs and divert management time and attention in pursuing these proceedings, which could have a material adverse effect on us. If we are unable to avoid infringing the patent rights of others, we may be required to seek a license, defend an infringement action or challenge the validity of the patents in court, or redesign our products. Patent litigation is costly and time-consuming. We may not have sufficient resources to bring these actions to a successful conclusion. In addition, intellectual property litigation or claims could force us to do one or more of the following:

- cease developing, selling or otherwise commercializing our product candidates;
- pay substantial damages for past use of the asserted intellectual property;
- obtain a license from the holder of the asserted intellectual property, which license may not be available on reasonable terms, if at all; and
- in the case of trademark claims, redesign or rename some or all of our product candidates or other brands to avoid infringing the intellectual property rights of third parties, which may not be possible and, even if possible, could be costly and time-consuming.

Any of these risks coming to fruition could have a material adverse effect on our business, results of operations, financial condition and prospects.

Issued patents covering our product candidates could be found invalid or unenforceable or could be interpreted narrowly if challenged in court.

Competitors may infringe our intellectual property, including our patents or the patents of our licensors. As a result, we may be required to file infringement claims to stop third-party infringement or unauthorized use. This can be expensive, particularly for a company of our size, and time-consuming. If we initiated legal proceedings against a third party to enforce a patent, if and when issued, covering one of our product candidates, the defendant could counterclaim that the patent covering our product candidate is invalid and/or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity and/or unenforceability are commonplace. Grounds for a validity challenge include alleged failures to meet any of several statutory requirements, including lack of novelty, obviousness or non-enablement, or failure to claim patent eligible subject matter. Grounds for unenforceability assertions include allegations that someone connected with prosecution of the patent withheld relevant information from the USPTO or made a misleading statement during prosecution. Third parties may also raise similar claims before administrative bodies in the United States or abroad, even outside the context of litigation. Such mechanisms include re-examination, post grant review and equivalent proceedings in foreign jurisdictions, such as opposition proceedings. Such proceedings could result in revocation or amendment of our patents in such a way that they no longer cover our product candidates or competitive products. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to validity, for example, we cannot be certain that there is no invalidating prior art of which we and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity and/or unenforceability, we would lose at least part, and perhaps all, of the patent protection on our product candidates. Moreover, even if not found invalid or unenforceable, the claims of our patents could be construed narrowly or in a manner that does not cover the allegedly infringing technology in question. Such a loss of patent protection would have a material adverse impact on our business.

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 noncompliance with these requirements.

Periodic maintenance fees on any issued patent are due to be paid to the USPTO and foreign patent agencies in several stages over the lifetime of the patent and, in some jurisdictions, during the pendency of a patent application. The USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. While an inadvertent lapse can in many cases be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which noncompliance 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. Noncompliance events that could result in abandonment or lapse of a patent or patent application include, but are not limited to, failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. In such an event, our competitors might be able to enter the market, which would have a material adverse effect on our business.

We may be subject to claims challenging the inventorship or ownership of our patents and other intellectual property.

It is our policy to enter into confidentiality and intellectual property assignment agreements, including with our employees, consultants, contractors and advisors. These agreements generally provide that inventions conceived by the party in the course of rendering services to us will be our exclusive property. However, these agreements may not be honored and may not effectively assign intellectual property rights to us. For example, even if we have a consulting agreement in place with an academic advisor pursuant to which such academic advisor is required to assign any inventions developed in connection with providing services to us, such academic advisor may not have the right to assign such inventions to us, as it may conflict with his or her obligations to assign all such intellectual property to his or her employing institution.

Litigation may be necessary to defend against these and other claims challenging inventorship or ownership. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights such as exclusive ownership of, or right to use, valuable intellectual property. Such an outcome could have a material adverse effect on 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.

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

Many of our employees were previously employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. We may also engage advisors and consultants who are concurrently employed at universities or other organizations or who perform services for other entities. Although we try to ensure that our employees, advisors and consultants 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, advisors or consultants have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such party's former or current employer or in violation of an agreement with another party. Although we have no knowledge of any such claims being alleged to date, if such claims were to arise, litigation may be necessary to defend against any such claims.

In addition, while it is our policy to require our employees, consultants, advisors and contractors who may be involved in the development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who in fact develops intellectual property that we regard as our own. Our and their assignment agreements may not be self-executing or may be breached, and we may be forced to bring claims against third parties, or defend claims they may bring against us, to determine the ownership of what we regard as our intellectual property. Similarly, we may be subject to claims that an employee, advisor or consultant performed work for us that conflicts with that person's obligations to a third party, such as an employer, and thus, the third party has an ownership interest in the intellectual property arising out of work performed for us. Litigation may be necessary to defend against these claims. Although we have no knowledge of any such claims being alleged to date, if such claims were to arise, litigation may be necessary to defend against any such claims.

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

If our trademarks and trade names are not adequately protected, we may not be able to build name recognition in our markets of interest and our business may be adversely affected.

Our registered or unregistered trademarks or trade names may be challenged, infringed, circumvented or declared generic or determined to be infringing other marks. We may not be able to protect our rights to these trademarks and trade names which we need to build name recognition among potential collaborators or customers in our markets of interest. At times, competitors may adopt trade names or trademarks similar to ours, thereby impeding our ability to build brand identity and possibly leading to market confusion. In addition, there could be potential trade name or trademark infringement claims brought by owners of other registered trademarks or trademarks that incorporate variations of our registered or unregistered trademarks or trade names. Over the long term, if we are unable to establish name recognition based on our trademarks and trade names, then we may not be able to compete effectively and our business may be adversely affected. Our efforts to enforce or protect our proprietary rights related to trademarks, trade names, domain names or other intellectual property may be ineffective and could result in substantial costs and diversion of resources, and could adversely impact our financial condition or results of operations.

We will not seek to protect our intellectual property rights in all jurisdictions throughout the world and we may not be able to adequately enforce our intellectual property rights even in the jurisdictions where we seek protection.

Filing, prosecuting and defending patents on product candidates in all countries and jurisdictions throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States could be less extensive than in the United States, assuming that rights are obtained in the United States and assuming that rights are pursued outside the United States. The statutory deadlines for pursuing patent protection in individual foreign jurisdictions are based on the priority date of each of our patent applications. For some of the patent families in our portfolio, including the families that may provide coverage for our lead product candidates, the relevant statutory deadlines have not yet expired. Therefore, for each of the patent families that we believe provide coverage for our lead product candidates, we will need to decide whether and where to pursue protection outside the United States. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the United States. Consequently, even if we do elect to pursue patent rights outside the United States, we may not be able to obtain relevant claims and/or we may not be able to prevent third parties from practicing our inventions in all countries outside the United States or from selling or importing products made using our inventions in and into the United States or other jurisdictions.

Competitors may use our technologies in jurisdictions where we do not pursue and obtain patent protection to develop their own products and, further, may export otherwise infringing products to territories where we have patent protection but enforcement is not as strong as that in the United States. 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.

Even if we pursue and obtain issued patents in particular jurisdictions, our patent claims or other intellectual property rights may not be effective or sufficient to prevent third parties from so competing.

The laws of some foreign countries do not protect intellectual property rights to the same extent as the laws of the United States. Many companies have encountered significant problems in protecting and defending intellectual property rights in certain foreign jurisdictions. The legal systems of some countries, particularly developing countries, do not favor the enforcement of patents and other intellectual property protection, especially those relating to biotechnology. This could make it difficult for us to stop the infringement of our patents, if obtained, or the misappropriation of our other intellectual property rights. For example, many foreign countries have compulsory licensing laws under which a patent owner must grant licenses to third parties. In addition, many countries limit the enforceability of patents against third parties, including government agencies or government contractors. In these countries, patents may provide limited or no benefit. Patent protection must ultimately be sought on a country-by-country basis, which is an expensive and time-consuming process with uncertain outcomes. Accordingly, we may choose not to seek patent protection in certain countries, and we will not have the benefit of patent protection in such countries.

If our ability to obtain and, if obtained, enforce our patents to stop infringing activities is inadequate, third parties may compete with our products, and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing. Accordingly, our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property we develop or license.

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

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

We are highly dependent on Balkrishan (Simba) Gill, our President and Chief Executive Officer, as well as the other principal members of our management, scientific and clinical teams. Although we have entered into agreements with our executive officers, each of them may terminate their employment with us at any time. We do not maintain "key person" insurance for any of our executives or other employees.

Recruiting and retaining qualified scientific, clinical, manufacturing and sales and marketing personnel will also be critical to our success. The loss of the services of our executive officers or other key employees could impede the achievement of our research, development and commercialization objectives, and seriously harm our ability to successfully implement our business strategy. Furthermore, replacing executive officers and key employees may be difficult and may take an extended period of time due to the limited number of individuals in our industry with the breadth of skills and experience required to successfully develop, gain regulatory approval of and commercialize products. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate these key personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. 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 employed by employers 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 pursue our growth strategy will be limited.

We expect to expand our development and regulatory capabilities and potentially implement sales, marketing and distribution capabilities, and as a result, we may encounter difficulties in managing our growth, which could disrupt our operations.

We expect to experience significant growth in the number of our employees and the scope of our operations, particularly in the areas of product development, regulatory affairs, clinical affairs and manufacturing and, if any of our product candidates receives marketing approval, sales, marketing and distribution. To manage our anticipated future growth, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities 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. The expansion of our operations may lead to significant costs and may divert our management and business development resources. Any inability to manage growth could delay the execution of our business plans or disrupt our operations.

A variety of risks associated with operating internationally could materially adversely affect our business.

We currently have limited international operations, but our business strategy incorporates potentially expanding internationally if any of our product candidates receive regulatory approval. Doing business internationally involves a number of risks, including but not limited to:

- multiple, conflicting and changing laws and regulations, such as privacy regulations, tax laws, export and import restrictions, employment laws, regulatory requirements and other governmental approvals, permits and licenses;
- failure by us to obtain and maintain regulatory approvals for the use of our products in various countries;
- additional potentially relevant third-party patent rights;
- complexities and difficulties in obtaining protection and enforcing our intellectual property;

- difficulties in staffing and managing foreign operations;
- complexities associated with managing multiple payor reimbursement regimes, government payors or patient self-pay systems;
- limits in our ability to penetrate international markets;
- financial risks, such as longer payment cycles, difficulty collecting accounts receivable, the impact of local and regional financial crises on demand and payment for our products and exposure to foreign currency exchange rate fluctuations;
- natural disasters, political and economic instability, including wars, terrorism and political unrest (for example, the ongoing conflict between Russia and Ukraine), outbreak of disease (e.g. the COVID-19 pandemic), boycotts, curtailment of trade and other business restrictions;
- certain expenses including, among others, expenses for travel, translation and insurance; and
- regulatory and compliance risks that relate to maintaining accurate information and control over sales and activities that may fall within the purview of the U.S. Foreign Corrupt Practices Act, its books and records provisions, its anti-bribery provisions or other anti-bribery and anti-corruption laws.

Any of these factors could significantly harm our future international expansion and operations and, consequently, our results of operations.

The United Kingdom's withdrawal from the European Union may have a negative effect on global economic conditions, financial markets and our business.

The UK left the EU on January 31, 2020, following which existing EU legislation continued to apply in the UK during a transition period under the terms of the EU-UK Withdrawal Agreement. The transition period, which ended on December 31, 2020, maintained access to the EU single market and to global trade deals negotiated by the EU on behalf of its members. The transition period provided time for the UK and EU to negotiate a framework for partnership for the future, which was then crystallized in the Trade and Cooperation Agreement ("TCA") which became effective on January 1, 2021.

These developments, or the perception that any related developments could occur, have had and may continue to have a material adverse effect on global economic conditions and the stability of global financial markets, and may significantly reduce global market liquidity and restrict the ability of key market participants to operate in certain financial markets. Any of these factors could depress economic activity and restrict our access to capital, which could have a material adverse effect on our business, financial condition and results of operations and reduce the price of common stock.

The long term effects of Brexit will depend on the implementation and application of the TCA and any other relevant agreements between the UK and the EU. EU laws which have been transposed into UK law through secondary legislation continue to be applicable as "retained EU law". However, new legislation will not be applicable. The UK government has passed a new Medicines and Medical Devices Act 2021, which introduces delegated powers in favor of the Secretary of State or an 'appropriate authority' to amend or supplement existing regulations in the area of medical devices. This allows new rules to be introduced in the future by way of secondary legislation, which aims to allow flexibility in addressing regulatory gaps. There is a possibility that, over time, national laws will be amended and that consequently the regulatory framework in Great Britain will diverge from that of the EU. As of January 1, 2021, the MHRA is the UK's standalone medicines and medical devices regulator. As a result of the Northern Ireland protocol, different rules will apply in Northern Ireland than in England, Wales and Scotland, together, Great Britain. Broadly, Northern Ireland will continue to follow the EU regulatory regime, but its national competent authority will remain the MHRA.

The uncertainty regarding new or modified arrangements between the United Kingdom and other countries following the withdrawal may have a material adverse effect on the movement of personnel, goods, information or data between the United Kingdom and members of the EU and the United States, including the interruption of or delays in imports into the United Kingdom of goods originating within the EU and exports from the United Kingdom of goods originating there. For example, shipments into the United Kingdom of drug substance manufactured for us in the EU may be interrupted or delayed and thereby prevent or delay the manufacture in the United Kingdom of drug product. Similarly, shipments out of the United Kingdom of drug product to the United States or the EU may be interrupted or delayed and thereby prevent or delay the delivery of drug product to clinical sites. Such a situation could hinder our ability to conduct current and planned clinical trials and have an adverse effect on our business.

Our business and operations may suffer in the event of information technology and other system failures or security breaches of or unauthorized access to our systems.

We collect and maintain information in digital form that is necessary to conduct our business, and we are increasingly dependent on information technology systems and infrastructure to operate our business. In the ordinary course of our business, we collect, store and transmit large amounts of confidential information, including intellectual property, proprietary business information and personal information. It is critical that we do so in a secure manner to maintain the confidentiality and integrity of such confidential information.

Despite the implementation of security measures, our information technology systems and those of our current and future partners, service providers, contractors and consultants are vulnerable to attack and damage from computer viruses, unauthorized access, malware (e.g. ransomware), malicious code, natural disasters, terrorism, war, telecommunication and electrical failures, cyberattacks or cyber-intrusions, phishing attacks and other social engineering schemes, employee theft or misuse, human error, fraud, denial or degradation of service attacks, and other security breaches or unauthorized access by persons inside our organization or with access to our internal systems. The risk of a security breach or disruption, particularly through cyberattacks or cyber-intrusions, including by computer hackers, foreign governments and cyber terrorists, generally has increased as the number, intensity and sophistication of attempted attacks and intrusions from around the world have increased. In addition, our information technology systems safeguard important confidential data, including personal data regarding patients enrolled in our clinical trials. As a result of the COVID-19 pandemic, we may also face increased cybersecurity risks due to our greater reliance on internet technology and the number of our employees who are working remotely, which may create additional opportunities for cybercriminals to exploit vulnerabilities. Furthermore, because the techniques used to obtain unauthorized access to, or to sabotage, systems change frequently and often are not recognized until launched against a target, we may be unable to anticipate these techniques or implement adequate preventative measures. We may also experience security breaches that may remain undetected for an extended period. Even if identified, 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 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, it could result in a material disruption to our product development programs and our business operations. For example, the loss of clinical trial data from completed or future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. Likewise, we rely on third parties to manufacture our product candidates and conduct clinical trials, and we have also outsourced elements of our information technology infrastructure. Similar events relating to the computer systems of our third-party service providers and vendors could make us vulnerable to disruptions in service and unauthorized access to our confidential or proprietary information, and we could incur liability and reputational damage. Though immaterial to date and despite stringent precautions, we have in the past experienced, and may in the future experience, the inadvertent disclosure of information by our third party service providers. 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 confidential or proprietary information, we could incur liability and the further development and commercialization of our product candidates could be delayed. If such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our business. Furthermore, federal, state and international laws and regulations can expose us to enforcement actions and investigations by regulatory authorities, and potentially result in regulatory penalties, fines and significant legal liability, if our information technology security efforts fail. We may also be exposed to a risk of loss or litigation and potential liability, which could materially and adversely affect our business, results of operations or financial condition and prospects.

We rely on a set of cloud-based software services and access these services via the Internet for the vast majority of our computing, storage, bandwidth and other services. Any disruption of or interference with our use of our cloud-based services would negatively affect our operations and could seriously harm our business.

We use several distributed computing infrastructure platforms for business operations, or what is commonly referred to as "cloud" computing services, and we access these services via the Internet. Any transition of the cloud services currently provided by an existing vendor to another cloud provider would be difficult to implement and will cause us to incur significant time and expense. Given this, any significant disruption of or interference with our use of these cloud computing services would negatively impact our operations and our business would be seriously harmed. If our employees or partners are not able to access our cloud computing services or encounter difficulties in doing so, we may experience business disruption. The level of service provided by our cloud computing vendors, including the ability to secure our confidential information and the confidential information of third parties that is shared with us, may also impact the perception of our company and could seriously harm our business and reputation and create liability for us. If a cloud computing service that we use experiences interruptions in service regularly or for a prolonged basis, or other similar issues, our business could be seriously harmed.

In addition, a cloud computing service may take actions beyond our control that could seriously harm our business, including:

- discontinuing or limiting our access to its platform;
- increasing pricing terms;
- terminating or seeking to terminate our contractual relationship altogether;
- establishing more favorable relationships with one or more of our competitors; or
- modifying or interpreting its terms of service or other policies in a manner that impacts our ability to run our business and operations.

Our cloud computing service providers have broad discretion to change and interpret their terms of service and other policies with respect to us, and those actions may be unfavorable to us. Our cloud computing service providers may also alter how we are able to process data on the platform. If a cloud computing service provider makes changes or interpretations that are unfavorable to us, our business could be seriously harmed.

Our efforts to protect the information shared with us may be unsuccessful due to the actions of third parties, software bugs or other technical malfunctions, employee error or malfeasance or other factors. In addition, third parties may attempt to fraudulently induce employees or users to disclose information to gain access to our data or third-party data entrusted to us. If any of these events occur, our or third-party information could be accessed or disclosed improperly. Some partners or collaborators may store information that we share with them on their own computing system. If these third parties fail to implement adequate data-security practices or fail to comply with our policies, our data may be improperly accessed or disclosed. And even if these third parties take all these steps, their networks may still suffer a breach, which could compromise our data.

Any incidents where our information is accessed without authorization, is improperly used, or that violate our policies, could damage our reputation and our brand and diminish our competitive position. In addition, affected parties or government authorities could initiate legal or regulatory action against us over those incidents, which could cause us to incur significant expense and liability or result in orders or consent decrees forcing us to modify our business practices. Concerns over our privacy practices, whether actual or unfounded, could damage our reputation and brand and deter users, advertisers and partners from using our products and services. Any of these occurrences could seriously harm our business.

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, financial condition and prospects.

Legislation in various countries around the world with regard to cybersecurity, privacy and data protection is rapidly expanding and creating a complex compliance environment. We are subject to many federal, state and foreign laws and regulations, including those related to privacy, rights of publicity, data protection, content regulation, protection of minors and consumer protection. In the United States, HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009 and regulations promulgated thereunder (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. While we do not believe that we are currently acting as a covered entity or business associate under HIPAA and thus are not directly regulated under HIPAA, any person may be prosecuted under HIPAA's criminal provisions either directly or under aiding-and-abetting or conspiracy principles. Consequently, 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 U.S. 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. Such laws and regulations will be subject to interpretation by various courts and other governmental authorities, thus creating potentially complex compliance issues for us and our future customers and strategic partners. For example, California has enacted the California Consumer Privacy Act (the "CCPA"), which took effect on January 1, 2020. The CCPA creates individual privacy rights for California consumers and increases the privacy and security obligations of entities handling certain personal information. The CCPA provides for civil penalties for violations, as well as a private right of action for data breaches that is expected to increase data breach litigation. Additionally, the California Privacy Rights Act (the "CPRA") was recently enacted in California. The CPRA significantly amends the CCPA and will impose additional data protection obligations on covered companies doing business in California, 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 will also create a new California data protection agency authorized to issue substantive regulations and could result in increased privacy and information security enforcement. The majority of the provisions will go into effect on January 1, 2023, and additional compliance investment and potential business process changes may be required. Similar laws have passed in Virginia, Utah and Colorado, and have been proposed in other states and at the federal level, reflecting a trend toward more stringent privacy legislation in the United States.

We are also or may become subject to rapidly evolving data protection laws, rules and regulations in foreign jurisdictions. For example, the General Data Protection Regulation (the "GDPR"), which became effective in May 2018, imposes stringent data protection requirements for processing the personal data of individuals within the EEA. 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. Among other requirements, the GDPR prohibits the transfer of personal data from the EEA to the United States and other jurisdictions that the European Commission does not recognize as having "adequate" data protection laws unless a data transfer mechanism has been put in place. In July 2020, the Court of Justice of the European Union (the "CJEU") limited how organizations could lawfully transfer personal data from the EEA to the United States by invalidating the EU-US Privacy Shield for purposes of international transfers and imposing further restrictions on the use of standard contractual clauses ("SCCs"). The European Commission published revised SCCs for data transfers from the EEA on June 4, 2021. The revised clauses must be used for relevant new data transfers from September 27, 2021 onward; existing SCC arrangements must be migrated to the revised clauses by December 27, 2022. The new SCCs apply only to the transfer of personal data outside of the EEA and not the United Kingdom. The United Kingdom's Information Commissioner's Office has published new data transfer standard contracts for transfers from the United Kingdom under the United Kingdom GDPR ("UK GDPR"). This new documentation will be mandatory for relevant data transfers from September 21, 2022; existing standard contractual clauses arrangements must be migrated to the new documentation by March 21, 2024. We will be required to implement the revised SCCs, in relation to relevant existing contracts and certain additional contracts and arrangements, within the relevant time frames. There is some uncertainty around whether the revised clauses can be used for all types of data transfers, particularly whether they can be relied on for data transfers to non-EEA entities subject to the GDPR. These recent developments are likely to require us to review and amend the legal mechanisms by which we make and/or receive personal data transfers to/ in the United States. As supervisory authorities issue further guidance on personal data export mechanisms, including circumstances where the standard contractual clauses cannot be used, and/or start taking enforcement action, we could suffer additional costs, complaints and/or regulatory investigations or fines, and/or if we are otherwise unable to transfer personal data between and among countries and regions in which we operate, it could affect the manner in which we provide our services, the geographical location or segregation of our relevant systems and operations, and could adversely affect our financial results.

Relatedly, following the United Kingdom's withdrawal from the EEA and the EU and the expiration of the transition period, from January 1, 2021, companies have to comply with both the GDPR and the UK GDPR, the latter regime

having the ability to separately fine up to the greater of £17.5 million or 4% of global revenue. The relationship between the United Kingdom and the EU in relation to certain aspects of data protection law remains unclear, and it is unclear how United Kingdom data protection laws and regulations will develop in the medium to longer term. On June 28, 2021, the European Commission adopted an adequacy decision in favor of the United Kingdom enabling data transfers from EU member states to the United Kingdom without additional safeguards. However, the United Kingdom adequacy decision will automatically expire in June 2025 unless the European Commission renews or extends that decision and remains under review by the Commission during this period.

Although we work to comply with applicable laws, regulations and standards, our contractual obligations and other legal obligations, these requirements are evolving and may be modified, interpreted and applied in an inconsistent manner from one jurisdiction to another, and may conflict with one another or other legal obligations with which we must comply. Any failure or perceived failure by us or our employees, representatives, contractors, consultants, collaborators or other third parties to comply with such requirements or adequately address privacy and security concerns, even if unfounded, could result in additional cost and liability to us, damage our reputation, and adversely affect our business and results of operations.

Acquisitions or joint ventures could disrupt our business, cause dilution to our stockholders and otherwise harm our business.

We may acquire other businesses, products or technologies as well as pursue strategic alliances, joint ventures, technology licenses or investments in complementary businesses. We have limited experience in completing such transactions. Any of these transactions could be material to our financial condition and operating results and expose us to many risks, including:

- disruption in our relationships with future customers or with current or future distributors or suppliers as a result of such a transaction;
- unanticipated liabilities related to acquired companies;
- difficulties integrating acquired personnel, technologies and operations into our existing business;
- diversion of management time and focus from operating our business to acquisition integration challenges;
- increases in our expenses and reductions in our cash available for operations and other uses;
- possible write-offs or impairment charges relating to acquired businesses; and
- inability to develop a sales force for any additional product candidates.

Foreign acquisitions involve unique risks in addition to those mentioned above, including those related to integration of operations across different cultures and languages, currency risks and the particular economic, political and regulatory risks associated with specific countries.

Also, the anticipated benefit of any acquisition may not materialize. Future acquisitions or dispositions could result in potentially dilutive issuances of our equity securities, the incurrence of debt, contingent liabilities or amortization expenses or write-offs of goodwill, any of which could harm our financial condition. We cannot predict the number, timing or size of future joint ventures or acquisitions, or the effect that any such transactions might have on our operating results.

Risks Related to Our Common Stock

The price of our common stock may be volatile and fluctuate substantially, which could result in substantial losses for purchasers of our common stock, and we could be subject to securities class action litigation as a result.

Our stock price is likely to be volatile. The stock market in general and the market for smaller biopharmaceutical companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. As a result of this volatility, you may not be able to sell your shares of common stock at or above the price at which you purchase the shares. The market price for our common stock may be influenced by many factors, including:

- the success of competitive products or technologies;
- actual or anticipated changes in our growth rate relative to our competitors;

- results of clinical trials of our product candidates or those of our competitors;
- developments related to any future collaborations;
- regulatory or legal developments in the United States and other countries;
- adverse actions taken by regulatory agencies with respect to our preclinical studies or clinical trials, manufacturing or sales and marketing activities;
- any adverse changes to our relationship with third party contractors or manufacturers;
- development of new product candidates that may address our markets and may make our existing product candidates less attractive;
- changes in physician, hospital or healthcare provider practices that may make our product candidates less useful;
- announcements by us, our collaborators or our competitors of significant acquisitions, strategic partnerships, joint ventures, collaborations or capital commitments;
- developments or disputes concerning patent applications, issued patents or other proprietary rights;
- the recruitment or departure of key personnel;
- the level of expenses related to any of our product candidates or product development programs;
- failure to meet or exceed financial estimates and projections of the investment community or that we provide to the public;
- press reports or other negative publicity, whether or not true, about our business;
- the results of our efforts to discover, develop, acquire or in-license additional product candidates or products;
- actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts;
- 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;
- speculative trading in and short sales of our stock, as well as trading phenomena such as the “short squeeze”;
- general economic, industry and market conditions; and
- the other factors described in this "Risk Factors" section.

Any of these factors may result in large and sudden changes in the volume and trading price of our common stock. 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 biopharmaceutical 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.

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

Based on the number of shares of common stock outstanding as of December 31, 2021, our executive officers, directors and stockholders who own more than 5% of our outstanding common stock and their respective affiliates hold, in the aggregate, shares representing approximately 70% of our outstanding voting stock. As a result, if these stockholders were to 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 persons, if they choose to act together, would control or significantly influence the election of directors and approval of any merger, consolidation or sale of all or substantially all of our assets. They may also have interests that differ from yours and may vote in a way with which you disagree, and which may be adverse to your interests. This concentration of ownership control may have the effect of delaying, deferring or preventing a change in control of our company, could deprive our stockholders of an opportunity to receive a premium for their common stock as part of a sale of our company and might ultimately affect the market price of our common stock.

A significant portion of our total outstanding shares are eligible to be sold into the market, 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 approximately 18.4 million shares of our common stock as of December 31, 2021 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, including entities affiliated with Flagship Pioneering, until such shares can otherwise be sold without restriction under Rule 144 of the Securities Act or until the rights terminate pursuant to the terms of the investors' rights agreement between us and such holders. We have also registered and intend to continue to register all shares of common stock that we may issue under our equity compensation plans. Once we register these shares, they can be freely sold in the public market upon issuance, subject to volume limitations applicable to affiliates.

We have broad discretion in the use of our cash reserves and may not use them effectively.

Our management has broad discretion to use our cash reserves and could use our cash reserves in ways that do not improve our results of operations or enhance the value of our common stock. The failure by our management to apply these funds effectively could result in financial losses that could have a material adverse effect on our business, cause the price of our common stock to decline and delay the development of our product candidates. Pending their use, we may invest our cash reserves in a manner that does not produce income or that loses value.

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

We are an "emerging growth company" as that term is used in the Jumpstart Our Business Startups Act of 2012, (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 completion of the initial public offering of our common stock, or December 31, 2023, (b) in which we have total annual gross revenue of at least $1.07 billion, or (c) in which we are deemed to be a large accelerated filer, which means the market value of our outstanding common stock that are held by non-affiliates exceeds $700 million as of the prior June 30, 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:

- being permitted to provide only two years of audited financial statements, in addition to any required unaudited interim financial statements, with correspondingly reduced "Management's Discussion and Analysis of Financial Condition and Results of Operations" disclosure;
- not being required to comply with the auditor attestation requirements in the assessment of our internal control over financial reporting;
- not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements;
- reduced disclosure obligations regarding executive compensation; and
- exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and shareholder approval of any golden parachute payments not previously approved.

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. We have elected to take advantage of this extended transition period.

We are also a smaller reporting company, and we will remain a smaller reporting company until the fiscal year following the determination that our voting and non-voting common shares held by non-affiliates is more than $250 million measured on the last business day of our second fiscal quarter, and our annual revenues are more than $100 million during the most recently completed fiscal year and our voting and non-voting common shares held by non-affiliates is more than $700 million measured on the last business day of our second fiscal quarter. Similar to emerging growth companies, smaller reporting companies are able to provide simplified executive compensation disclosure, are exempt from the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002 ("Section 404") and have certain other reduced disclosure obligations, including, among other things, being required to provide only two years of audited financial statements and not being required to provide selected financial data, supplemental financial information or risk factors.

We have elected to take advantage of certain of the reduced reporting obligations, and may in the future take advantage of these or others. We cannot predict whether investors will find our common stock less attractive if we 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 price may be reduced or more volatile.

Provisions in our restated certificate of incorporation and amended and restated bylaws 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 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, such 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 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 restated certificate of incorporation provides that the Court of Chancery of the State of Delaware will be the exclusive forum for substantially all disputes between us and our stockholders, and our bylaws designate the federal district courts of the United States as the exclusive forum for actions arising under the Securities Act, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or other employees.

Our 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 any derivative action or proceeding brought on our behalf, any action asserting a claim of breach of

fiduciary duty owed by any director, officer, employee or stockholder to us or our stockholders, any action asserting a claim arising pursuant to any provision of the General Corporation Law of the State of Delaware or any action asserting a claim governed by the internal affairs doctrine. In addition, our bylaws provide that the federal district courts of the United States are the exclusive forum for any complaint raising a cause of action arising under the Securities Act. We believe these provisions benefit us by providing increased consistency in the application of Delaware law by chancellors particularly experienced in resolving corporate disputes and in the application of the Securities Act by federal judges, as applicable, efficient administration of cases on a more expedited schedule relative to other forums and protection against the burdens of multi-forum litigation. The provision may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes, and may have the effect of discouraging lawsuits, including those against our directors and officers. The enforceability of similar choice of forum provisions in other companies' certificates of incorporation and bylaws 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 restated certificate of incorporation or bylaws to be inapplicable or unenforceable in such action. If a court were to find the choice of forum provision contained in our restated certificate of incorporation or bylaws 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 results of operations and financial condition.

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

We have never declared or paid cash dividends on our capital stock. We currently intend to retain all of our future earnings, if any, to finance the operation and expansion of our business. Therefore, you should not rely on an investment in our common stock as a source for any future dividend income.

Our board of directors has significant discretion as to whether to distribute dividends. Even if our board of directors decides to declare and pay dividends, the timing, amount and form of future dividends, if any, will depend on, among other things, our future results of operations and cash flow, our capital requirements and surplus, our financial condition, contractual restrictions and other factors deemed relevant by our board of directors. Accordingly, the return on your investment in our common stock will likely depend entirely on any future capital appreciation, if any, of our common stock. There is no guarantee that our common stock will appreciate in value or even maintain the price at which you purchased our common stock.

Our ability to use net operating losses and research and development tax credits to offset future taxable income or tax liabilities may be subject to certain limitations.

As of December 31, 2021, we had approximately $189.7 million and $187.1 million of federal and state net operating losses ("NOLs"), respectively. The federal NOLs include $49.9 million which expire at various dates through 2036, and $139.7 million which carry forward indefinitely. Our ability to use such federal NOLs to offset taxable income is limited to 80% of taxable income with respect to taxable years beginning after December 31, 2020. Our state NOLs expire at various dates through 2041. As of December 31, 2021, we had federal and state research and development tax credits of $7.2 million and $3.3 million, respectively, which expire at various dates through 2041. A portion of these NOLs and the tax credit carryforwards could expire unused and be unavailable to offset future taxable income or income tax liabilities, respectively. In addition, in general, under Sections 382 and 383 of the United States Internal Revenue Code of 1986, as amended (the "Code"), a corporation that undergoes an "ownership change" is subject to limitations on its ability to utilize its pre-change NOLs or tax credits to offset future taxable income or tax liabilities. For these purposes, an ownership change generally occurs where the aggregate stock ownership of one or more stockholders or groups of stockholders who owns at least 5% of a corporation's stock increases its ownership by more than 50 percentage points over its lowest ownership percentage within a specified testing period. Our existing NOLs or tax credits may be subject to limitations arising from previous ownership changes. In addition, future changes in our stock ownership, many of which are outside of our control, could result in an ownership change under Sections 382 and 383 of the Code. Our state NOLs or tax credits may also be limited or impaired under state law. Our ability to utilize our NOLs or tax credits is also conditioned upon our attaining profitability and generating federal and state taxable income and income tax liabilities. We have incurred significant net losses since our inception and, therefore, we do not know whether or when we will generate the federal or state taxable income or income tax liabilities necessary to utilize our NOLs or tax credits. Accordingly, we may not be able to utilize a material portion of our NOLs or tax credits. In addition, we may be required to pay federal income taxes due to the 80% limitation on utilization of certain federal NOLs to offset taxable income, even if we have federal NOLs that are otherwise available for use.

General Risk Factors

We have incurred and expect to 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, we have incurred and expect to continue to incur significant legal, accounting and other expenses that we did not incur as a private company. These expenses will be even greater after we are no longer an emerging growth company and/or a smaller reporting 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 need to devote a substantial amount of time to these compliance initiatives.

Moreover, these rules and regulations have increased our legal and financial compliance costs and made some activities more time consuming and costly. For example, we expect that these rules and regulations may make it more difficult and more expensive for us to maintain 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 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, 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, 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, we 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 will need to continue to dedicate internal resources, potentially engage outside consultants and adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, there is a risk that we will not be able to conclude, within the prescribed timeframe or at all, that our internal control over financial reporting is effective as required by Section 404. 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 consolidated financial statements.

Our failure to maintain effective control over financial reporting and disclosure controls and procedures could result in errors in our financial statements, our failure to meet our reporting obligations, reduce investor confidence and adversely impact our stock price.

As a public company, we are required to maintain effective disclosure controls and procedures and internal control over financial reporting, and to report any material weaknesses in such internal controls. A material weakness is a deficiency, or combination of deficiencies, in internal control over financial reporting such that there is a reasonable possibility that a material misstatement of the annual or interim financial statements will not be prevented or detected on a timely basis. In October 2021, we identified a material weakness relating to an insufficient process for confirming final approvals for the release of reviewed and approved documentation prior to filing such documentation with the SEC. This material weakness did not result in any financial statement modifications, and there were no changes to our previously disclosed financial results. Additionally, in connection with the preparation of our financial statements in our Annual Report on Form 10-K for the fiscal year ended December 31, 2021 which we filed with the SEC on March 24, 2022, we identified a different material weakness relating to the review of certain financial transactions and the preparation and review of account reconciliations which were not performed using a sufficient level of precision and accuracy. No material financial statement misstatements were identified in relation to this material weakness in our internal control over financial reporting. The remediation efforts that we take to address a material weakness need to be completed and operating effectively for a sufficient period of time before

we are able to deem such material weakness fully remediated. See Part I, Item 4 “Controls and Procedures” for additional information about these material weaknesses and our remediation efforts.

If we identify other material weaknesses or identify deficiencies that individually or together constitute significant deficiencies or material weaknesses, or if the additional controls and processes that we implement to remediate any identified material weaknesses prove to be insufficient, our ability to accurately record, process and report financial information and, consequently, our ability to prepare financial statements within required time periods could be adversely affected and we may be unable to assure that information required to be disclosed by us in reports that 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.

Furthermore, disclosure controls and procedures or internal 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.

The discovery of additional deficiencies could result in violations of applicable securities laws, stock exchange listing requirements and agreements to which we are subject, subject us to litigation and investigations, negatively affect investor confidence in our financial statements and adversely impact our stock price and ability to hinder our ability to access capital markets.

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 business, our stock price and trading volume could decline.

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. If any of the analysts who cover us issue an adverse or misleading opinion regarding us, our business model, our intellectual property or our stock performance, or if our preclinical studies or clinical trials and/or operating results fail to meet the expectations of analysts, our stock price would likely decline. If one or more of these analysts cease coverage of us or fail 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.

Unfavorable global political or economic conditions could adversely affect our business, financial condition or results of operations.

Our results of operations could be adversely affected by general conditions in the global economy and in the global financial markets. For example, the global financial crisis caused extreme volatility and disruptions in the capital and credit markets. A severe or prolonged economic downturn, such as the global financial crisis, could result in a variety of risks to our business, including our ability to raise additional capital when needed on acceptable terms, if at all. There can be no assurance that further deterioration in credit and financial markets and confidence in economic conditions will not occur. A weak or declining economy could also strain our suppliers, possibly resulting in supply disruption, or cause our customers to delay making payments for our services. In addition, military conflict such as that between Russia and Ukraine could disrupt or otherwise adversely impact our operations and those of third parties upon which we rely. Related sanctions, export controls or other actions have and may in the future be initiated by nations including the U.S., the EU or Russia (e.g., potential cyberattacks, disruption of energy flows, etc.), which could adversely affect our business and/or our supply chain, our CROs, CMOs and other third parties with which we conduct business. Any of the foregoing could harm our business and we cannot anticipate all of the ways in which the current economic climate and financial market conditions could adversely impact our business.

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

There were no sales of unregistered equity securities during the three months ended March 31, 2022.

Item 3. Defaults Upon Senior Securities.

None.

Item 4. Mine Safety Disclosures

Not applicable.

Item 5. Other Information

On May 11, 2022, we provided notice to terminate the patent license agreement between us and the University of Chicago, which we initially entered into in March 2016 (the "2016 University of Chicago Agreement"). Pursuant to the terms of the 2016 University of Chicago Agreement, such termination will be effective on July 11, 2022. None of our current or anticipated product candidates depends on any license subject to the 2016 University of Chicago Agreement.

Item 6. Exhibits

Exhibit Number	Exhibit Description	Incorporated by Reference				Filed Herewith
		Form	File No.	Exhibit	Filing Date	
3.1	Restated Certificate of Incorporation of Evelo Biosciences, Inc.	8-K	001-38473	3.1	5/11/2018	
3.2	Amended and Restated Bylaws of Evelo Biosciences, Inc.	8-K	001-38473	3.1	3/18/2021	
10.1	Evelo Biosciences, Inc. Non-Employee Director Compensation Program, as amended, effective April 1, 2022	10-K	001-38473	10.5	3/24/2022	
10.2	Amendment No. 1 to Clinical Master Services Agreement between Evelo Biosciences, Inc. and Halo Pharmaceutical, Inc. d/b/a Cambrex Whippany, dated February 8, 2022	10-K	001-38473	10.21	3/24/2022	
31.1	Certification of Principal Executive Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.					*
31.2	Certification of Principal Financial Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.					*
32.1	Certification of Principal Executive Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.					**
32.2	Certification of Principal Financial Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.					**
101.INS	Inline XBRL Instance Document- the Instance Document does not appear in the interactive data file because its XBRL tags are embedded within the Inline XBRL document					*
101.SCH	Inline XBRL Taxonomy Extension Schema Document					*
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document					*
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document					*
101.LAB	Inline XBRL Taxonomy Extension Label Linkbase Document					*
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document					*
104	Cover Page Interactive Data File (formatted as Inline XBRL and contained in Exhibit 101)					*

* Filed herewith

** Furnished herewith

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed by the following persons on behalf of the registrant in the capacities and on the dates indicated.

EVELO BIOSCIENCES, INC.

Date: May 12, 2022 By: /s/ Balkrishan (Simba) Gill, Ph.D.

Balkrishan (Simba) Gill, Ph.D.
President and Chief Executive Officer
(Principal Executive Officer)

Date: May 12, 2022 By: /s/ Luca Scavo

Luca Scavo
Chief Financial Officer
(Principal Financial Officer)

Exhibit 31.1

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

I, Balkrishan (Simba) Gill, Ph.D., certify that:

1. I have reviewed this Quarterly Report on Form 10-Q for the quarterly period ended March 31, 2022 of Evelo Biosciences, Inc.;

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

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

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

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

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

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

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

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

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

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

Date: May 12, 2022

By: /s/ Balkrishan (Simba) Gill, Ph.D.
Balkrishan (Simba) Gill, Ph.D.
President and Chief Executive Officer
(Principal Executive Officer)

Exhibit 31.2

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

I, Luca Scavo, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q for the quarterly period ended March 31, 2022 of Evelo Biosciences, Inc.;

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

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

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

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

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

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

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

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

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

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

Date: May 12, 2022

By: /s/ Luca Scavo

Luca Scavo

Chief Financial Officer, Senior Vice President and Treasurer

(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

I, Balkrishan (Simba) Gill, Ph.D., President and Chief Executive Officer of Evelo Biosciences, Inc. (the "Company"), hereby certify, pursuant to 18 U.S.C. § 1350, as adopted pursuant to § 906 of the Sarbanes-Oxley Act of 2002, that, to the best of my knowledge:

(1) the Company's Quarterly Report on Form 10-Q for the quarterly period ended March 31, 2022 (the "Report") fully complies with the requirements of Sections 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended; and

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

Date: May 12, 2022

By: /s/ Balkrishan (Simba) Gill, Ph.D.

Balkrishan (Simba) Gill, Ph.D.
President and Chief Executive Officer
(Principal Executive Officer)

Exhibit 32.2

CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

I, Luca Scavo, Chief Financial Officer, Senior Vice President and Treasurer of Evelo Biosciences, Inc. (the "Company"), hereby certify, pursuant to 18 U.S.C. § 1350, as adopted pursuant to § 906 of the Sarbanes-Oxley Act of 2002, that, to the best of my knowledge:

(1) the Company's Quarterly Report on Form 10-Q for the quarterly period ended March 31, 2022 (the "Report") fully complies with the requirements of Sections 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended; and

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

Date: May 12, 2022

By: /s/ Luca Scavo

Luca Scavo

Chief Financial Officer, Senior Vice President and Treasurer

(Principal Financial Officer)