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

(Mark One)

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

For the quarterly period ended September 30, 2019

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)

N/A

(Former name, former address and former fiscal year, if changed since last report)

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 October 31, 2019, the registrant had 32,085,829 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. We intend such forward-looking statements to be covered by the safe harbor provisions for forward-looking statements contained in Section 27A of the Securities Act of 1933, as amended (the "Securities Act") and Section 21E of the Securities Exchange Act of 1934, as amended (the "Exchange Act"). All statements other than statements of historical facts contained in this Quarterly Report on Form 10-Q, including statements regarding our future results of operations and financial position, business strategy, prospective products, product approvals, research and development costs, timing and plans for clinical trials, expected timing of the release of clinical trial data, new formulations and product candidates, plans and objectives of management for future operations and future results of anticipated products, are forward-looking statements. These statements involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements.

In some cases, you can identify forward-looking statements by terms such as “may,” “will,” “should,” “expect,” “plan,” “anticipate,” “could,” “intend,” “target,” “project,” “contemplate,” “believe,” “estimate,” “predict,” “potential” or “continue” or the negative of these terms or other similar expressions. 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. These forward-looking statements speak only as of the date of this Quarterly Report on Form 10-Q and are subject to a number of risks, uncertainties and assumptions described under the sections in this Quarterly Report on Form 10-Q entitled “Risk Factors” and “Management’s Discussion and Analysis of Financial Condition and Results of Operations” and elsewhere in this Quarterly Report on Form 10-Q. These forward-looking statements are subject to numerous risks, including, without limitation, the following:

- our status as a development-stage company and our expectation to incur losses in the future;
- our future capital needs and our need to raise additional funds;
- our ability to build a pipeline of product candidates and develop and commercialize drugs;
- our unproven approach to therapeutic intervention;
- our ability to enroll patients and volunteers in clinical trials, timely and successfully complete those trials and receive necessary regulatory approvals;
- our ability to establish our own manufacturing facilities and to receive or manufacture sufficient quantities of our product candidates;
- our ability to protect and enforce our intellectual property rights;
- federal, state, and foreign regulatory requirements, including FDA regulation of our product candidates;
- the timing of clinical trials and the likelihood of regulatory filings and approvals;
- our ability to obtain and retain key executives and attract and retain qualified personnel; and
- our ability to successfully manage our growth.

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.

As forward-looking statements are inherently subject to risks and uncertainties, some of which cannot be predicted or quantified and some of which are beyond our control, you should not rely on these forward-looking statements as predictions of future events. The events and circumstances reflected in our forward-looking statements may not occur or be achieved, and actual results could differ materially from those projected in the forward-looking statements. We qualify all of our forward-looking statements by these cautionary statements. Except as required by applicable law, we do not plan to publicly update or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise.

Evelo Biosciences, Inc.
Form 10-Q for the Quarterly Period Ended September 30, 2019

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PART I—FINANCIAL INFORMATION

Item 1. Financial Statements.

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

	September 30, 2019	December 31, 2018
Assets		
Current assets:		
Cash and cash equivalents	$ 97,061	$ 93,101
Short-term investments	—	54,818
Prepaid expenses and other current assets	4,170	3,703
Total current assets	101,231	151,622
Property and equipment, net	8,339	6,925
Other assets	1,570	1,320
Total assets	$ 111,140	$ 159,867
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 1,358	$ 1,519
Accrued expenses	7,919	4,965
Other current liabilities	398	2,751
Total current liabilities	9,675	9,235
Noncurrent liabilities:		
Long-term debt, net of current portion	19,549	12,305
Deferred rent, net of current portion	1,146	1,071
Other noncurrent liabilities	224	307
Total liabilities	30,594	22,918
Commitments and contingencies		
Stockholder's equity:		
Preferred stock, $0.001 par value; 10,000,000 shares authorized; no shares issued or outstanding at September 30, 2019 and December 31, 2018, respectively	—	—
Common stock, $0.001 par value; 200,000,000 shares authorized; 32,147,073 and 31,951,540 shares issued and 32,072,030 and 31,825,769 shares outstanding at September 30, 2019 and December 31, 2018, respectively	32	32
Additional paid-in capital	256,768	250,316
Accumulated other comprehensive loss	—	(18)
Accumulated deficit	(176,254)	(113,381)
Total stockholders' equity	80,546	136,949
Total liabilities and stockholders' equity	$ 111,140	$ 159,867

See accompanying notes to condensed consolidated financial statements.

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

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2019	2018	2019	2018
Operating expenses:				
Research and development	$ 15,610	$ 11,227	$ 46,751	$ 28,542
General and administrative	5,886	5,230	16,936	13,568
Total operating expenses	21,496	16,457	63,687	42,110
Loss from operations	(21,496)	(16,457)	(63,687)	(42,110)
Other income (expense):				
Interest income, net	81	600	1,032	1,013
Other expenses	(218)	—	(218)	(406)
Other income (expense), net	(137)	600	814	607
Net loss	$ (21,633)	$ (15,857)	$ (62,873)	$ (41,503)
Convertible preferred stock dividends	—	—	—	(3,937)
Net loss attributable to common stockholders	$ (21,633)	$ (15,857)	$ (62,873)	$ (45,440)
Net loss per share attributable to common stockholders, basic and diluted	$ (0.67)	$ (0.50)	$ (1.96)	$ (2.45)
Weighted-average number of common shares outstanding, basic and diluted	32,060,747	31,741,683	32,009,571	18,532,408
Comprehensive loss:				
Net loss	$ (21,633)	$ (15,857)	$ (62,873)	$ (41,503)
Other comprehensive loss:				
Unrealized gain (loss) on investments, net of tax of $0	(1)	(38)	18	(38)
Comprehensive loss	$ (21,634)	$ (15,895)	$ (62,855)	$ (41,541)

See accompanying notes to condensed consolidated financial statements.

Evelo Biosciences, Inc.
Condensed Consolidated Statements of Preferred Stock and Stockholders' Equity
(Unaudited, in thousands, except share amounts)

	Nine Month Periods Ended September 30, 2019							
	Preferred Stock		Common Stock		Additional Paid-in Capital	Accumulated Other Comprehensive Loss	Accumulated Deficit	Total
	Shares	Amount	Shares	Amount				
Balance-December 31, 2018	—	$ —	31,825,769	$ 32	$ 250,316	$ (18)	$ (113,381)	$ 136,949
Vesting of restricted common stock	—	—	23,345	—	7	—	—	7
Exercise of stock options and warrants	—	—	181,521	—	257	—	—	257
Stock-based compensation expense	—	—	—	—	1,953	—	—	1,953
Unrealized gain on investments	—	—	—	—	—	16	—	16
Net loss	—	—	—	—	—	—	(20,299)	(20,299)
Balance-March 31, 2019	—	$ —	32,030,635	$ 32	$ 252,533	$ (2)	$ (133,680)	$ 118,883
Vesting of restricted common stock	—	—	13,692	—	7	—	—	7
Exercise of stock options	—	—	1,379	—	1	—	—	1
Stock-based compensation expense	—	—	—	—	2,135	—	—	2,135
Unrealized gain on investments	—	—	—	—	—	3	—	3
Net loss	—	—	—	—	—	—	(20,941)	(20,941)
Balance-June 30, 2019	—	$ —	32,045,706	$ 32	$ 254,676	$ 1	$ (154,621)	$ 100,088
Vesting of restricted common stock	—	—	13,691	—	7	—	—	7
Exercise of stock options	—	—	12,633	—	23	—	—	23
Stock-based compensation expense	—	—	—	—	2,062	—	—	2,062
Unrealized gain on investments	—	—	—	—		(1)	—	(1)
Net loss	—	—	—	—	—	—	(21,633)	(21,633)
Balance-September 30, 2019	—	$ —	32,072,030	$ 32	$ 256,768	$ —	$ (176,254)	$ 80,546

See accompanying notes to condensed consolidated financial statements.

Evelo Biosciences, Inc.
Condensed Consolidated Statements of Convertible Preferred Stock, Preferred Stock and Stockholders' Equity (Deficit)
(Unaudited, in thousands, except share amounts)

	Nine Month Periods Ended September 30, 2018									
	Convertible Preferred Stock		Preferred Stock		Common Stock		Additional Paid-in Capital	Accumulated Other Comprehensive Loss	Accumulated Deficit	Total
	Shares	Amount	Shares	Amount	Shares	Amount				
Balance-December 31, 2017	65,833,096	$ 83,702	—	$ —	3,880,607	$ 4	$ 1,708	$ —	$ (56,435)	$ (54,723)
Issuance of Series B and Series C Preferred Stock, net of issuance costs	25,482,199	82,076	—	—	—	—	—	—	—	—
Vesting of restricted common stock	—	—	—	—	31,557	—	11	—	—	11
Exercise of stock options and warrants	—	—	—	—	31,765	—	35	—	—	35
Stock-based compensation expense	—	—	—	—	—	—	652	—	—	652
Net loss	—	—	—	—	—	—	—	—	(10,500)	(10,500)
Balance-March 31, 2018	91,315,295	$ 165,778	—	$ —	3,943,929	$ 4	$ 2,406	$ —	$ (66,935)	$ (64,525)
Proceeds from Initial Public Offering, net of underwriting costs and commissions	—	—	—	—	5,312,500	5	75,793	—	—	75,798
Conversion of preferred stock into common stock	(91,315,295)	(165,778)	—	—	22,386,677	22	165,756	—	—	165,778
Reclassification of warrant liability	—	—	—	—	—	—	879	—	—	879
Vesting of restricted common stock	—	—	—	—	31,572	—	11	—	—	11
Exercise of stock options and warrants	—	—	—	—	51,408	1	4	—	—	5
Stock-based compensation expense	—	—	—	—	—	—	2,247	—	—	2,247
Unrealized gain on investments	—	—	—	—	—	—	—	—	—	—
Net loss	—	—	—	—	—	—	—	—	$ (15,146)	$ (15,146)
Balance-June 30, 2018	—	$ —	—	$ —	31,726,086	$ 32	$ 247,096	$ —	$ (82,081)	$ 165,047
Vesting of restricted common stock	—	—	—	—	25,816	—	7	—	—	7
Exercise of stock options	—	—	—	—	5,805	—	5	—	—	5
Stock-based compensation expense	—	—	—	—	—	—	1,595	—	—	1,595
Unrealized gain on investments	—	—	—	—	—	—	—	(38)	—	(38)
Net loss	—	—	—	—	—	—	—	—	$ (15,857)	$ (15,857)
Balance-September 30, 2018	—	$ —	—	$ —	31,757,707	$ 32	$ 248,703	$ (38)	$ (97,938)	$ 150,759

See accompanying notes to condensed consolidated financial statements.

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

	Nine Months Ended September 30,	
	2019	**2018**
Operating activities		
Net loss	$ (62,873)	$ (41,503)
Adjustments to reconcile net loss to net cash used in operating activities:		
Stock-based compensation expense	6,150	4,494
Depreciation expense	1,264	1,575
Change in fair value of warrant and debt derivative liability	—	406
Net (accretion of discount)/amortization of premium on marketable securities	(164)	—
Non-cash interest expense	263	78
Gain on sale of fixed assets	(2)	—
Changes in assets and liabilities:		
Prepaid expenses and other current assets	(633)	(3,180)
Accounts payable	90	1,375
Accrued expenses and other current liabilities	2,907	4,314
Other liabilities	12	618
Net cash used in operating activities	(52,986)	(31,823)
Investing activities		
Purchase of investments	—	(84,653)
Proceeds from sales and maturities of investments	55,000	—
Purchases of property and equipment	(2,569)	(4,227)
Proceeds from the sale of fixed assets	2	171
Net cash provided by/(used in) investing activities	52,433	(88,709)
Financing activities		
Proceeds from the issuance of common stock upon completion of initial public offering	—	85,000
Net proceeds from the issuance of convertible preferred stock	—	81,336
Net proceeds from the issuance of long-term debt	19,481	4,975
Repayment of long-term debt	(15,000)	—
Cash payment of initial public offering issuance costs	—	(9,171)
Settlement of derivative liability	—	(250)
Proceeds from the exercise of stock options, restricted common stock and warrants	282	104
Net cash provided by financing activities	4,763	161,994
Net increase in cash, cash equivalents and restricted cash	4,210	41,462
Cash, cash equivalents and restricted cash – beginning of period	94,351	39,746
Cash, cash equivalents and restricted cash – end of period	$ 98,561	$ 81,208
Supplemental disclosure of cash flow information		
Cash paid for interest	$ 728	$ 535
Noncash investing and financing activities		
Conversion of convertible preferred stock into common stock upon closing of initial public offering	$ —	$ 165,778
Property and equipment additions in accounts payable and accrued expenses	$ 290	$ 176
Conversion of convertible preferred stock warrants into common stock warrants	$ —	$ 819
Issuance of debt derivative liability in connection with long-term debt facility	$ —	$ 150
Issuance of warrants in connection with long-term debt facility	$ —	$ 89

See accompanying notes to the condensed consolidated financial statements.

EVELO BIOSCIENCES, INC.

NOTES TO CONDENSED CONSOLIDATED FINANCIAL STATEMENTS (unaudited)

1. Organization

Evelo Biosciences, Inc. ("Evelo" or the "Company") is a biotechnology company which was incorporated in Delaware on May 6, 2014. The Company is discovering and developing oral biologics designed to engage immune cells in the small intestine and drive therapeutic effects throughout the body. The Company is advancing these monoclonal microbials with the aim of treating a broad range of immune mediated diseases with an initial focus on inflammatory diseases and oncology. The Company is headquartered in Cambridge, Massachusetts.

Since inception, the Company has devoted substantially all of its efforts to research and development and raising capital. The Company has not generated any revenue related to its primary business purpose to date. The Company is subject to a number of risks similar to those of other development stage companies, including dependence on key individuals, the need to develop commercially viable products, 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 its products.

The Company has funded its operations from the issuance of convertible notes, convertible preferred stock, common stock and debt financing. At September 30, 2019, the Company had cash and cash equivalents of $97.1 million and an accumulated deficit of $176.3 million.

The Company has incurred operating losses since inception and expects such losses and negative operating cash flows to continue for the foreseeable future. The transition to profitability is dependent upon the successful development, approval, and commercialization of its products and product candidates and the achievement of a level of revenues adequate to support its cost structure. Based on the Company's current operating plan, the Company believes that its cash and cash equivalents at September 30, 2019, along with the capacity to borrow an additional $10.0 million under the 2019 Credit Facility (see note 6), will 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. Management's belief with respect to its ability to fund operations is based on estimates that are subject to risks and uncertainties. If actual results are different from management's estimates, the Company may need to seek additional funding sooner than would otherwise be expected. There can be no assurance that the Company will be able to obtain additional funding on acceptable terms, if at all.

2. Summary of Significant Accounting Policies

Basis of Presentation

The accompanying unaudited interim condensed consolidated financial statements have been 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 Accounting Standards Updates ("ASU") of the Financial Accounting Standards Board ("FASB"). Certain information and footnote disclosures normally included in financial statements prepared in accordance with U.S. GAAP have been condensed or omitted from this report, as is permitted by such rules and regulations. Accordingly, these financial statements should be read in conjunction with the Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2018 and notes thereto. The unaudited interim consolidated financial statements have been prepared on the same basis as the audited financial statements. In the opinion of the Company's management, the accompanying unaudited interim condensed consolidated financial statements contain all adjustments which are necessary to present fairly the Company's financial position as of September 30, 2019, the results of its operations and stockholders' equity for the three and nine months ended September 30, 2019 and 2018 and cash flows for the nine months ended September 30, 2019 and 2018. Such adjustments are of a normal and recurring nature. The results for the three and nine months ended September 30, 2019 are not necessarily indicative of the results for the year ending December 31, 2019, or for any future period.

Use of Estimates

The preparation of 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 condensed consolidated financial statements include, but are not limited to, the accrual of research and development expenses and the valuation of stock-based awards. The Company bases its estimates on historical experience and other market-specific or other relevant assumptions that it believes 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 the Company and its wholly owned, controlled subsidiaries. All intercompany transactions and balances have been eliminated in consolidation.

Subsequent Event Considerations

The Company considers events or transactions that occur after the balance sheet date but prior to the issuance of the consolidated financial statements to provide additional evidence for certain estimates or to identify matters that require additional disclosure. Subsequent events have been evaluated as required. The Company has evaluated all subsequent events and determined that there are no material recognized or unrecognized subsequent events requiring disclosure, other than those disclosed in this Quarterly Report on Form 10-Q.

Emerging Growth Company Status

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

Comprehensive Loss

Comprehensive loss includes net loss and certain changes in stockholders’ equity that are excluded from net loss. The Company's only element of other comprehensive income (loss) is unrealized gains and losses on available-for-sale investments. Comprehensive loss totaled $21.6 million and $62.9 million for the three and nine months ended September 30, 2019, respectively, and $15.9 million and $41.5 million for the three and nine months ended September 30, 2018, and was not significantly different than net loss in any period. For the nine months ended September 30, 2018 comprehensive loss was equal to net loss.

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. Cash and cash equivalents include cash held in banks and amounts held in money market funds and U.S. treasuries with original maturities of three months or less. Cash equivalents are stated at cost, which approximates market value. The Company’s restricted cash consists of restricted cash in connection with building leases for the Company’s office and laboratory premises and deposits held in relation to the company's credit card facility. Restricted cash totaled approximately $1.5 million and $1.3 million at September 30, 2019 and December 31, 2018, respectively, and is classified within other assets on the accompanying condensed consolidated balance sheet. The following reconciles cash, cash equivalents and restricted cash as of September 30, 2019 and December 31, 2018, as presented on the Company's statements of cash flows, to its related balance sheet accounts (in thousands):

	September 30, 2019	December 31, 2018
Cash and cash equivalents:		
Cash	$ 1,304	$ 1,300
Money market funds	95,757	91,801
Total cash and cash equivalents	97,061	93,101
Restricted cash	1,500	1,250
Cash, cash equivalents and restricted cash	$ 98,561	$ 94,351

Investments

The Company accounts for and classifies its investments as either “available-for-sale,” “trading,” or “held-to-maturity,” in accordance with the accounting guidance related to the accounting and classification of certain investments in debt and equity securities. The determination of the appropriate classification is based primarily on management’s intent to sell the investment at the time of purchase. The Company did not have any investments at September 30, 2019. As of December 31, 2018 all of the Company's investments were classified as available-for-sale securities.

Available-for-sale securities are those securities which the Company views as available for use in current operations, if needed. The Company generally classifies its available-for-sale securities as short-term investments, even though the stated maturity date may be one year or more beyond the current balance sheet date. Available-for-sale investments are stated at fair value with their unrealized gains and losses included in accumulated other comprehensive loss within stockholders’ (deficit) equity, until such gains and losses are realized in other income (expense) within the condensed consolidated statements of operations and comprehensive loss or until an unrealized loss is considered other-than-temporary.

The Company recognizes other-than-temporary impairments of its investments in debt securities when there is a decline in fair value below the amortized cost basis and if (a) it has the intent to sell the security or (b) it is more likely than not that the Company will be required to sell the security prior to recovery of its amortized cost basis. If either of these conditions is met, the Company recognizes the difference between the amortized cost of the security and its fair value at the impairment measurement date in the condensed consolidated statements of operations and comprehensive loss. If neither of these conditions is met, the Company must perform an additional analysis to evaluate whether the unrealized loss is associated with the creditworthiness of the issuer of the security rather than other factors, such as interest rates or market factors. If the Company determines from this analysis that it does not expect to receive cash flows sufficient to recover the entire amortized cost of the security, a credit loss exists, the impairment is considered other-than-temporary and is recognized in its condensed consolidated statements of operations and comprehensive loss.

Fair Value of Financial Instruments

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 the Company’s own assumptions (unobservable inputs). Observable inputs are inputs that market participants would use in pricing the asset or liability based on market data obtained from sources independent of the Company. Unobservable inputs are inputs that reflect the Company’s assumptions about the inputs that market participants would use in pricing the asset or liability and are developed based on the best information available in the circumstances.

ASC 820 identifies fair value as the exchange price, or exit price, representing the amount that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants. 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 the Company’s 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 exercised by the Company in determining fair value is greatest for instruments categorized in Level 3. A financial instrument's level within the fair value hierarchy is based on the lowest level of any input that is significant to the fair value measurement.

An entity may choose to measure many financial instruments and certain other items at fair value at specified election dates. Subsequent unrealized gains and losses on items for which the fair value option has been elected will be reported in earnings. The Company did not elect to measure any additional financial instruments or other items at fair value.

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 such as payroll, consulting, and manufacturing costs associated with the development of the Company's 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 the Company by its 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 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.

The Company has and may continue to acquire the rights to develop and commercialize new product candidates from third parties. The upfront payments to acquire 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

The Company records stock-based compensation for options 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. The Company uses the Black-Scholes option-pricing model to determine the fair value of stock options. The determination of the fair value of stock options on the date of grant using an option-pricing model is affected by the Company's common stock price, as well as a number of other assumptions. The Company records forfeitures as they occur.

The Company accounts for stock-based compensation arrangements with non-employees based upon the fair value of the consideration received or the equity instruments issued, whichever is more reliably measurable. The measurement date for non-employee awards is generally the date performance of services required from the non-employee is complete. Stock-based compensation costs for non-employee awards are recognized as services are provided, which is generally the vesting period, on a straight-line basis. The unvested portion of the stock options is subject to re-measurement over the vesting period and forfeitures are recorded as they occur.

Segments

The Company has one operating segment. The Company's chief operating decision maker, its Chief Executive Officer, manages the Company's operations on a consolidated basis for the purposes of allocating resources.

Recently Adopted Accounting Pronouncements

In May 2014, the FASB issued ASU No. 2014-09, *Revenue from Contracts with Customers* (Topic 606) (“ASU 2014-09”), and further updated through ASU 2016-12 (“ASU 2016-12”), which amends the existing accounting standards for revenue recognition. ASU 2014-09 is based on principles that govern the recognition of revenue at an amount to which an entity expects to be entitled when products are transferred to customers. This guidance is effective for annual reporting periods, and interim periods within those years, beginning after December 15, 2017, for public entities and no later than for annual reporting periods beginning after December 15, 2018, for non-public entities. The new revenue standard may be applied retrospectively to each prior period presented or retrospectively with the cumulative effect recognized as of the date of adoption. The Company adopted ASU 2014-09 on January 1, 2019 and has concluded that the adoption did not have a material impact on its consolidated financial statements as the Company is not yet generating revenues.

In November 2018, the FASB issued ASU No. 2018-18, *Collaborative Arrangements* (Topic 808)-Clarifying the Interaction between Topic 808 and Topic 606 ("ASU 2018-18"). The amendments in ASU 2018-18 make targeted improvements to U.S. GAAP for collaborative arrangements by clarifying that certain transactions between collaborative arrangement participants should be accounted for as revenue under Topic 606 when the collaborative arrangement participant is a customer in the context of a unit of account. In those situations, all the guidance in Topic 606 should be applied, including recognition, measurement, presentation, and disclosure requirements. In addition, unit-of-account guidance in Topic 808 was aligned with the guidance in Topic 606 (that is, a distinct good or service) when an entity is assessing whether the collaborative arrangement or a part of the arrangement is within the scope of Topic 606. ASU 2018-18 is effective for fiscal years beginning after December 15, 2019, and interim periods within those fiscal years. Early adoption is permitted, including adoption in any interim period. The amendments in this Update should be applied retrospectively to the date of initial application of Topic 606. The Company adopted ASU 2018-18 on January 1, 2019 and has concluded the adoption did not have a material impact on its consolidated financial statements as the Company does not have any collaborative agreements under which any participant is considered a customer of the Company.

Accounting Pronouncements Issued and Not Adopted as of September 30, 2019

In February 2016, the FASB issued ASU 2016-2, Leases (Topic 842) (“ASU 2016-2”), which supersedes the guidance in former ASC 840, Leases. The new standard requires lessees to apply a dual approach, classifying leases as either finance or operating leases based on the principle of whether or not the lease is effectively a financed purchase by the lessee. This classification will determine whether lease expense is recognized based on an effective interest method or on a straight-line basis over the term of the lease. A lessee is also required to record a right-of-use asset and a lease liability for all leases with a term of greater than 12 months regardless of their classification. Leases with a term of 12 months or less will be accounted for similar to the historical guidance for operating leases. This guidance is effective for annual reporting periods, and interim periods within those years, beginning after December 15, 2018 for most public entities. Early adoption is permitted for all entities. Although its assessment is not complete, the Company currently expects the adoption of this guidance to result in the addition of material balances of leased assets and corresponding lease liabilities to its consolidated balance sheets, primarily relating to leases of office space.

In June 2018, the FASB issued ASU No. 2018-07, Stock-based Compensation: Improvements to Nonemployee Share-based Payment Accounting (Topic 718) ("ASU 2018-07"), which amends the existing accounting standards for share-based payments to nonemployees. This ASU aligns much of the guidance on measuring and classifying nonemployee awards with that of awards to employees. Under the new guidance, the measurement of nonemployee equity awards is fixed on the grant date. This ASU becomes effective in the first quarter of fiscal year 2020 and early adoption is permitted but no earlier than the Company's adoption date of Topic 606. Entities will apply the ASU by recognizing a cumulative-effect adjustment to retained earnings as of the beginning of the annual period of adoption. The Company is currently evaluating the impact that ASU 2018-07 will have on its consolidated financial statements.

3. Investments

As of September 30, 2019 the Company did not hold any short-term investments. As of December 31, 2018, the Company had short-term investments, consisting entirely of U.S. treasury securities, of $54.8 million, respectively.

The following tables summarize the Company's investments held at December 31, 2018, which are all classified as available-for-sale (in thousands):

Description	Amortized cost	Unrealized Gain	Unrealized Loss	Fair Value
December 31, 2018:				
U.S. treasury securities	$ 54,836	$ —	$ (18)	$ 54,818
Total	$ 54,836	$ —	$ (18)	$ 54,818

The amortized cost of available-for-sale securities is adjusted for amortization of premiums and accretion of discounts to maturity. At September 30, 2019 the Company had no accumulated other comprehensive loss. There were no material realized gains or losses recognized on the sale or maturity of available-for-sale securities during the three and nine months ended September 30, 2019 or 2018, and as a result, the Company did not reclassify any amounts out of accumulated other comprehensive loss for the same periods.

As of December 31, 2018, the aggregate fair value of securities held by the Company in an unrealized loss position for less than twelve months was $54.8 million, and none of these securities had remaining maturities of greater than three years. The Company has the intent and ability to hold such securities until recovery. The Company determined that there has been no material change in the credit risk of the above investments. As a result, the Company determined it did not hold any investments with any other-than-temporary impairment as of December 31, 2018.

4. Fair Value Measurements

The following tables present information about the Company's financial assets and liabilities that have been measured at fair value as of September 30, 2019 and December 31, 2018 (in thousands):

Description	September 30, 2019	Active Markets (Level 1)	Observable Inputs (Level 2)	Unobservable Inputs (Level 3)
Assets:				
Money market funds included within cash and cash equivalents	$ 95,757	$ 95,757	$ —	$ —
Total	$ 95,757	$ 95,757	$ —	$ —

Description	December 31, 2018	Active Markets (Level 1)	Observable Inputs (Level 2)	Unobservable Inputs (Level 3)
Assets:				
Money market funds included within cash and cash equivalents	$ 91,801	$ 91,801	$ —	$ —
U.S. treasury securities included within short-term investments	54,818	—	54,818	—
Total	$ 146,619	$ 91,801	$ 54,818	$ —

As of September 30, 2019 and December 31, 2018, the Company's cash equivalents and short-term investments have been initially valued at the transaction price and subsequently valued utilizing a third party pricing service. The Company validates the prices provided by its third-party pricing service by understanding the models used and obtaining market values from other pricing sources.

5. Property and Equipment, Net

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

	September 30, 2019	December 31, 2018
Property and equipment:		
Lab equipment	$ 7,300	$ 5,393
Leasehold improvements	1,944	1,824
Furniture and fixtures	701	525
Computers and software	200	115
Office equipment	9	9
Construction-in-process	1,394	1,011
Property and equipment	11,548	8,877
Less: accumulated depreciation	(3,209)	(1,952)
Property and equipment, net	$ 8,339	$ 6,925

The Company recognized $0.5 million and $1.3 million of depreciation expense for the three and nine months ended September 30, 2019, respectively, and $0.3 million and $1.6 million for the three and nine months ended September 30, 2018, respectively.

6. Loan and Security Agreements

2016 Credit Facility

In 2016, the Company entered into a credit facility (the “2016 Credit Facility”) with a bank that allowed the Company to borrow up to $15.0 million. Borrowings under the 2016 Credit Facility were secured by a lien on all Company assets, excluding intellectual property.

Prior to 2018, a total of $10.0 million was drawn under the 2016 Credit Facility, and in February 2018, the Company drew the remaining $5.0 million available. This resulted in an increase to the interest rate to the higher of (i) prime plus 0.25% or (ii) 4.50% per annum and extended the interest only payment period was extended through to August 15, 2019. Upon the expiration of the interest only period, amounts borrowed will be repaid over 24 equal monthly payments of principal plus interest accrued through August 15, 2021. The Company had the ability to prepay the outstanding balance of the 2016 Credit Facility at its option with a prepayment fee of 2% of principal amount if prepayment was made before August 15, 2018 or 0.5% if the prepayment was made between August 15, 2018 and August 15, 2019.

In conjunction with the February 2018 drawdown, the Company issued a warrant to purchase up to 34,722 shares of the Company’s Series B preferred stock at an exercise price of $1.80 per share. As part of the February 2018 drawdown, the loan and security agreement was amended to include the payment of a $0.3 million success fee to the financial institution in the event of a liquidation event, including an initial public offering. The success fee represented an embedded derivative which the Company bifurcated from the debt arrangement and carried at fair value. In May 2018, the Company completed its initial public offering (the "IPO") and paid the success fee of $0.3 million. In addition, the warrant issued in February 2018 was exercised in May 2018.

The 2016 Credit Facility contained negative covenants restricting the Company’s activities, including limitations on cash deposits, dispositions, mergers or acquisitions, incurring indebtedness or liens, paying dividends or making investments and certain other business transactions. There were no financial covenants associated with the agreement.

2019 Credit Facility

On July 19, 2019, the Company entered into a loan and security agreement (as amended, the "2019 Credit Facility") with K2 HealthVentures LLC ("K2HV") pursuant to which the K2HV agreed to make term loans in an aggregate principal amount of up to $45.0 million available to the Company in three tranches. The initial tranche of $20.0 million was funded upon closing on July 19, 2019. The second tranche of $10.0 million is available to be funded at the Company's election between December 1, 2019 and June 1, 2020, subject to certain customary conditions. The third tranche of

$15.0 million is available to be funded at the Company's election on or before January 15, 2021, subject to certain customary conditions and the achievement of certain clinical development milestones. Borrowings under the Loan Agreement are collateralized by substantially all of the Company's personal property, excluding intellectual property, and the Company pledged its equity interests in its subsidiaries, subject to certain limitations with respect to its foreign subsidiaries.

Interest on the outstanding loan balance will accrue at a variable annual rate equal to the greater of (i) 8.65% and (ii) the prime rate plus 3.15%. The Company is required to make interest-only payments on the loans on a monthly basis through February 28, 2022. If the Company elects to draw the third tranche, the interest-only period is extended through August 31, 2022. Subsequent to the interest only periods, the Company is required to make equal monthly payments of principal plus interest until the loans mature on August 1, 2024. Upon final payment or prepayment of the loans, the Company must pay a final payment equal to 4.3% of the loans borrowed, which is being accrued to interest expense over the term of the loan using the effective-interest method. The Company incurred fees associated with establishing the facility of $0.4 million. The Company has an option to prepay the loans in whole, subject to a prepayment fee of 2% of the amount prepaid or, if the prepayment occurs after the 18-month anniversary of the funding date of the loans, 1% of the amount prepaid.

The Loan Agreement contains customary representations, warranties and covenants and also includes customary events of default, including payment defaults, breaches of covenants, change of control and occurrence of a material adverse effect. The Company has determined that the risk of subjective acceleration under the material adverse events clause was remote and therefore has classified the long-term portion of the outstanding principal in non-current liabilities. Upon the occurrence and continuation of an event of default, a default interest rate of an additional 5% per annum may be applied to the outstanding loan balances, and the administrative agent, collateral agent, and lenders may declare all outstanding obligations immediately due and payable and exercise all of their rights and remedies as set forth in the Loan Agreement and under applicable law.

The Company used the proceeds from the initial $20.0 million tranche to prepay the full $15.0 million loan balance outstanding under the 2016 Credit Facility on July 19, 2019.

The Company has the following minimum aggregate future loan payments at September 30, 2019 (in thousands):

Twelve month period ending September 30,	Amount
2020	$ 1,759
2021	1,754
2022	6,318
2023	9,022
2024	8,515
Total minimum payments	$ 27,368
Less amounts representing interest and discount	(7,819)
Long-term debt	$ 19,549

Interest expense related to the Company's 2016 Credit Facility was approximately $0.5 million for the nine months ended September 30, 2019 and $0.2 million and $0.6 million for the three and nine months ended September 30, 2018, respectively.

Interest expense related to the Company's 2019 Credit Facility was approximately $0.4 million for both the three and nine months ended September 30, 2019.

7. In-License Agreements

Mayo Foundation for Medical Education and Research

On June 10, 2016, the Company entered into a Research and License Agreement, (the "2016 Mayo License Agreement") with Mayo Foundation for Medical Education and Research ("Mayo"). Under the Mayo License Agreement, Mayo was entitled to certain participation rights in connection with the issuance and sale of Series B Preferred Stock. The 2016 Mayo License Agreement allowed Mayo to purchase shares at the same price paid as other investors and is considered to be a fair value contract. In 2017, Mayo purchased 1,666,667 shares of Series B Preferred Stock at $1.80 per share. Also pursuant to the 2016 Mayo License Agreement, Mayo received 490 shares of common stock upon the completion of certain project milestones as well as warrants to purchase common stock (the "Mayo Warrants") exercisable for 18 shares and 116 shares of common stock upon the completion of certain additional project milestones. The Mayo Warrants were fully vested and expensed in 2016. On April 9, 2018, Mayo Foundation exercised its warrant and was issued 134 shares of common stock.

On August 6, 2017, the Company and Mayo entered into a license agreement ("2017 Mayo License Agreement"). Under the 2017 Mayo License Agreement, Mayo granted the Company (i) an exclusive, worldwide, sublicensable license under Mayo's rights to certain intellectual property and microbial strains (ii) a non-exclusive, worldwide, sublicensable license to certain related know-how, in each case, to develop and commercialize certain microbial strains and licensed products incorporating any such strains. As consideration, the Company paid a nonrefundable upfront fee of $0.2 million and annual license maintenance fees. Nonrefundable upfront fees were expensed in full to research and development expense in 2017. Annual maintenance fees will be expensed as incurred over the term of the agreement. The Company may owe Mayo milestone payments upon the achievement of certain development, regulatory, and commercial milestones, up to a maximum of $56.0 million in the aggregate, as well as royalties on net sales of licensed products in low single-digit percentages. As of September 30, 2019, the Company has incurred milestone payments to date totaling approximately $0.2 million under the agreement of which no amounts are currently due.

University of Chicago

On March 10, 2016, the Company and the University of Chicago entered into a patent license agreement ("2016 University of Chicago Agreement"). Under the 2016 University of Chicago Agreement, the University of Chicago granted the Company (i) an exclusive, royalty-bearing and sublicensable license under the Licensed Patents and (ii) a non-exclusive, royalty-bearing, sublicensable license to access the technical information to diligently develop and commercialize Licensed Products. As consideration, the Company paid a nonrefundable upfront fee of less than $0.5 million and will pay annual license maintenance fees. Nonrefundable upfront fees were expensed in full to research and development expense in 2016. Annual maintenance fees will be expensed as incurred over the term of the agreement. The Company may owe the University of Chicago milestone payments, totaling an aggregate of approximately $60.9 million upon the achievement of certain development, regulatory, and commercial milestones, as well as royalties on net sales of licensed products ranging from low to high single-digit percentages. As of September 30, 2019, the Company has incurred milestone payments to date totaling approximately $0.4 million.

In addition, the Company also agreed to pay the University of Chicago a share of sublicense revenue. The University of Chicago maintains control of patent prosecution, defense and maintenance on their patent rights. The Company has the first right, but not obligation, to control any post-grant proceedings and to take action in the prosecution or prevention of any infringement by a third party to patent rights. The Company is responsible for reimbursing the University of Chicago, or directly paying, for patent prosecution, defense and/or maintenance costs incurred. This includes any costs associated with defense activities related to one of the patents underlying the 2016 University of Chicago Agreement and to which in April 2019 the United States Patent and Trademark Office instituted a post-grant review based on a petition from a third party. For the nine months ended September 30, 2019, the Company has incurred expenses of $1.1 million related to the post grant review.

8. Commitments and Contingencies

Lease Obligations

In January 2018, the Company entered into an operating sublease arrangement to lease approximately 40,765 square feet for its office and research development space at 620 Memorial Drive, Cambridge, MA 02139 from February 2018 to September 2025. The Company maintains an additional separate operating lease for office and laboratory space that is scheduled to expire in 2020. The leases require security deposits, which the Company has primarily met with letters of credit from a financial institution that are secured with cash on deposit.

In June 2018, the Company entered into a sublease arrangement with a third party to lease space subject to an operating lease that is scheduled to expire in 2020. The future minimum rental payments to be received under this agreement total $0.3 million and are equivalent to the minimum payments due from the Company to the landlord.

The Company recorded rent expense of $0.7 million and $2.0 million for the three and nine months ended September 30, 2019, respectively. Rent expense for the three and nine months ended September 30, 2019 is net of sublease rental income of $0.1 million and $0.4 million, respectively. Rent expense totaled $0.8 million and $1.5 million for the three and nine months ended September 30, 2018, which is net of sublease rental income of $0.1 million in both periods.

The minimum aggregate future lease commitments, exclusive of any offsetting sublease rental payments, at September 30, 2019, are as follows (in thousands):

Twelve month period ending September 30,	Amount
2020	$ 3,187
2021	2,951
2022	3,040
2023	3,131
2024	3,225
Thereafter	3,321
	$ 18,855

Collaboration Agreement with Sacco S.r.l.

In July 2019, the Company entered into a Collaboration Agreement with Sacco S.r.l. ("Sacco"), an affiliate of one of the Company's existing contract manufacturing organizations, pursuant to which and subject to certain exceptions for pre-existing products for pre-existing customers, Sacco will manufacture and supply single strain, non-genetically modified microbes intended for oral delivery or oral use in pharmaceutical products exclusively for the Company 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. The Company has agreed to pay Sacco an aggregate of €3.0 million, €0.6 million annually, during the exclusivity period. The Company recognized €0.6 million in expense associated with this agreement during the three months ended September 30, 2019.

Equipment Funding Arrangement

In July 2019, the Company entered into an arrangement with one of its external manufacturing partners providing the Company with priority access to future manufacturing services which will be rendered using certain dedicated equipment. In return for such access, the Company committed to provide funding for the purchase of the dedicated equipment in an aggregate amount of £0.8 million, £0.4 million of which to be paid upfront and, subject to the manufacturer's installation and qualification of the equipment, an additional two installments of £0.2 million will be paid in January and April 2020.

Biose Industrie

On February 15, 2018, the Company entered into an Exclusivity and Commitment Agreement with Biose Industrie (“Biose”), a French corporation, in which Biose has agreed to exclusively manufacture certain microbial biotherapeutic products for the Company and reserve agreed upon manufacturing resources to conduct manufacturing runs for such products. Under the terms of this agreement, the Company agreed to annual fees in the mid-six digits in consideration of both exclusivity for the manufacture of monoclonal microbials and for a set minimum number of manufacturing runs per year. Exclusivity fees paid and any minimum commitments are expensed as incurred. The Company has agreed to pay an exclusivity fee of $0.3 million per year.

Litigation and Other Proceedings

The Company may periodically become subject to legal proceedings and claims arising in connection with on-going business activities, including claims or disputes related to patents that have been issued or that are pending in the field of research on which the Company is focused. The Company is not a party to any material litigation and does not have contingency reserves established for any litigation liabilities.

In April 2019, the United States Patent and Trademark Office ("USPTO"), granted a third party petition to initiate a post-grant review of a patent issued to the University of Chicago, to which the Company has an exclusive license from the University of Chicago. Although the Company believes that the subject patent is valid, there is a possibility that the USPTO could invalidate the patent or require the University of Chicago to narrow the claims contained in the patent. Under the terms of the license agreement, the Company is responsible for reimbursing the University of Chicago for patent defense costs.

9. Stockholders’ Equity and Convertible Preferred Stock

Common Stock

On April 27, 2018, the Company filed an amendment to its certificate of incorporation with the Secretary of State of the State of Delaware, to effect a 1-for-4.079 reverse stock split of the Company’s common stock. All share and per share data shown in the accompanying condensed consolidated financial statements and related notes have been retroactively revised to reflect the reverse stock split.

On May 11, 2018, the Company completed an IPO of 5,312,500 shares of its common stock for aggregate gross proceeds of $85.0 million. The Company received approximately $75.8 million in net proceeds after deducting underwriting discounts and commissions and other estimated offering expenses payable by the Company. Upon closing of the IPO, all of the outstanding shares of convertible preferred stock automatically converted into 22,386,677 shares of common stock at the applicable conversion ratio then in effect

On May 11, 2018, the Company filed a restated certificate of incorporation with the Secretary of the State of Delaware, which became effective in connection with the closing of the IPO. Pursuant to the restated certificate of incorporation, the Company is authorized to issue 200,000,000 shares of common stock and 10,000,000 shares of preferred stock.

On June 3, 2019, the Company filed a Registration Statement on Form S-3 (File No. 333-231911) (the “Shelf”) with the SEC in relation to the registration of common stock, preferred stock, debt securities, warrants and/or units of any combination thereof in the aggregate amount of up to $200.0 million for a period up to three years from the date of the filing. The Company also simultaneously entered into a sales agreement with Cowen and Company, LLC, as sales agent, providing for the offering, issuance and sale by the Company of up to an aggregate $50.0 million of its common stock from time to time in “at-the-market” offerings under the Shelf. As of September 30, 2019, no securities have been issued pursuant to the sales agreement.

Convertible Preferred Stock

Upon closing of the IPO in May 2018, all 91,315,295 outstanding shares of the Series A, Series A-1, Series A-2, Series A-3, Series B and Series C Preferred Stock (collectively, the "Preferred Stock") automatically converted into 22,386,677 shares of the Company’s common stock at the applicable conversion ratio of 1-for-4.079. Prior to conversion, all shares of Preferred Stock accrued a cumulative dividend of 8% per annum. Dividends for the applicable periods are included in net loss attributable to common shareholders on the condensed consolidated statement of operations through the conversion date. All accrued dividends earned on Preferred Stock were forfeited as of the conversion.

In February and March 2018, the Company issued a total of 25,232,199 shares of Series C Preferred Stock at purchase price of $3.23 for gross proceeds of $81.5 million under the same terms as the Series B Preferred Stock.

10. Stock-Based Compensation

2018 Incentive Award Plan

The Company's board of directors adopted on April 18, 2018, and the Company's stockholders approved, the 2018 Incentive Award Plan (the "2018 Plan"), which became effective May 8, 2018 and under which the Company may grant cash and equity-based incentive awards to the Company's employees, officers, directors, consultants and advisors. Following the effectiveness of the 2018 Plan, the Company ceased making grants under the 2015 Stock Incentive Plan (as amended the "2015 Plan"). The 2018 Plan allows the Company 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, that expire, lapse or become terminated or are exchanged for cash, surrendered, repurchased, canceled without having been fully exercised or forfeited. Each year starting with 2019 and ending in and including 2028, the, 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 the Company's board of directors. Accordingly, effective January 1, 2019, the number of shares authorized for issuance under the 2018 Plan was increased by 1,273,031 shares. The 2015 Plan continues to govern the terms and conditions of the outstanding awards granted under it.

The exercise price of stock options granted under the 2018 Plan is not less than the fair market value of a share of the Company's 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 more than 10 years from the date of grant. As of September 30, 2019, equity-based incentive awards for the purchase of up to 2,135,946 shares of the Company's common stock have been issued under the 2018 Plan, of which 99,196 have been canceled and none have been exercised. As of September 30, 2019, 947,381 shares of common stock are available for future grant under the 2018 Plan, which includes 366,408 shares subject to awards that were originally granted, and have, since the effective date of the 2018 Plan, been canceled or repurchased under the 2015 Plan.

2015 Stock Incentive Plan

Prior to the approval of the 2018 Plan, the Company granted equity awards under the 2015 Plan, which originally provided for grant of incentive stock options, non-qualified stock options, restricted stock awards ("RSAs"), and other stock-based awards to the Company's employees, officers, directors, consultants and advisors.

The terms of stock awards agreements, including vesting requirements, are 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, the Company records expense in the period in which such determination is made through any estimated remaining 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 more than 10 years from the date of grant. As of the adoption of the 2018 Plan, the Company ceased making awards under the 2015 Plan.

Under the 2015 Plan, the Company was authorized to grant equity awards up to an aggregate of 5,417,044 shares of common stock. As of September 30, 2019, an aggregate of 5,758,518 options and other equity awards had been granted under the 2015 Plan, of which 1,100,083 have been exercised and 802,417 have been canceled and 18,468 have been repurchased as of September 30, 2019. 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 included in the Company's condensed consolidated statements of operations and comprehensive loss is as follows (in thousands):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2019	2018	2019	2018
General and administrative	$ 1,082	$ 831	$ 3,306	$ 2,727
Research and development	980	764	2,844	1,767
Total stock-based compensation expense	$ 2,062	$ 1,595	$ 6,150	$ 4,494

Stock Options

A summary of the Company's stock option activity and related information is as follows:

	Shares	Weighted-Average Exercise Price
Options outstanding at December 31, 2018	4,917,811	$ 5.64
Granted	1,431,970	11.35
Exercised	(195,533)	1.44
Canceled	(261,467)	8.38
Options outstanding at September 30, 2019	5,892,781	$ 7.05
Exercisable as of September 30, 2019	2,230,234	$ 4.00

The weighted-average fair value of options granted during the nine months ended September 30, 2019 and 2018 was $7.66 and $8.18, respectively.

On January 30, 2018, the Company issued 250,000 shares of Series B Preferred Stock to a non-employee consultant as part of the consideration for services performed and completed in 2017. The Company has recognized $0.7 million as general and administrative expense in the condensed consolidated statement of operations and comprehensive loss, of which $0.1 million was recorded in the nine months ended September 30, 2018.

As of September 30, 2019, total unrecognized stock-based compensation expense relating to unvested stock options was $21.6 million. This amount is subject to change as the unvested portion of the stock options granted to non-employees is subject to re-measurement over the vesting period. This amount is expected to be recognized over a weighted average period of 2.71 years.

2018 Employee Stock Purchase Plan

The Company's board of directors adopted on April 18, 2018, and the Company's stockholders approved, the 2018 Employee Stock Purchase Plan (the "ESPP"), which became effective on May 8, 2018. A total of 336,356 shares of common stock were initially reserved for issuance under the ESPP. In addition, the number of shares of common stock that may be issued under the ESPP will automatically increase 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 the Company's common stock outstanding on the last day of the applicable preceding calendar year and (ii) an amount determined by the Company's board of directors. The plan administrators have proposed, and the Company's board of directors has authorized, an initial offering period under the ESPP commencing on February 1, 2020.

11. Income Taxes

Deferred tax assets and deferred tax liabilities are recognized based on temporary differences between the financial reporting and tax basis of assets and liabilities using statutory rates. A valuation allowance is recorded against deferred tax assets if it is more likely than not that some or all of the deferred tax assets will not be realized.

There were no significant income tax provisions or benefits for the three or nine months ended September 30, 2019. Due to losses incurred since inception and the uncertainty surrounding the realization of the favorable tax attributes in future tax returns, the Company has recorded a full valuation allowance against the Company's otherwise recognizable net deferred tax assets.

12. 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. The Company has computed diluted net loss per common share after giving consideration to all potentially dilutive common shares, including options to purchase common stock, restricted common stock, convertible preferred stock and warrants to purchase convertible preferred stock, outstanding during the period determined using the if-converted and treasury stock methods, except where the effect of including such securities would be antidilutive. Because the Company has reported net losses since inception, these potential common shares have been anti-dilutive and therefore basic and diluted net loss per share have been equivalent.

The following table presents securities that have been excluded from the computations of diluted weighted-average shares outstanding as they would be anti-dilutive:

	Nine Months Ended September 30,	
	2019	2018
Unvested common stock from early exercise of options	75,043	168,947
Stock options to purchase common stock	5,892,781	4,912,281
Total	5,967,824	5,081,228

13. Related Party Transactions

The Company receives clinical advisory services from Weatherden Ltd. ("Weatherden") under agreements that were entered into during 2017 and 2018. Duncan McHale, the Company's Chief Medical Officer, is a part owner of Weatherden. During the nine months ended September 30, 2019 and 2018, the Company paid Weatherden $0.7 million and $0.5 million, respectively. As of September 30, 2019 and 2018, the amounts due to Weatherden under the supply of service agreement were $0.1 million in both periods.

In June 2018, the Company entered into a subleasing arrangement with Ring Therapeutics (formerly VL46), an affiliate of one of its stockholders, Flagship Venture Funds. Under the terms of the sublease, the Company will invoice Ring Therapeutics for an aggregate $0.9 million in rent payments which are due during the period from July 1, 2018 through May 31, 2020 plus any related taxes and lease operating costs. For the nine months ended September 30, 2019, $0.5 million related to this sublease agreement, inclusive of taxes and operating expenses, has been recorded as an offset to operating expense within the consolidated statements of operations and comprehensive loss.

The Company entered into a consulting agreement with David Epstein (the "Consulting Agreement"), the Company's Chairman of the Board, effective September 16, 2019 pursuant to which Mr. Epstein will provide strategic advisory and other consulting services to the Company. The Consulting Agreement has an one year term and may be earlier terminated by either Mr. Epstein or the Company upon 30 days' notice, or 24 hours' notice by the non-breaching party in the event of a breach. In accordance with the terms of the Consulting Agreement, Mr. Epstein was granted an option to purchase 75,000 shares of the Company's common stock, which award vests in 36 equal monthly installments subject to his continued provision of consulting services to the Company pursuant to the Consulting Agreement on the applicable vesting date. Under the Consulting Agreement, Mr. Epstein also is 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 the Company's common stock having an aggregate grant date fair market value equal to approximately $0.2 million, as determined by the Board in its discretion based on customary option pricing methodologies, which award vests in full on the first anniversary of the grant date, subject to his continued provision of consulting services to the Company pursuant to the Consulting Agreement on the applicable vesting date, and (ii) an aggregate annual cash consulting fee of $0.3 million for his consulting services. All of the foregoing options, to the extent then outstanding, will be subject to accelerated vesting upon the occurrence of a change in control of the Company.

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 our Annual Report on Form 10-K for the year ended December 31, 2018 (the "2018 Annual Report"), including the audited consolidated financial statements and notes thereto contained in our 2018 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 the ''Risk Factors'' section 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

Evelo Biosciences is discovering and developing oral biologics that act on cells in the small intestine with systemic therapeutic effects. These cells in the small intestine play a central role in governing the immune, metabolic and neurological systems. Our first product candidates are monoclonal microbials, single strains of microbes selected for defined pharmacological properties. They have been observed in preclinical models to have systemic dose-dependent effects, modulating multiple clinically-validated pathways. Our product candidates have the potential to be effective, safe and affordable medicines to improve the lives of people with chronic diseases and cancer.

We currently have three product candidates in clinical trials, EDP1066 and EDP1815 for the treatment of inflammatory diseases and EDP1503 for the treatment of cancer. We also are advancing additional oral biologics through preclinical development in other disease areas.

Recent Clinical Developments

EDP1815

EDP1815 is a monoclonal microbial candidate for inflammatory diseases. In November 2018 we initiated our ongoing Phase 1b placebo-controlled dose-escalating safety and tolerability study of EDP1815 in approximately 24 healthy volunteers and up to 108 individuals with mild to moderate psoriasis or atopic dermatitis. The primary endpoint of this trial is safety and tolerability. Prospectively defined secondary and exploratory endpoints include clinical measures of disease, cellular histological biomarkers and blood immune cell biomarkers taken from biopsies and blood samples, respectively, at the start and end of the 28-day dosing period. Safety and tolerability, and secondary clinical endpoints are also measured at day 42, 2 weeks after completion of dosing.

In August 2019, we reported positive interim data from this Phase 1b trial from an initial cohort of 12 individuals with mild to moderate psoriasis dosed once per day for 28 days with 550mg ("1x" or "low" dose) of the enteric capsule formulation of EDP1815. EDP1815 was well tolerated in this cohort with no overall difference reported from placebo.

At the end of the 28-day dosing period, individuals dosed with EDP1815 showed a statistically significant ($p<0.05$) reduction in mean lesion severity score ("LSS") at 28 days of 2 points, compared to a mean increase of 0.25 points in individuals who received placebo. LSS reductions over the dosing period of individuals dosed with EDP1815 ranged from 0-67 percent. LSS, a secondary endpoint, is a component of the Psoriasis Area and Severity Index ("PASI") score and measures redness, thickness, and scaling of an individual psoriatic lesion and is a sensitive clinical measure for individuals with mild to moderate disease. Trends consistent with the LSS reductions were observed in the reduction of the PASI scores in individuals treated with EDP1815 compared to individuals treated with placebo.

Analysis of the basal epithelium mitotic count, a secondary endpoint and cellular driver of psoriasis pathology, showed a mean reduction over the dosing period of 2.25 cells/mm^2 in individuals who received EDP1815 compared to no change in individuals receiving placebo. Lower basal epithelium mitotic counts indicate a reduction of psoriasis pathology. In an analysis of the change over the dosing period of blood immune cell cytokine production following stimulation with lipopolysaccharide, an exploratory endpoint, the individuals dosed with EDP1815 showed a reduction in cytokine production indicative of a systemic anti-inflammatory response, compared to no reduction in the placebo group.

In November 2019, we reported additional positive interim clinical data from this ongoing Phase 1b trial in a cohort of eighteen individuals with mild to moderate psoriasis who were randomized 2:1 to receive a daily dose of 2.76g (5x or high dose) of the enteric capsule formulation of EDP1815 or placebo for 28 days.

EDP1815 continued to be well tolerated in this cohort, with no overall difference reported from placebo. At the end of the 28-day dosing period, the high dose cohort showed a mean reduction in LSS consistent with previously reported data from the low dose cohort.

Two weeks following the completion of the dosing period, at day 42, the high dose cohort showed continued reductions from baseline in both mean LSS and PASI, which may be indicative of a sustained clinical effect and dose response.

A summary of the LSS and PASI results are shown in the tables below.

Mean (+/-SE) Percentage Change in LSS vs. Start of Dosing Period [(1)]

	n	At end of 28-day dosing period	At day 42
Placebo [(2)]	10	0.6% (9.0%)	-7.2% (6.2%)
EDP1815 (high dose)	12	-15.1% (6.4%)	-24.1% (7.1%)
EDP1815 (low dose)	8	-22.8% (9.9%)	-9.0% (12.7%)

Mean (+/-SE) Percentage Change in PASI vs. Start of Dosing Period [(1)]

	n	At end of 28-day dosing period	At day 42
Placebo [(2)]	10	-1.0% (13.2%)	-3.3% (14.8%)
EDP1815 (high dose)	12	-16.0% (8.1%)	-20.7% (8.2%)

Note:
[(1)] This study was not sufficiently powered to detect statistically significant differences in clinical effect between treatment groups.
[(2)] Represents the combination of placebo arms for the low dose (n=4) and high dose (n=6) cohorts

A range of histological and molecular biomarkers were measured in the high dose cohort, with trends in line with the clinical effects of EDP1815 at the cohort level.

Based on the psoriasis data from the ongoing Phase 1b clinical trial, we plan to advance EDP1815 into Phase 2 in early 2020. This placebo-controlled trial will investigate daily dosing of EDP1815 in individuals with mild to moderate psoriasis over 16 weeks, and the primary endpoint will be a reduction in PASI score. Part A of the trial is designed to select an optimal formulation and will test the high dose of the enteric capsule formulation versus the high dose of a new formulation of EDP1815 versus placebo in approximately 180 individuals. We expect to perform an interim analysis, and to report initial data from Part A of the trial, in late 2020, which will enable the selection of the optimal formulation and potential initiation of Part B. Part B is designed to test three doses of the optimal formulation determined in Part A against placebo in approximately 250 individuals.

Based on the positive results of the ongoing Phase 1b trial and the planned Phase 2 psoriasis study, we will not enroll any further cohorts of individuals with psoriasis in the ongoing Phase 1b trial.

We expect to report additional data from the Phase 1b trial in a cohort of individuals with atopic dermatitis to be dosed with a new formulation of EDP1815 in the second quarter of 2020.

We expect to advance EDP1815 into further inflammatory disease indications after the Phase 2 interim data analysis. Potential indications include psoriatic arthritis, axial spondylarthritis, rheumatoid arthritis atopic dermatitis and asthma.

EDP1066

EDP1066 is a monoclonal microbial candidate for inflammatory diseases. In April 2018 we initiated our ongoing Phase 1b placebo-controlled dose-escalating safety and tolerability study of EDP1066 in approximately 36 healthy volunteers and up to 96 subjects with mild to moderate psoriasis or atopic dermatitis. The primary endpoint of this trial is safety and tolerability. Prospectively defined secondary and exploratory endpoints include clinical measures of disease, cellular histological biomarkers and blood immune cell biomarkers taken from biopsies and blood samples, respectively, at the start and end of the 28-day dosing period.

In August 2019, we reported interim clinical data from two cohorts of mild to moderate psoriasis subjects from this Phase 1b trial. EDP1066 was well tolerated with no overall difference reported from placebo. In an analysis of the change over the dosing period of blood immune cell cytokine production following stimulation by lipopolysaccharide, an exploratory endpoint, subjects who received a 3.3g ("5x dose") of EDP1066 showed a reduction in cytokine production consistent with a pharmacodynamic effect. No reduction was observed in subjects receiving a 660mg ("1x dose") of EDP1066 or placebo. No effects were observed in the secondary endpoints of clinical measures of disease or cellular histological biomarkers at either the 660mg or 3.3g dose of EDP1066.

Based on this data and the EDP1815 psoriasis data reported in August 2019, we refocused the ongoing EDP1066 Phase 1b trial on the enrollment of a cohort of mild to moderate atopic dermatitis subjects to be dosed with a new formulation which demonstrated significantly higher potency in preclinical studies. We expect to report data from this cohort in the first quarter of 2020. There will be no further development of EDP1066 in psoriasis.

EDP1503

EDP1503 is a monoclonal microbial candidate for oncology. In December 2018, we initiated our ongoing Phase 1/2 open-label study of EDP1503 in combination with KEYTRUDA (pembrolizumab), Merck's anti-PD-1 therapy, in three groups of patients: microsatellite stable colorectal cancer; triple-negative breast cancer; and patients across multiple tumor types who have relapsed on prior PD-1/L1 inhibitor treatment. We estimate that we will enroll up to 120 subjects in this study which will assess the safety and tolerability, immune response markers and overall response rates achieved with EDP1503 in combination with KEYTRUDA.

In November 2019, we announced that the microsatellite stable colorectal cancer cohort is fully recruited. No clinical responses have been evident, however, several patients in this cohort have experienced extended stable disease. Cellular infiltration biomarker changes were also observed in tumor biopsies taken from those patients during the EDP1503 monotherapy period, which are consistent with preclinical observations for EDP1503. We continue to monitor patients in this cohort.

Given newly approved treatments for triple-negative breast cancer, we anticipate that the majority of triple negative breast cancer patients to be recruited will have relapsed following prior PD-1/L1 therapy, similarly to those in the PD-1 relapsed cohort. We expect to report further clinical data from this trial in the first half of 2020.

In January 2019, the University of Chicago initiated a Phase 2a investigator-sponsored clinical study of EDP1503 in combination with KEYTRUDA in melanoma patients. The University of Chicago will enroll up to 70 PD-1-naïve and PD-1-relapsed melanoma patients in this study which is assessing the safety, tolerability and overall response rates achieved with EDP1503 in combination with KEYTRUDA. Additionally, the University of Chicago will evaluate immune response markers from biopsies taken during the study. Evelo is not issuing guidance related to this investigator-sponsored trial.

In addition to these ongoing clinical trials, we expect to initiate future additional clinical trials related to these product candidates and potential new product candidates. For instance, we expect to continue to conduct immuno-pharmacology clinical trials in healthy volunteers with EDP1066 and EDP1815.

Recent Collaboration Activities

On July 9, 2019, we entered into a Collaboration Agreement with Sacco, an affiliate of one of our existing contract manufacturing partners. Pursuant to the Collaboration Agreement, and subject to certain exceptions for pre-existing products for pre-existing customers, 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 have agreed to pay Sacco an aggregate of €3.0 million, €0.6 million annually, during the exclusivity period.

Recent Financing Activities

On July 19, 2019 we entered into a Loan and Security Agreement, as amended with K2 HealthVentures LLC providing for up to $45.0 million in potential debt financing, the proceeds of which were used to prepay our entire existing outstanding loan balance, and additional amounts are intended for the advancement of our research and development activities related to our pipeline of oral biologics and for general corporate purposes. Under terms of the Loan Agreement, the aggregate principal amount of $45.0 million is available in three tranches of term loans of $20.0 million, $10.0 million, and $15.0 million, respectively. At closing on July 19, 2019, we borrowed $20.0 million, representing the first tranche under the 2019 Credit Facility. The second tranche will be available to us between December 1, 2019 and June 1, 2020. The third tranche will be available to us through January 15, 2021, subject to the achievement of certain clinical development milestones. Interest on the outstanding loan balance will accrue at a variable rate equal to the greater of (i) 8.65% and (ii) the prime rate as published in the Wall Street Journal, plus 3.15%. We are required to make monthly interest-only payments through February 2022. If we elect to draw the third tranche, the interest-only period is extended through August 2022. Subsequent to the interest-only period, we are required to make equal monthly principal payments plus any accrued interest until the loans mature in August 2024. Upon final payment or prepayment of the loans, we are required to pay a final payment equal to 4.3% of the loans borrowed.

Contemporaneous with the closing of the first tranche of funding described above, our $15.0 million loan balance outstanding under an existing credit facility, was repaid in full. In accordance with the agreement underlying the prior debt facility, we paid an additional 0.5% prepayment fee as additional expense.

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. On May 11, 2018, we completed our IPO of 5,312,500 shares of our common stock at a public offering price of $16.00 per share. The net proceeds from the IPO were approximately $75.8 million. Prior to our IPO, we financed our operations primarily with proceeds from sales of convertible preferred stock to our equity investors and borrowings under a loan and security agreement, as amended, with a financial institution. Through September 30, 2019, we had received aggregate gross proceeds of $262.6 million from sales of common stock, convertible preferred stock and borrowings under our loan and security agreements.

We are a development stage company and have not generated any revenue. All of our product candidates are in early 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 nine months ended September 30, 2019, our net loss was $21.6 million. As of September 30, 2019, we had an accumulated deficit of $176.3 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 proof of concept trials for EDP1066, EDP1815 and EDP1503;
- potentially initiate additional clinical trials for EDP1066, EDP1815 and EDP1503;
- initiate or advance the clinical development of 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. 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, then we may be unable to continue our operations at planned levels and be forced to reduce or terminate our operations.

As of September 30, 2019, our principal source of liquidity is cash and cash equivalents, which totaled approximately $97.1 million. We expect that our existing cash and cash equivalents, along with the potential to borrow, at Evelo's election between December 1, 2019 and June 1, 2020, the second tranche of $10.0 million under the 2019 Credit Facility, will enable us to fund our planned operating expenses and capital expenditure requirements to the end of 2020. We have based these estimates on assumptions that may prove to be wrong, and we may use our available capital resources sooner than we currently expect. See “Liquidity and Capital Resources.”

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. 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 contract research organizations ("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, even 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 expense 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, continue our ongoing clinical trials for our product candidates, including EDP1066, EDP1815 and EDP1503, initiate additional clinical trials, continue to discover and develop additional product candidates, seek regulatory approvals for any products that successfully complete clinical trials, 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 in and completion of clinical trials;
- 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 Investigational New Drug-enabling toxicology studies;

- our ability to establish and maintain agreements with third-party manufacturers 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 the 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.

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 and business development, and administrative functions. General and administrative expenses also include legal fees relating to patent and corporate matters; 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 and 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 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 Income (Expense), Net

Interest income (expense), net primarily consists of interest earned on our cash, cash equivalents and short-term investments balances offset by interest expense incurred on our debt. During each of the three and nine month periods ended September 30, 2019 and 2018, interest income (expense), net consisted primarily of interest earned on institutional money market instruments and U.S. treasury securities offset by interest at the stated rate on borrowings under our loan and security agreements and amortization of deferred financing costs and interest expense related to the accretion of debt discount.

Other Expenses

Other expenses for the three and nine months ended September 30, 2019 primarily consist of loss on extinguishment of debt related to unamortized debt discount and a prepayment penalty for the repayment of the prior debt facility. For the three and nine months ended September 30, 2018, other expenses consist of non-cash changes in the fair value of warrants issued in connection with our previous loan and security agreement with Pacific Western Bank, all of which were settled in 2018.

Income Taxes

Since our inception in 2014, we have not recorded any U.S. federal or state income tax benefits for the net losses we have incurred in each year or 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 September 30, 2019 and 2018

The following table summarizes our results of operations for the three months ended September 30, 2019 and 2018 (in thousands):

	Three Months Ended September 30,		
	2019	2018	Change
Operating expenses:			
Research and development	$ 15,610	$ 11,227	$ 4,383
General and administrative	5,886	5,230	656
Total operating expenses	21,496	16,457	5,039
Loss from operations	(21,496)	(16,457)	(5,039)
Other (expense) income:			
Interest income, net	81	600	(519)
Other expense	(218)	—	(218)
Other income (expense), net	(137)	600	(737)
Net loss	$ (21,633)	$ (15,857)	$ (5,776)

Research and Development Expenses (in thousands):

	Three Months Ended September 30,		
	2019	2018	Change
Platform expenses	$ 4,182	$ 2,287	$ 1,895
Inflammation programs	5,039	3,759	1,280
Oncology programs	1,697	1,976	(279)
Research and development personnel costs (including stock-based compensation)	4,692	3,205	1,487
Total research and development expenses	$ 15,610	$ 11,227	$ 4,383

Research and development expenses were $15.6 million for the three months ended September 30, 2019, compared to $11.2 million for the three months ended September 30, 2018. The increase of $4.4 million was due primarily to an increase of $1.3 million in costs for our inflammation programs, driven primarily by clinical trial expenses, as well as an increase of $1.9 million in platform expenses in line with our strategy to maximize the potential of our platform. Personnel costs increased $1.5 million due primarily to increases in research and development headcount and compensation, including an increase of $0.2 million in stock-based compensation expense. These increases were partially offset by a decrease of $0.3 million for our oncology program due to the timing of clinical activity. We expect that our research and development expenses will continue to increase in the foreseeable future as we continue our clinical trials for our product candidates, initiate new clinical trials, continue discovery and development efforts for additional product candidates, hire additional research and development personnel and seek to increase manufacturing capabilities and possibly expand into additional therapeutic areas.

General and Administrative Expenses (in thousands):

	Three Months Ended September 30,		
	2019	2018	Change
General and administrative personnel costs (including stock-based compensation)	$ 3,154	$ 2,372	$ 782
Professional fees	1,682	1,819	(137)
Facility costs, office expense and other	1,050	1,039	11
Total general and administrative expenses	$ 5,886	$ 5,230	$ 656

General and administrative expenses were $5.9 million for the three months ended September 30, 2019, compared to $5.2 million for the three months ended September 30, 2018. The increase of $0.7 million primarily reflects costs required to support our growing organization and public company status. Professional fees decreased $0.1 million, reflecting a decrease in consulting expenses offset by increases in legal and patent costs, including $0.6 million related to the ongoing post-grant review of a patent issued to the University of Chicago, as well as increases in other professional fees. Personnel costs increased by $0.8 million, due primarily to increases in general and administrative headcount and compensation. The increase in personnel costs includes an increase of $0.3 million in stock-based compensation expense. We expect general and administrative expenses to continue to increase due to higher personnel and related costs, professional fees, and consulting expenses in support of our continued growth.

Other Income (Expense), Net

Other income (expense), net for the three months ended September 30, 2019 was expense of $0.1 million compared to income of $0.6 million for the three months ended September 30, 2018. This change was primarily driven by an increase in interest expense due to a higher interest rate on a greater principal balance from our 2019 Credit Facility. Additionally, we recorded $0.2 million for extinguishment of debt due to the repayment of our prior debt facility in July 2019.

Net Loss

Net loss for the three months ended September 30, 2019 was $21.6 million, compared to $15.9 million for the three months ended September 30, 2018.

Comparison of the Nine Months Ended September 30, 2019 and 2018

The following table summarizes our results of operations for the nine months ended September 30, 2019 and 2018 (in thousands):

	Nine Months Ended September 30,		
	2019	2018	Change
Operating expenses:			
Research and development	$ 46,751	$ 28,542	$ 18,209
General and administrative	16,936	13,568	3,368
Total operating expenses	63,687	42,110	21,577
Loss from operations	(63,687)	(42,110)	(21,577)
Other (expense) income:			
Interest income (expense), net	1,032	1,013	19
Other expense	(218)	(406)	188
Other income (expense), net	814	607	207
Net loss	$ (62,873)	$ (41,503)	$ (21,370)

Research and Development Expenses (in thousands):

	Nine Months Ended September 30,		
	2019	2018	Change
Platform expenses	$ 9,228	$ 6,117	$ 3,111
Inflammation programs	17,191	9,821	7,370
Oncology programs	6,723	3,905	2,818
Other program expenses	—	43	(43)
Research and development personnel costs (including stock-based compensation)	13,609	8,658	4,951
Total research and development expenses	$ 46,751	$ 28,544	$ 18,207

Research and development expenses were $46.8 million for the nine months ended September 30, 2019, compared to $28.5 million for the nine months ended September 30, 2018. The increase of $18.2 million was due primarily to increases of $7.4 million in costs for our inflammation programs, driven primarily by clinical trial expenses and external manufacturing costs, an increase of $2.8 million for our oncology programs, related primarily to increased costs associated with clinical development activities, as well as an increase of $3.1 million in platform expenses in line with our strategy to maximize the potential of our platform. Personnel costs increased $5.0 million due primarily to increases in research and development headcount and compensation, including an increase of $1.1 million in stock-based compensation expense.

General and Administrative Expenses (in thousands):

	Nine Months Ended September 30,		
	2019	2018	Change
General and administrative personnel costs (including stock-based compensation)	$ 9,087	$ 6,474	$ 2,613
Professional fees	4,524	4,116	408
Facility costs, office expense and other	3,325	2,978	347
Total general and administrative expenses	$ 16,936	$ 13,568	$ 3,368

General and administrative expenses were $16.9 million for the nine months ended September 30, 2019, compared to $13.6 million for the nine months ended September 30, 2018. The increase of $3.4 million primarily reflects costs required to support our growing organization and public company status. Personnel costs increased by $2.6 million, due primarily to increases in general and administrative headcount and compensation, including an increase of $0.6 million in stock-based compensation expense. Professional fees increased $0.4 million, reflecting increases in legal and patent costs, including $1.1 million related to the ongoing post-grant review of a patent issued to the University of Chicago, as well as increases in other professional consulting fees. Facility, office and other costs increased $0.3 million, primarily due to increased costs to support corporate operational activities including the expansion of our leased space to support our continued growth.

Other Income (Expense), Net

Other income (expense), net for the nine months ended September 30, 2019 was income of $0.8 million, compared to $0.6 million for the nine months ended September 30, 2018. This change was primarily driven by a decrease in net other expense of approximately $0.2 million, driven by the prior period including expense associated with the change in fair value of our warrant liabilities which were settled in the prior year period, partially offset by debt extinguishment charges in the nine months ended September 30, 2019

Net Loss

Net loss for the nine months ended September 30, 2018 was $62.9 million, compared to $41.5 million for the nine months ended September 30, 2018.

Liquidity and Capital Resources

We have incurred losses and generated negative operating cash flows since our inception and anticipate that we will continue to incur losses for at least the next several years. We incurred net losses of approximately $21.6 million and $15.9 million for the three months ended September 30, 2019 and 2018, respectively. To date, we have financed our operations primarily with proceeds from the initial public offering of our common stock, sales of our convertible preferred stock to our equity investors and borrowings under our debt facilities. From our inception through September 30, 2019, we have received gross proceeds of $262.6 million from such transactions, including a net $20.0 million borrowed under our debt facilities. As of September 30, 2019, we had cash and cash equivalents of $97.1 million and an accumulated deficit of $176.3 million.

On June 3, 2019, we entered into a sales agreement with Cowen and Company, LLC, as sales agent, pursuant to which we may, from time to time, issue and sell up to an aggregate of $50.0 million of our common stock in "at-the-market" offerings. As of September 30, 2019, no securities had been issued pursuant to the sales agreement.

On May 11, 2018, we completed our IPO of 5,312,500 shares of common stock at a public offering price of $16.00 per share. The gross proceeds from the IPO were $85.0 million and the net proceeds were approximately $75.8 million, after deducting underwriting discounts and commissions and other estimated offering expenses payable by us.

On July 19, 2019 we entered into the 2019 Credit Facility with K2HV providing for up to $45.0 million of current and future potential debt financing. The aggregate principal amount is available in three tranches of term loans of $20.0 million, $10.0 million, and $15.0 million, respectively. At closing on July 19, 2019, we withdrew initial proceeds of $20.0 million representing the first tranche under the 2019 Credit Facility. The second tranche will be available to us between December 1, 2019 and June 1, 2020. The third tranche will be available to us through January 15, 2021, subject to the achievement of certain clinical development milestones.

Interest on the outstanding loan balance will accrue at a variable rate equal to the greater of (i) 8.65% and (ii) the prime rate as published in the Wall Street Journal, plus 3.15%. We are required to make monthly interest-only payments through February 2022. If we elect to draw the third tranche, the interest-only period is extended through August 2022. Subsequent to the interest-only period, we are required to make equal monthly principal payments plus any accrued interest until the loans mature in August 2024. Upon final payment or prepayment of the loans, we are required to pay a final payment equal to 4.3% of the loans borrowed. We have an option to prepay the loans in whole, subject to a prepayment fee of 2% of the amount prepaid or, if the prepayment occurs after the 18-month anniversary of the funding date of the loans, 1% of the amount prepaid.

Contemporaneous with the closing of the first tranche of funding described above, we repaid the entire $15.0 million loan balance outstanding under an existing loan and security agreement with a separate financial institution. In accordance with the agreement underlying the prior debt facility, we paid an additional 0.5% prepayment fee as additional expense.

We expect that our existing cash and cash equivalents, along with the capacity to borrow an additional $10.0 million under the 2019 Credit Facility, will enable us to fund our planned operating expenses and capital expenditure requirements to the end of 2020.

Until such time, if ever, as we can generate revenue from product sales, we expect to finance our cash needs through a combination of equity offerings, debt financings and potential collaborations, license and development agreements. To the extent that we raise additional capital through future equity offerings or debt financings, ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of the common stockholders. Debt and equity financings, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. There can be no assurance that such financings will be obtained on terms acceptable to us, if at all. If we are unable to raise additional capital in sufficient amounts or on terms acceptable to us we may have to significantly delay, scale back or discontinue our research and development programs or future commercialization efforts. If we raise additional funds through collaborations, strategic alliances or marketing, distribution or licensing arrangements with third parties for one or more of our current or future drug candidates, we may be required to relinquish valuable rights to our technologies, future revenue streams, research programs or drug candidates or to grant licenses on terms that may not be favorable to us. Our failure to raise capital as and when needed would have a material adverse effect on our financial condition and our ability to pursue our business strategy.

Cash Flows

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

	Nine Months Ended September 30,	
	2019	2018
Cash used in operating activities	$ (52,986)	$ (31,823)
Cash provided by/(used in) investing activities	52,433	(88,709)
Cash provided by financing activities	4,763	161,994
Net increase in cash, cash equivalents and restricted cash	$ 4,210	$ 41,462

Operating Activities

Net cash used in operating activities for the nine months ended September 30, 2019 was $53.0 million driven primarily by our net loss of $62.9 million partially offset by non-cash charges including stock-based compensation expense of $6.2 million and depreciation expense of $1.3 million and changes in components of working capital.

Net cash used in operating activities for the nine months ended September 30, 2018 was $31.8 million driven primarily by our net loss of $41.5 million. This was partially offset by a net change in working capital of $3.1 million, non-cash charges including stock-based compensation expense of $4.5 million, depreciation expense of $1.6 million, and a change in fair value of warrant liability and debt derivative of $0.4 million.

Investing Activities

Net cash provided by investing activities for the nine months ended September 30, 2019 was $52.4 million, primarily consisting of the maturity of investments totaling $55.0 million. This was partially offset by the purchase of capital equipment which totaled $2.6 million during the period.

Net cash used in investing activities for the nine months ended September 30, 2018 was $88.7 million, primarily consisting of the purchase of investments totaling $84.7 million. Additionally, the purchase of capital equipment totaled $4.2 million during the period, which was slightly offset by $0.2 million of cash received for the sale of equipment.

Financing Activities

Net cash provided by financing activities for the nine months ended September 30, 2019 was $4.8 million, primarily due to proceeds from the issuance of long-term debt under our 2019 Credit Facility and proceeds from the issuance of common stock in connection with the exercise of option totaling $0.3 million, partially offset by the repayment of our prior debt facility.

Net cash provided by financing activities for the nine months ended September 30, 2018 was $162.0 million, primarily consisting of the net proceeds of $75.8 million from our IPO, net proceeds of $81.3 million from the issuance of our Series C Preferred Stock as well as net proceeds of approximately $5.0 million from the issuance of long-term debt, partially offset by a payment made for the settlement of a derivative liability of $0.3 million.

Contractual Obligations and Commitments

On July 19, 2019 we entered into the Loan Agreement with K2HV providing for up to $45.0 million of current and future potential debt financing in three tranches. At closing, we drew $20.0 million of proceeds which were available under the first tranche of this debt facility and contemporaneously repaid the entire $15.0 million outstanding under the 2016 Credit Facility, including a 0.5% prepayment fee. Under the Loan Agreement, a second tranche of $10.0 million will be available to us, at our election, between December 1, 2019 and June 1, 2020, subject to certain customary conditions, and a third tranche of $15.0 million will be available to us through January 15, 2021, subject to the achievement of certain clinical development milestones. Interest on the outstanding loan balance will accrue at a variable rate equal to the greater of (i) 8.65% and (ii) the prime rate as published in the Wall Street Journal, plus 3.15%. We are required to make monthly interest-only payments through February 2022 or, if the third tranche is drawn, August 2022. Subsequent to the interest-only period, principal payments will commence in March 2022 or September 2022, as

applicable, with equal payments plus accrued interest being made by us in consecutive monthly installments until the loans mature in August 2024. Upon final payment or prepayment of the loans, we are required to make a final payment equal to 4.3% of the loans borrowed. At our option, we may prepay the loans in whole, subject to a prepayment fee of 2% of the amount prepaid or, if the prepayment occurs after the 18-month anniversary of the funding date of the loans, 1% of the amount prepaid. Based on the above and using our initial interest rate of 8.65%, minimum contractual interest and principal payments due under our 2019 Credit Facility from December 31, 2018 will total approximately: $0.6 million within 1 year; $3.5 million between 1 to 3 years; $17.1 million between 4-5 years; and $6.4 million thereafter.

In July 2019, we entered into the Collaboration Agreement with a CMO. Pursuant to the agreement, the CMO has agreed that subject to certain exceptions, it will exclusively provide specified manufacturing services for us over a period of five years. We have committed to pay the CMO an aggregate of €3.0 million, €0.6 million annually, during the exclusivity period.

Also in July 2019, we entered into an arrangement with one of our external manufacturing partners to fund the purchase of certain dedicated equipment that will be used in manufacturing for an aggregate amount of £0.8 million, £0.4 million to be paid upfront and, subject to the manufacturer's installation and qualification of the equipment, the additional two equal installments of £0.2 million will be paid in January and April 2020.

Other than as described immediately above, there have been no material changes to our contractual obligations and commitments included in our Annual Report on Form 10-K for the year ended December 31, 2018.

Off-Balance Sheet Arrangements

We did not have during the periods presented, and we do not currently have, any off-balance sheet arrangements, as defined in the rules and regulations of the SEC.

Recent Accounting Pronouncements

For a discussion of recently adopted or issued accounting pronouncements please refer to Note 2 to 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 consolidated financial statements, which have been prepared in accordance with accounting principles generally accepted in the United States ("GAAP"). The preparation of these financial statements requires us to make estimates and judgments that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities in our consolidated financial statements, as well as the reported revenues and expenses during the reporting periods. These items, including accrued research and development expenses and stock-based compensation, are monitored and analyzed by us for changes in facts and circumstances, and material changes in these estimates could occur in the future. We base our estimates on historical experience, known trends and events, and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. 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. In making estimates and judgments, management employs critical accounting policies.

There have been no material changes to our critical accounting policies from those described in “Management’s Discussion and Analysis of Financial Condition and Results of Operations,” included in our Annual Report on Form 10-K that was filed with the SEC on February 15, 2019.

Item 3. Quantitative and Qualitative Disclosures About Market Risk.

Interest Rate Fluctuation Risk

We are exposed to market risk related to changes in interest rates. As of September 30, 2019, our cash and cash equivalents consisted of cash, money market accounts and U.S. treasury securities. Our primary exposure to market risk is interest income sensitivity, which is affected by changes in the general level of U.S. interest rates. However, because of the short-term nature of the instruments in our portfolio, an immediate 10% change in market interest rates would not have a material impact on the fair market value of our investment portfolio or on our financial position or results of operations.

In July 2019, we received proceeds of $20.0 million under the 2019 Credit Facility. This term loan bears interest at a variable annual rate equal to the greater of (i) 8.65% and (ii) the prime rate plus 3.15%, thereby exposing us to interest rate risk. Based upon the prime rate at September 30, 2019 of 5.00% and considering the $20.0 million of borrowings described above, an immediate 10% change in the prime rate would have no impact on our interest to be paid annually and therefore would not have a material impact on our debt-related obligations, financial position or results of operations.

Foreign Currency Fluctuation Risk

We are not currently exposed to significant market risk related to changes in foreign currency exchange rates; however, we have contracted with and may continue to contract with foreign vendors that are located in Europe.

Our operations may be subject to fluctuations in foreign currency exchange rates in the future.

Inflation Fluctuation Risk

Inflation generally affects us by increasing our cost of labor and clinical trial costs. We do not believe that inflation had a material effect on our business, financial condition or results of operations during the three and nine months ended September 30, 2019 and 2018.

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 Chief Executive Officer and Chief 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 in Rules 13a-15(e) and 15d-15(e) under the Exchange Act. Based on that evaluation, our Chief Executive Officer and Chief Financial Officer concluded that our disclosure controls and procedures were effective at a reasonable assurance level as of September 30, 2019.

Changes in Internal Control over Financial Reporting

There was no change in our internal control over financial reporting that occurred during the period covered by this Quarterly Report on Form 10-Q that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

PART 2—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 claims or proceedings, regardless of the merits, is inherently uncertain. For example, in April 2019, the United States Patent and Trademark Office ("USPTO") granted Genome & Co.'s petition to initiate a post-grant review of a patent issued to the University of Chicago, to which we have an exclusive license from the University of Chicago. Although we believe that the subject patent is valid, there is a possibility that the USPTO could invalidate the patent or require the University of Chicago to narrow the claims contained in the patent. Under the terms of our license agreement we are responsible for reimbursing the University of Chicago for patent defense costs.

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 consolidated financial statements and the related notes and "Management's Discussion and Analysis of Results of Operations and Financial Condition," 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 $21.6 million and $62.9 million for the three and nine months ended September 30, 2019, respectively, and $56.9 million, $28.0 million and $13.3 million for the years ended December 31, 2018, 2017 and 2016, respectively. As of September 30, 2019, we had an accumulated deficit of $176.3 million. Through September 30, 2019, we have financed our operations through private placements of our preferred stock, borrowings under our previous loan and security agreement with Pacific Western Bank and our current loan and security agreement with K2 HealthVentures LLC and other parties ("K2HV") and proceeds from our initial public offering which was completed in May 2018. We have devoted substantially all of our financial resources and efforts to developing our monoclonal microbial platform, identifying potential product candidates and conducting preclinical and clinical studies. We are in the early stages of developing our product candidates, and we have not completed the development of any monoclonal microbial therapies or other drugs or biologics. 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 enhance our monoclonal microbial 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 U.S. Food and Drug Administration ("FDA") or the European Medicines Agency ("EMA") or other regulatory authorities to perform preclinical or clinical studies 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, along with the capacity to borrow an additional $10.0 million under the 2019 Credit Facility, will enable us to fund our planned operating expenses and capital expenditure requirements to the end of 2020. 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 EDP1066, EDP1815 and EDP1503;
- 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, although we currently have no commitments or agreements to complete any such transactions.

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. Moreover, the terms of any financing may adversely affect the holdings or the rights of our stockholders and the issuance of additional securities,

whether equity or debt, by us, or the possibility of such issuance, may cause the market price of our shares to decline. The sale of additional equity or convertible securities would dilute all of our stockholders. The incurrence of 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. 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 dosed the first subjects in our clinical trial of our first monoclonal microbial candidate in our inflammation portfolio, EDP1066, in April 2018, and commenced initial clinical trials for our second inflammation candidate, EDP1815, and our first oncology candidate, EDP1503, in the fourth quarter of 2018, but have not completed any clinical trials for these or any other product candidates. We have not yet demonstrated our ability to successfully complete any non-clinical toxicology study, Phase 1 clinical study, Phase 2 clinical study or any Phase 3 or other pivotal clinical trials, obtain regulatory approvals, manufacture a commercial scale product, or arrange for a third party to do so on our behalf, or conduct sales and marketing activities necessary for successful 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.

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.

We have a $45.0 million term loan credit facility with K2HV, (as amended, the "Loan Agreement") that is 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 Loan Agreement, we repaid the entire $15.0 million loan balance outstanding under our prior loan and security agreement with Pacific Western Bank. As of September 30, 2019, the outstanding principal balance under the credit facility is $20.0 million resulting from the closing of the first tranche of funding which occurred on July 19, 2019. The Loan Agreement contains customary representations, warranties, affirmative and negative covenants and events of default applicable to us and our subsidiaries.

If we default under the Loan Agreement, K2HV may accelerate all of our repayment obligations and exercise all of their rights and remedies under the Loan Agreement 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' right 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 Loan Agreement, 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 the lenders of an event of default could 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 very 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 monoclonal microbial platform, with an initial focus on developing therapies in immunology, specifically inflammatory diseases, and also oncology. While we believe our preclinical and clinical studies 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 monoclonal microbials, 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 third-party manufacturers for, 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 technological 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 intended 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 data.

We believe our product candidates, including EDP1066, EDP1815 and EDP1503, work by modulating systemic responses via interactions with cells in the small intestine. This requires our monoclonal microbials, when dosed, to pass safely through the tissues of the gut, where they can interact with cells in the interior of the small intestine called the lumen. Dosing to achieve sufficient exposure may require an inconvenient dosing regimen. Even with successful formulation and delivery to achieve proper exposure of our microbes 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, these principles and the ability to use monoclonal microbials to modulate the immune system and other systems has not yet been proven in humans.

Our product candidates are monoclonal microbials, which are an unproven approach to therapeutic intervention.

All of our product candidates are based on monoclonal microbials. 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 monoclonal microbial therapies 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 monoclonal microbials, 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 monoclonal microbial 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 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 EDP1066, EDP1815 and EDP1503, are designed to work by modulating the immune system. While we have observed in preclinical studies that our monoclonal microbials have limited systemic exposure, the pharmacological immune effects we induce are systemic. Systemic immunomodulation from taking our monoclonal microbials 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 monoclonal microbials 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, EMA 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 monoclonal microbial. 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 remerge. These events, while unlikely, could cause a delay in our clinical development and/or could increase the regulatory standards for the entire class of monoclonal microbials. 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.

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, EMA or comparable foreign regulatory authorities, the institutional review boards ("IRBs") at the institutions in which our studies are conducted, or ethics committees, or the data safety monitoring board ("DSMB") could suspend or terminate our clinical trials or the FDA, EMA 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 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;
- 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 the 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 monoclonal microbials, and may negatively impact regulatory approval of, or demand for, our potential products.

Our monoclonal microbial product candidates are pharmaceutical compositions of commensal microbes. 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 monoclonal microbials. 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 monoclonal microbial technologies, even if not ultimately attributable to our product candidates, and the resulting publicity could result in increased governmental regulation, unfavorable public perception, 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 monoclonal microbial product candidates require that we manufacture from master cell banks ("MCBs") of 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. Recreating and recertifying 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. We dosed the first subjects in our clinical trial of our first monoclonal microbial candidate in our inflammation portfolio, EDP1066, in April 2018, and commenced initial clinical trials for our second inflammation candidate, EDP1815, and our first oncology candidate, EDP1503, in the fourth quarter of 2018, but have not completed any clinical trials for these or any other product candidates. 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 our initial clinical trials, investigationals drug products are being delivered in a capsule coated 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 coated for targeted release in the small intestine. Our ongoing and planned 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 studies, and we cannot be certain that we will not face similar setbacks.

The results from early 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. For example, in August and November 2019, we announced positive Phase 1b clinical data, as measured using certain secondary and exploratory endpoints, from our ongoing clinical trial of EDP1815 in subjects with mild to moderate psoriasis and also from our EDP1066 trial in subjects with mild to moderate psoriasis. Although the initial clinical data from these trials may be encouraging, the data are preliminary in nature, based on a limited number of people with psoriasis, and the Phase 1 studies are not complete. These data, or other positive data, may not continue for these people with psoriasis or occur for any future

patients in these studies, and may not be repeated or observed in any future studies. There can be no assurance that these studies will ultimately be successful or support further clinical advancement of this product candidate.

In addition, we cannot be certain as to the type and number of clinical trials the FDA will require us to conduct before we may successfully gain approval, referred to as licensure in the United States, to market any of our product candidates. Prior to approving a new therapeutic product, the FDA generally requires that efficacy be demonstrated in two adequate and well-controlled clinical trials. In some situations, evidence from a Phase 2 trial and a Phase 3 trial or from a single Phase 3 trial can be sufficient for FDA approval, such as in cases where the trial or trials provide highly reliable and statistically strong evidence of an important clinical benefit. Additionally, the FDA requires that investigation include adequate tests to demonstrate the safety of the new therapeutic product. Additional clinical trials 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 slower than we anticipate or participants may drop out of these clinical trials at a higher rate than we anticipate;
- our third-party contractors may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all;
- we may have to, or regulators, IRB or ethics committees 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 participants 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.

Our product development costs will increase if we experience delays in clinical testing or 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.

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, such as the EMA. We are developing our product candidates, EDP1066 and EDP1815, to treat inflammatory diseases, beginning with psoriasis and atopic dermatitis, and EDP1503 to treat multiple types of cancer. There are a limited number of patients from which to draw for clinical studies.

Patient enrollment is also affected by other factors including:

- the severity of the disease under investigation;
- the patient eligibility criteria for the study 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.

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 by the FDA and other regulatory agencies in the United States and by the EMA and similar 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 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 studies than those conducted by a sponsor, especially for novel product candidates such as our monoclonal microbials. The FDA, EMA 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, EMA 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, EMA or the applicable foreign regulatory agency approval for their products. The FDA, EMA 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, EMA 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 biologics license application ("BLA") or foreign marketing authorization for one of our product candidates, the FDA, EMA 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, EMA 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, EMA 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 therapeutic products targeting the underlying biology of monoclonal microbials and their interactions with cells in the small intestine is an emerging field, and it is possible that the FDA, EMA or other regulatory authorities could issue regulations or new policies in the future affecting our monoclonal microbials that could adversely affect 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.

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 may also be eligible for accelerated approval.

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.

We may seek orphan drug designation for some of our product candidates, but may not be able to obtain it.

Regulatory authorities in some jurisdictions, including the United States and Europe, may designate drugs and biologics for relatively small patient populations as orphan drugs. In the United States, the FDA may designate a drug or biologic as an orphan drug if it is intended to treat a rare disease or condition, which is defined as a disease or condition that affects fewer than 200,000 individuals in the United States, or if it affects more than 200,000 individuals in the United States, there is no reasonable expectation that the cost of developing and making the product available in the United States for the disease or condition will be recovered from sales of the product.

Generally, if a product with an orphan drug designation subsequently receives the first marketing approval for the indication for which it has such designation, the product is entitled to a period of marketing exclusivity, which precludes the EMA or the FDA from approving another marketing application for the same drug or biologic for that time period. The applicable period is seven years in the United States and ten years in Europe. Market exclusivity based on orphan drug designation is distinct from exclusivity conveyed by other regulations and under issued patents; the periods of exclusivity may run concurrently. The European exclusivity period can be reduced to six years if a product no longer meets the criteria for orphan drug designation or if the product is sufficiently profitable so that market exclusivity is no longer justified.

In addition, exclusive marketing rights in the United States may be limited if we seek approval for an indication broader than the orphan-designated indication or may be lost if the FDA or EMA later determines that the request for designation was materially defective or if we are unable to assure sufficient quantities of the product to meet the needs of patients with the rare disease or condition. We may seek orphan drug designation and exclusivity for some of our product candidates. However, even if we obtain orphan drug designation for a product candidate, we may not be able to obtain or maintain orphan drug exclusivity for that product candidate. Orphan drug exclusivity may be lost if the FDA or EMA determines that the request for designation was materially defective or if we are unable to assure sufficient quantity of the drug or biologic to meet the needs of patients with the rare disease or condition. We also may not be the first to obtain marketing approval of any product candidate for which we have obtained orphan drug designation for the orphan-designated indication due to the uncertainties associated with developing pharmaceutical products.

Further, even if we obtain orphan drug exclusivity for a product, that exclusivity may not effectively protect the product from competition because different drugs with different active moieties may be approved for the same condition. Even after an orphan drug is approved, the FDA can subsequently approve the same drug with the same active moiety for the same condition if the FDA concludes that the later drug is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care or if the manufacturer of the product with orphan exclusivity is unable to maintain sufficient product quantity. Orphan drug designation neither shortens the development time or regulatory review time of a drug nor gives the drug any advantage in the regulatory review or approval process.

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 contract research organizations ("CROs"), clinical data management organizations, medical institutions, clinical investigators and potential pharmaceutical partners, to conduct and manage our clinical trials, including our clinical trials of EDP1066, EDP1815 and EDP1503.

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 trial participants 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*, 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 to, 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, 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.

This reliance on third parties 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 any 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 nonrenewal 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 current Good Manufacturing Practices ("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. The contract manufacturers we rely on to produce our product candidates have never produced a FDA-approved therapeutic. If our contract manufacturers are unable to comply with cGMP regulation or if the FDA does 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 regulations and 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 supply or a second source for required raw materials used in the manufacture of our product candidates or for the manufacture of finished 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.

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 a manufacturing facility for our product candidates for production at a commercial scale. We have no experience in commercial-scale manufacturing of our product candidates. We currently intend to develop our manufacturing capacity in part by expanding our current facility or building additional facilities. This activity will 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 studies, 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 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, 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, Celgene Corporation, F. Hoffmann-La Roche A.G., Gilead Sciences, Inc., Incyte Corporation, Johnson & Johnson, Merck, 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 based on scientific approaches that are the same as or similar to our approach, and others 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 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 third parties 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 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 a 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 an adequate level of reimbursement for our products by third-party payors. Even if we do obtain adequate levels of reimbursement, third-party payors, such as government or private healthcare insurers, carefully review and increasingly question the coverage of, and challenge the prices charged for, drugs. Reimbursement rates from private health insurance companies vary depending on the company, the insurance plan and other factors. 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 are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for drugs. 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, and negatively impact the revenues we are able to generate from the sale of the product in that country. Adverse pricing limitations may hinder our ability to recoup our investment in one or more product candidates, even if 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 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 participants;
- 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 Patient Protection and Affordable Care Act ("Affordable Care Act") signed into law on March 23, 2010, includes a subtitle called the Biologics Price Competition and Innovation Act of 2009 ("BPCIA") which 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. The law is complex and is still being interpreted and implemented by the FDA. As a result, its ultimate impact, implementation, and meaning are subject to uncertainty. While it is uncertain when such processes intended to implement BPCIA may be fully adopted by the FDA, any such processes could have a material adverse effect on the future commercial prospects for our biological products.

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 recent 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 Europe, 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 Europe, a competitor may reference data supporting approval of an innovative biological product, but will not be able to get on the market until 10 years after the time of approval of the innovative product. This 10-year marketing exclusivity period will be extended to 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 European Union and many other jurisdictions, we or our collaborators must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. The approval procedure varies among countries and can involve additional testing. The time required to obtain approval in foreign countries may differ substantially from that required to obtain FDA, EMA 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, EMA or other applicable regulatory 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.

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 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. 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 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 closely regulates 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 imposes 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 restrictions relating to the promotion of prescription drugs may also lead to investigations alleging violations of federal and state health care fraud and abuse laws, as well as state 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 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 European Union 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 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.

We also cannot predict the likelihood, nature or extent of adverse government regulation that may arise from pending or future legislation or administrative action, either in the United States or abroad. For example, certain policies of the current presidential administration may impact our business and industry. Namely, the current presidential administration has taken several executive actions, including the issuance of a number of Executive Orders, that could

impose significant burdens on, or otherwise materially delay, the FDA's ability to engage in routine regulatory and oversight activities such as implementing statutes through rulemaking, issuance of guidance, and review and approval of marketing applications. It is difficult to predict how these requirements will be implemented, and the extent to which they will impact the FDA's ability to exercise its regulatory authority. If these executive actions impose constraints on the FDA's ability to engage in oversight and implementation activities in the normal course, our business may be negatively impacted.

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 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 and state 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. 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 (described below);

- 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;

- the federal Health Insurance Portability and Accountability Act of 1996 ("HIPAA") 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;

- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act and its implementing regulations, also imposes obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;

- the federal Physician Payment Sunshine Act requires applicable manufacturers of covered drugs to report payments and other transfers of value to physicians and 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;

- 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 that 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; and

- state and foreign laws that govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

The risk of our being found in violation of these laws 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, 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 will comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental 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, President Obama signed into law the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act (collectively the "Affordable Care Act"), a sweeping law 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 Affordable Care Act 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;
- expansion of healthcare fraud and abuse laws, including the False Claims Act and the Anti-Kickback Statute, new government investigative powers and enhanced penalties for noncompliance;
- a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% 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;
- new requirements to report financial arrangements with physicians and teaching hospitals;

- 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 in and conduct comparative clinical effectiveness research, along with funding for such research.

There have been judicial and Congressional challenges to certain aspects of the Affordable Care Act, and we expect there will be additional challenges and amendments to the Affordable Care Act in the future, particularly in light of the new presidential administration and U.S. Congress. At this time, the full effect that the Affordable Care Act would have on our business remains unclear.

In addition, other legislative changes have been proposed and adopted since the Affordable Care Act was enacted. In August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. This includes 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 2025 unless additional Congressional action is taken. On January 2, 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, which, among other things, reduced Medicare payments to several providers, including hospitals, and an increase in the statute of limitations period for the government to recover overpayments to providers from three to five years. These new laws may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain.

We expect that the Affordable Care Act, as well as other healthcare reform measures that may be adopted in the future, may result in additional reductions in Medicare and other healthcare funding, more rigorous coverage criteria, new payment methodologies and 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 aggressive 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.

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

In some countries, particularly the countries of the European Union, 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 European Union 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 such as human stool. 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 we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against 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. Prosecution of our patent portfolio is at a very early stage, and we are just beginning to reach the statutory deadlines for deciding whether and where to initiate prosecution in specific foreign jurisdictions by filing national stage applications based on our Patent Cooperation Treaty applications. As those deadlines come due, we will have to decide whether and where to pursue patent protection for the various inventions claimed in our patent portfolio, and we will only have the opportunity to obtain patents in those jurisdictions where we pursue protection. 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. Therefore, these patents and applications may not be prosecuted and enforced in a manner consistent with the best interests of our business.

Our patent portfolio is in the early stages of prosecution. We currently have seven issued U.S. patents. Although we have numerous patent applications pending, substantive prosecution has begun in only a small number of those applications. 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 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 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, given the early stage of prosecution of our portfolio, it may be some time before we understand how patent offices react to our patent claims and whether they identify prior art of relevance that we have not already considered, which could be an impediment to our patents issuing.

Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing, 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 owned 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 either the patent laws 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 United States Patent and Trademark Office ("USPTO") or become involved in opposition, derivation, reexamination, inter partes review, 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 April 2019, the USPTO granted Genome & Co.'s petition to initiate a post grant review of a patent issued to the University of Chicago, to which we have an exclusive license from the University of Chicago. Although the outcome of the post grant review is uncertain, there is a possibility that the USPTO could invalidate the subject patent or require the University of Chicago to narrow the claims contained in the patent. 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 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 exclusive license agreements with the University of Chicago and 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 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 on 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 University of Chicago and 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 University of Chicago and Mayo Clinic. These agreements indicate 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 (the "Bayh-Dole Act"). 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 U.S. patent law 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. In addition, patent reform legislation could further increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents. On September 16, 2011, the Leahy-Smith America Invents Act (the "Leahy-Smith Act") was signed into law. The Leahy-Smith Act includes a number of significant changes to U.S. patent law. These include provisions that affect the way patent applications are prosecuted and may also affect patent litigation. The USPTO has also developed regulations and procedures to govern administration of the Leahy-Smith Act, and many of the substantive changes to patent law associated with the Leahy-Smith Act, in particular the first to file provisions, only became effective on March 16, 2013. A third party that files a patent application in the USPTO after that date but before us could therefore be awarded a patent covering an invention of ours even if we had made the invention before it was made by the third party. This will require us to be cognizant going forward of the time from invention to filing of a patent application. Thus, for our U.S. patent applications containing a priority claim after March 16, 2013, there is a greater level of uncertainty in the patent law.

Moreover, some of the patent applications in our portfolio will be subject to examination under the pre-Leahy-Smith Act law and regulations, while other patents applications in our portfolio will be subject to examination under the law and regulations, as amended by the Leahy-Smith Act. This introduces additional complexities into the prosecution and management of our portfolio.

In addition, the Leahy-Smith Act limits where a patentee may file a patent infringement suit and provides opportunities for third parties to challenge any issued patent in the USPTO. These provisions apply to all of our U.S. patents, even those issued before March 16, 2013. Because of a lower evidentiary standard in USPTO proceedings compared to the evidentiary standard in U.S. federal court necessary to invalidate a patent claim, a third party could potentially provide evidence in a USPTO proceeding sufficient for the USPTO to hold a claim invalid even though the same evidence would be insufficient to invalidate the claim if first presented in a federal court action. Accordingly, a third party may attempt to use the USPTO procedures to invalidate our patent claims because it may be easier for them to do so relative to challenging the patent in a federal court action. It is not clear what, if any, impact the Leahy-Smith Act will have on the operation of our business. However, the Leahy-Smith Act and its implementation could 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 have a material adverse effect on our business 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.

A number of cases decided by the Supreme Court have involved questions of when claims reciting abstract ideas, laws of nature, natural phenomena and/or natural products are eligible for a patent, regardless of whether the claimed subject matter is otherwise novel and inventive. These cases include *Association for Molecular Pathology v. Myriad Genetics, Inc.* , 569 U.S. 12-398 (2013) or *Myriad*; *Alice Corp. v. CLS Bank International*, 573 U.S. 13-298 (2014); and *Mayo Collaborative Services v. Prometheus Laboratories, Inc.* , or *Prometheus*, 566 U.S. 10-1150 (2012). In response to these cases, the USPTO has issued guidance to the examining corps.

The full impact of these decisions is not yet known. The *Myriad* decision, issued on June 13, 2013, is the most recent Supreme Court decision to address patent eligibility of natural products. 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. In *Myriad*, the 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. However, on March 4, 2014, the USPTO issued a memorandum to patent examiners providing guidance for examining claims that recite laws of nature, natural phenomena or natural products under the *Myriad* and *Prometheus* decisions. The guidance did not limit the application of *Myriad* to DNA but, rather, applied the decision broadly to other

natural products, which may include our product candidates. The March 4, 2014 memorandum and the USPTO's interpretation of the cases and announced examination rubric received widespread criticism from stakeholders during a public comment period and was superseded by interim guidance published on December 15, 2014. The USPTO's interpretation of the case law and new guidelines for examination may influence, possibly adversely, prosecution and defense of certain types of claims in our portfolio.

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 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.

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 these proceedings, 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 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, that 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, then 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 on 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 all 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 team. Although we have entered into employment 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, outbreak of disease, 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, or its anti-bribery provisions.

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

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

Following a national referendum in which a majority of voters in the United Kingdom elected to withdraw from the European Union, the government of the United Kingdom formally initiated the process for withdrawal in March 2017 ("Brexit"). The terms of any withdrawal are subject to a complex and ongoing negotiation between the United Kingdom and the European Union whose result and timing remain unclear and which has created significant political and economic uncertainty about the future trading relationship between the United Kingdom and the European Union in the event of a withdrawal, including with respect to the laws and regulations that will apply as the United Kingdom determines which European Union laws to replace or replicate in the event of a withdrawal and particularly in light of the possibility that a withdrawal could occur without a negotiated agreement

These developments, or the perception that any of them 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.

Depending on the terms of Brexit, the United Kingdom could lose its present rights or terms of access to the single EU market and EU customs areas and to the global trade deals negotiated by the European Union on behalf of its members. The uncertainty regarding new or modified arrangements, or initially the absence of such arrangements, between the United Kingdom and other countries following Brexit may have a material adverse effect on the movement of goods between the United Kingdom and members of the European Union and the United States, including the interruption of or delays in imports into the United Kingdom of goods originating within the European Union and exports from the United Kingdom of goods originating there. For example, shipments into the United Kingdom of drug substance manufactured for the Company in the European Union 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 European Union 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 would suffer in the event of information technology and other system failures or security breaches of or unauthorized access to our systems.

Despite the implementation of security measures, our internal computer systems and those of our current and future contractors and consultants are vulnerable to damage from computer viruses, unauthorized access, malware, natural disasters, terrorism, war, telecommunication and electrical failures, cyber-attacks or cyber-intrusions over the Internet, or to attachments to emails 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 cyber-attacks 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 systems safeguard important confidential personal data regarding patients enrolled in our clinical trials. While we are not aware of any such material 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 similar events relating to their computer systems could also have a material adverse effect on our business. 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.

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 services have broad discretion to change and interpret its terms of service and other policies with respect to us, and those actions may be unfavorable to us. Our cloud computing services may also alter how we are able to process data on the platform. If a cloud computing services 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, or is improperly used, or incidents 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.

We are also subject to many federal, state, and foreign laws and regulations, including those related to privacy, rights of publicity, data protection, content regulation, intellectual property, health and safety, competition, protection of minors, consumer protection, employment, and taxation. These laws and regulations are constantly evolving and may be interpreted, applied, created, or amended in a manner that could seriously harm our business.

Changes in funding for the FDA, the SEC and other government agencies could hinder their ability to hire and retain key leadership and other personnel, and prevent those agencies from performing normal functions on which the operation of our business may rely, which could negatively impact our business.

The ability of the FDA to take action with respect to regulatory matters can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel and accept payment of user fees and statutory, regulatory and policy changes. In addition, government funding of the FDA, the SEC and other government agencies on which our operations may rely is subject to the political process, which is inherently fluid and unpredictable.

Disruptions at the FDA and other agencies may also slow the time necessary for regulatory submissions to be reviewed or approved, or for other actions to be taken, by relevant government agencies, which would adversely affect our business. For example, over the last several years, including as recently as December 22, 2018, the U.S. government has shut down several times and certain regulatory agencies, such as the FDA and the SEC, have had to furlough critical FDA, SEC and other government employees and stop critical activities. If a prolonged government shutdown occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Similarly, a prolonged government shutdown could prevent the timely review of our patent applications by the USPTO, which could delay the issuance of any U.S. patents to which we might otherwise be entitled. Additionally, government shutdowns could impact our ability to access the public markets and obtain necessary capital in order to properly fund our business.

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 only made one acquisition to date, and our ability to do so successfully is unproven beyond this instance. 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;
- 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 September 30, 2019, 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 73% 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. For example, in November 2018, holders of approximately 28.3 million shares of our common stock formerly subject to a lock-up agreement entered into in connection with our IPO became eligible to resell their shares in the open market (subject to volume limitations as to resales by affiliates of the Company pursuant to Rule 144 of the Securities Act). Moreover, holders of an aggregate of approximately 18.4 million shares of our common stock have rights, subject to specified conditions, to require us to file registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or other stockholders, 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 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 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, (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, or 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, 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. 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.

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, and particularly after we are no longer an emerging growth 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. 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 are evaluating these rules and regulations, and cannot predict or estimate the amount of additional costs we may incur or the timing of such costs. These rules and regulations are often subject to varying interpretations, in many cases due to their lack of specificity, and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. This could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices.

Pursuant to Section 404 of the Sarbanes-Oxley Act of 2002, or Section 404, we will be 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 will be engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to continue to dedicate internal resources, potentially engage outside consultants and adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, there is a risk that we will not be able to conclude, 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 disclosure controls and procedures may not prevent or detect all errors or acts of fraud.

Our disclosure controls and procedures are designed to reasonably assure that information required to be disclosed by us in reports we file or submit under the Exchange Act is accumulated and communicated to management, and recorded, processed, summarized and reported within the time periods specified in the rules and forms of the SEC.

We believe that any disclosure controls and procedures 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.

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 stock, 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 target preclinical studies or clinical studies 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.

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, these provisions include those establishing:

- a classified board of directors with three-year staggered terms, which may delay the ability of stockholders to change the membership of a majority of our board of directors;
- no cumulative voting in the election of directors, which limits the ability of minority stockholders to elect director candidates;
- the exclusive right of our board of directors to elect a director to fill a vacancy created by the expansion of the board of directors or the resignation, death or removal of a director, which prevents stockholders from filling vacancies on our board of directors;
- the ability of our board of directors to authorize the issuance of shares of preferred stock and to determine the terms of those shares, including preferences and voting rights, without stockholder approval, which could be used to significantly dilute the ownership of a hostile acquirer;
- the ability of our board of directors to alter our bylaws without obtaining stockholder approval;
- the required approval of the holders of at least two-thirds of the shares entitled to vote at an election of directors to adopt, amend or repeal our bylaws or repeal the provisions of our 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 provide that the Court of Chancery of the State of Delaware will be the exclusive forum for substantially all disputes between us and our stockholders, 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. We believe these provisions benefit us by providing increased consistency in the application of Delaware law by chancellors particularly experienced in resolving corporate disputes, 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 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 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 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 credits to offset future taxable income may be subject to certain limitations.

As of December 31, 2018, we had federal and state net operating loss carryforwards of $98.0 million and $91.2 million, respectively. A portion of the federal net operating losses will begin to expire at various dates through 2037. The state net operating losses will begin to expire at various dates through 2038. As of December 31, 2018, we also had federal research and development tax credit carryforwards of $2.1 million and state research and development tax credit carryforwards of $0.8 million, which begin to expire in 2033. These net operating loss and tax credit carryforwards could expire unused and be unavailable to offset future income tax liabilities. In addition, in general, under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended, or the Code, a corporation that undergoes an “ownership change” is subject to limitations on its ability to utilize its pre-change net operating losses or tax credits, or NOLs or credits, to offset future taxable income or taxes. 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 credits may be subject to limitations arising from previous ownership changes, and if we undergo an ownership change in the future, our ability to utilize NOLs or credits could be further limited by Sections 382 and 383 of the Code. 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 NOLs or credits may also be impaired under state law. Accordingly, we may not be able to utilize a material portion of our NOLs or credits. The reduction of the corporate tax rate under the Tax Cuts and Jobs Act of 2017 (the "TCJA") may cause a reduction in the economic benefit of our net operating loss carryforwards and other deferred tax assets available to us. Furthermore, under the TCJA, although the treatment of NOLs generated before December 31, 2017 has generally not changed, NOLs generated in calendar year 2018 and beyond will not be subject to expiration but will only be able to offset 80% of taxable income. This change may require us to pay federal income taxes even if we have NOL carryforwards that could otherwise offset our taxable income.

Changes in U.S. tax legislation may materially adversely affect our financial condition, results of operations and cash flows.

The TCJA has significantly changed the U.S. federal income taxation of U.S. corporations, including by reducing the U.S. corporate income tax rate, limiting interest deductions, modifying or repealing many business deductions and credits (including reducing the business tax credit for certain clinical testing expenses incurred in the testing of certain drugs for rare diseases or conditions generally referred to as “orphan drugs”), adopting elements of a territorial tax system, imposing a one-time transition tax, or repatriation tax, on all undistributed earnings and profits of certain U.S.-owned foreign corporations, revising the rules governing net operating losses and the rules governing foreign tax credits, and introducing new anti-base erosion provisions. In addition, it is unclear how these U.S. federal income tax changes will affect state and local taxation, which often uses federal taxable income as a starting point for computing state and local tax liabilities.

While some of the changes made by the TCJA may adversely affect us in one or more reporting periods and prospectively, other changes may be beneficial on a going forward basis. We continue to work with our tax advisors

and auditors to determine the full impact that the TCJA will have on us. We urge our investors to consult with their legal and tax advisors with respect to the TCJA.

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

None.

Item 3. Defaults Upon Senior Securities.

None.

Item 4. Mine Safety Disclosures

Not applicable.

Item 5. Other Information

None.

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	3.2	5/11/2018	
10.1	Loan and Security Agreement between Pacific Western Bank and Evelo Biosciences, Inc., dated August 15, 2016, as amended on June 14, 2017, August 18, 2017, February 7, 2018, March 14, 2018 and April 18, 2019.	10-Q	001-38473	10.1	8/6/2019	
10.2	Loan and Security Agreement by and among Evelo Biosciences, Inc. and the other borrowers party thereto, the lenders party thereto, K2 HealthVentures LLC, as administrative agent for such lenders, and Ankura Trust Company, LLC, as collateral agent for such lenders, dated July 19, 2019, as amended.	10-Q	001-38473	10.3	8/6/2019	
10.3 †	Collaboration Agreement between Evelo Biosciences, Inc. and Sacco S.r.l., dated July 9, 2019.	10-Q	001-38473	10.4	8/6/2019	
10.4	Amendment No. 1 to Exclusivity and Commitment Agreement between Evelo Biosciences, Inc. and Biose Industrie, dated as of August 1, 2019.					*
10.5	Letter Agreement between Evelo Biosciences, Inc. and David R. Epstein dated September 16, 2019.	8-K	001-38473	10.1	9/18/2019	
10.6	Consulting Agreement between Evelo Biosciences, Inc. and David R. Epstein dated September 16, 2019.	8-K	001-38473	10.2	9/18/2019	
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	XBRL Instance Document					*

Exhibit Number	Exhibit Description	Incorporated by Reference				Filed Herewith
		Form	File No.	Exhibit	Filing Date	
101.SCH	XBRL Taxonomy Extension Schema Document					*
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document					*
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document					*
101.LAB	XBRL Taxonomy Extension Label Linkbase Document					*
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document					*

* Filed herewith.

** Furnished herewith.

† Portions of this exhibit have been omitted pursuant to Item 601(b)(10)(iv) of Regulation S-K

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: November 5, 2019

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

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

Date: November 5, 2019

By: /s/ Jonathan Poole

Jonathan Poole
Chief Financial Officer
(Principal Financial and Accounting Officer)

Certain information marked as [***] has been excluded from this exhibit because it is both (i) not material and (ii) would be competitively harmful if publicly disclosed.

Exhibit 10.4

AMENDMENT NO. 1 TO EXCLUSIVITY AND COMMITMENT AGREEMENT

This Amendment No. 1 to an Exclusivity and Commitment Agreement is entered into as of August 1, 2019 by and between Biose Industrie, a French corporation with offices at rue des Freres Lumieres 15130, Arpajon sur Cere, France (registration number B529 243 271) (***"Biose"***) and Evelo Biosciences, Inc. a Delaware corporation with a principal place of business at 620 Memorial Drive, Cambridge, Massachusetts 02139, USA (***"Evelo"***). Evelo and Biose are each individually a "Party" and collectively referred to as the "Parties".

WHEREAS, Biose and Evelo are parties to an Exclusivity and Commitment Agreement entered into as of February 15, 2018 (the ***"Commitment Agreement"***), pursuant to which Biose reserves for Evelo agreed manufacturing resources to conduct Runs (as defined in the Commitment Agreement) and Evelo pays for Committed Run Resources (as defined in the Commitment Agreement);

WHEREAS, Biose and Evelo are parties to a Master Services Agreement effective as of August 3, 2017 (the ***"Service Agreement"***), pursuant to which Biose performs manufacturing activities, including Runs; and

WHEREAS, the Parties desire to modify the Commitment Agreement, including the Committed Run Schedule appended to the Commitment Agreement as Exhibit A, to address manufacturing issues experienced by Biose in the conduct of Runs in the first and second Agreement Years (as defined in the Commitment Agreement) and adjustments to Evelo's business requirements for Runs in the second Agreement Year;

NOW, THEREFORE, in consideration of the agreements and obligation set forth herein and for other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, the Parties, intending to be legally bound, do hereby agree as follows:

1. Definition of Run. Section 1.10 is amended to read as follows:

   "Run" means either, at the discretion of Evelo, (i) a [***] batch or (ii) a [***] batch fermentation for a particular Strain. A Run may be (a) an Engineering Run or (b) a GMP Run.

2. Run Fees. Sections 3.3(a) and (c)(iii) are amended to read as follows:

   (a) For a Run, Evelo will pay to Biose amounts as follows: (i) an Engineering Run fee will be [***] (but not less than [***]) for one [***] batch or [***] (but not less than [***]) for one [***] batch, as applicable; and (ii) a GMP Run fee will be [***] (but not less than [***]) for one [***] batch or [***] (but not less than [***]) for one [***] batch, as applicable; provided, however, if Evelo elects to forego a [***] batch Engineering Run for a given Strain before having Biose perform a GMP Run with such Strain, Evelo will pay to Biose an additional [***] for such GMP Run. Any Run fee shall be stated in and subject to a SOW and shall be paid according to the payment terms in the MSA. The Run fees above are fixed for the term of this Agreement, not subject to increases under the MSA and do not include any raw materials.

   (c)(iii) If Biose is unable to locate an alternative customer to use such Released Resources and Biose does not use such Released Resources for manufacturing purposes, then Evelo shall be obligated to pay Biose for the applicable unused Released Resources at the rate of [***] for a [***] batch or [***] for a [***] batch, taking into account any advance payments made by Evelo for such Released Resources.

3. Committed Run Schedule. Exhibit A (Committed Run Schedule) to the Commitment Agreement is deleted in its entirety and replaced with Exhibit A appended to this Amendment.

4. One-Time Payment. In recognition of Biose's efforts in connection with Runs [***] through [***] during Agreement Year 2 and the associated technical difficulties, notwithstanding the [***] of those Runs, Evelo shall pay to Biose the sum of [***] -- representing (i) the previously agreed Run fees in respect of [***] and [***], less advance payments previously paid to Biose for such Runs [***], plus the cost of materials consumed during such Runs [***]. For the avoid of doubt, no fees shall be owed or payable by Evelo to Biose in respect of [***] and [***] and the advance payments previously paid to Biose shall be credited to other Runs scheduled in Agreement Year 2.

5. No Other Changes. All other provisions of the Commitment Agreement shall remain unchanged and in full force and effect.

IN WITNESS WHEREOF, the Parties have executed this Amendment No. 1 through their duly authorized representatives.

Evelo Biosciences, Inc.	Biose Industrie
By: /s/ Daniel S. Char	By: /s/ Adrien Nivoliez
Name: Daniel S. Char	Name:
Title: General Counsel & Secretary	Title:
Date: August 8, 2019	Date: August 8, 2019

Exhibit A

Committed Run Schedule
(effective August 1, 2019)

Year	Number of Committed Runs
Agreement Year 1	*completed*
Agreement Year 2*Ü	[***], as specified below
Agreement Year 3*	[***], with such Run Resources allocated as follows: at least [***] Run [***] during each of Q1, Q2, Q3 and Q4**

The Run schedule above may be modified with the written agreement of the Parties. The payment for such Runs shall be made in accordance with Section 3.3.

* Evelo has the option to add up to [***] additional Runs per year in each Agreement Year 2 and Agreement Year 3, with 3 months notice to Biose for the subject Run(s) prior to the proposed Run start date(s). If Biose performs more than [***] Runs in Agreement Year 2, at the request and with the approval of Evelo, (i.e., beyond the Runs specified in the Run schedule below), then the number of committed Runs in Agreement Year 3 shall be reduced on a one for one basis for each additional Run performed in Agreement Year 2.

† The Run schedule for Agreement Year 2 shall be as set forth below:

No.	Project/Lot	Date	Comments
[***]	[***]		[***]
[***]	[***]		[***]
[***]	[***]		[***]
[***]	[***]		[***]
[***]	[***]		*completed*
[***]	[***]	[***]	*completed*
[***]	[***]	[***]	*credit of* [***] *applied*
[***]	[***]	[***]	*credit of* [***] *applied*
[***]	[***]	[***]	
[***]	[***]	[***]	
[***]	[***]	[***]	
[***]	[***]	[***]	
[***]	[***]	[***]	
[***]	[***]	[***]	
[***]	[***]	[***]	

Biose and Evelo shall execute one or more SOWs memorializing the Runs comprising the Committed Run Schedule for Agreement Year 2 (and confirming the start dates), and Evelo shall pay to Biose an advance payment of [***] in respect of the [***] through [***] Runs, promptly following the execution of Amendment No. 1 to Exclusivity and Commitment Agreement.

** For Agreement Year 3, a schedule for Runs subject to the Committed Run Resources shall be agreed by the Parties within 90 days prior to the start of Agreement Year 3.

In order to allow Biose to manufacture Runs for itself or other customers, Evelo may not schedule Runs such that Biose's [***] fermenter would be used for Evelo for more than [***] continuous days, unless otherwise agreed in writing by the Parties.

Evelo shall specify in the applicable SOW whether a specific Run is to be a [***] batch or a [***] batch, but either batch size shall constitute a Run for purposes of the above Committed Run Schedule and Section 3.3(b). For specific Runs listed in executed SOWs, Evelo may reschedule Runs with 3 months notice to Biose for the subject Run prior to the proposed rescheduled Run start date.

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 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)) 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) [omitted];
   (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: November 5, 2019

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, Jonathan Poole, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q 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(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) 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) [omitted];
   (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
   (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

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

   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: November 5, 2019

By: /s/ Jonathan Poole

Jonathan Poole

Chief Financial Officer

(Principal Financial and Accounting 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 Quarterly Report on Form 10-Q of the Company for the period ended September 30, 2019 (the "Report") fully complies with the requirements of section 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 result of operations of the Company.

Date: November 5, 2019

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, Jonathan Poole, Chief Financial 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 Quarterly Report on Form 10-Q of the Company for the period ended September 30, 2019 (the "Report") fully complies with the requirements of section 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 result of operations of the Company.

Date: November 5, 2019

By: /s/ Jonathan Poole

Jonathan Poole

Chief Financial Officer

(Principal Financial and Accounting Officer)