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

FORM 10-Q

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

For the quarterly period ended March 31, 2022

or

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

For the transition period from____to____

Sigilon Therapeutics, Inc.

(Exact name of registrant as specified in its charter)

Delaware	**001-39746**	**47-4005543**
(State or other jurisdiction of incorporation or organization)	(Commission File No.)	(I.R.S. Employer Identification No.)

100 Binney Street, Suite 600
Cambridge, MA 02142
(Address, including zip code, of registrant's principal executive offices)

(617) 336-7540
(Registrant's telephone number, including area code)

Securities Registered Pursuant to Section 12(b) of the Act:

Title of Each Class	**Trading Symbol(s)**	**Name of Each Exchange on Which Registered**
Common Stock, $0.001 par value per share	SGTX	The Nasdaq Global Select Market

Securities Registered Pursuant to Section 12(g) of the Act: None

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

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

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

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

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

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

As of May 2, 2022, there were 32,399,257 shares of the registrant's Common Stock, par value $0.001 per share, outstanding

Sigilon Therapeutics, Inc.
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RISK FACTORS SUMMARY

Our business is subject to a number of risks, including risks that may adversely affect our business, results of operations, cash flows, and prospects. These risks are discussed more fully in "Item 1.A Risk Factors" and include, but are not limited to, risks related to:

- We have incurred significant losses since inception. We expect to incur losses for the foreseeable future and may never achieve or maintain profitability.
- If we fail to achieve the expected financial and operational benefits of our corporate restructuring, our business and financial results may be harmed.
- The results of our investigation of the preliminary results of our Phase 1/2 clinical trial of SIG-001 in Hemophilia A or a failure of SIG-005 in clinical development could adversely affect our business and may require us to discontinue or delay development of other product candidates, which are all based on the same SLTx platform.
- The SLTx platform consists of novel technologies that are not yet clinically validated for human therapeutic use. The approaches we are taking to discover and develop novel therapeutics are unproven and may never lead to marketable products.
- We may not be successful in our efforts to identify and develop product candidates. If these efforts are unsuccessful, we may never become a commercial stage company or generate any revenues.
- We are early in our development efforts. It will be many years before we or our collaborators commercialize a product candidate, if ever.
- We only have preliminary data from the patients dosed with SIG-001 and no results from our product candidates in clinical trials and any favorable preclinical results are not predictive of results that may be observed in future clinical trials.
- Our product candidates are composed of engineered human cell lines, encapsulated in a biocompatible matrix sphere. To date, there have been no completed human clinical trials for product candidates arising from our SLTx platform or consisting of our cell or sphere technologies. There may be SAEs in addition to the SAE reported in our Phase 1/2 clinical trial of SIG-001 in Hemophilia A, undesirable side effects related to either component of our product candidates, or limited efficacy of product candidates arising from our SLTx platform.
- If clinical trials of our current and future product candidates fail to demonstrate safety and efficacy to the satisfaction of regulatory authorities or do not otherwise produce positive results, we may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of such product candidates.
- If we are unable to obtain and maintain patent and other intellectual property protection for SIG-001, SIG-005 or any other product candidates and for our SLTx platform, or if the scope of the patent and other intellectual property protection obtained is not sufficiently broad, our SLTx platform may be adversely affected.

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Quarterly Report on Form 10-Q contains forward-looking statements. All statements other than statements of historical facts contained in this Quarterly Report on Form 10-Q are forward-looking statements. In some cases, forward-looking statements include 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, although not all forward-looking statements contain these words. Forward-looking statements include, but are not limited to, statements concerning:

- the initiation, timing, enrollment, progress and results of our research and development programs, preclinical studies and clinical trials, the timing and enrollment of our clinical trial for SIG-005 and the submission or approval of INDs or CTAs for our other product candidates, including SIG-002;
- our ability to advance any product candidates that we may develop and successfully complete any clinical studies, including the manufacture of any such product candidates;
- our plan to develop next generation product candidates designed to penetrate the blood brain barrier;
- our ability to leverage our initial programs to develop additional product candidates using the SLTx platform and our ability to leverage the modularity of our SLTx platform across our lysosomal disease programs;
- the impact of the COVID-19 pandemic on our business operations, including our research and development programs, preclinical studies and clinical trials;
- our ability to treat, identify or otherwise expand or access the target populations of our programs;
- our ability to identify and enter into future license agreements and collaborations; and
- estimates of our expenses, capital requirements and needs for additional financing.

There may be events in the future that we are not able to accurately predict or control and that may cause our actual results to differ materially from the expectations we describe in our forward-looking statements. We undertake no obligation to publicly update any forward-looking statement, whether as a result of new information, future developments or otherwise, except as may be required by law. You should, therefore, not rely on these forward-looking statements as representing our views as of any date subsequent to the date of this Quarterly Report on Form 10-Q. We cannot guarantee future results, levels of activity, performance or achievements.

PART I – FINANCIAL INFORMATION

Item 1. Financial Statements

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

	March 31, 2022	December 31, 2021
Assets		
Current assets:		
Cash and cash equivalents	$ 64,487	$ 107,143
Marketable securities	38,618	16,213
Accounts receivable (inclusive of $23 and $23 from a related party at March 31, 2022 and December 31, 2021, respectively)	62	59
Prepaid expenses and other current assets	6,234	2,729
Restricted cash—current	250	250
Total current assets	109,651	126,394
Property and equipment, net	3,689	3,994
Right-of-use assets	11,708	12,863
Restricted cash	1,118	1,118
Total assets	$ 126,166	$ 144,369
Liabilities and stockholders' equity (deficit)		
Current liabilities:		
Accounts payable	$ 2,040	$ 2,344
Accrued expenses and other current liabilities	8,060	8,998
Lease liabilities, current portion	4,407	4,845
Current portion of long-term debt	3,333	1,667
Deferred revenue from related party, current portion	19,206	17,034
Total current liabilities	37,046	34,888
Deferred revenue from related party, net of current portion	—	5,333
Lease liability, net of current portion	7,721	8,577
Long-term debt, net of discount and current portion	16,811	18,411
Total liabilities	$ 61,578	$ 67,209
Commitments and contingencies (Note 9)		
Stockholders' equity		
Common stock, par value $0.001 per share; 175,000,000 shares authorized at March 31, 2022 and December 31, 2021; 32,399,257 and 32,359,895 shares issued and outstanding at March 31, 2022 and December 31, 2021, respectively	32	32
Preferred stock, par value $0.001 per share; 25,000,000 shares authorized at March 31, 2022 and December 31, 2021; no shares issued and outstanding at March 31, 2022 and December 31, 2021	—	—
Additional paid-in capital	292,043	290,377
Accumulated other comprehensive income	(389)	(10)
Accumulated deficit	(227,098)	(213,239)
Total stockholders' equity	64,588	77,160
Total liabilities and stockholders' equity	$ 126,166	$ 144,369

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

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

	Three Months Ended March 31,	
	2022	2021
Revenue		
Collaboration revenue (inclusive of $3,161 and $2,932 from a related party for the three months ended March 31, 2022 and 2021, respectively)	$ 3,165	$ 2,958
Operating expenses:		
Research and development	11,618	15,985
General and administrative	5,024	5,540
Total operating expenses	16,642	21,525
Loss from operations	(13,477)	(18,567)
Other income (expense), net:		
Interest income	64	86
Interest expense	(491)	(488)
Other income (expense)	45	(4)
Total other expense, net	(382)	(406)
Net loss	$ (13,859)	$ (18,973)
Net loss per share—basic and diluted	$ (0.43)	$ (0.60)
Weighted average common stock outstanding—basic and diluted	32,360,786	31,487,710
Other comprehensive loss		
Unrealized loss on marketable debt securities	(379)	—
Total other comprehensive loss	(379)	—
Total comprehensive loss	$ (14,238)	$ (18,973)

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

Sigilon Therapeutics, Inc.
Condensed Consolidated Statements of
Stock and Stockholders' Equity (Deficit)
(Unaudited, in thousands, except share amounts)

	Common Stock		Additional Paid-In Capital	Accumulated Other Comprehensive Loss	Accumulated Deficit	Total Stockholders' Equity (Deficit)
	Shares	Amount				
Balances at December 31, 2021	32,359,895	$ 32	$ 290,377	$ (10)	$ (213,239)	$ 77,160
Issuance of common stock upon exercise of stock options	833	—	1	—	—	1
Issuance of ESPP shares	38,529	—	47	—	—	47
Stock-based compensation expense	—	—	1,618	—	—	1,618
Unrealized loss on marketable debt securities	—	—	—	(379)	—	(379)
Net loss	—	—	—	—	(13,859)	(13,859)
Balances at March 31, 2022	32,399,257	$ 32	$ 292,043	$ (389)	$ (227,098)	$ 64,588
Balances at December 31, 2020	31,464,989	$ 31	$ 282,053	$ —	$ (135,928)	$ 146,156
Issuance of common stock upon exercise of stock options	36,963	1	144	—	—	145
Stock-based compensation expense	—	—	1,704	—	—	1,704
Net loss	—	—	—	—	(18,973)	(18,973)
Balances at March 31, 2021	31,501,952	$ 32	$ 283,901	$ —	$ (154,901)	$ 129,032

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

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

	Three Months Ended March 31,	
	2022	2021
Cash flows from operating activities:		
Net loss	$ (13,859)	$ (18,973)
Adjustments to reconcile net loss to net cash (used in) provided by operating activities:		
Depreciation and amortization expense	316	247
Gain on disposal of fixed assets	(20)	—
Stock-based compensation expense	1,618	1,704
Non-cash lease expense	1,223	1,197
Non-cash interest expense	66	67
Amortization of premium on marketable securities	35	—
Changes in operating assets and liabilities:		
Accounts receivable	(3)	37
Prepaid expenses and other current assets	(3,336)	(2,329)
Accounts payable	(186)	578
Accrued expenses and other current liabilities	(819)	(991)
Lease liabilities	(1,362)	(1,292)
Deferred revenue	(3,161)	(2,918)
Net cash used in operating activities	(19,488)	(22,673)
Cash flows from investing activities:		
Purchases of marketable securities	(22,819)	—
Purchase of property and equipment	(397)	(290)
Net cash used in investing activities	(23,216)	(290)
Cash flows from financing activities:		
Payments of deferred offering costs	—	(622)
Proceeds from employee equity plans	48	145
Net cash provided by (used in) financing activities	48	(477)
Net decrease in cash, cash equivalents and restricted cash	(42,656)	(23,440)
Cash, cash equivalents and restricted cash at beginning of period	108,511	203,422
Cash, cash equivalents and restricted cash at end of period	$ 65,855	$ 179,982
Supplemental disclosure of cash flow information:		
Cash paid for interest	$ 420	$ 420
Supplemental disclosures of noncash investing and financing activities:		
Right-of-use assets obtained in exchange for lease liabilities	$ 68	$ 564
Receivable for proceeds from the sale of property and equipment in prepaid expenses and other current assets	$ 169	$ —
Purchases of property and equipment included in accounts payable and accrued expenses	$ 85	$ 108

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

Sigilon Therapeutics, Inc.
Notes to the Condensed Consolidated Financial Statements
(Unaudited)

1. Nature of the Business and Basis of Presentation

Sigilon Therapeutics, Inc. (the "Company" or "Sigilon") is a biopharmaceutical company with a platform of biomedical technologies and cell therapies created to avoid host detection and foreign body responses with a goal of providing functional cures to patients with chronic diseases. The Company was incorporated on May 14, 2015 under the laws of the State of Delaware.

The Company is subject to risks and uncertainties common to early-stage companies in the biotechnology industry, including, but not limited to, the successful completion of research and development, development by competitors of new technological innovations, dependence on key personnel, protection of technology, compliance with government regulations, and the ability to secure additional capital to fund operations and commercial success of its product candidates.

Since its inception, the Company has devoted substantially all of its efforts to raising capital, obtaining financing, and incurring research and development costs related to advancing its biomedical platform. Product candidates currently under development will require significant additional research and development efforts, including extensive preclinical and clinical testing and regulatory approval prior to commercialization. These efforts require significant amounts of additional capital, adequate personnel and infrastructure and extensive compliance-reporting capabilities. Even if the Company's product development efforts are successful, it is uncertain when, if ever, the Company will realize significant revenue from product sales.

Basis of Presentation

The accompanying Unaudited Condensed Consolidated Financial Statements have been prepared in accordance with (i) U.S. generally accepted accounting principles ("U.S. GAAP") for interim financial information and (ii) the instructions to Form 10-Q and Article 8 of Regulation S-X. Accordingly, such financial statements do not include all the information and footnotes required by U.S. GAAP for a complete set of financial statements. In the opinion of management, the Unaudited Condensed Financial Statements include all adjustments, consisting of normal recurring accruals and other adjustments, considered necessary for a fair statement of the Company's financial position, results of operations, stockholders' equity (deficit) and cash flows as of and for the periods presented. The accompanying Condensed Consolidated Balance Sheet as of December 31, 2021 was derived from the Company's audited financial statements at that date but does not include all of the footnote disclosures required by U.S. GAAP.

The Unaudited Condensed Consolidated Financial Statements should be read in conjunction with the Company's audited financial statements and related notes included in its Annual Report on Form 10-K for the year ended December 31, 2021 (the "2021 Form 10-K"). The Company's significant accounting policies are described in Note 2 to the Notes to Financial Statements in the 2021 Form 10-K and are updated, as necessary, in subsequent Form 10-Q filings.

Going Concern

The Company has evaluated whether there are conditions and events, considered in the aggregate, that raise substantial doubt about the Company's ability to continue as a going concern within one year after the date the financial statements are issued.

From its inception through March 31, 2022, the Company has funded its operations primarily with proceeds from its IPO, sales of convertible preferred stock, payments received under its collaboration agreement and proceeds from borrowings under loan and security agreements. The Company has incurred recurring losses since inception, including net losses of $13.9 million for the three months ended March 31, 2022 and $77.3 million for the year ended December 31, 2021. In addition, as of March 31, 2022, the Company had an accumulated deficit of $227.1 million. The Company expects to generate significant losses and negative cash flows from operations for the foreseeable future.

Based on its current operating plans, the Company believes its cash, cash equivalents and marketable securities of $103.1 million as of March 31, 2022 will be sufficient to fund its anticipated level of operations, capital expenditures and satisfy debt repayments for a period of at least 12 months from the issuance date of this Quarterly Report. The Company expects to generate operating losses for the foreseeable future. Accordingly, the Company will seek additional funding through equity financings, debt financing, or additional collaboration agreements. If the Company is unable to raise additional funds through equity financing, debt financings or additional collaboration agreements the Company may be required to delay, limit, reduce or terminate product development or future commercialization efforts or grant rights to develop and market products or product candidates that the Company would otherwise prefer to develop and market itself.

Impact of COVID-19

The COVID-19 pandemic has impacted and may continue to impact the clinical sites and startup activities for the Company's Phase 1/2 clinical trials, including the operations of the Company's third-party manufacturing and logistics providers, which has disrupted its clinical supply chain or the availability or cost of materials, and it may affect the Company's ability to timely complete its clinical trials and delay the initiation and/or enrollment of any future clinical trials, disrupt regulatory activities or have other adverse effects on its business and operations.

The Company is monitoring the potential impact of COVID-19 on its business and financial statements. The effects of the public health directives may negatively impact productivity, disrupt its business and delay clinical programs and timelines and future clinical trials, the magnitude of which will depend, in part, on the length and severity of the restrictions and other limitations on its ability to conduct business in the ordinary course. These and similar, and perhaps more severe, disruptions in the Company's operations could negatively impact business, results of operations and financial condition, including its ability to obtain financing.

To date, the Company has not incurred impairment losses in the carrying values of its assets as a result of the COVID-19 pandemic and are not aware of any specific related event or circumstance that would require the Company to revise its estimates reflected in financial statements.

The Company cannot be certain what the overall impact of the COVID-19 pandemic will be on its business and prospects. The extent to which the COVID-19 pandemic will directly or indirectly impact its business, results of operations, financial condition and liquidity, including planned and future clinical trials and research and development costs, will depend on future developments that are highly uncertain, including as a result of new information that may emerge concerning COVID-19, the actions taken to contain or treat it, and the duration and intensity of the related effects.

2. Summary of Significant Accounting Policies

Use of Estimates

The preparation of financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities, the disclosure of contingent assets and liabilities at the date of the financial statements and the reported amounts of revenue and expenses during the period. Estimates and assumptions reflected in these financial statements include, but are not limited to, revenue recognition, research and development expenses, the valuations of common stock, stock-based awards and the preferred stock warrant liability. The Company bases its estimates on historical experience, known trends and other market-specific or other relevant factors that it believes to be reasonable under the circumstances. On an ongoing basis, management evaluates its estimates as there are changes in circumstances, facts and experience. Changes in estimates are recorded in the period in which they become known. Actual results may differ from those estimates or assumptions.

Concentration of Credit Risk and of Significant Suppliers

The financial instruments that potentially subject the Company to concentrations of credit risk are cash and accounts receivable. The Company does not believe that it is subject to unusual credit risk beyond the normal credit risk associated with commercial banking relationships. As of March 31, 2022 and December 31, 2021, all of the Company's accounts receivable were related to two customers. As of March 31, 2022 and December 31, 2021, 36% and 39%,

respectively, of the Company's total receivables were related to the Company's collaboration agreements with Eli Lilly and Company (Note 8).

The Company is dependent on third-party manufacturers to supply certain products for research and development activities in its programs. The Company currently has a supplier of certain raw materials that would be considered a sole supplier. If the Company cannot access additional suppliers, its programs could be adversely affected by an interruption in the availability of these raw materials.

Net Income (Loss) per Share

The Company only has one class of shares outstanding and basic net income (loss) per common share is computed by dividing the net income (loss) by the weighted average number of shares of common stock outstanding for the period. Diluted net income (loss) per common share is computed by dividing net income (loss) by the weighted average number of shares of common stock outstanding for the period, including potential dilutive common shares assuming the dilutive effect of outstanding stock awards. For periods in which the Company reports a net loss, diluted net loss per common share is the same as basic net loss per common share, since dilutive common shares are not assumed to have been issued if their effect is anti-dilutive.

Recently Issued Accounting Pronouncements

In June 2016, the FASB issued ASU 2016-13, *Financial Instruments—Credit Losses (Topic 362): Measurement of Credit Losses on Financial Statements* ("ASU 2016-13"). The new standard requires that expected credit losses relating to financial assets measured on an amortized cost basis and available-for-sale debt securities be recorded through an allowance for credit losses. It also limits the amount of credit losses to be recognized for available-for-sale debt securities to the amount by which carrying value exceeds fair value and also requires the reversal of previously recognized credit losses if fair value increases. The targeted transition relief standard allows filers an option to irrevocably elect the fair value option of ASC 825-10, Financial Instruments-Overall, applied on an instrument-by-instrument basis for eligible instruments. For public entities that are Securities and Exchange Commission ("SEC") filers, excluding entities eligible to be smaller reporting companies, ASU 2016-13 is effective for annual periods beginning after December 15, 2019, including interim periods within those fiscal years. For all other entities, ASU 2016-13 is effective for annual periods beginning after December 15, 2022, including interim periods within those fiscal years. Early adoption is permitted and the Company adopted ASU 2016-13 on January 1, 2022. The adoption of this standard did not have a material impact on its financial statements.

In December 2019, the FASB issued ASU 2019-12, *Income Taxes (Topic 740): Simplifying the Accounting for Income Taxes* ("ASU 2019-12"), which is intended to simplify the accounting for income taxes. ASU 2019-12 removes certain exceptions to the general principles in Topic 740 and also clarifies and amends existing guidance to improve consistent application. The new standard will be effective for public business entities, for fiscal years beginning after December 15, 2020, and for all other entities, for fiscal years beginning after December 15, 2021 and the Company adopted ASU 2016-13 on January 1, 2022. The adoption of ASU 2019-12 did not have a material impact on the Company's financial statements.

In March 2020, the FASB issued ASU No. 2020-04, *Reference Rate Reform (Topic 848): Facilitation of the Effects of Reference Rate Reform on Financial Reporting* ("ASU 2020-04"), which provide optional expedients and exceptions for applying generally accepted accounting principles to contracts, hedging relationships, and other transactions that reference the London Interbank Offered Rate ("LIBOR") or another reference rate expected to be discontinued because of reference rate reform if contract modifications are made on or before December 31, 2022. The amendments in this update are effective for all entities as of March 12, 2020 and do not apply to contract modifications made, and hedging relationships entered into or evaluated, after December 31, 2022. The Company is currently evaluating the potential impact ASU 2020-04 may have on its financial statements.

3. Fair Value Measurements and marketable securities

Value Measurements

The following tables present information about the Company's financial assets that have been measured at fair value as of March 31, 2021 and indicate the fair value of the hierarchy of the valuation inputs utilized to determine such fair value. In general, fair values determined by Level 1 inputs utilize quoted prices (unadjusted) in active markets for identical assets or liabilities. Fair value determined by Level 2 inputs utilize observable inputs other than Level 1 prices, such as quoted prices for similar assets or liabilities, quoted market prices in markets that are not active or other inputs that are observable or can be corroborated by observable market data for substantially the full term of the related assets or liabilities. Fair values determined by Level 3 inputs are unobservable data points for the asset or liability, and include situations where there is little, if any, market activity for the asset or liability. During the three months ended March 31, 2021, there were no transfers between Level 1 and Level 2 financial assets.

The following table summarizes the Company's cash equivalents and marketable securities as of March 31, 2022 and December 31, 2021 (in thousands):

	Fair value measurements as of March 31, 2022			
	Level 1	Level 2	Level 3	Total
Cash equivalents				
Money market funds	$ 28,897	$ —	$ —	$ 28,897
Commercial paper	—	20,158	—	20,158
U.S. Treasuries	—	4,999	—	4,999
Total cash equivalents	$ 28,897	$ 25,157	$ —	$ 54,054
Marketable securities				
Corporate bonds	$ —	$ 25,735	$ —	$ 25,735
Commercial paper	—	10,654	—	10,654
U.S. Government Agencies	—	1,235	—	1,235
U.S. Treasuries	—	994	—	994
Total marketable securities	$ —	$ 38,618	$ —	$ 38,618
Total	$ 28,897	$ 63,775	$ —	$ 92,672

	Fair value measurements as of December 31, 2021			
	Level 1	Level 2	Level 3	Total
Cash equivalents				
Money market funds	$ 50,847	$ —	$ —	$ 50,847
Commercial paper	—	25,995	—	25,995
Corporate bonds	—	1,000	—	1,000
Total cash equivalents	$ 50,847	$ 26,995	$ —	$ 77,842
Marketable securities				
Corporate bonds	$ —	$ 10,238	$ —	$ 10,238
Commercial paper	—	5,975	—	5,975
Total marketable securities	$ —	$ 16,213	$ —	$ 16,213
Total	$ 50,847	$ 43,208	$ —	$ 94,055

Marketable Securities

The following tables summarizes the Company's available-for-sale marketable debt securities as of March 31, 2022 and December 31, 2021 (in thousands):

	Fair value measurements as of March 31, 2022				
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Credit Losses	Total
Corporate bonds	$ 26,052	$ —	$ (317)	$ —	$ 25,735
Commercial paper	10,704	—	(50)	—	10,654
U.S. Treasuries	1,248	—	(13)	—	1,235
U.S. Government Agencies	998	—	(4)	—	994
Total	$ 39,002	$ —	$ (384)	$ —	$ 38,618

	Fair value measurements as of December 31, 2021			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Total
Commercial paper	$ 10,244	$ —	$ (6)	$ 10,238
Corporate bonds	5,977	—	(2)	5,975
Total	$ 16,221	$ —	$ (8)	$ 16,213

No declines in value were deemed to be other than temporary during the three months ended March 31, 2022 and the year ended December 31, 2021.

The following table summarizes the Company's available-for-sale marketable debt securities by contractual maturity, as of March 31, 2022 and December 31, 2021 (in thousands):

	March 31, 2022	December 31, 2021
Maturities in one year or less	$ 23,459	$ 9,004
Maturities between one and two years	15,159	7,209
Total	$ 38,618	$ 16,213

As of March 31, 2022 and December 31, 2020 the Company did not have any other financial assets and liabilities that were measured at fair value on a recurring basis.

The carrying value of the Company's long-term debt approximates its fair value at March, 31 2022 and December 31, 2021 because the debt bears interest at a variable market rate and the Company's credit risk has not materially changed since the inception of the agreement.

4. Property and Equipment, Net

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

	March 31, 2022	December 31, 2021
Laboratory equipment	$ 6,301	$ 6,297
Leasehold improvements	78	78
Furniture and fixtures	620	620
Computers and software	141	163
	7,140	7,158
Less: Accumulated depreciation and amortization	(3,451)	(3,164)
Total property and equipment, net	$ 3,689	$ 3,994

Depreciation and amortization expense for the three months ended March 31, 2022 and 2021 was $0.3 million and $0.2 million, respectively.

5. Accrued Expenses and Other Current Liabilities

Accrued expenses and other current liabilities consisted of the following (in thousands):

	March 31, 2022	December 31, 2021
Employee compensation and benefits	$ 1,154	$ 3,071
External research and development costs	6,127	5,056
Legal and professional fees	593	656
Other	186	215
Total accrued expenses and other current liabilities	$ 8,060	$ 8,998

6. Debt

The following discussion of the Company's debt should be read in conjunction with Note 8 to the Notes to the Consolidated Financial Statements in the 2021 Form 10-K.

As of March 31, 2022 and December 31, 2021, long-term debt consisted of the following (in thousands):

	March 31, 2022	December 31, 2021
Principal amount of long-term debt	$ 20,000	$ 20,000
Less: Current portion of long-term debt	(3,333)	(1,667)
Long-term debt, net of current portion	16,667	18,333
Final debt payment liability	700	700
Debt discount, net of accretion	(556)	(622)
Long-term debt, net of discount and current portion	$ 16,811	$ 18,411

As of March 31, 2022 and December 31, 2021, the interest rate applicable to borrowings under the 2020 Credit Facility was 8.47% and 8.40%, respectively.

The estimated future principal payments due were as follows (in thousands):

	March 31, 2022
2022 (Remaining nine months)	$ 1,666
2023	6,667
2024	6,667
2025	5,000
2026	—
	$ 20,000

As of March 31, 2022, the Company was in full compliance with all financial covenants of the Loan Agreement.

7. Stock Based Compensation

The Company uses stock options to provide long-term incentives to its employees, non-employee directors and certain consultants. The Company has two equity compensation plans under which awards are currently authorized for issuance: the 2020 Employee Stock Purchase Plan and the 2020 Equity Incentive Plan. The Company also has outstanding stock-based awards under its 2016 Equity Incentive Plan but is no longer granting awards under this plan. As of March 31, 2022, there were 882,827 shares available for issuance under the 2020 Employee Stock Purchase Plan and 1,725,763 shares available for issuance under the 2020 Equity Incentive Plan.

The fair value of each option is estimated on the date of grant using the Black-Scholes option-pricing model. The Company was a private company prior to the initial public offering and lacked company-specific historical and implied volatility information for its stock. Therefore, it estimates its expected stock price volatility based on the historical volatility of a publicly traded set of peer companies and expects to continue to do so until such time as it has adequate historical data regarding the volatility of its own traded stock price. The expected term of the Company's stock options has been determined utilizing the "simplified" method for awards that qualify as "plain-vanilla" options. The expected term of options granted to non-employees is equal to the contractual term of the option award. The risk-free interest rate is determined by reference to the U.S. Treasury yield curve in effect at the time of grant of the award for time periods approximately equal to the expected term of the award. Expected dividend yield of 0% is based on the fact that the Company has never paid cash dividends on common stock and does not expect to pay any cash dividends in the foreseeable future.

The following table presents, on a weighted average basis, the assumptions used in the Black-Scholes option-pricing model to determine the grant-date fair value of stock options granted to employees and directors:

	Three months ended March 31,	
	2022	2021
Risk-free interest rate	1.61 %	0.66 %
Expected dividend yield	0.00 %	0.00 %
Expected term (in years)	6.0	6.1
Expected volatility	84.28 %	78.39 %

Stock Option Activity

The following table summarizes the Company's stock option activity since December 31, 2021:

	Number of options	Weighted average exercise price	Weighted average remaining contractual term (in years)	Aggregate intrinsic value (in thousands)
Balances at December 31, 2021	3,138,646	$ 10.74	7.6	$ 328
Options granted	2,250,674	2.39		
Options cancelled	(385,026)	7.11		
Options exercised	(833)	0.57		
Outstanding and expected to vest at March 31, 2022	5,003,461	7.27	8.4	94
Exercisable at March 31, 2022	1,718,102	$ 6.83	6.6	$ 94

The aggregate intrinsic value of options is calculated as the difference between the exercise price of the stock options and the fair value of the Company's common stock for those options that had exercise prices lower than the fair value of the Company's common stock.

The aggregate intrinsic value of stock options exercised during the three months ended March 31, 2022 and 2021 were less than $0.1 million and $1.0 million, respectively. The weighted average grant date fair value of stock options during the three months ended March 31, 2022 and 2021 were $1.69 and $26.64, respectively.

Restricted Stock Units

The Company has granted restricted stock units with time-based vesting conditions to employees. The restricted stock units primarily vest over 3 years from the grant date. The Company values restricted stock units on the grant-date using the market price of the Company's common stock.

The following table summarizes restricted stock unit activity since December 31, 2021:

	Shares	Weighted average grant date fair value
Unvested shares as of December 31, 2021	275,400	$ 5.57
Forfeited	(53,500)	5.60
Unvested shares as of March 31, 2022	221,900	$ 5.56

Stock-based Compensation Expense

Stock-based compensation expense related to stock options and restricted stock units was classified in the statement of operations and comprehensive loss as follows (in thousands):

	Three months ended March 31,	
	2022	2021
Research and development	$ 516	$ 839
General and administrative	1,102	865
	$ 1,618	$ 1,704

As of March 31, 2022, total unrecognized stock-based compensation expense related to unvested stock-based awards and units was $16.2 million, which is expected to be recognized over a weighted average period of 2.6 years.

8. License and Collaboration Agreement

Lilly License and Collaboration Agreement

On April 2, 2018, the Company entered into a License and Collaboration Agreement with Lilly (the "2018 Lilly Agreement"). Under the 2018 Lilly Agreement, the Company granted Lilly an exclusive worldwide, royalty-bearing license, including the right to grant sublicenses, to the Company's encapsulation technology applied to islet cells. The Company is responsible for research and development activities, including supply and manufacturing activities, through investigational new drug ("IND") filing readiness for the first product candidate, including costs up to $47.5 million and certain supply and manufacturing of products and materials in Phase 1 clinical trials and for clinical and commercial use following Phase 1 clinical trials; provided, however, that, pursuant to an amendment to the 2018 Lilly Agreement entered in May 2022, Lilly may take on certain research and development activities, at its own cost and expense, including supply and manufacturing activities. In addition, Lilly will be responsible for development and commercialization of any licensed product post-IND filing readiness and research and development costs for the IND product candidate above the $47.5 million cost threshold. Lilly is also responsible for all research, development and commercialization related to any subsequent product candidate. The parties are collaborating with the intent of developing encapsulated cell therapies for the potential treatment of type 1 diabetes. The activities under the agreement are governed by a joint research committee ("JRC"), which meets quarterly and consists of at least three members each from the Company and Lilly.

Under the 2018 Lilly Agreement, Lilly was obligated to pay the Company a one-time, non-refundable and non-creditable license issuance fee of $62.5 million. Lilly is also obligated to make aggregate milestone payments to the Company of up to $165.0 million upon achievement of certain regulatory milestones for the first licensed product and regulatory milestones up to $160.0 million for additional licensed products. Lilly is also obligated to pay the company sales-based milestones of up to $250.0 million for each licensed product and tiered (from mid-single-to-low-double digit) sales-based royalties for each licensed product. The 2018 Lilly Agreement will expire upon the expiration of the last royalty term, on a product-by-product and country-for country basis. The royalty term, by product and country, commences upon the first commercial sale and ends upon the later to occur of (i) the expiration of the Company's patent rights of a product candidate developed under the Lilly Agreement, (ii) the expiration of any data exclusivity period in a country or (iii) 10 years after the first commercial sale.

The Company will have the right, and the obligation, to supply Lilly's requirements for the material to be used in the manufacture of licensed products for clinical and commercial use. In connection with the supply responsibilities, the parties may enter into supply and quality agreements for both clinical and commercial supply.

The Company evaluated the 2018 Lilly Agreement under ASC 606 as the transactions underlying the agreement were considered transactions with a customer. The Company identified the following material promises under the arrangement: (i) exclusive license to research, develop, manufacture and commercialize licensed products, (ii) initial technology transfer, (iii) research activities (including pre-IND supply), (iv) cell line development and supply, (v) product trademark election, (vi) requirement to supply Lilly with the licensed product related to Phase 1 clinical trial ("Phase 1 Supply") and (vii) participation in the JRC.

The Company determined that the exclusive license to research, develop, manufacture and commercialize the licensed product was not distinct from the related research and manufacturing activities to be provided by the Company as a result of Lilly being unable to benefit on its own or with other resources reasonably available in the marketplace because the license to the Company's intellectual property requires significant specialized capabilities in order to be further developed, the research services necessary to develop the product are highly specialized and the Company's proprietary technology is a key capability of that development. The cell line development and supply and research activities were determined not to be distinct because they are performed in conjunction with the research activities to further develop the underlying technology. The product trademark was determined not to be distinct because the benefit that Lilly receives from the Company's trademark license only exists when combined with the right to commercialize the licensed product. In addition, the Company determined that the impact of the participation in the JRC was insignificant and had an immaterial impact on the accounting model. Therefore, the Company determined that the first five promises should be combined into a single performance obligation (the "Combined Performance Obligation"). The Company determined the sixth promise, the Phase 1 Supply promise, is distinct in the contract. As this is at no cost to Lilly, the right to receive this supply represents

a material right and a distinct performance obligation. As such, the Company determined there were two distinct performance obligations at the outset of the 2018 Lilly Agreement.

The Company determined that the $62.5 million upfront payment represents the entirety of the consideration to be included in the transaction price as of the outset of the arrangement. The potential milestone payments that the Company may have been eligible to receive were initially excluded from the transaction price at the outset of the arrangement because (i) all development and regulatory milestone payments did not meet the criteria for inclusion using the most-likely-amount method and (ii) the Company recognizes as revenue sales-based milestones and royalties when the related sales occur. As of March 31, 2022 no milestones or royalties have been deemed likely to be achieved or have been achieved.

The Company recognizes revenue for the Combined Performance Obligation as the research, development and manufacturing services are provided using an input method, based on the cumulative costs incurred compared to the total estimated costs expected to be incurred to satisfy the Combined Performance Obligation. The transfer of control to the customer occurs over the time period that the research and development services are to be provided by the Company, and this cost-to-cost method is, in management's judgement, the best measure of progress toward satisfying this performance obligation. The Company allocated $56.6 million of the transaction price to the Combined Performance Obligation at the outset of the arrangement.

The Phase 1 Supply was determined to be a material right, and the standalone selling price was estimated using the expected cost-plus margin approach. The Company allocated $5.9 million of the transaction price to the Phase 1 Supply at the outset of the arrangement. The Company has determined that the Phase 1 Supply will be satisfied at a point in time when the customer obtains control of each unit of product. Therefore, the Company will recognize revenue as shipments of the Phase 1 Supply are made to Lilly.

The Company reevaluates the transaction price and the total estimated costs expected to be incurred to satisfy the performance obligations at the end of each reporting period and as uncertain events, such as changes to the expected timing and cost of certain research, development and manufacturing activities that the Company is responsible for, are resolved or other changes in circumstances occur, and, if necessary, the Company will adjust its estimate of the transaction price and total estimated costs expected to be incurred.

During the three months ended March 31, 2022, consistent with the Company's presentation to the JRC, the Company revised its estimate of total costs to complete the activities under the 2018 Lilly Agreement to reflect the Company's experiences to date and the impact this has on its expected future research and development activities to satisfy the Combined Performance Obligation. During the three months ended March 31, 2022, there has been an increase to the total estimated costs expected to be incurred of $1.8 million verse the estimate as of December 31, 2021. The increase in total estimated costs impacted both the Company's estimated transaction price for the 2018 Lilly Agreement, as Lilly is obligated to reimburse the Company if the costs exceed $47.5 million to complete the services, and the Company's input method used to recognize revenue, as this measure compares the Company's cumulative costs incurred to the Company's total estimated costs expected to be incurred. During the three months ended March 31, 2022, based on the allocation of total transaction price to each performance obligation using the relative stand-alone selling price of each performance obligation under the 2018 Lilly Agreement, the transaction price for the Combined Performance Obligation increased by $1.6 million and the Phase 1 supply performance obligation increased by $0.2 million.

During the three months ended March 31, 2022 and 2021, the Company recognized $3.2 million and $2.9 million, respectively, of collaboration revenue. As of March 31, 2022 and December 31, 2021, the Company recorded as a contract liability deferred revenue of $19.2 million and $22.4 million, respectively, of which $19.2 million and $17.0 million, respectively, were classified as current liabilities in the accompanying balance sheet. As of March 31, 2022 and December 31, 2021, the research and development services related to the Combined Performance Obligation were expected to be performed over a remaining period of approximately 1.75 years and 2.0 years, respectively.

Contract Liability

The changes in the total contract liability (deferred revenue) balances related to the Company's license and collaboration agreements with Lilly were as follows (in thousands):

	Three Months Ended March 31,	
	2022	2021
Deferred revenues at beginning of period	$ 22,367	$ 31,777
Revenues deferred during the period	—	—
Revenues recognized during the period	(3,161)	(2,918)
Deferred revenues at end of period	$ 19,206	$ 28,859

9. Commitments and Contingencies

Indemnification Agreements

In the ordinary course of business, the Company may provide indemnification of varying scope and terms to vendors, lessors, business partners and other parties with respect to certain matters including, but not limited to, losses arising out of breach of such agreements or from intellectual property infringement claims made by third parties. In addition, the Company has entered into indemnification agreements with members of its board of directors and certain of its executive officers that will require the Company, among other things, to indemnify them against certain liabilities that may arise by reason of their status or service as directors or officers. The maximum potential amount of future payments the Company could be required to make under these indemnification agreements is, in many cases, unlimited. The Company has not incurred any material costs as a result of such indemnifications and is not currently aware of any indemnification claims.

Legal Proceedings

The Company is not a party to any material legal proceedings. At each reporting date, the Company evaluates whether or not a potential loss amount or a potential range of loss is probable and reasonably estimable under the provisions of the authoritative guidance that addresses accounting for contingencies. The Company expenses as incurred the costs related to such legal proceedings.

10. Net Loss per Share

Net Loss per Share

Basic and diluted net loss per share attributable to common stockholders was calculated as follows (in thousands, except share and per share amounts):

	Three Months Ended March 31,	
	2022	2021
Numerator:		
Net loss	$ (13,859)	$ (18,973)
Net loss attributable to common stockholders	$ (13,859)	$ (18,973)
Denominator:		
Weighted average common stock outstanding—basic and diluted	32,360,786	31,487,710
Net loss per share attributable to common stockholders—basic and diluted	$ (0.43)	$ (0.60)

The Company's potential dilutive securities have been excluded from the computation of diluted net loss per share as the effect would be to reduce the net loss per share. Therefore, the weighted-average number of common shares outstanding used to calculate both basic and diluted net loss per share attributable to common stockholders is the same. The Company excluded the following potential common shares, presented based on amounts outstanding at each period end, from the computation of diluted net loss per share attributable to common stockholders for the periods indicated because including them would have had an anti-dilutive effect:

	Three Months Ended March 31,	
	2022	2021
Warrants to purchase common stock	19,044	19,044
Unvested restricted stock units	221,900	—
Stock options to purchase common stock	5,003,461	4,638,399
	5,244,405	4,657,443

11. Related Party Transactions

As described in Note 8 above, the Company entered into the 2018 Lilly Agreement with Lilly in April 2018. During the three months ended March 31, 2022 and 2021, the Company recognized $3.2 million and $2.9 million, respectively, of related party revenue associated with Lilly collaboration agreements. As of March 31, 2022 and December 31, 2021, the Company had deferred revenue related to the collaboration agreements with Lilly of $19.2 million and $22.4 million, respectively. As of March 31, 2022 and December 31, 2021, the Company had less than $0.1 million of outstanding receivables with Lilly.

In January 2021, the Company entered into a shared space arrangement with a portfolio company of Flagship Pioneering, one of the Company's significant stockholders, to sublease a portion of its office and laboratory space in Cambridge, Massachusetts. The term of the shared space arrangement commenced in January 2021 and the initial term ended on December 31, 2021. Under this agreement, the Company recorded other income, net, of less than $0.1 million during the three months ended March 31, 2021 and the Company received cash payments of less than $0.1 million during the three months ended March 31, 2021.

On February 1, 2022, the Company entered into a shared space arrangement with a portfolio company of Flagship Pioneering, to sublease a portion of its office and laboratory space in Cambridge, Massachusetts. The term of the shared space arrangement commenced on February 1, 2022 and continues for an initial term ending on July 31, 2023. The agreement may be renewed for six successive one-month periods. The Company will be paid a fee based on the portfolio company's occupancy of the office and laboratory space. Under this agreement, the Company recorded other income, net, of less than $0.1 million during the three months ended March 31, 2022. The Company also agreed to sell to the portfolio company of Flagship Pioneering, certain fixed assets of the Company for $0.2 million. The Company did not receive cash payments during the three months ended March 31, 2022 and as of March 31, 2022 the Company had $0.5 million of outstanding receivables under these agreements that were recorded within other current assets.

12. Subsequent Event

On April 14, 2022, the Company entered into an Equity Distribution Agreement with Canaccord Genuity LLC, or Canaccord, pursuant to which the Company may issue and sell shares of common stock, from time to time, having an aggregate offering price of up to $10.0 million. Sales of common stock through Canaccord may be made by any method that is deemed an "at the market" offering as defined in Rule 415 promulgated under the Securities Act of 1933, as amended. The Company is not obligated to make any sales of its common stock under the Equity Distribution Agreement. Any sales under the Equity Distribution Agreement will be made pursuant to the Company's registration statement on Form S-3 (File No 333- 264296), which became effective on April 22, 2022 and the prospectus relating to such offering.

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 the financial statements and notes appearing elsewhere in this Quarterly Report on Form 10-Q. In addition to historical financial information, the following discussion contains forward-looking statements that reflect our plans, estimates and beliefs. Some of the numbers included herein have been rounded for the convenience of presentation. As a result of many factors, including those factors set forth in the "Risk Factors" section of this Quarterly Report, our actual results could differ materially from the results described in, or implied by, these forward-looking statements.

Overview

We are a clinical stage biotechnology company pioneering a new class of therapeutics and seeking to develop functional cures for patients with chronic diseases by providing stable and durable levels of therapeutic molecules to patients. We have developed our Shielded Living Therapeutics, or SLTx, platform, which combines advanced cell engineering with cutting-edge innovations in biocompatible materials and enables our product candidates to produce a wide range of therapeutic molecules that may be missing or deficient, such as proteins (including therapeutic proteins and antibodies) and hormones. We are designing our product candidates to be off-the-shelf, durable, controllable and redosable, without requiring modification of the patient's genes or complete suppression of the patient's immune system.

Since our inception, we have devoted substantially all of our efforts to raising capital, obtaining financing, filing and prosecuting patent applications, organizing and staffing our company and incurring research and development costs related to advancing our biomedical platform. We do not have any products approved for sale and have not generated any revenue from product sales. To date, we have funded our operations primarily with proceeds from sales of common stock and convertible preferred stock, payments received under our collaboration agreement with Lilly and proceeds from borrowings under our credit facilities. Through March 31, 2022, we have received gross proceeds of $144.9 million from the sale of common stock in the IPO, $142.4 million from sales of our convertible preferred stock and net proceeds of $19.8 million through borrowings under our loan and security agreement with Oxford Finance LLC, or the 2020 Credit Facility, partially offset by the $15.0 million repayment of debt from our 2019 Credit Facility. We have also partnered one of our encapsulation technology programs with Lilly. Under the terms of the partnership, we received an upfront payment of $62.5 million and we are eligible to receive additional milestone payments of up to $165.0 million upon achievement of certain regulatory milestones and sales-based milestones of up to $250.0 million for SIG-002. We are also eligible to receive tiered royalty payments in the mid-single digit to low-double digit percentages based on certain sales thresholds. Finally, Lilly is obligated to reimburse us for costs incurred to perform the research and development activities for the first developed product candidate, including costs up to $47.5 million.

We have incurred significant operating losses since our inception. Our ability to generate any product revenue sufficient to achieve profitability will depend on the successful development and eventual commercialization of one or more of our product candidates. We reported a net loss of $13.9 million for the three months ended March 31, 2022. As of March 31, 2022, we had an accumulated deficit of $227.1 million and cash, cash equivalents and marketable securities totaling $103.1 million. Based on our current operating plans, we believe our cash will be sufficient to fund our anticipated level of operations, capital expenditures and satisfy debt repayments for a period of at least 12 months from the issuance date of this Quarterly Report. We expect to generate operating losses for the foreseeable future. Accordingly, we will seek additional funding through equity financings, debt financing, or additional collaboration agreements. If we are unable to raise additional funds through equity financing, debt financings or additional collaboration agreements we may be required to delay, limit, reduce or terminate product development or future commercialization efforts or grant rights to develop and market products or product candidates that we would otherwise prefer to develop and market itself.

Our Shielded Living Therapeutics Platform and Prioritized Areas of Development

Our SLTx platform is comprised of two primary elements: the cells and the sphere. We engineered cells to express the therapeutic molecule of choice, which are subsequently encapsulated in our proprietary spheres. Our human cell line for our internal product candidates was selected for its safety, durability, scalability and engineerability, which has been extensively tested in preclinical and clinical settings. The spheres are composed of an Afibromer outer layer, an alginate conjugated with a novel, proprietary anti-fibrotic small molecule, which was derived from 10 years of work in the MIT

labs of Professors Robert Langer and Daniel Anderson. We developed an inner compartment consisting of a proprietary conjugation of alginate and peptide molecules to enhance cell survival and productivity.

Modularity, a key attribute of our SLTx platform, is comprised of three pillars: the cells, the sphere and the manufacturing process. In addition to the cells and the sphere described above, we have also spent significant time and resources to create a state-of-the-art modular manufacturing platform for all potential product candidates developed using our cell and sphere components. This cost-effective manufacturing platform is designed to provide a true "off-the-shelf" product for patients. Furthermore, virtually all aspects of the platform, from raw materials to processing steps, are shared across our development programs, enabling a potentially streamlined path from discovery to clinical trials.

In December 2021, we announced a strategic reprioritization focusing our development efforts on mucopolysaccharidosis type 1, or MPS-1, diabetes and platform optimization. Our programs and most advanced clinical-stage and pre-clinical product candidates are outlined below:

MPS-1: SIG-005 is our product candidate that contains a cell line genetically modified with a non-viral vector to express human α-L-iduronidase, or IDUA, encapsulated within our spheres. SIG-005 is being developed to treat the non-neurological manifestations of mucopolysaccharidosis type 1, or MPS-1, in patients with the disease. We were granted Orphan Drug designation for SIG-005 for the treatment of MPS-1 by the U.S. Food and Drug Administration, or FDA, in December 2020 and by the European Commission in October 2021. We have completed pre-IND and scientific advisory meetings with the FDA, the Medicines and Healthcare products Regulatory Agency, or MHRA, and the Brazilian Health Regulatory Agency, or ANVISA. We received a Clinical Trial Application, or CTA, clearance, for SIG-005 in the United Kingdom in the third quarter of 2021 and a CTA acceptance for SIG-005 in Brazil in the first quarter of 2022. Prior to initiating this study, we expect to submit amendments to the CTAs for SIG-005 in the United Kingdom and Brazil in the second half of 2022.

We believe our product candidates for lysosomal diseases can leverage the well understood mechanism of enzyme replacement therapies, or ERTs, by using engineered cells to express functional human enzyme or other protein that more closely resemble normal physiology in a continuous manner. We are also developing next-generation product candidates to address the neurological manifestations of lysosomal diseases, starting with MPS-1, using transporter molecules designed to penetrate the blood brain barrier and molecules designed to extend plasma half-life.

Diabetes: SIG-002 is our product candidate designed to replace islet cells for the treatment of Type 1 Diabetes, or T1D. In T1D, the immune system attacks and destroys the insulin-producing beta cells within the endocrine islets of the pancreas. Insulin deficiency results in dysregulation of glucose metabolism. In April 2018, we partnered with Eli Lilly and Company, or Lilly, to develop cell therapies for the treatment of T1D, including SIG-002. Under the terms of the partnership, we are currently leading execution of the program through Investigational New Drug, or IND, submission and Lilly, a global leader in diabetes, will develop and commercialize the program worldwide. We expect to conduct IND-enabling studies for SIG-002 in 2023.

Platform optimization: We are continuing to optimize our Shielded Living Therapeutics, or SLTx, platform, which combines advanced cell engineering with cutting-edge innovations in biocompatible materials to pioneer a new class of therapeutics. In November 2021, we reported that spheres covered with pericapsular fibrotic overgrowth, or PFO, were observed during a retrieval procedure in its Phase 1/2 study of SIG-001 in severe or moderately severe hemophilia A. With the modularity of the SLTx platform, we are evaluating changes designed to modulate or otherwise reduce the potential for a patient's immune response to our product candidates.

Impact of COVID-19

The COVID-19 pandemic has impacted and may continue to impact the clinical sites and startup activities for our Phase 1/2 clinical trials, including third-party manufacturing and logistics providers, which would disrupt our clinical supply chain or the availability or cost of materials, and it may affect our ability to timely complete our clinical trials and

delay the initiation and/or enrollment of any future clinical trials, disrupt regulatory activities or have other adverse effects on our business and operations.

We are monitoring the potential impact of the COVID-19 pandemic on our business and financial statements. We cannot be certain what the overall impact of the COVID-19 pandemic will be on our business and prospects. The extent to which the COVID-19 pandemic will directly or indirectly impact our business, results of operations, financial condition and liquidity, including planned and future clinical trials and research and development costs, will depend on future developments that are highly uncertain, including as a result of new information that may emerge concerning COVID-19, the actions taken to contain or treat it, the effects of any variants as new strains evolve, vaccination efforts, and the duration and intensity of the related effects.

Components of Results of Operations

Revenue

To date, we have not generated any revenue from product sales and do not expect to generate any revenue from the sale of products in the near future. Substantially all of our revenue to date has been derived from the collaboration agreement with Lilly, which we entered into in 2018.

If our development efforts for our product candidates are successful and result in regulatory approval or if we enter into license or collaboration agreements with third parties, we may generate revenue in the future from product sales, payments from license or collaboration agreements that we may enter into with third parties, or any combination thereof. We expect that our revenue for the next several years will be derived primarily from our collaboration agreement with Lilly as well as any additional collaborations that we may enter into in the future. We cannot provide assurance as to the timing of future milestone or royalty payments or that we will receive any of these payments at all.

Collaboration Revenue

In April 2018, we entered into a License and Collaboration Agreement with Lilly, or the 2018 Lilly Agreement. Under the 2018 Lilly Agreement, we granted Lilly an exclusive worldwide, royalty-bearing license, including the right to grant sublicenses, to our encapsulation technology applied to islet cells. We are responsible for our own costs and expenses associated with pre-clinical development of a product candidate, and completion of the studies and other criteria required for filing the first IND, up to $47.5 million; provided, however, pursuant to an amendment to the 2018 Lilly Agreement entered in May 2022, Lilly may take on certain research and development activities, at its own cost and expense, including supply and manufacturing activities. Lilly is responsible for filing the first IND, all subsequent clinical development and commercialization, all research, development and commercialization for any subsequent product candidates, as well as reimbursing us for research and development costs required for filing the first IND related to the first developed product candidate that exceed $47.5 million.

We evaluated the 2018 Lilly Agreement under ASC 606 and concluded at the outset that there were two performance obligations under the arrangement: (1) exclusive license to research, develop, manufacture and commercialize licensed products, initial technology transfer, research activities (including pre-IND supply), cell line development and supply and product trademark election, or the Combined Performance Obligation; and (2) requirement to supply Lilly with the licensed product related to Phase 1 clinical trial, or Phase 1 Supply. We determined that the $62.5 million upfront payment represents the entirety of the consideration to be included in the transaction price as of the outset of the arrangement. We allocated $56.6 million of the transaction price to the Combined Performance Obligation and $5.9 million of the transaction price to the Phase 1 Supply at the outset of the arrangement. We recognize revenue for the Combined Performance Obligation as the research and development services are provided using an input method, based on the cumulative costs incurred compared to the total estimated costs expected to be incurred to satisfy the Combined Performance Obligation. The transfer of control to the customer occurs over the time period that the research and development services are to be provided by us, and this cost-to-cost method is, in management's judgment, the best measure of progress toward satisfying this performance obligation. We have determined that the Phase 1 Supply will be satisfied at a point in time when the customer obtains control of each unit of product. Therefore, we will recognize revenue as shipments of the Phase 1 Supply are made to Lilly.

We reevaluate the transaction price and our total estimated costs expected to be incurred at the end of each reporting period and as uncertain events, such as changes to the expected timing and cost of certain research, development and manufacturing activities that we are responsible for, are resolved or other changes in circumstances occur, and, if necessary, we will adjust our estimate of the transaction price or our total estimated costs expected to be incurred.

Additional information regarding the 2018 Lilly Agreement can be found in Note 8 to our financial statements in this Quarterly Report on Form 10-Q.

Operating Expenses

Research and Development Expenses

Research and development expenses consist primarily of costs incurred for our research activities, including our drug discovery efforts and the development of our platform and product candidates. We expense research and development costs as incurred, which include:

- employee-related expenses, including salaries, bonuses, benefits, stock-based compensation, other related costs for those employees involved in research and development efforts;
- expenses incurred in connection with the clinical and preclinical development of our product candidates and research programs, including under agreements with third parties, such as consultants, contractors, and CROs;
- the cost of raw materials and developing and scaling our manufacturing process and manufacturing product candidates for use in our research and preclinical studies, including under agreements with third parties, such as consultants, contractors, and CMOs;
- laboratory supplies and research materials;
- facilities, depreciation, and other expenses, which include direct and allocated expenses for rent and maintenance of facilities and insurance; and
- payments made under third-party licensing agreements.

We expense research and development costs as incurred. Non-refundable advance payments that we make for goods or services to be received in the future for use in research and development activities are recorded as prepaid expenses. The prepaid amounts are expensed as the related goods are delivered or the services are performed, or when it is no longer expected that the goods will be delivered or the services rendered. Upfront payments under license agreements are expensed upon receipt of the license, and annual maintenance fees under license agreements are expensed in the period in which they are incurred. Milestone payments under license agreements are accrued, with a corresponding expense being recognized, in the period in which the milestone is determined to be probable of achievement and the related amount is reasonably estimable.

Our direct external research and development expenses are tracked on a program-by-program basis, including our early-stage programs, and consist of costs that include fees, reimbursed materials, and other costs paid to consultants, contractors, contract manufacturing organizations or CMOs, and contract research organizations or CROs, in connection with our preclinical and manufacturing activities. Except for personnel expenses related to SIG-002, we do not allocate employee costs, costs associated with our discovery efforts, laboratory supplies and facilities expenses, including depreciation or other indirect costs, to specific product development programs because these costs are deployed across multiple programs and our platform and, as such, are not separately classified. The personnel expenses allocated to SIG-002 do not include stock-based compensation expense.

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 increase substantially in connection with our planned preclinical and clinical development activities in the near term and in the future. At this time, we cannot accurately estimate or know the nature, timing and costs of the efforts that will be necessary to complete the preclinical and clinical development of any of our product candidates. The successful development and commercialization of our product candidates is highly uncertain. This is due to the numerous risks and uncertainties associated with product development and commercialization, including the following:

- investigation of the preliminary results from our Phase 1/2 clinical trial for SIG-001, including the finding of spheres with PFO and the reported SAE;
- the timing and progress of preclinical and clinical development activities;
- the number and scope of preclinical and clinical programs we decide to pursue;
- raising additional funds necessary to complete preclinical and clinical development of and commercialize our product candidates;
- the progress of the development efforts of parties with whom we may enter into collaboration arrangements;
- our ability to maintain our current research and development programs and to establish new ones;
- our ability to establish new licensing or collaboration arrangements;
- the successful initiation and completion of clinical trials with safety, tolerability and efficacy profiles that are satisfactory to the FDA, or any comparable foreign regulatory authority;
- the receipt and related terms of regulatory approvals from applicable regulatory authorities;
- the availability of raw materials for use in production of our product candidates;
- our ability to consistently manufacture our product candidates for use in clinical trials;
- our ability to establish and operate a manufacturing facility, or secure manufacturing supply through relationships with third parties;
- our ability to obtain and maintain patents, trade secret protection and regulatory exclusivity, both in the United States and internationally;
- our ability to protect our rights in our intellectual property portfolio;
- the commercialization of our product candidates, if and when approved;
- obtaining and maintaining third-party insurance coverage and adequate reimbursement;
- the acceptance of our product candidates, if approved, by patients, the medical community and third-party payors;
- competition with other products; and
- a continued acceptable safety profile of our therapies following approval.

A change in the outcome of any of these variables with respect to the development of any of our product candidates could significantly change the costs and timing associated with the development of these product candidates. We may never succeed in obtaining regulatory approval for any of our product candidates.

General and Administrative Expenses

General and administrative expenses consist primarily of salaries and personnel expenses, including stock-based compensation, for our personnel in executive, legal, finance and accounting, human resources, and other administrative functions. General and administrative expenses also include legal fees relating to patent and corporate matters; professional fees paid for accounting, auditing, consulting, and tax services; insurance costs; travel expenses; and facility costs not otherwise included in research and development expenses.

We anticipate that our general and administrative expenses will increase in the future as we increase our headcount to support our continued research activities and development of our product candidates. We also anticipate that we will incur significantly increased accounting, audit, legal, regulatory, compliance and director and officer insurance costs as well as investor and public relations expenses associated with operating as a public company. Additionally, if and when we believe a regulatory approval of a product candidate appears likely, we anticipate an increase in payroll and other employee-related expenses as a result of our preparation for commercial operations, especially as it relates to the sales and marketing of that product candidate.

Other Income (Expense)

Interest Income

Interest income consists of interest earned on our cash, cash equivalents and marketable securities balances. We expect our interest income will fluctuate based on the timing and ability to raise additional funds as well as the amount of expenditures for our platform development and ongoing business operations.

Interest Expense

Interest expense consists of interest expense on outstanding borrowings under our loan and security agreements as well as amortization of debt discount and deferred financing costs.

Other Income (Expense)

Other expense consists primarily of losses on the disposal of fixed assets, net foreign exchange losses and net sublease income from subleasing a portion of our facilities.

Income Taxes

Since our inception in 2015, 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. We did not provide for any income taxes in the three months ended March 31, 2022 or 2021.

Critical Accounting Estimates

Our condensed consolidated financial statements are prepared in accordance with accounting principles generally accepted in the United States. The preparation of these condensed consolidated financial statements requires us to make estimates and judgments that affect the reported amounts of assets, liabilities, costs and expenses, and the disclosure of contingent assets and liabilities in our financial statements. We base our estimates on historical experience, known trends and events, and various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. We evaluate our estimates and assumptions on an ongoing basis. Our actual results may differ from these estimates under different assumptions or conditions. The accounting estimates and policies discussed in our Annual Report on Form

10-K for the fiscal year ended December 31, 2021, filed with the SEC on March 14, 2022, or the Annual Report, are considered by management to be the most important to an understanding of the consolidated financial statements because of their significance to the portrayal of our financial condition and results of operations. There have been no material changes to that information disclosed in our Annual Report on Form 10-K for the year ended December 31, 2021 filed with the SEC on March 14, 2022.

Results of Operations

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

The following table summarizes our results of operations for the three months ended March 31, 2022 and 2021:

	Three Months Ended March 31,		Increase (Decrease)
	2022	2021	
	(in thousands)		
Revenue			
Collaboration revenue	$ 3,165	$ 2,958	$ 207
Operating expenses:			
Research and development	11,618	15,985	(4,367)
General and administrative	5,024	5,540	(516)
Total operating expenses	16,642	21,525	(4,883)
Loss from operations	(13,477)	(18,567)	5,090
Other income (expense):			
Interest income	64	86	(22)
Interest expense	(491)	(488)	(3)
Other expense	45	(4)	49
Total other expense, net	(382)	(406)	24
Net loss and comprehensive loss	$ (13,859)	$ (18,973)	$ 5,114

Revenue

Revenue was $3.2 million for the three months ended March 31, 2022, compared to $3.0 million for the three months ended March 31, 2021. The increase in revenue of $0.2 million was due to the timing of costs of the activities performed under the 2018 Lilly Agreement. We recognizes revenue under the 2018 Lilly Agreement based on the input method and as the costs incurred increased by $0.2 million from the three months ended March 31, 2021 to the three months ended March 31, 2022 the income recognized also increased.

Research and Development Expenses

The following table summarizes our research and development expenses for the three months ended March 31, 2022 and 2021:

	Three Months Ended March 31,		Increase
	2022	2021	(Decrease)
	(in thousands)		
Direct research and development expenses by program:			
SIG-005	$ 1,869	$ 1,564	$ 305
SIG-002	2,727	2,616	111
SIG-001	1,457	1,581	(124)
SIG-007	197	695	(498)
Platform and pipeline development	2,006	4,460	(2,454)
Unallocated expenses			
Personnel expenses (including stock-based compensation)	2,513	4,030	(1,517)
Facility related and other	849	1,039	(190)
Total research and development expenses	$ 11,618	$ 15,985	$ (4,367)

Research and development expenses were $11.6 million for the three months ended March 31, 2022, compared to $16.0 million for three months ended March 31, 2021. The decrease in research and development expenses was primarily related to decreased ongoing platform and pipeline development activities, personnel expenses and our SIG-007 program, which were offset by increases in our SIG-005 program. The decrease in platform and pipeline development, personnel expenses and SIG-007 and the increase in SIG-005 is primarily due to our reprioritization of the development of MPS-1, diabetes and platform optimization following the Company's restructuring activities in December 2021.

General and Administrative Expenses

General and administrative expenses for the three months ended March 31, 2022 were $5.0 million, compared to $5.5 million for the three months ended March 31, 2021. General and administrative expenses for the three months ended March 31, 2022 versus March 31, 2021 decreased by $0.5 million as a result of decreased personnel expenses primarily in connection with our restructuring activities that occurred in December 2021.

Other expense, net

Other expense, net, for each of the three months ended March 31, 2022 and 2021 was $0.4 million.

Liquidity and Capital Resources

Sources of Liquidity

Since our inception, we have incurred significant operating losses. We have not yet commercialized any of our product candidates and we do not expect to generate revenue from sales of any product candidates for the foreseeable future, if at all. To date, we have funded our operations primarily with proceeds from sales of common stock, convertible preferred stock, payments received under our collaboration agreement with Lilly and proceeds from borrowings under our credit facilities. Through March 31, 2022, we had received net proceeds of $131.8 million from the sale of common stock in the IPO, $141.9 million from the net sales of our convertible preferred stock and net proceeds of $19.8 million through borrowings under the 2020 Credit Facility. We have also partnered one of our encapsulation technology programs with Lilly. Under the terms of the partnership, we received an upfront payment of $62.5 million and we are eligible to receive additional milestone payments of up to $165.0 million upon achievement of certain regulatory milestones and sales-based milestones of up to $250.0 million for SIG-002. We are also eligible to receive tiered royalty payments in the mid-single digit to low-double digit percentages based on certain sales thresholds. Finally, Lilly is obligated to reimburse us for costs incurred to perform the research and development activities for the first developed product candidate that exceed $47.5

million. We are also eligible to receive additional payments upon the achievement of specified regulatory and sales milestones and royalty payments. As of March 31, 2022, we had cash, cash equivalents and marketable securities of $103.1 million.

Cash Flows

The following table summarizes our sources and uses of cash, cash equivalents and restricted cash for each of the periods presented:

	Three Months Ended March 31,	
	2022	2021
	(in thousands)	
Net cash used in operating activities	$ (19,488)	$ (22,673)
Net cash used in investing activities	(23,216)	(290)
Net cash provided by (used in) financing activities	48	(477)
Net decrease in cash, cash equivalents and restricted cash	$ (42,656)	$ (23,440)

Operating Activities

During the three months ended March 31, 2022, operating activities used $19.5 million of cash, primarily resulting from our net loss of $13.9 million and net cash used in changes in our operating assets and liabilities of $8.9 million, partially offset by non-cash charges of $3.2 million. Net changes in our operating assets and liabilities for the three months ended March 31, 2022 consisted primarily of a $3.2 million decrease in deferred revenue, $3.0 million increase in prepaid expenses and other current assets, a $1.4 million decrease in lease liabilities, a $1.0 million decrease in accounts payable and accrued expenses and other current liabilities and a $0.4 million increase in accounts receivable. The decrease in deferred revenue was due to recognition of revenue related to our collaboration agreement. The increase in prepaid expenses and other current assets were the result of timing of payments for services to be performed in future periods. The decrease in accounts payables and accrued expenses and other current liabilities was the result of timing of payments for services performed by our vendors. The decrease in lease liabilities was primarily due to payment of rent for our leased property. The increase in accounts receivable was the result of timing of collections.

During the three months ended March 31, 2021, operating activities used $22.7 million of cash, primarily resulting from our net loss of $19.0 million and net cash used in changes in our operating assets and liabilities of $6.9 million, partially offset by non-cash charges of $3.2 million. Net changes in our operating assets and liabilities for the three months ended March 31, 2021 consisted primarily of a $2.9 million decrease in deferred revenue, a $2.3 million increase in prepaid expenses and other current assets, a $1.2 million decrease in lease liabilities and a $0.9 million decrease in accrued expenses and other current liabilities, partially offset by a $0.6 million increase in accounts payable. The decrease in deferred revenue was due to recognition of revenue related to our collaboration agreement. The increase in prepaid expenses and other current liabilities was the result of timing of payments for services. The decrease in lease liabilities was primarily due to payment of rent for our leased property.

Investing Activities

During the three months ended March 31, 2022, cash used in investing activities was $23.2 million and consisted of $22.8 million in purchases of marketable securities and $0.4 million in purchases of laboratory equipment and furniture and fixtures.

During the three months ended March 31, 2021, cash used in investing activities was $0.3 million and consisted of purchases of laboratory equipment and furniture and fixtures.

Financing Activities

During the three months ended March 31, 2022, cash provided by financing activities was less than $0.1 million and consisted of proceeds from the exercise of common stock options.

During the three months ended March 31, 2021, cash used in financing activities was $0.4 million. The cash used in financing activities consisted of $0.6 million for the payment of deferred offering costs associated with our initial public offering and was offset by $0.2 million that was provided from the exercise of common stock options.

Loan and security agreement

In September 2020, we entered into the 2020 Credit Facility, with Oxford Finance LLC, or Oxford, and paid off in full our borrowings under the 2019 Credit Facility with a portion of the proceeds from the 2020 Credit Facility. The 2020 Credit Facility provided for an initial term loan borrowing in an aggregate amount of $20.0 million. The Company elected not to borrow any additional eligible borrowings under the 2020 Credit Facility. Borrowings under the 2020 Credit Facility bear interest at an annual rate equal to the greater of 8.40% and the sum of U.S. Dollar LIBOR rate reported on the *Wall Street Journal* plus 8.23%.

Borrowings under the 2020 Credit Facility are collateralized by substantially all of our personal property, other than our intellectual property. There are no financial covenants associated with the 2020 Credit Facility; however, we are subject to certain affirmative and negative covenants to which we will remain subject until maturity. These covenants include limitations on dispositions, mergers or acquisitions; encumbering our intellectual property; incurring indebtedness or liens; paying dividends; making certain investments; and engaging in certain other business transactions. Obligations under the 2020 Credit Facility are subject to acceleration upon the occurrence of specified events of default, including a material adverse change in our business, operations or financial or other condition.

As of March 31, 2022 and December 31, 2021, the interest rate applicable to borrowings under the 2020 Credit Facility was 8.47% and 8.40%, respectively.

As of March 31, 2022, we were in compliance with all covenants pursuant to the 2020 Credit Facility. We cannot be assured that we will be able to obtain additional covenant waivers or amendments in the future which may have a material adverse effect on our results or operations or liquidity.

Funding requirements

We expect our expenses to increase substantially in connection with our ongoing activities, particularly as we advance the preclinical activities and clinical trials for our product candidates in development. In addition, we expect to continue to incur additional cost associated with operating as a public company. The timing and amount of our operating and capital expenditures will depend largely on:

- the costs of our investigation of the SAE and PFO reported in our Phase 1/2 clinical trial for SIG-001 in Hemophilia A and the costs of additional preclinical or clinical studies as may be requested by the FDA;
- the cost of patient treatment for medical events related to the SAE reported in our Phase 1/2 clinical trial for SIG-001 if and when we are asked to pay for such treatments;
- the costs of continuing to develop our SLTx platform, including the cost of any changes to our cells, spheres or manufacturing processes and the costs of any additional preclinical studies we may conduct as a result of our ongoing investigation into the results of our Phase 1/2 clinical trial of SIG-001;
- the costs of acquiring licenses for the components and engineered cell lines that will be used with our current and future product candidates;

- the scope, progress, results, and costs of discovery, preclinical development, formulation development, and clinical trials for our current and future product candidates;
- the costs of preparing, filing, and prosecuting patent applications, maintaining and enforcing our intellectual property and proprietary rights, and defending intellectual property-related claims;
- the costs, timing, and outcome of regulatory review of SIG-005 or any other product candidates;
- the costs of future activities, including product sales, medical affairs, marketing, manufacturing, distribution, coverage and reimbursement for SIG-005 or any other product candidates for which we receive regulatory approval;
- the cost of developing and expanding our manufacturing capabilities and advancing these manufacturing capabilities to manufacture product candidates that are commercially viable;
- the potential additional expenses attributable to adjusting our development plans (including any supply-related matters) due to the COVID-19 pandemic;
- our ability to establish and maintain additional collaborations on favorable terms, if at all;
- the success of any collaborations that we may establish and of our license agreements;
- the achievement of milestones or occurrence of other developments that trigger payments under any additional collaboration agreements we obtain; and
- the extent to which we acquire or in-license product candidates, intellectual property and technologies.

We believe that our existing cash will enable us to fund our operating expenses and capital expenditure requirements into 2024. We have based this estimate on assumptions that may prove to be wrong, and we could utilize our available capital resources sooner than we expect.

Until such time, if ever, as we can generate substantial product revenue, we expect to finance our operations through a combination of equity offerings, debt financings, collaborations, strategic alliances and marketing, distribution or licensing arrangements. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interest of our stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our common stockholders. Debt financing and preferred equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making acquisitions or capital expenditures or declaring dividends. If we raise additional funds through additional collaborations, strategic alliances or marketing, distribution or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates, or grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings or other arrangements when needed, we may be required to delay, limit, reduce or terminate our research, product development or future commercialization efforts, or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Item 3. Quantitative and Qualitative Disclosure About Market Risk

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

Item 4. Controls and Procedures

Disclosure Controls and Procedures

Our management, with the participation of our Chief Executive Officer (our principal executive officer and principal financial officer), evaluated the effectiveness of our disclosure controls and procedures as of March 31, 2022 and concluded that our disclosure controls and procedures were effective at the reasonable assurance level as of that date. The term "disclosure controls and procedures," as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended, or the Exchange Act, means controls and other procedures of a company that are designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the SEC's rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is accumulated and communicated to the company's management, including its principal executive and principal financial officers, as appropriate to allow timely decisions regarding required disclosure. Management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures.

Changes in Internal Control over Financial Reporting

There were no change in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) occurred during the quarter ended March 31, 2022 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

PART II – OTHER INFORMATION

Item 1. Legal Proceedings

From time to time, we may be involved in legal proceedings arising in the ordinary course of our business. We are not presently a party to any legal proceedings that, in the opinion of management, would have a material adverse effect on our business. Regardless of outcome, litigation can have an adverse impact on us due to defense and settlement costs, diversion of management resources, negative publicity and reputational harm and other factors.

Item 1A. Risk Factors

You should carefully consider the risks and uncertainties described below together with all of the other information contained in this Quarterly Report on Form 10-Q. The risks and uncertainties described below are not the only ones we face. Additional risks and uncertainties not presently known to us or that we currently believe to be immaterial may also adversely affect our business. If any of the following risks occur, our business, financial condition, results of operations and future growth prospects could be materially and adversely affected.

Risks Related to Our Financial Position and Need for Additional Capital

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

We are currently advancing our pipeline of programs in development. Discovering development candidates and developing investigational therapeutics is expensive, and we expect to continue to spend substantial amounts to (i) perform basic research, perform preclinical studies, and conduct clinical trials of our current and future programs, (ii) continue to develop and expand our Shielded Living Therapeutics, or SLTx, platform and infrastructure and supply preclinical studies and clinical trials with appropriate grade materials, including current good manufacturing practices, or cGMP, materials, (iii) seek regulatory approvals for our product candidates, and (iv) launch and commercialize any product candidates for which we receive regulatory approval.

Since inception, we have incurred significant operating losses. Our net loss was $13.9 million and $77.3 million for the three months ended March 31, 2022 and for the year ended December 31, 2021, respectively. As of March 31 2022, we had an accumulated deficit of $227.1 million. We have financed our operations primarily through the sale of equity securities, payments received under our collaboration agreement and proceeds from borrowings under our credit facilities. We have devoted all of our efforts to research and development. We expect to continue to incur significant expenses and increasing operating losses for the foreseeable future. The net losses we incur may fluctuate significantly from quarter to quarter. We anticipate that our expenses will increase substantially if and as we:

- investigate the preliminary results from our Phase 1/2 clinical trial for SIG-001, including the reported SAE, and the finding of PFO;
- incur the cost of patient treatment for medical events related to the SAE reported in our Phase 1/2 clinical trial for SIG-001 if we are asked to pay for such treatments;
- initiate clinical trials for SIG-005 or any other product candidates;
- continue our current research programs and our preclinical development of product candidates from our current research programs;
- seek to identify additional research programs and additional product candidates;
- comply with regulatory requirements established by the FDA, the European Medicines Agency, or EMA, and other comparable foreign regulatory authorities;
- conduct preclinical studies for our product candidates;
- seek marketing approvals for any of our product candidates;
- ultimately establish a sales, marketing, and distribution infrastructure to commercialize any medicines for which we may obtain marketing approval;
- further develop our SLTx platform;
- hire additional research, development and manufacturing personnel;
- continue to hire and retain clinical and commercial personnel;
- add operational, financial, corporate development and management information systems and legal personnel, including personnel to support our product development and planned future commercialization efforts;
- expand our facilities;
- acquire or in-license product candidates, intellectual property and technologies;
- develop an automated encapsulation system for future commercial scale manufacturing of our SLTx platform or otherwise build or expand our manufacturing capabilities or capacity, including future manufacturing facilities;
- file, prosecute, defend, and enforce our patent claims and other intellectual property rights, including patent infringement actions brought by third parties against us regarding our investigational medicines or actions by us challenging the patent or intellectual property rights of others, and provide reimbursement of third-party expenses related to our patent portfolio; and

- operate as a public company.

We expect that it will be many years, if ever, before we have a product candidate ready for commercialization. To become and remain profitable, we must, either directly or through collaborators, develop and eventually commercialize a medicine or medicines with significant market potential. This will require us to be successful in a range of challenging activities, including identifying product candidates, completing preclinical testing and clinical trials of product candidates, obtaining marketing approval for these product candidates, manufacturing, marketing, and selling those medicines for which we may obtain marketing approval, and satisfying any post-marketing requirements. We may never succeed in these activities and, even if we do, may never generate revenues that are significant or large enough to achieve profitability. We are currently in the preclinical testing stages for all of our research programs other than SIG-001 and SIG-005. Because of the numerous risks and uncertainties associated with developing product candidates, we are unable to predict the extent of any future losses or when we will become profitable, if at all. If we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would decrease the value of our company and could impair our ability to raise capital, maintain our research and development efforts, expand our business, or continue our operations. A decline in the value of our company could also cause you to lose all or part of your investment.

If we fail to achieve the expected financial and operational benefits of our corporate restructuring, our business and financial results may be harmed.

In December 2021, we conducted a reduction in workforce, which represented approximately 38% of our full-time employee workforce. The reduction in workforce was primarily comprised of positions related to research, manufacturing, and general and administrative services and was implemented in connection with our determination to focus and reprioritize our resources on our Mucopolysaccharidosis Type I, or MPS-1, and diabetes programs. As a result of the reduction in force, we incurred expenses of approximately $1.4 million, comprised of termination benefits including severance, benefits and other payroll-related charges. The expected cost savings and operational efficiencies from the restructuring activities were based on assumptions and expectations about our future needs and strategic priorities, which may not be achieved due to unforeseen difficulties and challenges that are beyond our control. If these assumptions and expectations are incorrect, our business operations and financial results may be harmed. Further, the restructuring and possible additional cost containment measures may yield unintended consequences, such as attrition beyond our intended reduction in workforce and reduced employee morale. In addition, employees who were not affected by the reduction in force may seek alternate employment, which could result in us seeking contract support at unplanned additional expense or harm our productivity. In addition, due to our limited resources, we may not be able to manage our operations effectively or recruit and retain qualified personnel, which may result in weaknesses in our infrastructure and operations, risks that we may not be able to comply with legal and regulatory requirements and loss of business opportunities. If our management is unable to manage this transition and reduction in force and additional cost containment measures effectively, we may not be able to implement our business strategy.

We will need substantial additional funding. If we are unable to raise capital when needed, we would be forced to delay, reduce, reprioritize, or eliminate our research and product development programs or future commercialization efforts.

We expect our expenses to increase in connection with our ongoing activities, particularly as we identify, continue the research and development of, initiate clinical trials of, and seek marketing approval for product candidates. We expect that our cash, cash equivalents and marketable securities as of March 31, 2022 of $103.1 million would enable us to fund our operating expenses, capital expenditures requirements and debt service payments into 2024. If we obtain marketing approval for SIG-005 any other product candidates, we expect to incur significant commercialization expenses related to product sales, marketing, manufacturing, and distribution to the extent that such sales, marketing, manufacturing, and distribution are not the responsibility of a collaborator. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations, including operating as a public company. If we are unable to raise capital when needed or on attractive terms, we would be forced to delay, reduce, reprioritize, or eliminate our research and product development programs or future commercialization efforts.

Our operating plan may change as a result of factors currently unknown to us, and we may need to seek funding sooner than planned. Our future capital requirements will depend on many factors, including:

- the costs of our investigation of the SAE and PFO reported in our Phase 1/2 clinical trial for SIG-001 in Hemophilia A and the costs of additional preclinical or clinical studies as may be requested by the FDA;
- the cost of patient treatment for medical events related to the SAE reported in our Phase 1/2 clinical trial for SIG-001 if and when we are asked to pay for such treatments;
- the timing of our investigations of the SAE and PFO reported in our Phase 1/2 clinical trial of SIG-001 in Hemophilia A;
- the costs of continuing to develop our SLTx platform, including the cost of any changes to our cells, spheres or manufacturing processes and the costs of any additional preclinical studies we may conduct as a result of our ongoing investigation into the results of our Phase 1/2 clinical trial of SIG-001;
- the costs of acquiring licenses for the components of our products and engineered cell lines that will be used with our current and future product candidates;
- the scope, progress, results, and costs of discovery, preclinical development, formulation development, and clinical trials for our current and future product candidates;
- the costs of preparing, filing, and prosecuting patent applications, maintaining and enforcing our intellectual property and proprietary rights, and defending intellectual property-related claims;
- the costs, timing, and outcome of regulatory reviews associated with SIG-005 or any other product candidates;
- the costs of future activities, including product sales, medical affairs, marketing, manufacturing, distribution, coverage and reimbursement for SIG-005 or any other product candidates for which we receive regulatory approval;
- the cost of developing and expanding our manufacturing capabilities and advancing these manufacturing capabilities to manufacture product candidates that are commercially viable;
- the potential additional expenses attributable to adjusting our development plans (including any supply-related matters) due to the COVID-19 pandemic;
- our ability to establish and maintain additional collaborations on favorable terms, if at all;
- the success of any collaborations that we may establish and of our license agreements;
- the achievement of milestones or occurrence of other developments that trigger payments under any additional collaboration agreements we obtain; and
- the extent to which we acquire or in-license product candidates, intellectual property and technologies.

Identifying product candidates and conducting preclinical testing and clinical trials is a time-consuming, expensive, and uncertain process that takes years to complete, and we may never generate the necessary data or results required to obtain marketing approval and achieve product sales. In addition, even if we successfully identify and develop product candidates and those are approved, we may not achieve commercial success. Our commercial revenues, if any, will be derived from sales of medicines that we do not expect to be commercially available for many years, if at all. Accordingly, we will need to continue to rely on additional financing to achieve our business objectives. Adequate additional financing may not be available to us on acceptable terms, or at all.

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. Disruptions in the financial markets could make equity and debt financing more difficult to obtain and may have a material adverse effect on our ability to meet our fundraising needs. We cannot be certain that additional funding will be available on acceptable terms, or at all. If we are unable to raise additional capital in sufficient amounts or on terms acceptable to us, we may have to significantly delay, scale back or discontinue the development or commercialization of our product candidates or other research and development initiatives. Our license agreements and any future collaboration agreements may also be terminated if we are unable to meet the payment or other obligations under the agreements. We could be required to seek collaborators for SIG-005 and our other product candidates at an earlier stage than otherwise would be desirable or on terms that are less favorable than might otherwise be available or relinquish or license on unfavorable terms our rights to SIG-005 or any other product candidates in markets where we otherwise would seek to pursue development or commercialization ourselves.

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

The transition away from LIBOR may adversely affect our cost to obtain financing.

On July 27, 2017, the U.K. Financial Conduct Authority announced that it intends to stop persuading or compelling banks to submit London Interbank Offered Rate, or LIBOR, rates after 2021. The Financial Conduct Authority and the ICE Benchmark Administration recently announced that LIBOR may continue for legacy contracts until June 2023. The Alternative Reference Rates Committee, a steering committee comprised of U.S. financial market participants, selected and the Federal Reserve Bank of New York, has recommended the Secured Overnight Finance Rate, or SOFR, as an alternative to LIBOR. SOFR is a broad measure of the cost of borrowing cash in the overnight U.S. treasury repo market. There can be no assurance that rates linked to SOFR or associated changes related to the adoption of SOFR will be as favorable to us as LIBOR and may result in an effective increase in the applicable interest rate on our current or future debt obligations, including our 2020 Credit Facility.

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

Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of equity offerings, including through our at-the-market, or ATM, equity offering program, debt financings, collaborations, strategic alliances, and licensing arrangements. To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect your rights as a common stockholder. Additional debt financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures, declaring dividends, and possibly other restrictions.

If we raise funds through additional collaborations, strategic alliances, or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs, or product candidates we may develop, or we may have to grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce, or terminate our product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

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

We are an early-stage company. We were founded in 2015 and commenced operations in 2016. Our operations to date have been limited to organizing and staffing our company, business planning, raising capital, acquiring and

developing our SLTx platform, identifying product candidates, undertaking preclinical studies and have initiated clinical studies for SIG-001. We have not yet commenced clinical trials for any product candidate other than SIG-001, and the risk of failure for our programs is high. We have not yet demonstrated an ability to successfully complete any clinical trials, including large-scale, pivotal clinical trials, obtain marketing approvals, manufacture a commercial-scale medicine, or arrange for a third party to do so on our behalf, or conduct sales and marketing activities necessary for successful commercialization. Typically, it takes about 10 to 15 years to develop a product candidate from the time it is discovered to when it is available for treating patients, if ever. Consequently, any predictions you make about our future success or viability may not be as accurate as they could be if we had a longer operating history.

Our limited operating history may make it difficult to evaluate our technologies and industry and predict our future performance. Our short history as an operating company makes any assessment of our future success or viability subject to significant uncertainty. We will encounter risks and difficulties frequently experienced by early-stage companies in rapidly evolving fields. If we do not address these risks successfully, our business will suffer.

We have never generated revenue from product sales and may never become profitable.

Our ability to generate revenue from product sales and achieve profitability depends on our ability, alone or with collaborative partners, to successfully complete the development of, and obtain the regulatory approvals necessary to commercialize our current and future product candidates. We do not anticipate generating revenues from product sales for the next several years, if ever. Our ability to generate future revenues from product sales depends heavily on our, or our collaborators', ability to successfully:

- complete research and preclinical and clinical development of our current and future product candidates, including addressing any additional clinical holds that may be placed on our development activities by regulatory authorities;
- seek and obtain regulatory and marketing approvals for any of our product candidates for which we complete clinical trials;
- launch and commercialize any of our product candidates for which we obtain regulatory and marketing approval by establishing a sales force, marketing, and distribution infrastructure or, alternatively, collaborating with a commercialization partner;
- qualify for coverage and establish adequate reimbursement by government and third-party payors for any of our product candidates for which we obtain regulatory and marketing approval;
- develop, maintain, and enhance a sustainable, scalable, reproducible, and transferable manufacturing process for the product candidates we may develop;
- establish and maintain supply and manufacturing capabilities or capacities internally or with third parties that can provide adequate, in both amount and quality, products, and services to support clinical development and the market demand for any of our product candidates for which we obtain regulatory and marketing approval;
- obtain market acceptance of current or any future product candidates as viable treatment options;
- address competing technological and market developments;
- implement internal systems and infrastructure, as needed;
- negotiate favorable terms in any collaboration, licensing, or other arrangements into which we may enter and performing our obligations in such collaborations;

- maintain, protect, enforce, defend, and expand our portfolio of intellectual property rights, including patents, trade secrets, and know-how;
- avoid and defend against third-party interference, infringement, and other intellectual property claims; and
- attract, hire, and retain qualified personnel.

Even if one or more of our current and future product candidates are approved for commercial sale, we anticipate incurring significant costs associated with commercializing any approved product candidate. Our expenses could increase beyond expectations if we are required by the FDA or the EMA, or other regulatory authorities to perform clinical and other studies in addition to those that we currently anticipate. Even if we are able to generate revenues from the sale of any approved product candidates, we may not become profitable and may need to obtain additional funding to continue operations.

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

Risks Related to Preclinical and Clinical Development of Our Technologies

The results of our investigation of the preliminary results of our Phase 1/2 clinical trial of SIG-001 in Hemophilia A or a failure of SIG-005 in clinical development could adversely affect our business and may require us to discontinue or delay development of other product candidates, which are all based on the same SLTx platform.

While we have certain preclinical programs in development, including SIG-002 for the treatment of Type 1 Diabetes, or T1D, and intend to develop other product candidates, it will take additional investment and time for such programs to reach the same stage of development as SIG-005 for MPS-1. Since all of the product candidates in our current pipeline are based on the same SLTx platform, if our investigation of the preliminary results of our Phase 1/2 clinical trial of SIG-001 in Hemophilia reveal that either the reported SAE or the finding of PFO was as a result of any underlying problem with our SLTx platform, then we may be required to discontinue development of all of our product candidates and our portfolio of product candidates would have little value.

In addition, a failure of SIG-005 in clinical development would also adversely affect our business. If SIG-005 fails in development as a result of any underlying problem with our SLTx platform, then we may also be required to discontinue development of all of our product candidates.

Further, the FDA or other regulatory authorities may not allow us to pursue further development of SIG-005 or any other of product candidates as a result of the issues presented by the SAE reported in our Phase 1/2 clinical trial of SIG-001 or our finding of PFO, particularly if we are unable to demonstrate an acceptable risk-benefit profile for product candidates developed using our SLTx platform. If the FDA or other regulatory agencies continue to express safety, tolerability or efficacy concerns, additional preclinical studies or clinical trials involving SIG-005 or other product candidates, amendments to the enrollment criteria and/or clinical trial protocols for our studies or changes to our platform, including our cells, spheres or manufacturing processes, may be needed and may be difficult to implement or complete. In such instance, our progress in the development of SIG-005 and other product candidates may be significantly slowed or stopped and the associated costs may be significantly increased, adversely affecting our business.

The SLTx platform consists of novel technologies that are not yet clinically validated for human therapeutic use. The regulatory requirements applicable to our product candidates may change over time. The approaches we are taking to discover and develop novel therapeutics are unproven and may never lead to marketable products.

The regulatory approval process for novel cellular therapy product candidates such as ours is unclear and may be lengthier and more expensive than the process for other, better-known or more extensively studied product candidates, such as biologics, small molecule drugs and other more traditional pharmaceuticals.

Regulatory requirements governing cell therapy products have changed and may continue to change in the future. The FDA has established the Office of Tissues and Advanced Therapies, or OTAT, within its Center for Biologics Evaluation and Research, or CBER, to consolidate the review of cell therapy and related products, and has established the Cellular, Tissue and Gene Therapies Advisory Committee to advise CBER in its review. Our product candidates have been reviewed by OTAT to date, but this could change if the FDA changes any of its guidance or regulations. If we were to engage an NIH-funded institution to conduct a clinical trial, that institution's biosafety committee, a local institutional committee that reviews and oversees research utilizing recombinant or synthetic nucleic acid molecules, as well as its institutional review board, or IRB, would need to review the proposed clinical trial to assess the safety of the trial. Similarly, the EMA may issue new guidelines concerning the development and marketing authorization for cell therapy medicinal products and require that we comply with these new guidelines.

Regulatory review committees and advisory groups, and any new guidelines they promulgate, may lengthen the regulatory review process, require us to perform additional preclinical studies or clinical trials, increase our development costs, lead to changes in regulatory positions and interpretations, delay or prevent approval and commercialization of our current or future product candidates or lead to significant post-approval limitations or restrictions. As we advance our product candidates, we will be required to consult with these regulatory and advisory groups and comply with applicable guidelines. If we fail to do so, we may be required to delay or discontinue development of our product candidates. These additional processes may result in a review and approval process that is longer than we otherwise would have expected.

Delay or failure to obtain, or unexpected costs in obtaining, the regulatory approval necessary to bring a product to market could decrease our ability to generate sufficient product revenue, and our business, financial condition, results of operations and prospects would be harmed. Even if our product candidates are approved, we expect that the FDA will require us to submit follow-up data regarding our clinical trial subjects for a number of years after any approval. If this follow-up data shows negative long-term safety or efficacy outcomes for these patients, the FDA may revoke its approval or change the label of our products in a manner that could have an adverse impact on our business.

In addition, adverse developments in clinical trials of cell therapy products conducted by others or regulatory review of the SAE that occurred in our Phase 1/2 clinical trial of SIG-001 or the finding of PFO, may cause the FDA or other oversight bodies to change the requirements for approval of our other product candidates, including, SIG-005. As a result, it is difficult to determine how long it will take or how much it will cost to obtain regulatory approvals for our product candidates.

We may not be successful in our efforts to identify and develop product candidates. If these efforts are unsuccessful, we may never become a commercial stage company or generate any revenues.

The success of our business depends primarily upon our ability to identify, develop, and commercialize product candidates using on our SLTx platform. We have not yet commenced clinical trials for any product candidate other than SIG-001, which is currently subject to a clinical hold. Because most of our programs are in the research or preclinical stage, we have not yet been able to assess safety, tolerability or efficacy of our product candidates in humans, and there may be effects from treatment with any of our current or future product candidates that we cannot predict at this time. In connection with our investigations of the SAE and of the PFO reported in our Phase 1/2 clinical trial of SIG-001 in Hemophilia A, we may also determine that changes to our platform, including our cells, spheres or manufacturing processes, are needed that may be difficult, costly, or timing-consuming to implement or complete. Additionally, our research programs may fail to identify product candidates for clinical development for a number of reasons. Our research methodology may be unsuccessful in identifying product candidates, our product candidates may be shown to have harmful side effects in preclinical *in vitro* experiments or animal model studies, they may not show promising signals of therapeutic effect in such experiments or studies or they may have other characteristics that may make the product candidates impractical to manufacture or dose, unmarketable, or unlikely to receive marketing approval.

If any of these events occur, we may be forced to abandon our research or development efforts for a program or programs, which would have a material adverse effect on our business, financial condition, results of operations, and prospects. Research programs to identify new product candidates require substantial technical, financial, and human resources. We may focus our efforts and resources on potential programs or product candidates that ultimately prove to be unsuccessful, which would be costly and time-consuming.

We are early in our development efforts. It will be many years before we or our collaborators commercialize a product candidate, if ever. If we are unable to advance our product candidates to clinical development, obtain regulatory approval and ultimately commercialize our product candidates, or experience significant delays in doing so, our business will be materially harmed.

We are early in our development efforts and have focused our research and development efforts to date on select indications, including rare blood disorders, lysosomal diseases, endocrine and other chronic disorders, when identifying our initial targeted disease indications and our initial product candidates. We initiated our first-in-human trial for SIG-001, which has been placed on clinical hold by the FDA. We have completed IND-enabling studies for one of our other product candidates, SIG-005 and we are conducting IND-enabling studies for our other product candidates, but there is no guarantee that the results from such IND-enabling studies will enable us to commence clinical trials of our product candidates in a timely manner, or at all. Our future success depends heavily on the successful development of our product candidates.

We have not submitted INDs to the FDA or similar filings to any other regulatory agency for any product candidate other than SIG-001 and SIG-005. We have invested substantially all of our efforts and financial resources in building our SLTx platform, and the identification and preclinical development of our current product candidates. Our ability to generate product revenue, which we do not expect will occur for many years, if ever, will depend heavily on the

successful development and eventual commercialization of our product candidates, which may never occur. We currently generate no revenue from sales of any product and we may never be able to develop or commercialize a marketable product.

In the first half of 2020, we submitted a Clinical Trial Application, or CTA, in the United Kingdom and an IND in the United States for SIG-001 for the treatment of Hemophilia A, which were accepted by MHRA and the FDA, respectively. We initiated enrollment and dosed three patients for our multicenter Phase 1/2 clinical trial of SIG-001 in Hemophilia A in the United Kingdom and United States. In July 2021, the FDA placed a clinical hold on our Phase 1/2 clinical trial of SIG-001 in Hemophilia A, in light of a reported SAE. The FDA requested additional information or data on factors potentially contributing to the development of inhibitors in this patient, such as family history and immune stimulation from a recent vaccination. In November 2021, we reported that spheres covered with PFO were observed during a retrieval procedure in a patient in our Phase 1/2 clinical trial of SIG-001. As a result of the clinical hold, the finding of PFO or other observations, the FDA or other regulatory authorities could require us to complete additional preclinical studies or clinical trials or impose stricter approval conditions than we currently expect for any of our product candidates.

In the third quarter of 2021, we announced that the MHRA accepted the CTA for our multicenter Phase 1/2 clinical trial of SIG-005 in MPS-1. We also filed a CTA with Brazil in July 2021, which was accepted in the first quarter of 2022, and plan to submit an IND to the FDA. We may pursue studies for SIG-005 or our other product candidates in additional jurisdictions, where we will be subject to equivalent processes and risks applicable to clinical trial applications in other countries, including in Europe.

Commercialization of our product candidates will require additional preclinical and clinical development; regulatory and marketing approval in multiple jurisdictions, including by the FDA and the EMA; obtaining manufacturing supply, capacity and expertise; building of a commercial organization; and significant marketing efforts. The success of our current and future product candidates will depend on many additional factors, including the following:

- successful completion of preclinical studies resulting in data that is supportive of advancing to an IND or CTA submission;
- successful submissions of INDs or comparable foreign applications that allow commencement of our planned or future clinical trials, including resolving any clinical holds that may be imposed on such submissions;
- successful initiation, enrollment in, and completion of, clinical trials;
- positive results from our clinical trials that support a finding of safety and effectiveness and an acceptable risk-benefit profile in the intended populations;
- receipt of marketing approvals from applicable regulatory authorities;
- establishment of arrangements with third-party manufacturers for clinical supply and commercial manufacturing and, where applicable, commercial manufacturing capabilities;
- successful development of our internal manufacturing processes and transfer to larger-scale facilities operated by either a contract manufacturing organization, or CMO, or by us;
- obtaining and maintaining patent, trade secret, and other intellectual property protection and non-patent exclusivity for our product candidates;
- launching commercial sales of the product candidates, if and when approved, whether alone or in collaboration with others;
- acceptance of the products, if and when approved, by patients, the medical community, and third-party payors;

- effectively competing with other therapies and treatment options;
- a continued acceptable safety profile of the product candidates following approval;
- enforcing and defending intellectual property and proprietary rights and claims; and
- supplying the products at a price that is acceptable to the pricing or reimbursement authorities in different countries.

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

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 focus on research programs and product candidates that we identify for specific indications among many potential options. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs and product candidates for specific indications may not yield any commercially viable medicines. 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. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations, and prospects.

We only have preliminary data from patients dosed with SIG-001 and no results from our product candidates in clinical trials and any favorable preclinical results are not predictive of results that may be observed in clinical trials.

Data obtained from preclinical and clinical activities are subject to varying interpretations and analyses, which may delay, limit or prevent regulatory approval. Many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical development have nonetheless failed to obtain marketing approval of their product candidates. As we generate preclinical results, such results will not ensure that later preclinical studies or clinical trials will demonstrate similar results.

We have not yet initiated clinical trials for any product candidate other than SIG-001, and to date, we have not generated clinical trial results other than preliminary data from the first three patients dosed with SIG-001. At the dose levels tested in the first two patients, our initial results showed low-to-mid single digit activity levels of FVIII. The third patient enrolled in this trial, who received the highest dose of study drug, developed inhibitors to FVIII. As a result of this reported SAE, the FDA placed a clinical hold on our Phase 1/2 clinical trial for SIG-001 in Hemophilia A. We may not generate additional clinical trial results from this clinical trial. There is a high failure rate for drugs and biologics proceeding through clinical trials. SIG-001, if we were to pursue this program, SIG-005 and other product candidates may fail to demonstrate sufficient safety and efficacy levels. In addition, even if initial clinical trials in any of our current or future product candidates are successful, these product candidates may fail to show the desired safety and efficacy in later stages of clinical development despite having successfully advanced through preclinical studies and initial clinical trials. A number of companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in later stage clinical trials even after achieving promising results in earlier stage clinical trials.

In addition, regulatory delays or rejections may be encountered as a result of many factors, including changes in regulatory policy during the period of product development and clinical holds that may be imposed on our clinical trials. Any such adverse events may cause us to delay, limit, or terminate current or planned clinical trials, any of which would have a material adverse effect on our business, financial condition, results of operations, and prospects.

Our reported SAE in our Phase 1/2 clinical trial of SIG-001 or any other serious adverse events, undesirable side effects or unexpected characteristics caused by any of the product candidates we may develop, or the delivery modes we rely on to administer them, could delay or prevent regulatory approval of the product candidates, limit the commercial potential, or result in significant negative consequences following any potential marketing approval.

Our product candidates are composed of engineered human cell lines, encapsulated in a biocompatible matrix sphere. To date, there have been no completed human clinical trials for product candidates arising from our SLTx platform or consisting of our cell or sphere technologies. There may be SAEs in addition to the SAE reported in our Phase 1/2 clinical trial of SIG-001 in Hemophilia A, undesirable side effects related to either component of our product candidates, or limited efficacy of product candidates arising from our SLTx platform.

If any other product candidates we develop, in addition to SIG-001, are associated with serious adverse events, undesirable side effects, unexpected characteristics or limited efficacy or if the risk-benefit profile of such products is adversely impacted, we may need to abandon or modify their development or limit development to certain uses or subpopulations in which the serious adverse events, undesirable side effects, other characteristics or limited efficacy are less prevalent, less severe, or more acceptable from a risk-benefit perspective, any of which would have a material adverse effect on our business, financial condition, results of operations, and prospects. For example, if our future preclinical and clinical studies of our product candidates result in additional incidences of PFO, we may be unable to support an appropriate risk-benefit profile of our product candidates. Many product candidates that initially showed promise in early-stage testing for rare blood disorders, lysosomal diseases, endocrine and other chronic disorders have later been found to cause side effects that prevented further clinical development of the product candidates.

If our clinical trials result in a high and unacceptable severity and/or prevalence of adverse events or limited efficacy due to the formation of inhibitors or PFO or other characteristics, the FDA, the EMA or other regulatory authorities could require us to cease further development of, or deny approval of, any product candidates we are able to develop for any or all targeted indications. Even if we are able to demonstrate that all future serious adverse events or incidences of PFO are not product related, such occurrences could affect patient recruitment or the ability of enrolled patients to complete the trial. Moreover, if we elect, or are required, to delay, suspend or terminate any clinical trial of any product candidate we may develop, the commercial prospects of such product candidates may be harmed and our ability to generate product revenues from any of these product candidates may be delayed or eliminated. Any of these occurrences may harm our ability to identify and develop product candidates, and may harm our business, financial condition, result of operations, and prospects significantly.

Additionally, if we successfully develop a product candidate and it receives marketing approval, the FDA could require us to adopt a Risk Evaluation and Mitigation Strategy, or REMS, to ensure that the benefits of treatment with such product candidate outweighs the risks for each potential patient, which may include, among other things, a medication guide outlining the risks of the product for distribution to patients, a communication plan to health care practitioners, extensive patient monitoring, or distribution systems and processes that are highly controlled, restrictive, and more costly than what is typical for the industry. Furthermore, if we or others later identify undesirable side effects caused by any product candidate that we develop, if the results of our clinical trials or tests are not positive or are only modestly positive or if there are safety concerns, several potentially significant negative consequences could result, including:

- regulatory authorities may suspend or withdraw approvals of such product candidate, or may refuse to approve supplemental applications for such product candidate;
- regulatory authorities may require additional warnings on the label, such as a “Boxed Warning” or contraindication, or limit the approved use of such product candidate;
- regulatory authorities may impose additional restriction on the marketing of, or the manufacturing processes for, the particular product candidate;
- we may be required to recall the product or change the way it is administered in patients;
- we may be required to conduct additional clinical trials;

- we may lose the support of collaborators, requiring us to bear more of the costs associated with research and development;
- we may only obtain approval for indications or patient populations that are not as broad as intended or desired;
- we may only obtain marketing approval in some countries but not others;
- we could be sued and held liable for harm caused to patients; and
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of our current and future product candidates and could have a material adverse effect on our business, financial condition, results of operations, and prospects.

If clinical trials of our current and future product candidates fail to demonstrate safety and efficacy to the satisfaction of regulatory authorities or do not otherwise produce positive results, we may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of such product candidates.

Before obtaining marketing approval from regulatory authorities for the sale of any of our current and future product candidates, we must complete preclinical development and then conduct extensive clinical trials to demonstrate the safety and efficacy in humans. Clinical testing is expensive, difficult to design and implement, can take many years to complete, and is uncertain as to outcome. A failure of one or more clinical trials 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.

We and our collaborators have and may continue to experience numerous unforeseen events during, or as a result of, clinical trials that could delay or prevent our ability to complete such clinical trials, receive marketing approval or commercialize our current and future product candidates, including:

- delays in reaching a consensus with regulators on trial design;
- regulators, IRBs, or independent ethics committees may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- delays in reaching or failing to reach agreement on acceptable clinical trial contracts or clinical trial protocols with prospective contract research organizations, or CROs, and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- difficulties in recruiting investigators of appropriate competence and experience for our clinical trials;
- the number of patients required for clinical trials of any of our current and future product candidates may be larger than we anticipate; enrollment of suitable participants in these clinical trials may be delayed or slower than we anticipate; or patients 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;
- regulators, IRBs, or independent ethics committees may impose a clinical hold and require that we or our investigators suspend or terminate clinical research or clinical trials of any of our current and future product candidates for various reasons,

- noncompliance with regulatory requirements, a finding of undesirable side effects or other unexpected characteristics, or that the participants are being exposed to unacceptable health risks or after an inspection of our clinical trial operations or trial sites;
- failure to perform clinical trials in accordance with study protocols, Good Clinical Practice, or GCP, requirements, and other regulatory requirements;
- the cost of clinical trials of any of our current and future product candidates may be greater than we anticipate;
- delays in having patients complete participation in a trial or return for post-treatment follow-up;
- delays in participation in a trial as a result of failure to deliver treatment doses to clinical trial sites in a timely manner, the logistical burden of dose delivery or failure by clinical trial sites to store treatment doses according to protocols;
- clinical trial sites deviating from trial protocol or dropping out of a trial;
- selection of clinical endpoints that require prolonged periods of clinical observation or analysis of the resulting data;
- occurrence of new or recurring serious adverse events associated with any of our current and future product candidates that are viewed to outweigh their potential benefits, and related clinical holds;
- occurrence of serious adverse events in trials of the same class of agents conducted by other sponsors;
- the supply or quality of any of our current and future product candidates or other materials necessary to conduct clinical trials of any of our current and future product candidates may be insufficient or inadequate, including as a result of delays in the testing, validation, manufacturing, and delivery of any of our current and future product candidates to the clinical sites by us or by third parties with whom we have contracted to perform certain of those functions;
- changes in regulatory requirements and guidance that require amending or submitting new clinical protocols; and
- clinical trials of any of our current and future product candidates may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional clinical trials or abandon product development or research programs altogether.

In addition, disruptions caused by the COVID-19 pandemic, including new variants of the COVID-19 virus, may increase the likelihood that we encounter such difficulties or delays in initiating, enrolling, conducting or completing our planned and ongoing clinical trials, and the duration of the COVID-19 pandemic may lead to an increase in the frequency at which our patient population receives additional doses of vaccines against the COVID-19 virus, new variants of the COVID-19 virus, or other common viruses, which could result in disqualification from our current or future clinical trials and lead to delay in the development of our product candidates. We could also encounter delays if a clinical trial is suspended or terminated by us, by the IRBs of the institutions in which such trials are being conducted, by a Data Safety Monitoring Board for such trial or by the FDA or comparable foreign regulatory authorities. Such authorities may impose such a suspension or termination due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA or comparable foreign regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit or sufficient benefit from using a drug, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial. In addition, changes in regulatory requirements and policies may occur, and we may need to amend clinical trial protocols to comply with these changes.

Amendments may require us to resubmit our clinical trial protocols to IRBs for reexamination, which may impact the costs, timing or successful completion of a clinical trial.

Product development costs will also increase if we or our collaborators experience delays in clinical trials or other testing or in obtaining marketing approvals. We do not know whether our clinical trials will begin as planned, will need to be restructured, or will be completed on schedule, or at all. Significant clinical trial delays, including those caused by the COVID-19 pandemic or similar events (including new strains of the COVID-19 virus and the potential impact of availability of COVID-19 vaccines on our eligible patient population for enrollment in our clinical trials), also could shorten any periods during which we may have the exclusive right to commercialize any product candidates we may develop, could allow our competitors to bring products to market before we do, and could impair our ability to successfully commercialize any product candidates we may develop, any of which may harm our business, financial condition, results of operations, and prospects.

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

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

Identifying and qualifying patients to participate in clinical trials of SIG-005 or any other product candidates is critical to our success. The timing of our clinical trials depends on our ability to recruit patients to participate in our studies as well as the dosing of such patients and completion of required follow-up periods. There are also a number of other product candidates in development by our competitors, who compete for the same limited patient populations. If we or our collaborators are unable to locate and enroll a sufficient number of eligible patients to participate in these trials as required by the FDA, the EMA or other analogous regulatory authorities outside the United States, or as needed to provide appropriate statistical power for a given trial, we may not be able to initiate or continue clinical trials for our current and future product candidates. Enrollment may be particularly challenging for some of the rare diseases we are targeting in our most advanced programs. For example, the approximate incidence of MPS-1 is one in 100,000 live births and only approximately 4,000 to 5,000 patients with Fabry disease are known in the United States. Additionally, we may face similar challenges or delays in our other or potential future clinical trials. In addition, the number of patients eligible to enroll in our clinical trials may turn out to be lower than expected if certain patient populations such as pediatric subpopulations are not eligible to participate in our clinical trials.

If patients are unwilling to participate in our studies because of negative publicity from adverse events related to the biotechnology or cell therapy, engineered cell therapy or encapsulated cell therapy fields, competitive clinical trials for similar patient populations or for other reasons, the timeline for recruiting patients, conducting studies and obtaining regulatory approval of SIG-005 or any other product candidates may be delayed. These delays could result in increased costs, delays in advancing our product candidates, delays in testing the effectiveness of our product candidates or termination of the clinical trials altogether.

Patient enrollment is also affected by other factors, including:

- severity of the disease under investigation;
- size of the patient population and process for identifying patients;
- design of the trial protocol;

- availability and efficacy of approved medications for the disease under investigation;
- convenience and ease of administration compared to approved medications for the disease under investigation and the willingness of patients to undergo the surgical procedures necessary to administer our product candidates, such as laparoscopy;
- ability to obtain and maintain patient informed consent;
- risk that enrolled patients will drop out before completion of the trial;
- eligibility and exclusion criteria for the trial in question;
- perceived risks and benefits of the product candidate under trial, including perceived additional risks as a result of any clinical holds;
- efforts to facilitate timely enrollment in clinical trials;
- patient referral practices of physicians;
- ability to monitor patients adequately during and after treatment;
- proximity and availability of clinical trial sites for prospective patients; and
- factors we may not be able to control, such as current or potential pandemics that may limit patients, principal investigators or staff or clinical site availability (e.g., the ongoing COVID-19 pandemic).

Our ability to successfully initiate, enroll, and complete a clinical trial in any foreign country is subject to numerous risks unique to conducting business in foreign countries, including:

- difficulty in establishing or managing relationships with CROs and physicians;
- different standards for the conduct of clinical trials;
- different standard-of-care for patients with a particular disease;
- difficulty in locating qualified local consultants, physicians, and partners; and
- potential burden of complying with a variety of foreign laws, medical standards, and regulatory requirements, including the regulation of pharmaceutical and biotechnology products and treatment.

Enrollment delays in our clinical trials may result in increased development costs for SIG-005 or any other product candidates, which would cause the value of our company to decline and limit our ability to obtain additional financing. If we or our collaborators have difficulty enrolling a sufficient number of patients to conduct our clinical trials as planned, we may need to delay, limit, or terminate clinical trials for SIG-005 or our other product candidates, or expand to additional jurisdictions, which could impose additional challenges on our company and expose us to risks. If we are not successful in conducting our clinical trials as planned, it would have an adverse effect on our business, financial condition, results of operations, and prospects.

Even if we complete the necessary clinical trials, we cannot predict when, or if, we will obtain regulatory approval to commercialize SIG-005 or any other product candidate in the United States or any other jurisdiction, and any such approval may be for a more narrow indication than we seek.

We cannot commercialize a product candidate until the appropriate regulatory authorities have reviewed and approved the product candidate. Even if SIG-005 and any other product candidates meet their safety and efficacy endpoints in clinical trials, the regulatory authorities may not complete their review processes in a timely manner, or we may not be able to obtain regulatory approval. Additional delays may result if an FDA Advisory Committee or other regulatory authority recommends non-approval or restrictions on approval. In addition, we may experience delays or rejections based upon additional government regulation from future legislation or administrative action, or changes in regulatory authority policy during the period of product development, clinical trials, and the review process.

Regulatory authorities also may approve a product candidate for more limited indications than requested or they may impose significant limitations in the form of narrow indications, warnings or a REMS. These regulatory authorities may require labeling that includes precautions or contraindications with respect to conditions of use, or they may grant approval subject to the performance of costly post-marketing clinical trials. In addition, regulatory authorities may not approve the labeling claims that are necessary or desirable for the successful commercialization of any product candidates we may develop, including claims that are necessary for certain patient populations such as pediatric patients. Any of the foregoing scenarios could materially harm the commercial prospects for SIG-005 or any other product candidates and materially adversely affect our business, financial condition, results of operations, and prospects.

To date, we have not submitted a biologics license application, or BLA, or other marketing authorization application to the FDA or similar drug approval submissions to comparable foreign regulatory authorities for any product candidate. Marketing approval by the FDA in the United States, if obtained, does not ensure approval by regulatory authorities in other countries or jurisdictions. In addition, clinical trials conducted in one country may not be accepted by regulatory authorities in other countries, and regulatory approval in one country does not guarantee regulatory approval in any other country. Approval processes vary among countries and can involve additional product candidate testing and validation and additional administrative review periods. Seeking foreign regulatory approval could result in difficulties and costs for us and require additional preclinical studies or clinical trials which could be costly and time-consuming. Regulatory requirements can vary widely from country to country and could delay or prevent the introduction of SIG-005 or any other product candidates in those countries. The foreign regulatory approval process involves all of the risks associated with FDA approval. We do not have any product candidates approved for sale in any jurisdiction, including international markets, and we do not have experience in obtaining regulatory approval in international markets. If we fail to comply with regulatory requirements in international markets or to obtain and maintain required approvals, or if regulatory approvals in international markets are delayed, our target market will be reduced and our ability to realize the full market potential of our product candidates will be unrealized.

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

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

From time to time, we may also disclose interim data from our preclinical studies and clinical trials. Interim data from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available. Adverse differences between preliminary

or interim data and final data could significantly harm our business prospects. Further, disclosure of interim data by us or by our competitors could result in volatility in the price of our common stock.

Further, others, including regulatory agencies, may not accept or agree with our assumptions, estimates, calculations, conclusions, or analyses or may interpret or weigh the importance of data differently, which could impact the value of the particular program, the approvability or commercialization of the particular product candidate or product and our company in general. If the interim, topline, or preliminary data that we report differ from actual results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for, and commercialize, our product candidates may be harmed, which may harm our business, financial condition, results of operations, and prospects.

Our product candidates may be considered combination products involving a proprietary delivery approach, which may result in additional regulatory and other risks.

Because our SLTx platform represents a novel approach to cell-based therapy development, we could be asked to perform additional preclinical or clinical studies, as well as develop additional manufacturing procedures and protocols, before we are able to obtain regulatory approvals for our product candidates. Our product candidates are comprised of both allogeneic human cells, which means the cells are obtained from a human donor other than the patient, and sphere components, and therefore we expect our product candidates to be regulated as biologic combination products, such as a biologic-device combination products for administration directly to the abdominal cavity or, as a novel cell-based therapies, which may subject our product candidates to additional regulatory requirements, such as CMC, preclinical or clinical requirements. If FDA regulates our product candidates as biologic-device combination products, we anticipate each component would be subject to the FDA medical requirements for that type of component. If that is the case, our delivery system device would be subject to FDA device requirements regarding design, performance, and validation, and human factor testing, as well as manufacturing requirements, including the FDA's Quality System regulations applicable to medical devices. Additionally, products that are regulated as biologic-device combination products would require coordination within the FDA for review of the product candidate's device and biologic components. The determination whether a combination product requires a single marketing application or two separate marketing applications for each component is made by the FDA on a case-by-case basis. Although a single marketing application may be sufficient for the approval of a combination product, the FDA may determine that separate marketing applications are necessary. This determination could significantly increase the resources and time required to bring our combination product to market. Although the FDA has systems in place for the review and approval of combination products such as ours, we may experience delays in the development and commercialization of our product candidates due to regulatory timing constraints and uncertainties in the product development and approval process, as well as coordination between two different centers within FDA responsible for review of the different components of the combination product.

Failure to obtain marketing approval in foreign jurisdictions would prevent SIG-005 or any other product candidates from being marketed in such jurisdictions, which, in turn, would materially impair our ability to generate revenue.

In order to market and sell SIG-005 or any other product candidates in the European Union, or the EU, and other foreign jurisdictions, including the United Kingdom, we or our third-party collaborators must obtain separate marketing approvals (a single one for the EU and a separate one for the United Kingdom, albeit potentially under a 67 day process following a positive CHMP opinion from the EU) and comply with numerous and varying regulatory requirements. The approval procedure varies among countries and can involve additional testing and/or clinical trials. The time required to obtain approval may differ substantially from that required to obtain FDA approval. The regulatory approval process outside the United States generally includes all of the risks associated with obtaining FDA approval. In addition, in many countries outside the United States, it is required that the product candidate be approved for reimbursement before the product candidate can be approved for sale in that country. We or these third parties may not obtain approvals from regulatory authorities outside the United States on a timely basis, if at all. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one regulatory authority outside the United States does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA. We may not be able to file for marketing approvals and may not receive necessary approvals to commercialize our medicines in any jurisdiction, which would materially impair our ability to generate revenue.

Even if we, or any collaborators we may have, obtain marketing approvals for any product candidates we develop, the terms of approvals and ongoing regulation of our product candidates could require the substantial expenditure of resources and may limit how we, or they, manufacture and market our product candidates, which could materially impair our ability to generate revenue.

Any product candidate for which we obtain marketing approval, along with the manufacturing processes, post-approval clinical data, labeling, packaging, distribution, import, export, adverse event reporting, storage, recordkeeping, advertising, and promotional activities for such product candidate, will be subject to extensive and ongoing requirements imposed by the FDA, EMA and other regulatory authorities. These requirements include submissions of safety and other post-marketing information and reports, facility registration and drug listing requirements, cGMP requirements relating to quality control, quality assurance and corresponding maintenance of records and documents, requirements regarding the distribution of samples to physicians and recordkeeping, and with respect to any medical device components of our product candidates, compliance with applicable provisions of the FDA's Quality System regulation. Even if marketing approval of a product candidate is granted, the approval may be subject to limitations on the indicated uses for which the product may be marketed or to the conditions of approval, or contain requirements for costly post-marketing testing and surveillance to monitor the safety or efficacy of the product.

Accordingly, assuming we, or any collaborators we may have, receive marketing approval for one or more product candidates we develop, we, and such collaborators, and our and their contract manufacturers will continue to expend time, money, and effort in all areas of regulatory compliance, including manufacturing, production, product surveillance, and quality control. If we and such collaborators are not able to comply with post-approval regulatory requirements, we and such collaborators could have the marketing approvals for our products withdrawn by regulatory authorities and our, or such collaborators', ability to market any future products could be limited, which could adversely affect our ability to achieve or sustain profitability. Further, the cost of compliance with post-approval regulations may have a negative effect on our business, operating results, financial condition, and prospects.

If there are changes in the application of legislation or regulatory policies, or if problems are discovered with a product or our manufacture of a product, or if we or one of our distributors, licensees or co-marketers fails to comply with regulatory requirements, the regulators could take various actions. These include issuing warning letters or untitled letters, imposing fines on us, imposing restrictions on the product or its manufacture and requiring us to recall or remove the product from the market. The regulators could also suspend or withdraw our marketing authorizations, requiring us to conduct additional clinical trials, change our product labeling or submit additional applications for marketing authorization. If any of these events occurs, our ability to sell such product may be impaired, and we may incur substantial additional expense to comply with regulatory requirements, which could materially adversely affect our business, financial condition and results of operations.

In addition, the FDA, the EMA, the MHRA and other regulatory agencies closely regulate the post-approval marketing and promotion of medicines to ensure that they are marketed only for the approved indications and in accordance with the provisions of the approved labeling. In particular, a product may not be promoted for uses that are not approved by the FDA, EMA, MHRA or other regulatory agencies as reflected in the product's approved labeling. If we receive marketing approval for a product candidate, physicians may nevertheless prescribe it to their patients in a manner that is inconsistent with the approved label. If we are found to have promoted such off-label uses, we may become subject to significant liability. The FDA, the EMA, the MHRA and other regulatory agencies impose stringent restrictions on manufacturers' communications regarding off-label use, and if we market our medicines for off-label use, we may be subject to enforcement action for off-label marketing by the FDA and other federal and state enforcement agencies, including the Department of Justice. Violation of the Federal Food, Drug, and Cosmetic Act and other statutes, including the False Claims Act, and equivalent legislation in other countries relating to the promotion and advertising of prescription products may also lead to investigations or allegations of violations of federal and state and other countries' health care fraud and abuse laws and state consumer protection laws. Even if it is later determined we were not in violation of these laws, we may be faced with negative publicity, incur significant expenses defending our actions and have to divert significant management resources from other matters.

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

- restrictions on such products, manufacturers, or manufacturing processes;
- restrictions on the labeling or marketing of a medicine;
- restrictions on the distribution or use of a medicine;
- requirements to conduct additional post-marketing clinical trials;
- receipt of warning or untitled letters;
- withdrawal of the products from the market, or suspension of marketing approvals;
- refusal to approve pending applications or supplements to approved applications that we submit;
- recall of our approved product candidates;
- fines, restitution, or disgorgement of profits or revenue;
- restrictions on future procurements with governmental authorities;
- suspension of any ongoing clinical trials;
- refusal to permit the import or export of our medicines;
- product seizure; and
- injunctions or the imposition of civil or criminal penalties.

Any government investigation of alleged violations of law could require us to expend significant time and resources in response and could generate negative publicity. The occurrence of any event or penalty described above may inhibit our ability to commercialize SIG-005 or any other product candidates, if approved, and adversely affect our business, financial condition, results of operations, and prospects.

Moreover, the policies of the FDA and of other regulatory authorities may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative or executive action, either in the United States or abroad. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained and we may not achieve or sustain profitability.

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

The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, statutory, regulatory, and policy changes, the FDA's ability to hire and retain key personnel and accept the payment of user fees, and other events that may otherwise affect the FDA's ability to perform routine functions. Average review times at the FDA have fluctuated in recent years as a result. In addition, government funding of other government agencies that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable. Disruptions at the FDA and other agencies may also slow the time necessary for new biologics or modifications to licensed biologics to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years, including for 35 days beginning on

December 22, 2018, the United States, or the U.S., government has shut down several times and certain regulatory agencies, such as the FDA, have had to furlough critical FDA employees and stop critical activities.

Separately, in response to the COVID-19 pandemic, on March 10, 2020 the FDA announced its intention to postpone most inspections of foreign manufacturing facilities, and on March 18, 2020, the FDA temporarily postponed routine surveillance inspections of domestic manufacturing facilities. Subsequently, on July 10, 2020, the FDA announced its intention to resume certain on-site inspections of domestic manufacturing facilities subject to a risk-based prioritization system. The FDA intends to use this risk-based assessment system to identify the categories of regulatory activity that can occur within a given geographic area, ranging from critical inspections to resumption of all regulatory activities. Regulatory authorities outside the United States may adopt similar restrictions or other policy measures in response to the COVID-19 pandemic. If a prolonged government shutdown occurs, or if global health concerns continue to prevent the FDA or other regulatory authorities from conducting their regular inspections, reviews or other regulatory activities, it could significantly impact the ability of the FDA or other regulatory authorities to timely review and process our regulatory submissions, which could have a material adverse effect on our business.

Risks Related to Our Industry and Future Commercialization

Even if SIG-005 or any other product candidate receives marketing approval, such product candidate may fail to achieve the degree of market acceptance by physicians, patients, healthcare payors, and others in the medical community necessary for commercial success.

The commercial success of SIG-005 or any other product candidates will depend upon the degree of market acceptance by physicians, patients, third-party payors, and others in the medical community. Even if SIG-005 or any other product candidate receives marketing approval, the product may nonetheless fail to gain sufficient market acceptance by physicians, patients, healthcare payors, and others in the medical community. The degree of market acceptance of any product candidates we may develop, if approved for commercial sale, will depend on a number of factors, including:

- the efficacy and safety of such product candidates as demonstrated in clinical trials;
- the potential and perceived advantages compared to alternative treatments;
- the limitation to our targeted patient population and limitations or warnings contained in approved labeling by the FDA or other regulatory authorities;
- the ability to offer our product candidates for sale at competitive prices;
- convenience and ease of administration compared to alternative treatments, including the logistical challenges of administering product candidates with a short shelf life and the willingness of patients to undergo the surgical procedures necessary to administer our product candidates, such as laparoscopy;
- the clinical indications for which the product candidate is approved by the FDA, the EMA, or other regulatory agencies;
- the willingness of the target patient population to try novel therapies and of physicians to prescribe these therapies;
- product labeling or product insert requirements of the FDA, the EMA, or other regulatory authorities, including any limitations or warnings contained in a product’s approved labeling;
- the timing of market introduction of competitive products;
- publicity concerning our products or competing products and treatments;

- the strength of marketing and distribution support;
- sufficient third-party coverage or reimbursement; and
- the prevalence and severity of any side effects.

Even if SIG-005 or any other product candidates are approved, such products may not achieve an adequate level of acceptance, we may not generate significant product revenues, and we may not become profitable.

If, in the future, we are unable to establish sales and marketing capabilities or enter into agreements with third parties to sell and market any product candidates we may develop, we may not be successful in commercializing those product candidates if and when they are approved.

We do not have a sales or marketing infrastructure and have limited experience in the sale, marketing, or distribution of pharmaceutical products. To achieve commercial success for any approved medicine for which we retain sales and marketing responsibilities, we must either develop a sales and marketing organization or outsource these functions to third parties. In the future, we may choose to build a focused sales, marketing, and commercial support infrastructure to sell, or participate in sales activities with our collaborators for, some of our current and future product candidates if and when they are approved.

There are risks involved with both establishing our own commercial capabilities and entering into arrangements with third parties to perform these services. For example, recruiting and training a sales force or reimbursement specialists 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 and other commercialization 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 commercialization personnel.

Factors that may inhibit our efforts to commercialize SIG-005 or any other product candidates on our own include:

- our inability to recruit and retain adequate numbers of effective sales, marketing, reimbursement, customer service, medical affairs, and other support personnel;
- the inability of sales personnel to obtain access to physicians to discuss our product candidates;
- the inability of reimbursement professionals to negotiate arrangements for formulary access, reimbursement, and other acceptance by payors;
- restricted or closed distribution channels that make it difficult to distribute SIG-005 or any other product candidates to segments of the patient population;
- the lack of complementary medicines to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines; and
- unforeseen costs and expenses associated with creating an independent commercialization organization.

If we enter into arrangements with third parties to perform sales, marketing, commercial support, and distribution services, our product revenues or the profitability of these product revenues to us may be lower than if we were to market and sell any product we may develop ourselves. In addition, we may not be successful in entering into arrangements with third parties to commercialize SIG-005 or any other product candidates or may be unable to do so on terms that are favorable to us. We may 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 commercialization capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing our products we may develop.

We face significant competition in an environment of rapid technological change, and there is a possibility that our competitors may achieve regulatory approval before us or develop therapies that are safer or more advanced or effective than ours, which may harm our financial condition and our ability to successfully market or commercialize any product candidates we may develop.

The development and commercialization of new therapeutic biologics is highly competitive. Moreover, the engineered cell therapy field is characterized by rapidly changing technologies, significant competition, and a strong emphasis on intellectual property. We will face competition with respect to any product candidates that we may seek to develop or commercialize in the future from major pharmaceutical companies, specialty pharmaceutical companies, and biotechnology companies worldwide. Potential competitors also include academic institutions, government agencies, and other public and private research organizations that conduct research, seek patent protection, and establish collaborative arrangements for research, development, manufacturing, and commercialization.

There are a number of large pharmaceutical and biotechnology companies that currently market and sell products or are pursuing the development of products for the treatment of the same disease indications as our product candidates, including rare blood disorders, lysosomal diseases, endocrine and other chronic disorders. We may face intense competition from large pharmaceutical companies with extensive resources and established relationships in these patient communities. Several large pharmaceutical companies and biotechnology companies currently market and sell products for the treatment of lysosomal disorders. This includes products developed by Amicus Therapeutics, Inc., BioMarin Pharmaceutical Inc., or BioMarin, and Ultragenyx Pharmaceutical Inc., or Ultragenyx, among others. Additionally, the current standard of care for T1D is highly competitive and established, and includes Novo Nordisk's Levemir and Tresiba, and Sanofi's Toujeo and Lantus. There are also diabetes programs in development at ViaCyte, Inc. and Vertex Pharmaceuticals, Inc., which may compete with any therapy to treat diabetes we may develop. Any product candidates that we or our collaborators successfully develop and commercialize will compete with existing therapies and new therapies that may become available in the future that are approved to treat the same diseases for which we may obtain approval for our product candidates.

Many of our current or potential competitors, either alone or with their collaboration partners, may have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals, and marketing approved products than we do. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize product candidates that are safer, more effective, have fewer or less severe side effects, are more convenient, or are less expensive than the product candidates we may develop or that would render any of our product candidates obsolete or non-competitive. Our competitors also may obtain FDA or other regulatory approval for their product candidates more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market.

Our commercial opportunity may also be reduced or limited if we or our partners are unable to manufacture large cryopreserved lots of our products candidates in a fully automated encapsulation system efficiently. Additionally, technologies developed by our competitors may render our product candidates, or our future developments, uneconomical or obsolete, and we may not be successful in marketing SIG-005 or any other product candidates against competitors.

In addition, we could face litigation with respect to the validity and/or scope of patents relating to our competitors' products. The availability of our competitors' products could limit the demand, and the price we are able to charge, for SIG-005 or any other product candidates. Further, intellectual property protection for human cell lines, including the engineered cell components of our product candidates are dynamic and rapidly evolving. The scope of intellectual property protection for the human cell line(s) used in our platform may be limited, and our commercial opportunity may be reduced or limited if our competitors are able to acquire or develop the same or similar cell lines.

Even if we are able to commercialize any product candidates, such products may become subject to unfavorable pricing regulations, third-party reimbursement practices, or healthcare reform initiatives, which would harm our business.

The regulations that govern pricing, and reimbursement for new medicines vary widely from country to country. Outside the United States, some countries require approval of the sale price of a medicine before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we might obtain marketing approval for a product candidate in a particular country, but then be subject to price regulations that delay or might even prevent our commercial launch of the product candidate, possibly for lengthy time periods, and negatively impact the revenues we are able to generate from the sale of the product candidate in that country. Adverse pricing limitations may hinder our ability to recoup our investment in one or more product candidates we may develop, even if SIG-005 or any other product candidates obtain marketing approval.

Our ability to commercialize any product candidates successfully also will depend in part on the extent to which reimbursement for these product candidates and related treatments will be available from government authorities, government healthcare programs, private health plans, and other organizations. Government authorities and third-party payors, such as private health plans, decide which medications they will pay for and establish reimbursement levels. 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 challenging the prices charged for medical products and requiring that drug companies provide them with predetermined discounts from list prices. Novel medical products, if covered at all, may be subject to enhanced utilization management controls designed to ensure that the products are used only when medically necessary. Such utilization management controls may discourage the prescription or use of a medical product by increasing the administrative burden associated with its prescription or creating coverage uncertainties for prescribers and patients. We cannot be sure that reimbursement will be available for any product candidate that we commercialize and, if reimbursement is available, that the level of reimbursement will be adequate. Reimbursement may impact the demand for, or the price of, any product candidate for which we obtain marketing approval. If reimbursement is not available or is available only to limited levels, we may not be able to successfully commercialize any product candidate for which we obtain marketing approval.

There may be significant delays in obtaining reimbursement for newly approved product candidates, and coverage may be more limited than the purposes for which the product candidate is approved by the FDA, the EMA or other regulatory authorities outside the United States. Moreover, eligibility for reimbursement does not imply that any product candidate 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 product candidates, 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 product candidate and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost therapies or medicines and may be incorporated into existing payments for other services. Net prices for product candidates may be reduced by mandatory discounts or rebates required for government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of medicines from countries where they may be sold at lower prices than in the United States. Our inability to promptly obtain coverage and profitable payment rates from both government-funded and private payors for any approved product candidates we may develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize medicines, and our overall financial condition.

Any product candidates for which we intend to seek approval as biologic products may face competition sooner than anticipated.

The Patient Protection and Affordable Care Act, signed into law on March 23, 2010, includes a subtitle called the Biologics Price Competition and Innovation Act of 2009, or 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.

There is a risk that any of our product candidates approved as a biological product under a BLA would not qualify for the 12-year period of exclusivity or 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.

Due to the novel nature of our technologies and the potential for SIG-005 or any other product candidates to offer therapeutic benefit in a single administration or limited number of administrations, we face uncertainty related to pricing and reimbursement for these product candidates.

If we are unable to obtain adequate levels of reimbursement, our ability to successfully market and sell any such product candidates will be adversely affected. The manner and level at which reimbursement is provided for services related to SIG-005 or any other product candidates (e.g., for administration of our product candidate to patients) is also important. Inadequate reimbursement for such services may lead to physician and payor resistance and adversely affect our ability to market or sell SIG-005 or any other product candidates. In addition, we may need to develop new reimbursement models in order to realize adequate value.

Payors may not be able or willing to adopt such new models, and patients may be unable to afford that portion of the cost that such models may require them to bear. If we determine such new models are necessary but we are unsuccessful in developing them, or if such models are not adopted by payors, our business, financial condition, results of operations, and prospects could be adversely affected.

We expect that coverage and reimbursement by government and private payors will be essential for most patients to be able to afford these treatments. Accordingly, sales of any such product candidates will depend substantially, both domestically and abroad, on the extent to which the costs of SIG-005 or any other product candidates will be paid by government authorities, private health plans, and other third-party payors. Payors may not be willing to pay high prices for a single administration. Coverage and reimbursement by a third-party payor may depend upon several factors, including the third-party payor's determination that use of a product is:

- a covered benefit under its health plan;
- safe, effective, and medically necessary;
- appropriate for the specific patient;
- cost-effective; and
- neither experimental nor investigational.

Obtaining coverage and reimbursement for a product from third-party payors is a time-consuming and costly process that could require us to provide to the payor supporting scientific, clinical, and cost-effectiveness data. There is significant uncertainty related to third-party coverage and reimbursement of newly approved products. We may not be able to provide data sufficient to gain acceptance with respect to coverage and reimbursement. If coverage and

reimbursement are not available, or are available only at limited levels, we may not be able to successfully commercialize any product candidates we may develop. Even if coverage is provided, the approved reimbursement amount may not be adequate to realize a sufficient return on our investment.

Moreover, the downward pressure on healthcare costs in general, particularly prescription drugs and surgical procedures and other treatments, has become intense. As a result, increasingly high barriers are being erected to the entry of new product candidates such as ours. If we are unable to obtain adequate levels of reimbursement, our ability to successfully market and sell SIG-005 or any other product candidates will be harmed.

If the market opportunities for SIG-005 or any other product candidates are smaller than we believe they are, our potential revenues may be adversely affected, and our business may suffer.

We focus certain research and product development pipelines and our product candidates on treatments for rare diseases including rare blood disorders, lysosomal diseases, endocrine and other chronic disorders. Our understanding of both the number of people who have these diseases, as well as the subset of people with these diseases who have the potential to benefit from treatment with our product candidates, are based on estimates. For example, the approximate incidence of MPS-1 is one in 100,000 live births and only approximately 4,000 to 5,000 patients with Fabry disease are known in the United States. These estimates may prove to be incorrect and new studies may reduce the estimated incidence or prevalence of these diseases. The number of patients in the United States and elsewhere may turn out to be lower than expected, may not be otherwise amenable to treatment with SIG-005 or our other product candidates or patients may become increasingly difficult to identify and access, all of which would adversely affect our business, financial condition, results of operations and prospects. In addition, the number of patients with these diseases who have the potential to benefit from treatment may turn out to be lower than expected if we are unable to treat certain patient populations such as pediatric subpopulations.

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

We face an inherent risk of product liability exposure related to the testing in human clinical trials of SIG-001 or any other product candidates for which we initiate human clinical trials and will face an even greater risk if we commercially sell any product candidates that we may develop. If we cannot successfully defend ourselves against claims that our product candidates caused injuries, we could incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- decreased demand for any product candidates that we may develop;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial participants;
- significant time and costs to defend the related litigation;
- substantial monetary awards to trial participants or patients;
- loss of revenue; and
- the inability to commercialize any product candidates that we may develop.

Although we maintain product liability insurance coverage, it may not be adequate to cover all liabilities that we may incur. We anticipate that we will need to increase our insurance coverage when we begin clinical trials and if we successfully commercialize any medicine. 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.

If we or any contract manufacturers and suppliers we engage fail to comply with environmental, health, and safety laws and regulations, we could become subject to fines or penalties or incur costs that could have a material adverse effect on the success of our business.

We and any contract manufacturers and suppliers we engage are subject to numerous federal, state, and local environmental, health, and safety laws, regulations, and permitting requirements, including those governing laboratory procedures; the generation, handling, use, storage, treatment, and disposal of hazardous and regulated materials and wastes; the emission and discharge of hazardous materials into the ground, air, and water; and employee health and safety. Our operations involve the use of hazardous and flammable materials, including chemicals and biological materials. Our operations also produce hazardous waste. 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. Under certain environmental laws, we could be held responsible for costs relating to any contamination at our current or past facilities and at third-party facilities. We also could incur significant costs associated with civil or criminal fines and penalties.

Compliance with applicable environmental laws and regulations may be expensive, and current or future environmental laws and regulations may impair our research and product development efforts. In addition, we cannot entirely eliminate the risk of accidental injury or contamination from these materials or wastes. 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 carry specific biological or hazardous waste insurance coverage, and our property, casualty, and general liability insurance policies (under which we currently have an aggregate of approximately $15.0 million in coverage) specifically exclude coverage for damages and fines arising from biological or hazardous waste exposure or contamination. Accordingly, in the event of contamination or injury, we could be held liable for damages or be penalized with fines in an amount exceeding our resources, and our clinical trials or regulatory approvals could be suspended, which could have a material adverse effect on our business, financial condition, results of operations, and prospects.

In addition, we may incur substantial costs in order to comply with current or future environmental, health, and safety laws, regulations, and permitting requirements. These current or future laws, regulations, and permitting requirements may impair our research, development, or production efforts. Failure to comply with these laws, regulations, and permitting requirements also may result in substantial fines, penalties, or other sanctions or business disruption, which could have a material adverse effect on our business, financial condition, results of operations, and prospects.

Any third-party contract manufacturers and suppliers we engage will also be subject to these and other environmental, health, and safety laws and regulations. Liabilities they incur pursuant to these laws and regulations could result in significant costs or an interruption in operations, which could have a material adverse effect on our business, financial condition, results of operations, and prospects.

Our technologies are novel, and any product candidates we develop may be complex and difficult to manufacture on a clinical or commercial scale. We could experience delays in satisfying regulatory authorities or production problems that result in delays in our development or commercialization programs, limit the supply of our product candidates we may develop, or otherwise harm our business.

Our SLTx platform is novel and the manufacture of products on the basis of our platform is untested at a large scale. Any current and future product candidates will likely require processing steps that are more complex than those required for most chemical pharmaceuticals and traditional biologics. Moreover, unlike small molecules, the physical and chemical properties of various components in our product candidates generally cannot be fully characterized. As a result, assays of the finished product candidate may not be sufficient to ensure that the product candidate will perform in the intended manner. Problems with the manufacturing process, even minor deviations from the normal process, could result in product defects or manufacturing failures that result in lot failures, product recalls, product liability claims, insufficient inventory, or potentially delay progression of our regulatory filings. If we successfully develop product candidates, we may encounter problems achieving adequate quantities and quality of clinical-grade materials that meet FDA, EMA or other comparable applicable foreign standards or specifications with consistent and acceptable production yields and costs.

If we or our contract manufacturers are unable to scale our manufacturing at the same levels of quality and efficiency, we may not be able to supply the required number of doses for clinical trials or commercial supply, and our business could be harmed.

As product candidates proceed through preclinical studies to clinical trials towards potential approval and commercialization, it is common that various aspects of the development program, such as manufacturing methods and formulation, are tested and then altered along the way in an effort to optimize processes and results. We may make changes to our manufacturing methods as part of our product development activities. Any such changes could cause any product candidates we may develop to perform differently and affect the results of clinical trials conducted with the materials manufactured using altered processes. Such changes may also require additional testing, FDA notification or FDA approval. This could delay completion of clinical trials, require the conduct of bridging clinical trials or the repetition of one or more clinical trials, increase clinical trial costs, delay approval of our product candidates and jeopardize our ability to commence sales and generate revenue.

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

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

The manufacture of biopharmaceutical products is complex and requires significant expertise, including the development of advanced manufacturing techniques and process controls. Manufacturers of cell therapy products often encounter difficulties in production, particularly in scaling out and validating initial production and ensuring the absence of contamination. Given the nature of biologics manufacturing and the cell therapy products used in our early-stage programs there is a risk of contamination during manufacturing. For example, given the aseptic controls required for the manufacture of our product candidates, if contaminants are discovered in our supply of product candidates or in the manufacturing facilities, such manufacturing facilities may need to be closed for an extended period of time to investigate and remedy the contamination. Any such contamination could materially harm our ability to produce product candidates on schedule and could delay our development programs and results of operations and cause reputational damage. We cannot assure you that any such issues relating to the manufacture of SIG-005 or any other product candidate will not occur in the future or that significant delays would not occur as a result of any such issue.

In addition, some of the raw materials that we anticipate will be required in our manufacturing process are derived from biologic sources. For example, engineered human cell lines serve as components of product candidates developed using the SLTx platform, and our alginates, which are naturally occurring polymers derived from seaweed. Such raw materials can be difficult to procure and may be subject to contamination or recall. A material shortage, recall, or restriction on the use of biologically derived substances in the manufacture of any of our product candidates could adversely impact or disrupt the commercial manufacturing or the production of clinical material, which could materially harm our development timelines and our business, financial condition, results of operations, and prospects.

Any problems in our manufacturing process or the facilities with which we contract to make, store or ship our product candidates or any problems caused by us, our vendors or other factors not in our control could result in the loss of usable product or prevent or delay the delivery of product candidates to patients in our clinical trials. Any such loss or delay could materially delay our development timelines and harm our business, financial condition and results of operations. Such losses or delays could also make us a less attractive collaborator for potential partners, including larger pharmaceutical companies and academic research institutions, which could limit our access to additional attractive development programs. Problems in third-party manufacturing process or facilities also could restrict our ability to ensure

sufficient clinical material for any clinical trials we may be conducting or are planning to conduct and meet market demand for any product candidates we develop and commercialize.

We purchase some of the starting material for our product candidates from a single source or a limited number of suppliers, and the partial or complete loss of one of these suppliers could cause production delays, clinical trial delays, substantial loss of revenue and contract liability to third parties.

We source a critical raw material used in our sphere alginate from a single supplier. A limited supply of this raw material and other raw materials with a limited number of suppliers could cause production delays, clinical trial delays, substantial lost revenue opportunities or contract liabilities to third parties. For example, there are only a limited number of qualified suppliers, and in some cases single source suppliers, for the raw materials included in our SLTx platform, including our current supply of alginates. Any interruption in supply, diminution in quality of raw materials supplied to us or failure to procure such raw materials on commercially feasible terms, including as a result of the COVID-19 pandemic, could harm our business by delaying our clinical trials, impeding commercialization of potential approved products or increasing our costs.

Additionally, our sphere alginate is derived from a naturally occurring seaweed. The availability or characteristics of this material may be impacted by disease to this species of seaweed, ocean pollution and climate change as a result of global warming.

Risks Related to Our Relationships with Third Parties

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

We expect to rely on third parties, such as CROs, medical institutions, and clinical investigators, to conduct our clinical trials. We currently rely and expect to continue to rely on third parties to conduct some aspects of our research and preclinical testing. Any of our collaborators and partners may terminate their engagements with us at any time. If we need to enter into alternative arrangements, it may delay our product development activities.

Our reliance on third parties for research and development activities will reduce our control over these activities but will not relieve us of our responsibilities. For example, we will remain responsible for ensuring that each of our clinical trials is conducted in accordance with study protocol for the trial. Moreover, the FDA, the EMA, the MHRA and other regulatory authorities require us to comply with GCP requirements for conducting, recording, and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity, and confidentiality of trial participants are protected. Regulatory authorities enforce these GCPs through periodic inspections of trial sponsors, principal investigators and trial sites. If we or any of our CROs fail to comply with applicable GCP, the clinical data generated in our clinical trials may be deemed unreliable and the FDA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our clinical trials comply with GCP regulations. In addition, our clinical trials must be conducted with product produced under cGMP regulations. Our failure to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process.

We also are required to register ongoing clinical trials and post the results of completed clinical trials on government-sponsored databases, including ClinicalTrials.gov in the United States and the EudraCT database in the EU, within certain timeframes. Failure to do so can result in fines, adverse publicity, and civil and criminal sanctions.

Although we intend to design the clinical trials for the majority of our product candidates, CROs will conduct some or all of the clinical trials. As a result, many important aspects of our development programs, including their conduct and timing, will be outside of our direct control. Our reliance on third parties to conduct future preclinical studies and clinical trials will also result in less direct control over the management of data developed through preclinical studies and clinical trials than would be the case if we were relying entirely upon our own staff.

Communicating with outside parties can also be challenging, potentially leading to mistakes as well as difficulties in coordinating activities. Outside parties may:

- have staffing difficulties;
- fail to comply with contractual obligations;
- experience regulatory compliance issues;
- undergo changes in priorities or become financially distressed; or
- form relationships with other entities, some of which may be our competitors.

These factors may materially adversely affect the willingness or ability of third parties to conduct our preclinical studies and clinical trials and may subject us to unexpected cost increases that are beyond our control. If the CROs and other third parties do not perform preclinical studies and future clinical trials in a satisfactory manner, breach their obligations to us or fail to comply with regulatory requirements, the development, regulatory approval and commercialization of our product candidates may be delayed or prevented, we may not be able to obtain regulatory approval and commercialize our product candidates, or our development programs may be materially and irreversibly harmed.

We also expect to rely on other third parties to store and distribute product supplies for our clinical trials. Any performance failure on the part of our distributors could delay clinical development or marketing approval of SIG-005 or any other product candidates or commercialization of our medicines, producing additional losses and depriving us of product revenue.

If any of our relationships with these third-party CROs terminate, we may not be able to enter into arrangements with alternative CROs or to do so on commercially reasonable terms. If CROs do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols, regulatory requirements or for other reasons, our clinical trials may be extended, delayed or terminated and we may not be able to obtain regulatory approval for or successfully commercialize our product candidates. As a result, our results of operations and the commercial prospects for our product candidates would be harmed, our costs could increase and our ability to generate revenues could be delayed.

Switching or adding additional CROs involves additional cost and requires management time and focus. In addition, there is a natural transition period when a new CRO commences work. As a result, delays occur, which can materially impact our ability to meet our desired clinical development timelines. Additionally, CROs may lack the capacity to absorb higher workloads or take on additional capacity to support our needs. Though we carefully manage our relationships with our CROs, there can be no assurance that we will not encounter similar challenges or delays in the future or that these delays or challenges will not have a material adverse impact on our business, financial condition and prospects.

Because we rely on third-party manufacturing and supply partners, our supply of research and development, preclinical and clinical development materials may become limited or interrupted or may not be of satisfactory quantity or quality.

We rely on third-party contract manufacturers, or CMOs, to manufacture our preclinical product candidate supplies and will rely on CMOs to manufacture our clinical trial supplies. We lack the internal resources and the capability to manufacture any product candidates on a clinical or commercial scale. The facilities used by our CMOs to manufacture our product candidates must be acceptable to the FDA and other comparable foreign regulatory agencies pursuant to inspections that would be conducted after we submit our marketing application or relevant foreign regulatory submission to the applicable regulatory agency. Our preclinical and clinical development product supplies may be limited, interrupted or may not be of satisfactory quality or continue to be available at acceptable prices. If our CMOs cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or applicable

foreign regulatory agencies, they will not be able to secure or maintain regulatory approval for their manufacturing facilities. Any replacement of our CMOs could require significant effort and expertise because there may be a limited number of qualified replacements.

The manufacturing process for our product candidates is subject to FDA and foreign regulatory authority review. Suppliers and manufacturers must meet applicable manufacturing requirements and undergo rigorous facility and process validation tests required by regulatory authorities in order to comply with regulatory standards, such as cGMP. We have no direct control over our CMOs' ability to maintain adequate quality control, quality assurance and qualified personnel. In the event that any of our manufacturers fails to comply with regulatory requirements or to perform its obligations to us in relation to quality, timing or otherwise, or if our supply of components or other materials becomes limited or interrupted for other reasons, we may be forced to manufacture the materials ourselves, for which we currently do not have the capabilities or resources, or enter into an agreement with another third party, which we may not be able to do on reasonable terms, if at all. In some cases, the technical skills or technology required to manufacture our product candidates may be unique or proprietary to the original manufacturer and we may have difficulty transferring such skills or technology to another third party and a feasible alternative may not exist. These factors would increase our reliance on such manufacturer or require us to obtain a license from such manufacturer in order to have another third party manufacture our product candidates. If we are required to change manufacturers for any reason, we will be required to verify that the new manufacturer maintains facilities and procedures that comply with quality standards and with all applicable regulations and guidelines. The delays associated with the verification of a new manufacturer could negatively affect our ability to develop product candidates in a timely manner or within budget. Our reliance on contract manufacturers also exposes us to the possibility that they, or third parties with access to their facilities, will have access to and may appropriate our trade secrets or other proprietary information.

We expect to continue to rely on third-party CMOs if we receive regulatory approval for any product candidate. To the extent that we have existing, or enter into future, manufacturing arrangements with third parties, we will depend on these third parties to perform their obligations in a timely manner consistent with contractual and regulatory requirements, including those related to quality control and assurance. If we are unable to obtain or maintain third-party manufacturing for our product candidates, or to do so on commercially reasonable terms, we may not be able to develop and commercialize our product candidates successfully. Our or a third party's failure to execute on our manufacturing requirements and comply with cGMP could adversely affect our business in a number of ways, including:

- an inability to initiate or continue clinical studies of product candidates under development;
- delay in submitting regulatory applications, or receiving regulatory approvals, for our product candidates;
- loss of the cooperation of an existing or future strategic partner;
- subjecting third-party manufacturing facilities or our manufacturing facilities to additional inspections by regulatory authorities;
- a requirement to cease distribution or to recall batches of our product candidates; and
- in the event of approval to market and commercialize a product candidate, an inability to meet commercial demands for our products.

We, or our third-party manufacturers, may be unable to successfully scale-up manufacturing of our product candidates in sufficient quality and quantity, which would delay or prevent us from developing our product candidates and commercializing approved products, if any.

In order to conduct clinical studies of our product candidates and commercialize any approved product candidates, we, or our manufacturing partners, will need to manufacture them in large quantities. We, or our manufacturing partners, may be unable to successfully increase the manufacturing capacity for any of our product candidates in a timely or cost-effective manner, or at all. In addition, quality issues may arise during scale-up activities. If we, or any manufacturing

partners, are unable to successfully scale up the manufacture of our product candidates in sufficient quality and quantity, the development, testing and clinical studies of that product candidate may be delayed or infeasible, and regulatory approval or commercial launch of any resulting product may be delayed or not obtained, which could significantly harm our business. We are currently evaluating which third-party manufactures to engage for scale-up to commercial supply of our product candidates, including SIG-005. If we are unable to obtain or maintain third-party manufacturing for commercial supply of product candidates, or to do so on commercially reasonable terms, or if we are unable to develop our own manufacturing capabilities, we may not be able to develop and commercialize our product candidates successfully.

We have entered and may in the future enter into collaborations with third parties for the research, development, and commercialization of SIG-002 or any other potential product candidates. If any such collaborations are not successful or our existing partners do not perform as expected, we may not be able to capitalize on the market potential of those product candidates.

We have engaged and may in the future seek third-party collaborators for the research, development, and commercialization of certain of the product candidates we may develop. For example, pursuant to our agreement with Eli Lilly and Company, or Lilly, for the development of SIG-002, Lilly will be responsible for submitting an IND and all clinical development and commercialization activities following such IND submission. We will therefore depend on Lilly to design and conduct their clinical studies. If we enter into similar collaboration agreements for any of our other product candidates, we may also depend on partners to design and conduct clinical trials. As a result, we may have limited control over the amount and timing of resources that our collaborators dedicate to the development or commercialization of SIG-002 or other product candidates we may decide to partner with third-party collaborators. Our ability to generate revenues from these arrangements will depend on our collaborators' abilities to successfully perform the functions assigned to them in these arrangements. We cannot predict the success of our current or any future collaboration that we enter into.

Our current and any future collaborations involving our research programs or our current or any future product candidates pose numerous risks to us, including the following:

- Collaborators may have significant discretion in determining the efforts and resources that they will apply to these collaborations.
- Collaborators may not pursue development and commercialization of any current or future product candidates or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in the collaborator's strategic focus or available funding or external factors such as an acquisition that diverts resources or creates competing priorities.
- Collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials, or require a new formulation of a product candidate for clinical testing.
- Collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with any current or future product candidates if the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours.
- Collaborators with marketing and distribution rights to one or more product candidates may not commit sufficient resources to the marketing and distribution of such product candidates.
- Collaborators may not properly obtain, maintain, enforce, or defend our intellectual property or proprietary rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our proprietary information or expose us to potential litigation.

- Disputes may arise between the collaborators and us that result in the delay or termination of the research, development, or commercialization of our product candidates or that result in costly litigation or arbitration that diverts management attention and resources.

- We may lose certain valuable rights under circumstances identified in our collaborations, including if we undergo a change of control.

- Collaborations may be terminated and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable product candidates we may develop.

- Collaboration agreements may not lead to development or commercialization of product candidates in the most efficient manner or at all. If a present or future collaborator of ours were to be involved in a business combination, the continued pursuit and emphasis on our product development or commercialization program under such collaboration could be delayed, diminished, or terminated.

If our collaborations do not result in the successful development and commercialization of product candidates, or if Lilly or any of our other collaborators terminates its agreement with us, we may not receive any future research funding or milestones or royalty payments under the collaboration. If we do not receive the funding we expect under these agreements, our development of product candidates could be delayed, and we may need additional resources to develop product candidates. In addition, if one of our collaborators terminates its agreement with us, we may find it more difficult to find a suitable replacement collaborator or attract new collaborators, and our development programs may be delayed or the perception of us in the business and financial communities could be adversely affected. All of the risks relating to product development, regulatory approval, and commercialization described in this Quarterly Report on Form 10-Q apply to the activities of our collaborators.

These relationships, or those like them, may require us to incur non-recurring and other charges, increase our near- and long-term expenditures, issue securities that dilute our existing stockholders, or disrupt our management and business. In addition, we could face significant competition in seeking appropriate collaborators, and the negotiation process is time-consuming and complex. Our ability to reach a definitive collaboration agreement will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration, and the proposed collaborator's evaluation of several factors. If we license rights to any of our future product candidates, as we have with Lilly for the development and commercialization of SIG-002, we may not be able to realize the benefit of such transactions if we are unable to successfully integrate them with our existing operations and company culture.

If conflicts arise between our partners and us, the other party may act in a manner adverse to us and could limit our ability to implement our strategies. If any of our partners terminate or breach our agreements with them, or otherwise fail to complete their obligations in a timely manner, it may have a detrimental effect on our financial position by reducing or eliminating the potential for us to receive technology access and license fees, milestones and royalties, reimbursement of development costs, as well as possibly requiring us to devote additional efforts and incur costs associated with pursuing internal development of product candidates. Furthermore, if our partners do not prioritize and commit sufficient resources to programs associated with our product candidates or collaboration product candidates, we or our partners may be unable to commercialize these product candidates, which would limit our ability to generate revenue and become profitable.

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

Our product development and research programs and the potential commercialization of any of our current and future product candidates will require substantial additional cash to fund expenses. For some of the product candidates we may develop, we may decide to collaborate with other pharmaceutical and biotechnology companies for the development and potential commercialization of those product candidates. For example, we have partnered with Lilly for the development and commercialization of SIG-002 for the treatment of T1D.

We face significant competition in seeking appropriate collaborators. Whether we reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration, and the proposed collaborator's evaluation of a number of factors. Those factors may include preclinical results, the design or results of clinical trials, the likelihood of approval by the FDA, the EMA, the MHRA or similar regulatory authorities outside the United States, the potential market for the subject product candidate, the costs and complexities of manufacturing and delivering such product candidate to patients, the potential of competing products, the existence of uncertainty with respect to our ownership of technology, which can exist if there is a challenge to such ownership without regard to the merits of the challenge, and industry and market conditions generally. The collaborator may also consider alternative product candidates or technologies for similar indications that may be available to collaborate on and whether such a collaboration could be more attractive than the one with us.

Collaboration agreements may also restrict us from entering into future agreements on certain terms with potential collaborators or from using intellectual property and product candidates resulting from such collaboration. Collaborations are complex and time-consuming to negotiate and document. In addition, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators.

We may not be able to negotiate collaborations on a timely basis, on acceptable terms, or at all. If we are unable to do so, we may have to curtail the development of the product candidate for which we are seeking to collaborate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms or at all. If we do not have sufficient funds, we may not be able to develop product candidates or bring them to market and generate product revenue.

Risks Related to Our Intellectual Property

If we are unable to obtain and maintain patent and other intellectual property protection for SIG-005 or any other product candidates and for our SLTx platform, or if the scope of the patent and other intellectual property protection obtained is not sufficiently broad, our competitors could develop and commercialize products and technologies similar or identical to ours, and our ability to successfully commercialize any product candidates we may develop, and our SLTx platform may be adversely affected.

Our commercial success will depend in large part on our ability to obtain and maintain patent, trademark, trade secret and other intellectual property protection of our SLTx platform technologies, product candidates and other technologies, methods used to manufacture them and methods of treatment, as well as successfully defending our patent and other intellectual property rights against third-party challenges. It is difficult, complex, time consuming and costly to protect cell-based technology, including our SLTx platform technologies. For example, important individual components of our platform and our product candidates may be in the prior art and available to third parties, and we may not be able to prevent use of such components in products that would compete with SIG-005 or our other product candidates. Our ability to stop unauthorized third parties from making, using, selling, offering to sell, importing or otherwise commercializing products similar to SIG-005 or any other product candidates is dependent upon the extent to which we have rights under valid and enforceable patents or trade secrets that cover these activities.

We seek to protect our proprietary position by continuing to develop our own intellectual property and in-licensed intellectual property relating to our SLTx platform technologies and product candidates in the United States and abroad. If we or our licensors are unable to obtain or maintain patent protection with respect to our SLTx platform technologies and product candidates we may develop, or if the scope of the patent protection secured is not sufficiently broad, our competitors could develop and commercialize products and technologies similar or identical to ours and our ability to commercialize SIG-005 or any other product candidates may be adversely affected.

The patent prosecution process is expensive, time-consuming, and complex, and we may not be able to file, prosecute, maintain, enforce, or license all necessary or desirable patent applications at a reasonable cost or in a timely

manner in the United States and other important markets. In addition, we may not pursue or obtain patent protection in all relevant markets. It is also possible that we will fail to identify patentable aspects of our research and development output in time to obtain patent protection. Although we enter into non-disclosure and confidentiality agreements with parties who have access to confidential or patentable aspects of our research and development output, such as our employees, corporate collaborators, outside scientific collaborators, CROs, contract manufacturers, consultants, advisors, and other third parties, any of these parties may breach the agreements and disclose such output before a patent application is filed, thereby jeopardizing our ability to seek patent protection. In addition, our ability to obtain and maintain valid and enforceable patents depends, in part, on whether the differences between our inventions and the prior art allow our inventions to be patentable over the prior art. Furthermore, 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 be certain that we or our licensors were the first to make the inventions claimed in our owned or any licensed patents or pending patent applications, or that we or our licensors were the first to file for patent protection of such inventions.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain, involves complex legal and factual questions, and has been the subject of much litigation in recent years. The field of cell-based therapies has been the subject of extensive patenting activity. As a result, the issuance, scope, validity, enforceability, and commercial value of our patent rights are highly uncertain, and we may become involved in complex and costly litigation. Our pending and future patent applications may not result in patents being issued that protect our SLTx platform technologies or any of our current and future product candidates or that effectively prevent others from commercializing competitive technologies and product candidates.

Moreover, the coverage claimed in a patent application can be significantly reduced before the patent is issued, and the scope of a patent claim may be reinterpreted after issuance. Even if our current or future owned and in-licensed patent applications issue as patents, the patents may not issue in a form that will provide us with any meaningful protection, prevent competitors or other third parties from competing with us, or otherwise provide us with any competitive advantage. Any patents that we own or in-license may be challenged, narrowed, circumvented, or invalidated by third parties. Consequently, we do not know whether any of our SLTx platform advances and any of our current and future product candidates will be protectable or remain protected by valid and enforceable patents. Our competitors or other third parties may be able to circumvent our patents by developing similar or alternative technologies or products in a non-infringing manner.

In addition, given the amount of time required for the development, testing, and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our intellectual property may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours. Any of the foregoing could have a material adverse effect on our competitive position, business, financial conditions, results of operations, and prospects.

Our rights to develop and commercialize our SLTx platform technologies and product candidates are subject, in part, to the terms and conditions of licenses granted to us by others.

A significant portion of our intellectual property portfolio has been licensed from third parties, and our licensors may not always act in our best interest. If we fail to comply with our obligations under our intellectual property licenses, if the licenses are terminated, or if disputes regarding these licenses arise, we could lose significant rights that are important to our business.

We have licensed and are dependent on certain patent rights and proprietary technology from third parties that are important or necessary to the development and commercialization of our technologies and product candidates. For example, we are a party to an exclusive patent license agreement with Massachusetts Institute of Technology, or MIT, pursuant to which we in-license key patents and patent applications co-owned by MIT and Boston Children’s Hospital, or BCH, covering our SLTx platform technologies and product candidates. We refer to this agreement as the MIT License. The MIT License imposes various diligence, milestone payment, royalty, insurance, and other obligations on us. If we fail to comply with these obligations, MIT may have the right to terminate our license, in which event we may not be able to develop or market our SLTx platform or any other technologies or product candidates covered by the licensed intellectual

property. In addition, if we conclude that technology licensed to us under the MIT license or other agreements failed to prevent the PFO reported in a patient in our Phase 1/2 clinical trial of SIG-001, such licenses may also be less valuable to us. In the future, we may also enter into additional license agreements that are material to the development or commercialization of our product candidates, and that may impose similar obligations as in the MIT License. For example, if we are required to license additional technology in order to change the development of our SLTx platform, we may not be able to enter into such licenses with third parties on reasonable terms if at all.

These and other licenses may not provide sufficient rights to use such intellectual property, including cell lines or therapeutic protein sequences, in all relevant fields of use and in all territories in which we may wish to develop or commercialize our SLTx platform technologies and product candidates in the future. If we determine that rights to excluded fields or territories are necessary to commercialize our product candidates or maintain our competitive advantage, we may need to obtain additional licenses in order to continue developing, manufacturing or marketing our product candidates. We may not be able to obtain such licenses on an exclusive basis, on commercially reasonable terms, or at all, which could prevent us from commercializing our product candidates or allow our competitors or others the chance to access technology that is important to our business.

We do not have complete control in the preparation, filing, prosecution, maintenance, enforcement, and defense of patents and patent applications covering the technology that we license from third parties. For example, pursuant to the MIT License, MIT retains control of preparation, filing, prosecution, and maintenance. We cannot be certain that these patents and patent applications will be prepared, filed, prosecuted, and maintained in a manner consistent with the best interests of our business. Also, in certain circumstances, MIT has the right to enforce and defend the licensed patents and patent applications. It is possible that any licensor enforcement of patents against infringers or defense of patents against challenges of validity or claims of enforceability may be less vigorous than if we had conducted them ourselves, or may not be conducted in accordance with our best interests. If we or our licensors fail to prosecute, maintain, enforce, and defend such patents, or if we or our licensors lose rights to those patents or patent applications, the rights we have licensed may be reduced or eliminated, our right to develop and commercialize SIG-005 and other potential product candidates that are the subject of such licensed rights could be adversely affected and we may not be able to prevent competitors from making, using, and selling competing products.

Our licensors may not be the sole and exclusive owners or may not have sole and exclusive control of the patents, patent applications and technology we in-licensed. If other third parties have rights to any of such in-licensed intellectual property, they may be able to license such intellectual property to our competitors, and our competitors could market competing products and technology. In addition, our rights to our in-licensed patents, patent applications and technology are dependent, in part, on inter-institutional or other operating agreements between the joint owners of such intellectual property. If one or more of such joint owners breaches such inter-institutional or operating agreements, our rights to such in-licensed intellectual property may be adversely affected. Any of these events could have a material adverse effect on our competitive position, business, financial conditions, results of operations, and prospects.

Furthermore, inventions contained within some of our in-licensed intellectual property, including patents and patent applications licensed from MIT, were made using funding from the U.S. government, and, in some cases, private, non-profit organizations. We rely on our licensors to ensure compliance with applicable obligations arising from such funding, such as timely reporting of the filing of patent applications arising out of the funded research and licenses granted to such patent applications. The failure of our licensors to meet their obligations may lead to a loss of rights to the relevant licensed intellectual property or the unenforceability of relevant patents.

Also, university licensors, governments and other funding entities could have certain rights in our in-licensed patents and technology. For example, in the MIT License, MIT and BCH retain the right on behalf of themselves and all other non-profit research institutions to practice under the licensed patent rights for non-profit research, teaching and educational purposes, including sponsored research and collaborations, and the U.S. government retains a non-exclusive license authorizing the U.S. government to use the inventions or to have others use the invention on its behalf. If the U.S. government decides to exercise these rights, it is not required to engage us as its contractor in connection with doing so. The U.S. government’s rights may also permit it to disclose the funded inventions and technology to third parties and to exercise march-in rights to use or allow third parties to use the technology we have licensed that was developed using U.S. government funding. The U.S. government may also exercise its march-in rights if it determines that action is necessary

because we or our licensors failed to achieve practical application of the U.S. government-funded technology, because action is necessary to alleviate health or safety needs, to meet requirements of federal regulations, or to give preference to U.S. industry. In addition, our rights in such in-licensed U.S. government-funded inventions may be subject to certain requirements to manufacture product candidates embodying such inventions in the United States. Any of the foregoing could harm our business, financial condition, results of operations, and prospects significantly.

In the event any of our third-party licensors determine that, in spite of our efforts, we have materially breached a license agreement or have failed to meet certain obligations thereunder, it may elect to terminate the applicable license agreement or, in some cases, one or more license(s) under the applicable license agreement and such termination could result in us no longer having the ability to develop and commercialize product candidates and technology covered by that license agreement or license. In the event of such termination of a third-party in-license, or if the underlying patents under a third-party in-license fail to provide the intended exclusivity, competitors could have the freedom to seek regulatory approval of, and to market, products identical to ours. Any of these events could have a material adverse effect on our competitive position, business, financial conditions, results of operations, and prospects.

Our owned patent applications and in-licensed patents and patent applications and other intellectual property may be subject to priority disputes or to inventorship disputes and similar proceedings.

We or our licensors may be subject to claims that former employees, collaborators, or other third parties have an interest in our owned patent applications or in-licensed patents, patent applications, trade secrets or other intellectual property as an inventor or co-inventor. For example, we or our licensors may have inventorship disputes arise from conflicting obligations of employees, consultants or others who are involved in developing our current or any future product candidates. While it is our policy to require our employees 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. Litigation may be necessary to defend against these and other claims challenging inventorship or ownership of our owned patent applications, in-licensed patents or patent applications, trade secrets or other intellectual property. If we or our licensors are unsuccessful in defending any such claims or disputes, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or the exclusive right to use, our owned or in-licensed patents or other intellectual property that is important to our current or any future product candidates. Even if we or our licensors are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees. Any of the foregoing could result in a material adverse effect on our business, financial condition, results of operations, or prospects.

We have limited foreign intellectual property rights and may not be able to protect our intellectual property and proprietary rights throughout the world.

We have limited intellectual property rights outside the United States. The process for obtaining patent protection outside the United States is particularly difficult, expensive, time consuming, and complex. Thus, filing, prosecuting, and defending patents on product candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States can be less extensive than those in the United States. In addition, the laws of foreign countries do not protect intellectual property rights to the same extent as federal and state laws of the United States. In addition, our intellectual property license agreements may not always include worldwide rights. Consequently, we may not be able to prevent third parties from practicing our owned and licensed inventions in all countries outside the United States, or from selling or importing products made using such inventions in and into the United States or other jurisdictions. Competitors may use our owned and licensed technologies in jurisdictions where we have not obtained patent protection, or in which our license rights are non-exclusive, to develop their own products and, further, may export otherwise infringing products to territories where we have patent protection but where enforcement is not as strong as that in the United States. These products may compete with our product candidates and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets, and other intellectual property protection, particularly those relating to biotechnology

and pharmaceutical products, which could make it difficult for us to stop the infringement of our patents or marketing of competing products against third parties in violation of our intellectual property and proprietary rights generally. Proceedings to enforce our patents and intellectual property rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly and our patent applications at risk of not issuing, and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate, and the damages or other remedies awarded, if any, may not be commercially meaningful. Moreover, the initiation of proceedings by third parties to challenge the scope or validity of our patent rights in foreign jurisdictions could result in substantial cost and divert our efforts and attention from other aspects of our business. Accordingly, our efforts to enforce our intellectual property and proprietary rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

Many countries have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In addition, many countries limit the enforceability of patents against government agencies or government contractors. In these countries, the patent owner may have limited remedies, which could materially diminish the value of such patent. If we or any of our licensors is forced to grant a license to third parties with respect to any patents relevant to our business, our competitive position may be impaired, and our business, financial condition, results of operations, and prospects may be adversely affected.

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

We have entered into license agreements with third parties and may need to obtain additional licenses from our existing licensors and others to advance our research or allow commercialization of our product candidates. It is possible that we may be unable to obtain any additional licenses at a reasonable cost or on reasonable terms, if at all. In either event, we may be required to expend significant time and resources to redesign our technologies, product candidates, or the methods for manufacturing them or to develop or license replacement technologies, all of which may not be feasible on a technical or commercial basis. If we are unable to do so, we may be unable to develop or commercialize the affected product candidates, which could harm our business, financial condition, results of operations, and prospects significantly. We cannot provide any assurances that third-party patents do not exist which might be enforced against our current technology, manufacturing methods, product candidates, or future methods or products resulting in either an injunction prohibiting our manufacture or future sales, or, with respect to our future sales, an obligation on our part to pay royalties and/or other forms of compensation to third parties, which could be significant.

In the MIT License, we have the first right to bring any actions against any third party for infringing on the patents we have exclusively licensed. Certain of our license agreements, including the MIT License, also require us to meet development thresholds to maintain the license, including establishing a set timeline for developing and commercializing products. In spite of our efforts, our licensors might conclude that we have materially breached our obligations under such license agreements and might therefore terminate the license agreements, thereby potentially removing or limiting our ability to develop and commercialize products and technologies covered by these license agreements. If these in-licenses are terminated, or if the underlying patents fail to provide the intended exclusivity, competitors or other third parties could have the freedom to seek regulatory approval of, and to market, products identical to ours and we may be required to cease our development and commercialization of our SLTx platform technologies or product candidates. Any of the foregoing could have a material adverse effect on our competitive position, business, financial conditions, results of operations, and growth prospects. Disputes may arise regarding intellectual property subject to a licensing agreement, including:

- the scope of rights granted under the license agreement and other interpretation-related issues;
- the extent to which our technologies and processes infringe on intellectual property of the licensor that is not subject to the licensing agreement;
- the sublicensing of patent and other rights to third parties under our collaborative development relationships;

- our diligence obligations under the license agreement with respect to the use of the licensed technology in relation to our development and commercialization of our product candidates and what activities satisfy those diligence obligations;

- the inventorship and ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our licensors and us and our partners;

- the effects of termination; and

- the priority of invention of patented technology.

In addition, the agreements under which we currently license intellectual property or technology from third parties are complex, and certain provisions in such agreements may be susceptible to multiple interpretations. The resolution of any contract interpretation disagreement that may arise could narrow what we believe to be the scope of our rights to the relevant intellectual property or technology, or increase what we believe to be our financial or other obligations under the relevant agreement, either of which could have a material adverse effect on our business, financial condition, results of operations, and prospects. Moreover, if disputes over intellectual property that we have licensed prevent or impair our ability to maintain our current licensing arrangements on commercially acceptable terms, we may be unable to successfully develop and commercialize the affected product candidates. As a result, any termination of or disputes over our intellectual property licenses could result in the delay of our development and commercialization of our SLTx platform or other product candidates, the loss of our ability to develop and commercialize our SLTx platform or other product candidates, or our loss of other significant rights, any of which could have a material adverse effect on our business, financial conditions, results of operations, and prospects. It is also possible that a third party could be granted limited licenses to some of the same technology, in certain circumstances. For more information regarding our obligations in these agreements, please see "Business—License and Collaboration Agreements."

We may not be successful in acquiring or in-licensing necessary rights to key technologies or any product candidates we may develop.

We currently have rights to intellectual property, through licenses from third parties, to identify and develop product candidates, and we may seek to in-license additional rights to key components of our SLTx platform. We may also seek to in-license rights to develop improvements to our SLTx platform or expand our product candidate pipeline. The future growth of our business may depend in part on our ability to in-license or otherwise acquire the rights to additional product candidates and technologies. Although we have succeeded in licensing technologies from third-party licensees including MIT in the past, we cannot assure you that we will be able to in-license or acquire the rights to any product candidates or technologies from third parties on acceptable terms or at all.

We may enter into agreements with third-party licensors that provide that our field of use excludes particular fields. If we determine that rights to such fields are necessary to commercialize our product candidates or maintain our competitive advantage, we may need to obtain a license from such third parties in order to continue developing, manufacturing or marketing our product candidates. We may not be able to obtain such a license on an exclusive basis, on commercially reasonable terms, or at all, which could prevent us from commercializing our product candidates or allow our competitors or others the chance to access technology that is important to our business. For more information regarding these agreements, please see "Business—License and Collaboration Agreements."

Furthermore, there has been extensive patenting activity in the fields of engineered cell therapy and encapsulated cell therapy, and pharmaceutical companies, biotechnology companies, and academic institutions are competing with us or are expected to compete with us in the field of cell therapy and filing patent applications potentially relevant to our business. Thus, there may be third-party patent applications, currently pending or filed in the future, that, if issued, may relate to our SLTx platform or product candidates. In order to market our product candidates, we may find it necessary or prudent to obtain licenses from such third-party intellectual property holders. However, we may be unable to secure such licenses or otherwise acquire or in-license any compositions, methods of use, processes, or other intellectual property rights from third parties that we identify as necessary for SIG-005 or any other product candidates. We may also require

licenses from third parties for certain technologies related to preexisting cell therapies to be incorporated in our SLTx platform.

Additionally, we may collaborate with academic institutions to accelerate our preclinical research or development under written agreements with these institutions. In certain cases, these institutions provide us with an option to negotiate a license to any of the institution's rights in technology resulting from the collaboration. Even if we hold such an option, we may be unable to negotiate a license from the institution within the specified timeframe or under terms that are acceptable to us. If we are unable to do so, the institution may offer the intellectual property rights to others, potentially blocking our ability to pursue our program.

Furthermore, the research resulting in certain of our owned and in-licensed patent rights and technology may have been funded in part by the U.S. federal or state governments. As a result, the government may have certain rights, including march-in rights, to such patent rights and technology. When new technologies are developed with government funding, the government generally obtains certain rights in any resulting patents, including a non-exclusive license authorizing the government to use the invention for noncommercial purposes. These rights may permit the government to disclose our confidential information to third parties or allow third parties to use our licensed technology. The government can exercise its march-in rights if it determines that action is necessary because we fail to achieve practical application of the government-funded technology, because action is necessary to alleviate health or safety needs, to meet requirements of federal regulations, or to give preference to U.S. industry. In addition, our rights in such inventions may be subject to certain requirements to manufacture products embodying such inventions in the United States. Any of the foregoing could harm our competitive position, business, financial condition, results of operations and prospects.

In addition, the licensing or acquisition of third-party intellectual property rights is a highly competitive area, and a number of more established companies are also pursuing strategies to license or acquire third-party intellectual property rights that we may consider attractive or necessary. These established companies may have a competitive advantage over us due to their size, capital resources and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We also may be unable to license or acquire third-party intellectual property rights on terms that would allow us to make an appropriate return on our investment or at all. If we are unable to successfully obtain rights to required third-party intellectual property rights or maintain the existing intellectual property rights we have, we may have to abandon development of the relevant program or product candidate, which could have a material adverse effect on our business, financial condition, results of operations, and prospects.

The biotechnology and pharmaceutical industries have experienced substantial litigation and other proceedings regarding intellectual property rights, and third parties may initiate legal proceedings alleging that we are infringing, misappropriating, or otherwise violating their intellectual property rights, the outcome of which would be uncertain and may prevent, delay or otherwise interfere with our product discovery and development efforts.

Our commercial success depends upon our ability and the ability of our collaborators and licensors to develop, manufacture, market, and sell SIG-005 or any other product candidates and use our proprietary technologies without infringing, misappropriating, or otherwise violating the intellectual property and proprietary rights of third parties. The biotechnology and pharmaceutical industries are characterized by extensive litigation regarding patents and other intellectual property rights as well as administrative proceedings for challenging patents, including interference, derivation, *inter partes* review, post grant review, and reexamination proceedings before the USPTO or oppositions and other comparable proceedings in foreign jurisdictions. We may be subject to and may in the future become party to, or threatened with, adversarial proceedings or litigation regarding intellectual property rights with respect to our SLTx platform technologies and any product candidates we may develop, including interference proceedings, post-grant review, *inter partes* review, and derivation proceedings before the USPTO and similar proceedings in foreign jurisdictions such as oppositions before the EPO. Numerous U.S. and foreign issued patents and pending patent applications that are owned by third parties exist in the fields in which we are developing our product candidates and they may assert infringement claims against us based on existing patents or patents that may be granted in the future, regardless of their merit.

As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our SLTx platform technologies and product candidates may give rise to claims of infringement of the patent rights of

others. Moreover, it is not always clear to industry participants, including us, which patents cover various types of therapies, products or their methods of use or manufacture. As with many technology-based products, there may be third-party patent applications that, if issued, may be construed to cover components of our SLTx platform and product candidates. There may also be third-party patents of which we are currently unaware with claims to technologies, compositions, methods of manufacture or methods of use.

Because of the large number of patents issued and patent applications filed in our fields, third parties may allege they have patent rights encompassing our product candidates, technologies or methods. Third parties may assert that we are employing their proprietary technology without authorization and may file patent infringement claims or lawsuit against us, and if we are found to infringe such third-party patents, we may be required to pay damages, cease commercialization of the infringing technology, or obtain a license from such third parties, which may not be available on commercially reasonable terms or at all.

Our ability to commercialize our product candidates in the United States and abroad may be adversely affected if we cannot obtain a license on commercially reasonable terms to relevant third-party patents that cover our product candidates or SLTx platform technologies. Even if we believe third-party intellectual property claims are without merit, there is no assurance that a court would find in our favor on questions of infringement, validity, enforceability, or priority. A court of competent jurisdiction could hold that these third-party patents are valid, enforceable, and infringed, which could materially and adversely affect our ability to commercialize SIG-005 or any other product candidates and any other product candidates or technologies covered by the asserted third-party patents. In order to successfully challenge the validity of any such U.S. patent in federal court, we would need to overcome a presumption of validity. As this burden is a high one requiring us to present clear and convincing evidence as to the invalidity of any such U.S. patent claims, there is no assurance that a court of competent jurisdiction would invalidate the claims of any such U.S. patent. If we are found to infringe a third party's intellectual property rights, and we are unsuccessful in demonstrating that such patents are invalid or unenforceable, we could be required to obtain a license from such third party to continue developing, manufacturing, and marketing SIG-005 or any other product candidates and our technologies. However, we may not be able to obtain any required license on commercially reasonable terms or at all. Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors and other third parties access to the same technologies licensed to us, and it could require us to make substantial licensing and royalty payments. If we are unable to obtain a necessary license to a third-party patent on commercially reasonable terms, we may be unable to commercialize our SLTx platform technology or product candidates or such commercialization efforts may be significantly delayed, which could in turn significantly harm our business. We also could be forced, including by court order, to cease developing, manufacturing, and commercializing the infringing technology or product candidates. In addition, we could be found liable for significant monetary damages, including treble damages and attorneys' fees, if we are found to have willfully infringed a patent or other intellectual property right. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar material adverse effect on our business, financial condition, results of operations, and prospects.

Defense of third-party claims of infringement of misappropriation, or violation of intellectual property rights involves substantial litigation expense and would be a substantial diversion of management and employee time and resources from our business. Some third-parties may be able to sustain the costs of complex patent litigation more effectively than we can because they have substantially greater resources. In addition, any uncertainties resulting from the initiation and continuation of any litigation could have a material adverse effect on our ability to raise the funds necessary to continue our operations or could otherwise have a material adverse effect on our business, financial condition, results of operations and prospects. There could also be public announcements of the results of hearings, motions, or other interim proceedings or developments, and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. Any of the foregoing events could have a material adverse effect on our business, financial condition, results of operations and prospects.

We may become involved in lawsuits to protect or enforce our future patents or the patents of our licensors, which could be expensive, time consuming, and unsuccessful and could result in a finding that such patents are unenforceable or invalid.

Competitors may infringe our future patents or the patents of our licensing partners, or we may be required to defend against claims of infringement. In addition, our future patents or the patents of our licensing partners also are, and

may in the future become, involved in inventorship, priority, validity or enforceability disputes. Countering or defending against such claims can be expensive and time consuming. In an infringement proceeding, a court may decide that a patent owned or in-licensed by us is invalid or unenforceable, or may refuse to stop the other party from using the technology at issue on the grounds that our owned and in-licensed patents do not cover the technology in question. An adverse result in any litigation proceeding could put one or more of our owned or in-licensed patents at risk of being invalidated or interpreted narrowly.

In patent litigation in the United States, defendant counterclaims alleging invalidity and/or unenforceability are commonplace, and there are numerous grounds upon which a third party can assert invalidity or unenforceability of a patent. Third parties may also raise similar claims before administrative bodies in the United States or abroad, even outside the context of litigation. These types of mechanisms include re-examination, post-grant review, *inter partes* review, interference proceedings, derivation proceedings, and equivalent proceedings in foreign jurisdictions (e.g., opposition proceedings). These types of proceedings could result in revocation or amendment to our patents such that they no longer cover our product candidates. The outcome for any particular patent following legal assertions of invalidity and unenforceability is unpredictable. With respect to the validity question, for example, we cannot be certain that there is no invalidating prior art, of which we, our licensors, our patent counsel and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity and/or unenforceability, or if we are otherwise unable to adequately protect our rights, we would lose at least part, and perhaps all, of the patent protection on our technology and/or product candidates. Defense of these types of claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business.

We may choose to challenge the patentability of claims in a third party's U.S. or foreign patent, regardless of whether the claims are a threat to our SLTx platform technologies or product candidates. In the United States, this may be done by requesting that the USPTO review the patent claims in re-examination, post-grant review, *inter partes* review, interference proceedings, derivation proceedings. There are equivalent proceedings in foreign jurisdictions (e.g., opposition proceedings). We may choose to challenge third-party patents in the EPO and other foreign patent offices. Even if successful, the costs of these opposition proceedings could be substantial, and may consume our time or other resources. If we fail to obtain a favorable result at the USPTO, EPO or other patent office then we may be exposed to litigation by a third party alleging that the patent may be infringed by our product candidates, SLTx platform technologies or other proprietary technologies.

Even if resolved in our favor, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses and could distract our personnel from their normal responsibilities. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. In addition, there could be public announcements of the results of hearings, motions, or other interim proceedings or developments, and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing, or distribution activities. We may not have sufficient financial or other resources to conduct such litigation or proceedings adequately. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources and more mature and developed intellectual property portfolios. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a material adverse effect on our ability to compete in the marketplace.

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

Periodic maintenance fees, renewal fees, annuity fees, and various other government fees on patents and applications are due to be paid to the USPTO and foreign patent agencies outside of the United States over the lifetime of our owned or licensed patents and applications. For our in-licensed patents and patent applications, we generally rely on our licensors, including MIT, to pay these fees due to U.S. and non-U.S. patent agencies. For our owned patent applications,

we rely on our outside patent counsel in the United States and in foreign countries to monitor these deadlines and to pay these fees when so instructed.

The USPTO and foreign patent agencies require compliance with several procedural, documentary, fee payment, and other similar provisions during the patent application process. We depend on our licensors to take the necessary action to comply with these requirements with respect to our licensed intellectual property, and for our owned patent applications, we engage counsel and other professionals to help us comply with these requirements. While an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations, however, in which non-compliance can result in a partial or complete loss of patent rights in the relevant jurisdiction. Were a noncompliance event to occur, our competitors might be able to enter the market with similar or identical products or technology, which could have a material adverse effect on our business, financial condition, results of operations, and prospects.

Changes in patent law in the United States and in non-U.S. jurisdictions could diminish the value of patents in general, thereby impairing our ability to protect our SLTx platform technologies and product candidates.

As is the case with other biotech and pharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biopharmaceutical industry involve both technological and legal complexity, and is therefore costly, time-consuming and inherently uncertain.

Changes in either the patent laws or interpretation of the patent laws could increase the uncertainties and costs surrounding the prosecution of patent applications and the enforcement or defense of our issued patents. For example, in March 2013, under the Leahy-Smith America Invents Act, or the America Invents Act, the United States transitioned from a “first to invent” to a “first-to-file” patent system. Under a “first-to-file” system, assuming that other requirements for patentability are met, the first inventor to file a patent application generally will be entitled to a patent on an invention regardless of whether another inventor had made the invention earlier. A third party that files a patent application in the USPTO after March 2013, 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 such third party. This will require us to be cognizant going forward of the time from invention to filing of a patent application. Since patent applications in the United States and most other countries are confidential for a period of time after filing or until issuance, we cannot be certain that we or our licensors were the first to either file any patent application related to our technologies or product candidates or invent any of the inventions claimed in our or our licensor’s patents or patent applications. The America Invents Act also includes a number of other significant changes to U.S. patent law, including provisions that affect the way patent applications will be prosecuted, allowing third-party submission of prior art and establishing a new post-grant review system, including post-grant review, *inter partes* review, and derivation proceedings. Because of a lower evidentiary standard in USPTO proceedings compared to the evidentiary standard in United States federal courts 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 district court action. Accordingly, a third-party may attempt to use the USPTO procedures to invalidate our patent claims that would not have been invalidated if first challenged by the third-party as a defendant in a district court action. The effects of these changes are currently unclear as the USPTO continues to promulgate new regulations and procedures in connection with the America Invents Act and many of the substantive changes to patent law, including the “first-to-file” provisions, only became effective in March 2013. In addition, the courts have yet to address many of these provisions and the applicability of the act and new regulations on the specific patents discussed in this filing have not been determined and would need to be reviewed. Therefore, the America Invents 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.

In addition, recent U.S. Supreme Court rulings have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the validity and enforceability of patents, once obtained. Depending on future actions by the U.S. Congress, the federal courts, and the USPTO, the laws and regulations governing patents could change in unpredictable ways that could weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future.

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

Patents have a limited lifespan. The terms of individual patents depend upon the legal term for patents in the countries in which they are granted. In most countries, including the United States, if all maintenance fees are timely paid, the natural expiration of a patent is generally 20 years from its earliest non-provisional filing date in the applicable country. However, the actual protection afforded by a patent varies from country to country, and depends upon many factors, including the type of patent, the scope of its coverage, the availability of regulatory-related extensions, the availability of legal remedies in a particular country and the validity and enforceability of the patent. Various extensions including patent term extension, or PTE, and patent term adjustment, or PTA, may be available, but the life of such extension, and the protection they afford, is limited. Even if patents covering our product candidates are obtained, once the patent life has expired, we may be open to competition from competitive products, including biosimilars and generics. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting our product candidates might expire before or shortly after we or our partners commercialize those candidates. As a result, our owned and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

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

In addition to seeking patents for our technologies and product candidates, we also rely on trade secret protection, as well as confidentiality agreements, non-disclosure agreements and invention assignment agreements with our employees, consultants and third-parties, to protect our know-how and other confidential and proprietary information, especially where we do not believe patent protection is appropriate or obtainable.

It is our policy to require our employees, corporate collaborators, outside scientific collaborators, CROs, contract manufacturers, consultants, advisors, and other third parties to execute confidentiality agreements upon the commencement of employment or consulting relationships with us. These agreements provide that all confidential information concerning our business or financial affairs developed by or made known to the individual or entity during the course of the party's relationship with us is to be kept confidential and not disclosed to third parties, except in certain specified circumstances. In the case of employees, the agreements provide that all inventions conceived by the individual, and that are related to our current or planned business or research and development or made during normal working hours, on our premises or using our equipment or proprietary information, are our exclusive property. In the case of consultants and other third-party service providers, the agreements provide us with certain rights to all inventions arising from the services. However, we cannot guarantee that we have entered into such agreements with each party that may have or have had access to our trade secrets or proprietary technologies and processes. Additionally, the assignment of intellectual property rights may not be self-executing, or the assignment agreements may be breached, and we may be forced to bring claims against third parties, or defend claims that they may bring against us, to determine the ownership of what we regard as our intellectual property. 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. 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 to contractual measures, we try to protect the confidential nature of our proprietary information through other appropriate precautions, such as physical and technological security measures. However, trade secrets and know-how can be difficult to protect. These measures may not, for example, in the case of misappropriation of a trade secret by an employee or third-party with authorized access, provide adequate protection for our proprietary information. Our security measures may not prevent an employee or consultant from misappropriating our trade secrets and providing them to a competitor, and any recourse we might take against this type of misconduct may not provide an adequate remedy to protect our interests fully. In addition, our trade secrets may be independently developed by others in a manner that could prevent us from receiving legal recourse. If any of our confidential or proprietary information, such as our trade secrets, were to be disclosed or misappropriated, or if any of that information was independently developed by a competitor, our competitive position could be harmed.

In addition, some courts inside and outside the United States are sometimes less willing or unwilling to protect trade secrets. If we choose to go to court to stop a third-party from using any of our trade secrets, we may incur substantial costs. Even if we are successful, these types of lawsuits may consume our time and other resources. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations and prospects.

Third parties may assert that our employees, consultants, or advisors have wrongfully used or disclosed confidential information or misappropriated trade secrets.

As is common in the biotechnology and pharmaceutical industries, we employ individuals that are currently or were previously employed at universities, research institutions or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although we try to ensure that our employees, consultants, and advisors do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that we or these individuals have inadvertently or otherwise used or disclosed intellectual property, including trade secrets or other proprietary information, of any such individual's current or former employer. We may then have to pursue litigation to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to our technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments, and, if securities analysts or investors perceive these results to be negative, that perception could have a substantial adverse effect on the price of our common stock. This type of litigation or proceeding could substantially increase our operating losses and reduce our resources available for development activities, and we may not have sufficient financial or other resources to adequately conduct this type of litigation or proceedings. For example, some of our competitors may be able to sustain the costs of this type of litigation or proceedings more effectively than we can because of their substantially greater financial resources. In any case, uncertainties resulting from the initiation and continuation of intellectual property litigation or other intellectual property related proceedings could adversely affect our ability to compete in the marketplace.

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 partners or customers in our markets of interest. At times, competitors or other third parties 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 secrets, domain names, copyrights or other intellectual property may be ineffective and could result in substantial costs and diversion of resources and could adversely affect our business, financial condition, results of operations and growth prospects.

Intellectual property rights do not necessarily address all potential threats.

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

- any of our current and future product candidates, if approved, will eventually become commercially available in generic or biosimilar product forms;

- others may be able to make cell therapy products that are similar to any of our current and future product candidates or utilize similar cell therapy technology but that are not covered by the claims of the patents that we license or may own in the future;
- we, or our licensors or current or future collaborators, might not have been the first to make the inventions covered by the issued patent or pending patent application that we license or may own in the future;
- we, or our licensors or current or future collaborators, might not have been the first to file patent applications covering certain of our or their inventions;
- we, or our licensors or current or future collaborators, may fail to meet our obligations to the U.S. government regarding any in-licensed patents and patent applications funded by U.S. government grants, leading to the loss or unenforceability of patent rights;
- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our owned or licensed intellectual property rights;
- it is possible that our pending, owned or licensed patent applications or those that we may own or license in the future will not lead to issued patents;
- it is possible that there are prior public disclosures that could invalidate our owned or in-licensed patents, or parts of our owned or in-licensed patents;
- it is possible that there are unpublished applications or patent applications maintained in secrecy that may later issue with claims covering our product candidates or technology similar to ours;
- it is possible that our owned or in-licensed patents or patent applications omit individual(s) that should be listed as inventor(s) or include individual(s) that should not be listed as inventor(s), which may cause these patents or patents issuing from these patent applications to be held invalid or unenforceable;
- issued patents that we hold rights to may be held invalid, unenforceable, or narrowed in scope, including as a result of legal challenges by our competitors;
- the claims of our owned or in-licensed issued patents or patent applications, if and when issued, may not cover our product candidates;
- the laws of foreign countries may not protect our proprietary rights or the proprietary rights of our licensors or current or future collaborators to the same extent as the laws of the United States;
- the inventors of our owned or in-licensed patents or patent applications may become involved with competitors, develop products or processes that design around our patents, or become hostile to us or the patents or patent applications on which they are named as inventors;
- our competitors might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;
- we have engaged in scientific collaborations in the past and will continue to do so in the future and our collaborators may develop adjacent or competing products that are outside the scope of our patents;
- we may not develop additional proprietary technologies that are patentable;

- any product candidates we develop may be covered by third parties' patents or other exclusive rights;
- the patents of others may harm our business; or
- we may choose not to file a patent in order to maintain certain trade secrets or know-how, and a third-party may subsequently file a patent covering such intellectual property.

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

Risks Related to Regulatory and Compliance Matters

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

Our operations and arrangements with third-party payors and customers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell, and distribute our medicines for which we obtain marketing approval. Restrictions under applicable federal and state healthcare laws and regulations, some of which will apply only if and when we market a product, include the following:

- federal false claims, false statements and civil monetary penalties laws prohibiting, among other things, any person from knowingly presenting, or causing to be presented, a false claim for payment of government funds or knowingly making, or causing to be made, a false statement to get a false claim paid;
- the federal Anti-Kickback Statute, which prohibits, among other things, persons from offering, soliciting, receiving or providing remuneration, directly or indirectly, to induce either the referral of an individual, or the purchasing or ordering of, a good or service for which payment may be made under federal healthcare programs such as Medicare and Medicaid. A person or entity does not need to have actual knowledge of this statute or specific intent to violate it in order 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 civil False Claims Act;
- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which, in addition to privacy protections applicable to healthcare providers and other entities, prohibits 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 the statute or specific intent to violate it in order to have committed a violation;
- the federal Food, Drug, and Cosmetic Act, or the FDCA, which among other things, strictly regulates pharmaceutical marketing, prohibits manufacturers from marketing such products for off-label use and regulates the distribution of samples;
- federal laws that require pharmaceutical manufacturers to report certain calculated product prices to the government or provide certain discounts or rebates to government authorities or private entities, often as a condition of reimbursement under government healthcare programs;
- the so-called "federal sunshine" law under the Affordable Care Act, which requires pharmaceutical companies to monitor and report certain financial interactions with certain healthcare providers as well as ownership and investment interests held by physicians and their immediate family members to the Centers for Medicare & Medicaid Services within the U.S. Department of Health and Human Services for re-disclosure to the public; and

- analogous state and foreign laws and regulations, such as state anti-kickback, anti-bribery and false claims laws, which may apply to healthcare items or services that are reimbursed by non-governmental third-party payors, including private insurers.

Some state laws also require pharmaceutical companies to comply with specific compliance standards, restrict financial interactions between pharmaceutical companies and healthcare providers or require pharmaceutical companies to report information related to payments to health care providers or marketing expenditures.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. Given the breadth of the laws and regulations, limited guidance for certain laws and regulations and evolving government interpretations of the laws and regulations, governmental authorities may possibly conclude that our business practices may not comply with healthcare laws and regulations. If our operations are found to be in violation of any of the laws described above or any other government regulations that apply to us, we may be subject to penalties, including civil and criminal penalties, damages, fines, exclusion from participation in government health care programs, such as Medicare and Medicaid, imprisonment, and the curtailment or restructuring of our operations, any of which could adversely affect our business, financial condition, results of operations, and prospects.

When carrying out any activity or inducement within the U.K. or EU designed to promote the prescription, supply, sale or consumption of medicinal products to persons qualified to prescribe or supply them (including, for example, physicians), no gifts, pecuniary advantages or benefits in kind may be supplied, offered or promised to such persons unless they are inexpensive and relevant to the practice of medicine or pharmacy. The provision of benefits or advantages to such individuals more generally is also governed by the national anti-bribery laws of the U.K. and the EU member states, such as the U.K. Bribery Act 2010. Infringement of these laws could result in substantial fines and imprisonment, or in being excluded from public tenders for our products.

Payments made by biopharmaceutical companies to healthcare organizations, healthcare professionals (including physicians) and patient organizations in the U.K. and EU are required to be publicly disclosed. Direct and indirect payments and transfers of value are caught, including donations, grants, sponsorships, hospitality, fees for research and development, consultancy services and gifts. Moreover, in some EU Members States, agreements with physicians often must be the subject of prior notification and approval by the physician's employer, his or her competent professional organization, and/or the relevant regulatory authorities. These requirements are provided in the national laws, industry codes, or professional codes of conduct applicable in the U.K. and EU member states. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines or imprisonment.

Healthcare and other reform legislation may increase the difficulty and cost for us and any collaborators we may have to obtain marketing approval of and commercialize SIG-005 or any other product candidates and affect the prices we, or they, may obtain.

In the United States and some foreign jurisdictions, there have been and continue to be ongoing efforts to implement legislative and regulatory changes regarding the healthcare system. Such changes could prevent or delay marketing approval of any product candidates that we may develop, restrict or regulate post-approval activities, and affect our ability to profitably sell any product candidates for which we obtain marketing approval. Although we cannot predict what healthcare or other reform efforts will be successful, such efforts may result in more rigorous coverage criteria, in additional downward pressure on the price that we, or our future collaborators, may receive for any approved products or in other consequences that may adversely affect our ability to achieve or maintain profitability.

In the United States, the federal government and individual states have aggressively pursued healthcare reform, as evidenced by the passing of the Affordable Care Act and the ongoing efforts to modify or repeal that legislation. The Affordable Care Act substantially changed the way healthcare is financed by both governmental and private insurers and contains a number of provisions that affect coverage and reimbursement of drug products and/or that could potentially reduce the demand for pharmaceutical products such as increasing drug rebates under state Medicaid programs for brand name prescription drugs and extending those rebates to Medicaid managed care and assessing a fee on manufacturers and importers of brand name prescription drugs reimbursed under certain government programs, including Medicare and Medicaid. The Affordable Care Act has been subject to modification and additional modifications may occur. There are,

and may continue to be, judicial challenges. Other health care reform efforts beyond the Affordable Care Act, including efforts related to drug coverage and pricing, have been ongoing. See "Government Regulation—Healthcare and Other Reform." We cannot predict the ultimate content, timing or effect of any changes to the Affordable Care Act or other federal and state reform efforts. There is no assurance that federal or state health care reform will not adversely affect our future business and financial results, and we cannot predict how future federal or state legislative, judicial or administrative changes relating to healthcare reform will affect our business.

Federal and state governments have shown significant interest in implementing cost-containment programs to limit the growth of government-paid healthcare costs, including price controls, waivers from Medicaid drug rebate law requirements, restrictions on reimbursement and requirements for substitution of generic products for branded prescription drugs. The private sector has also sought to control healthcare costs by limiting coverage or reimbursement or requiring discounts and rebates on products. We are unable to predict what additional legislation, regulations or policies, if any, relating to the healthcare industry or third-party coverage and reimbursement may be enacted in the future or what effect such legislation, regulations or policies would have on our business. Any cost containment measures could significantly decrease the available coverage and the price we might establish for our products, which would have an adverse effect on our net revenues and operating results.

Legislative and regulatory proposals have been made to expand post-approval requirements and restrict sales and promotional activities for biotechnology products. We cannot be sure whether additional legislative changes will be enacted, or whether FDA regulations, guidance or interpretations for biological products 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 the U.S. Congress of the FDA's approval and decision-making processes may significantly delay or prevent marketing approval, as well as subject us to more stringent product labeling and post-marketing testing and other requirements.

We have obtained orphan drug designation for SIG-005 for the treatment of MPS-1 and SIG-007 for the treatment of Fabry disease, and we intend to seek orphan drug designation for our product candidates, but any orphan drug designations we receive may not confer marketing exclusivity or other expected benefits.

We were granted Orphan Drug designations by the FDA and EMA for SIG-005 for the treatment of MPS-1 in December 2020 and October 2021, respectively, and by the FDA for SIG-007 for the treatment of Fabry disease in March 2021. However, we may not be able to obtain orphan drug designation for our other product candidates, and previously granted orphan drug designations may be revoked. Any product candidates we may develop for prevalent diseases, such as diabetes, will not be eligible to receive orphan drug designation. A separate application will have to be made in the United Kingdom at the time of the marketing authorization application and in which we might not be successful.

Even if we obtain U.S. orphan drug exclusivity for a product candidate, that exclusivity may not effectively protect the product candidate from competition because different product candidates can be approved for the same condition. In addition, even after an orphan drug is approved, the FDA can subsequently approve the same product candidate for the same condition if the FDA concludes that the later product candidate is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care compared with the product that has orphan exclusivity. The EU has its own criteria for designation as an orphan medicine but, as in the United States, orphan market exclusivity may not apply to the extent any further applicant can establish that its medicinal product is safer, more effective or otherwise clinically superior. Orphan drug exclusivity in the United States or the EU may also be lost if the FDA or EMA, respectively, determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the product to meet the needs of the patients with the rare disease or condition.

On August 3, 2017, the Congress passed the FDA Reauthorization Act of 2017, or FDARA. FDARA, among other things, codified the FDA's pre-existing regulatory interpretation, to require that a drug sponsor demonstrate the clinical superiority of an orphan drug that is otherwise the same as a previously approved drug for the same rare disease in order to receive orphan drug exclusivity. The new legislation reverses prior precedent holding that the Orphan Drug Act unambiguously requires that the FDA recognize the orphan exclusivity period regardless of a showing of clinical superiority. The FDA may further reevaluate the Orphan Drug Act and its regulations and policies. We do not know if, when, or how the FDA may change the orphan drug regulations and policies in the future, and it is uncertain how any

changes might affect our business. Depending on what changes the FDA may make to its orphan drug regulations and policies, our business could be adversely impacted.

Our employees, principal investigators, consultants, and commercial partners may engage in misconduct or other improper activities, including non-compliance with regulatory standards and requirements and insider trading.

We are exposed to the risk of fraud or other misconduct by our employees, consultants, and commercial partners, and, if we commence clinical trials, our principal investigators. Misconduct by these parties could include intentional failures to comply with FDA regulations or the regulations applicable in the EU, the United Kingdom and other jurisdictions, provide accurate information to the FDA, the EMA, the United Kingdom and other regulatory authorities, comply with healthcare fraud and abuse laws and regulations in the United States and abroad, report financial information or data accurately, or disclose unauthorized activities to us. In particular, sales, marketing, and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs, and other business arrangements. Such misconduct also could involve the improper use of information obtained in the course of clinical trials or interactions with the FDA, the EMA, the MHRA or other regulatory authorities, which could result in regulatory sanctions and cause serious harm to our reputation. It is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from government investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, financial condition, results of operations, and prospects, including the imposition of significant fines or other sanctions.

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

We are subject to numerous laws and regulations in each jurisdiction outside the United States in which we operate. The creation, implementation and maintenance of international business practices compliance programs is costly and such programs are difficult to enforce, particularly where reliance on third parties is required.

The Foreign Corrupt Practices Act, or FCPA, prohibits any U.S. individual or business from paying, offering, authorizing payment or offering of anything of value, directly or indirectly, to any foreign official, political party or candidate for the purpose of influencing any act or decision of the foreign entity in order to assist the individual or business in obtaining or retaining business. The FCPA also obligates companies whose securities are listed in the United States to comply with certain accounting provisions requiring the company to maintain books and records that accurately and fairly reflect all transactions of the corporation, including international subsidiaries, and to devise and maintain an adequate system of internal accounting controls for international operations. The anti-bribery provisions of the FCPA are enforced primarily by the Department of Justice. The SEC is involved with enforcement of the books and records provisions of the FCPA.

Similarly, the U.K. Bribery Act 2010 has extra-territorial effect for companies and individuals having a connection with the United Kingdom. The U.K. Bribery Act prohibits inducements both to public officials and private individuals and organizations. Compliance with the FCPA and the U.K. Bribery Act is expensive and difficult, particularly in countries in which corruption is a recognized problem. In addition, the FCPA presents particular challenges in the pharmaceutical industry, because, in many countries, hospitals are operated by the government, and doctors and other hospital employees are considered foreign officials. Certain payments to hospitals in connection with clinical trials and other work have been deemed to be improper payments to government officials and have led to FCPA enforcement actions.

Various laws, regulations and executive orders also restrict the use and dissemination outside of the United States, or the sharing with certain non-U.S. nationals, of information classified for national security purposes, as well as certain products and technical data relating to those products. If we expand our business outside of the United States, we will be required to dedicate additional resources to comply with these laws, and these laws may preclude us from developing,

manufacturing, or selling certain products and product candidates outside of the United States, which could limit our growth potential and increase our development costs. The failure to comply with laws governing international business practices may result in substantial penalties, including suspension or debarment from government contracting. Violation of the FCPA can result in significant civil and criminal penalties. Indictment alone under the FCPA can lead to suspension of the right to do business with the U.S. government until the pending claims are resolved. Conviction of a violation of the FCPA can result in long-term disqualification as a government contractor. The termination of a government contract or relationship as a result of our failure to satisfy any of our obligations under laws governing international business practices would have a negative impact on our operations and harm our reputation and ability to procure government contracts. The SEC also may suspend or bar issuers from trading securities on U.S. exchanges for violations of the FCPA's accounting provisions.

We are subject to stringent privacy laws, information security laws, regulations, policies and contractual obligations related to data privacy and security and changes in such laws, regulations, policies and contractual obligations could adversely affect our business.

We are subject to data privacy and protection laws and regulations that apply to the collection, transmission, storage and use of personally-identifying information, which among other things, impose certain requirements relating to the privacy, security and transmission of personal information, including comprehensive regulatory systems in the United States and EU. The legislative and regulatory landscape for privacy and data protection continues to evolve in jurisdictions worldwide, and there has been an increasing focus on privacy and data protection issues with the potential to affect our business. We cannot be sure how these evolving laws and regulations will be interpreted, enforced or applied to our operations. Failure to comply with any of these laws and regulations could result in contractual liabilities as well as enforcement action against us. As a result, we could be subject to fines, claims for damages by affected individuals, negative publicity, damage to our reputation and loss of goodwill, any of which could have a material adverse effect on our business, financial condition, results of operations or prospects. Even if we are not determined to have violated these laws, government investigations into these issues typically require the expenditure of significant resources and generate negative publicity, which could harm our business, financial condition, results of operations or prospects. Applicable privacy laws and court decisions in the EU could also impact our ability to transfer personal data internationally.

Within the United States, there are numerous federal and state laws and regulations related to the privacy and security of personal information. In particular, regulations promulgated pursuant to HIPAA establish privacy and security standards that limit the use and disclosure of personally identifiable health information, or protected health information, and require the implementation of administrative, physical and technological safeguards to protect the privacy of protected health information and ensure the confidentiality, integrity and availability of electronic protected health information. Determining whether protected information has been handled in compliance with the various applicable requirements and our contractual obligations can be complex and may be subject to changing interpretation.

Additionally, the California Consumer Privacy Act, or the CCPA, became effective on January 1, 2020 with enforcement beginning July 1, 2020. The CCPA imposes stringent data privacy and data protection requirements for the data of California residents. Among other things, it requires covered companies to provide new disclosures to California consumers and afford such consumers new data protection rights, including the ability to opt-out of certain sales of personal information. The CCPA provides for civil penalties for violations, as well as a private right of action for certain data breaches that result in the loss of personal data that may increase the likelihood of, and risks associated with, data breach litigation. The effects of this legislation are potentially far-reaching and may require us to modify our data processing practices and policies and to incur substantial costs and expenses in an effort to comply.

Data collected from patients enrolled in our Phase 1/2 clinical trial of SIG-001 is, and any data we may collect from patients enrolled in future clinical trials, including for SIG-005, in the United Kingdom or the EU will be, subject to the General Data Protection Regulation, or GDPR, which went into effect in May 2018 and which imposes obligations on companies that operate in our industry with respect to the processing of personal data and the cross border transfer of such data. The GDPR imposes onerous accountability obligations requiring data controllers and processors to maintain a record of their data processing and policies. If our or our partners' or service providers' privacy or data security measures fail to comply with the GDPR requirements, we may be subject to litigation, regulatory investigations, enforcement notices requiring us to change the way we use personal data and/or fines of up to 20 million Euros or up to 4% of the total

worldwide annual turnover of the preceding financial year, whichever is higher, as well as compensation claims by affected individuals, negative publicity, reputational harm and a potential loss of business and goodwill. Additionally, on July 16, 2020 the CJEU, Europe's highest court, held in the Schrems II case that the EU US Privacy Shield, a mechanism for the transfer of personal data from the EU to the United States, was invalid. The impact of this decision on the ability to lawfully transfer personal information from the EU to the United States, has led to increased scrutiny on data transfers from the European Economic Area to the U.S. generally and may increase our costs of compliance with data privacy legislation.

Data privacy regulations and data privacy remain an evolving landscape at both the domestic and international level, with new regulations coming into effect, such as the California Consumer Privacy Act, and continued legal challenges, and our efforts to comply with the evolving data protection rules may be unsuccessful. It is possible that these laws may be interpreted and applied in a manner that is inconsistent with our practices. We must devote significant resources to understanding and complying with this changing landscape and such changes may require ongoing modifications to our policies, procedures and systems.

Risks Related to Employee and Operations Matters, Managing Growth and Information Technology

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

We are highly dependent on Dr. Rogerio Vivaldi Coelho, our Chief Executive Officer, as well as the other principal members of our management and scientific teams. Dr. Vivaldi and such other principal members are employed "at will," meaning we or they may terminate the employment at any time. We do not maintain "key person" insurance for any of our executives or other employees. The loss of the services of any of these persons could impede the achievement of our research, development, and commercialization objectives.

Recruiting and retaining qualified scientific, clinical, manufacturing, business development, general and administrative and sales and marketing personnel will also be critical to our success. Our reduction in workforce, and the attrition thereafter, resulted in the loss of longer-term employees, the loss of institutional knowledge and expertise. We may not be able to attract and retain these personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel and recently observed increases in employee attrition and turnover in our industry. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. In addition, challenges or the failure to succeed in preclinical or clinical trials, including due to the clinical trial hold on SIG-001, or applications for marketing approval, may make it more challenging to recruit and retain qualified personnel. 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, including our scientific co-founders, 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. The inability to recruit, or loss of services of certain executives, key employees, consultants, or advisors, may impede the progress of our research, development, and commercialization objectives and have a material adverse effect on our business, financial condition, results of operations, and prospects.

Our internal computer systems, or those of our third-party vendors, collaborators or other contractors or consultants, may fail or suffer security breaches, which could result in a material disruption of our product development programs, compromise sensitive information related to our business or prevent us from accessing critical information, potentially exposing us to liability or otherwise adversely affecting our business.

Our internal computer systems and those of our current and any future third-party vendors, collaborators and other contractors or consultants are vulnerable to damage, interruption or data theft from computer viruses, computer hackers, malicious code, employee theft or misuse, ransomware, social engineering (including phishing attacks), denial-of-service attacks, sophisticated nation-state and nation-state-supported actors, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. Cybersecurity incidents, which may not be immediately or ever detected, are increasing in frequency and evolving in nature.

System failure, accident and security breach, could cause interruptions in our operations, or result in a disruption of our development programs and our business operations, whether due to a loss of our trade secrets or other proprietary information or other disruptions. For example, the loss of clinical trial data from future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. If we were to experience a significant cybersecurity breach of our information systems or data, the costs associated with the investigation, remediation and potential notification of the breach to counter-parties and data subjects could be material. In addition, our remediation efforts may not be successful. If we do not allocate and effectively manage the resources necessary to build and sustain the proper technology and cybersecurity infrastructure, we could suffer significant business disruption, including transaction errors, supply chain or manufacturing interruptions, processing inefficiencies, data loss or the loss of or damage to intellectual property or other proprietary information.

To the extent that any disruption or security breach were to result in a loss of, or damage to, our or our third-party vendors', collaborators' or other contractors' or consultants' data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability including litigation exposure, penalties and fines, we could become the subject of regulatory action or investigation, our competitive position could be harmed and the further development and commercialization of our product candidates could be delayed. Any of the above could have a material adverse effect on our business, financial condition, results of operations or prospects. While we maintain cyber-liability insurance (covering security and privacy matters), such insurance may not be adequate to cover any losses experienced as a result of a cybersecurity incident.

A pandemic, epidemic, or outbreak of an infectious disease, such the COVID-19 pandemic, may materially and adversely affect our business and our financial results and could cause a disruption to the development or supply of SIG-005 or any other product candidates.

COVID-19, including the continued spread of new variants of the virus, could adversely impact any preclinical or clinical trial operations in the United States and Europe, including our ability to recruit and retain patients and principal investigators and site staff who, as healthcare providers, may have heightened exposure to COVID-19 if an outbreak occurs in their geography, and our ability to conduct preclinical studies with reduced laboratory capacity. For example, similar to other biotechnology companies, we have, and may in the future, experience delays in initiating IND-enabling studies, protocol deviations, enrolling in any clinical trials or dosing of patients in any clinical trials as well as in activating any trial sites.

In addition, the patient populations that SIG-001, SIG-005 or any other product candidates target may be particularly susceptible to COVID-19, which may make it more difficult for us to review preliminary results of our Phase 1/2 clinical trial of SIG-001, including the finding of spheres with PFO and the reported SAE, identify patients able to enroll in our current and future clinical trials and may impact the ability of enrolled patients to complete any such trials. Any negative impact the COVID-19 pandemic has to patient enrollment or treatment or the execution of SIG-005 or any other product candidates could cause costly delays to clinical trial activities, which could adversely affect our ability to obtain regulatory approval for and to commercialize our product candidates, increase our operating expenses and have a material adverse effect on our financial results. Additionally, timely enrollment in planned clinical trials is dependent upon clinical trial sites which could be adversely affected by global health matters, such as pandemics. We plan to conduct clinical trials for SIG-005 and any other product candidates in geographies that continue to be affected by the COVID-19 pandemic. Some additional factors from the coronavirus outbreak that will delay or otherwise adversely affect future enrollment in the clinical trials of SIG-005 or any other product candidates, as well as our business generally, include:

- changes in local regulations as part of a response to the COVID-19 pandemic which may require us to change the ways in which our clinical trials are conducted, which may result in unexpected costs, or cause us to discontinue such clinical trials altogether;

- refusal of the FDA or other regulatory authorities to accept data from clinical trials gathered in affected geographies;

- the potential diversion of healthcare resources away from the conduct of clinical trials to focus on pandemic concerns, including the attention of physicians serving as our clinical trial investigators, hospitals serving as our clinical trial sites and hospital staff supporting the conduct of our prospective clinical trials;

- interruption in global shipping affecting the transport of clinical trial materials, such as patient samples, conditioning drugs and other supplies used in our prospective clinical trials; and

The COVID-19 pandemic has also impacted, and may continue to impact, our third-party suppliers and manufacturers, including through the effects of facility closures, reductions in operating hours, staggered shifts and other social distancing efforts, labor shortages, decreased productivity and unavailability of materials or components. While we maintain an inventory of materials used to conduct our research and development activities, a prolonged pandemic could lead to shortages in the raw materials necessary to manufacture our product candidates. We and our CMOs and CROs may also face challenges recruiting and retaining critical employees due to the high turnover rate of such employees during the COVID-19 pandemic. For example, similar to other biotechnology companies, we experienced increased rates of voluntary turnover as the demand for such employees has increased during the COVID-19 pandemic.

Risks Related to Our Common Stock

The market price of our common stock may be highly volatile, which could result in substantial losses for investors.

Our share price has been and may continue to be volatile. Some of the factors that may cause the market price of our common stock to fluctuate include:

- the success of existing or new competitive product candidates or technologies;

- the timing and results of preclinical studies for any product candidates that we may develop;

- failure or discontinuation of any of our product development and research programs;

- developments with respect to our investigation of the preliminary results of our Phase 1/2 clinical trial of SIG-001 in Hemophilia A , including the finding of spheres with PFO and the reported SAE;

- results of preclinical studies, clinical trials, or regulatory approvals of product candidates of our competitors, or announcements about new research programs or product candidates of our competitors;

- developments or changing views regarding the use of engineered cell therapy and encapsulated cell therapy;

- commencement or termination of collaborations for our product development and research programs;

- regulatory or legal developments in the United States and other countries;

- 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 research programs, clinical development programs, or product candidates that we may develop;

- the results of our efforts to develop additional product candidates or products;

- actual or anticipated changes in estimates as to financial results, development timelines, or recommendations by securities analysts;

- announcement or expectation of additional financing efforts;
- sales of our common stock by us, our insiders or other stockholders;
- variations in our financial results or those of companies that are perceived to be similar to us;
- changes in estimates or recommendations by securities analysts, if any, that cover our stock;
- market conditions in the pharmaceutical and biotechnology sectors;
- general economic, industry, and market conditions; and
- the other factors described in this “Risk Factors” section.

In recent years, the stock market in general, and the market for pharmaceutical and biotechnology companies in particular, has experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to changes in the operating performance of the companies whose stock is experiencing those price and volume fluctuations. The uncertain nature, magnitude and duration of hostilities stemming from the conflict in Ukraine, including the potential effects of sanctions limitations, retaliatory cyber-attacks on the world economy and markets, have contributed to increased market volatility and uncertainty. Broad market and industry factors may seriously affect the market price of our common stock, regardless of our actual operating performance. These fluctuations may be even more pronounced in the trading market for our stock. Following periods of such volatility in the market price of a company’s securities, securities class action litigation has often been brought against that company. Because of the potential volatility of our stock price, we may become the target of securities litigation in the future. Securities litigation could result in substantial costs and divert management’s attention and resources from our business.

Insiders have substantial influence over us, which could limit your ability to affect the outcome of key transactions, including a change of control.

As of December 31, 2021, our directors and executive officers and their affiliates beneficially owned shares representing approximately 32.2% of our outstanding common stock. As a result, these stockholders, if they act together, are able to influence our management and affairs and all matters requiring stockholder approval, including the election of directors and approval of significant corporate transactions. This concentration of ownership may have the effect of delaying or preventing a change in control of our company and might affect the market price of our common stock.

If we fail to establish and maintain proper and effective internal control over financial reporting, our operating results and our ability to operate our business could be harmed.

Ensuring that we have adequate internal financial and accounting controls and procedures in place so that we can produce accurate financial statements on a timely basis is a costly and time consuming effort that needs to be reevaluated frequently. Our internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements in accordance with generally accepted accounting principles.

Implementing any appropriate changes to our internal controls may distract our officers and employees, entail substantial costs to modify our existing processes and take significant time to complete. These changes may not, however, be effective in maintaining the adequacy of our internal controls, and any failure to maintain that adequacy, or consequent inability to produce accurate financial statements on a timely basis, could increase our operating costs and harm our business.

Our independent registered public accounting firm will not be required to formally attest to the effectiveness of our internal control over financial reporting pursuant to Section 404 of the Sarbanes-Oxley Act of 2002 until we are no longer an emerging growth company or a smaller reporting company. At such time, our independent registered public accounting firm may issue a report that is adverse in the event it is not satisfied with the level at which our controls are documented,

designed or operated. However, Section 404 of the Sarbanes-Oxley Act of 2002 requires management to furnish a report on our internal control over financial reporting. In this regard, we will need to continue to dedicate internal resources, potentially engage outside consultants, adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing whether such controls are functioning as documented, and implement a continuous reporting and improvement process for internal control over financial reporting.

If either we are unable to conclude that we have effective internal control over financial reporting or, at the appropriate time, our independent auditors are unwilling or unable to provide us with an unqualified report on the effectiveness of our internal control over financial reporting as required by Section 404, investors may lose confidence in our operating results, the price of our common stock could decline and we may be subject to litigation or regulatory enforcement actions.

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

We are an "emerging growth company," as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act, and may remain an emerging growth company for up to five years following our initial public offering. For so long as we remain an emerging growth company, we are permitted and plan to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not emerging growth companies. These exemptions include not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes Oxley Act, 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 stockholder approval of any golden parachute payments not previously approved. As a result, the information we provide stockholders is different than the information that is available with respect to other public companies. 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 more volatile.

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 certain accounting standards until those standards would otherwise apply to private companies. We have elected to not to "opt out" of the extended transition period, which means that when a standard is issued or revised and it has different application dates for public or private companies, we may adopt the new or revised standard at the time private companies adopt the new or revised standard.

Further, even after we no longer qualify as an emerging growth company, we may still qualify as a "smaller reporting company," which would allow us to take advantage of many of the same exemptions from disclosure requirements, including reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements. In addition, if we are a smaller reporting company, we would not be required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act. These exemptions and reduced disclosures in our SEC filings due to our status as a smaller reporting company may make it harder for investors to analyze our results of operations and financial prospects. We cannot predict if investors will find our common stock less attractive because we may rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock prices may be more volatile.

We do not expect to pay any dividends for the foreseeable future.

You should not rely on an investment in our common stock to provide dividend income. We do not anticipate that we will pay any dividends to holders of our common stock in the foreseeable future. Instead, we plan to retain any earnings to maintain and expand our existing operations. In addition, any future credit facility may contain terms prohibiting or limiting the amount of dividends that may be declared or paid on our common stock. Accordingly, investors must rely on sales of their common stock after price appreciation, which may never occur, as the only way to realize any return on their investment. As a result, investors seeking cash dividends should not purchase our common stock.

Our future ability to utilize our net operating loss carryforwards and certain other tax attributes may be limited.

We have incurred substantial losses during our history, and we may never achieve profitability. To the extent that we continue to generate taxable losses, unused losses will carry forward to offset a portion of future taxable income, if any, subject to expiration of such carryforwards in the case of carryforwards generated prior to 2018. Additionally, we continue to generate business tax credits, including research and development tax credits, which generally may be carried forward to offset a portion of future taxable income, if any, subject to expiration of such credit carryforwards. Under Sections 382 and 383 of the Code, if a corporation undergoes an "ownership change," generally defined as a greater than 50 percentage point change (by value) in its equity ownership over a three-year period, the corporation's ability to use its pre-change net operating loss carryforwards, or NOLs, and other pre-change tax attributes (such as research and development tax credits) to offset its post-change income or taxes may be limited. Our prior equity offerings and other changes in our stock ownership have resulted in such ownership changes. We may experience additional ownership changes in the future as a result of subsequent shifts in our stock ownership, some of which are outside of our control. As a result, if we earn net taxable income, our ability to use our pre-change NOLs or other pre-change tax attributes to offset U.S. federal taxable income may be subject to limitations, which could potentially result in increased future tax liability to us. Additionally, for taxable years beginning after December 31, 2017, the deductibility of such U.S. federal net operating losses is limited to 80% of our taxable income in any future taxable year. There is a risk that due to changes under the TCJA, regulatory changes, or other unforeseen reasons, our existing NOLs or business tax credits could expire or otherwise be unavailable to offset future income tax liabilities. At the state level, there may also be periods during which the use of NOLs or business tax credits is suspended or otherwise limited, which could accelerate or permanently increase state taxes owed. For these reasons, we may not be able to realize a tax benefit from the use of our NOLs or tax credits, even if we attain profitability.

Provisions in our amended and restated certificate of incorporation, our amended and restated by-laws and Delaware law may have anti-takeover effects that could discourage an acquisition of us by others, even if an acquisition would be beneficial to our stockholders, and may prevent attempts by our stockholders to replace or remove our current management.

Our amended and restated certificate of incorporation, amended and restated by-laws and Delaware law contain provisions that may have the effect of discouraging, delaying or preventing a change in control of us or changes in our management that stockholders may consider favorable, including transactions in which you might otherwise receive a premium for your shares. Our amended and restated certificate of incorporation and by-laws include provisions that:

- authorize "blank check" preferred stock, which could be issued by our board of directors without stockholder approval and may contain voting, liquidation, dividend and other rights superior to our common stock;
- create a classified board of directors whose members serve staggered three-year terms;
- specify that special meetings of our stockholders can be called only by our board of directors;
- prohibit stockholder action by written consent;
- establish an advance notice procedure for stockholder approvals to be brought before an annual meeting of our stockholders, including proposed nominations of persons for election to our board of directors;
- provide that vacancies on our board of directors may be filled only by a majority of directors then in office, even though less than a quorum;
- provide that our directors may be removed for cause only;
- specify that no stockholder is permitted to cumulate votes at any election of directors;
- expressly authorized our board of directors to modify, alter or repeal our amended and restated by-laws; and

- require supermajority votes of the holders of our common stock to amend specified provisions of our amended and restated certificate of incorporation and amended and restated by-laws.

These provisions, alone or together, could delay or prevent hostile takeovers and changes in control or changes in our management. 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 we are incorporated in the State of Delaware, we are governed by the provisions of Section 203 of the General Corporation Law of the State of Delaware, or the DGCL, 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.

Any provision of our amended and restated certificate of incorporation, amended and restated by-laws or Delaware law that has the effect of delaying or deterring a change in control could limit the opportunity for our stockholders to receive a premium for their shares of our common stock, and could also affect the price that some investors are willing to pay for our common stock.

Our amended and restated certificate of incorporation designates the state or federal courts within the State of Delaware as the exclusive forum for certain types of actions and proceedings that may be initiated by our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees.

Our amended and restated certificate of incorporation provides that, subject to limited exceptions, the state or federal courts within the State of Delaware are exclusive forums for (1) any derivative action or proceeding brought on our behalf, (2) any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers or other employees to us or our stockholders, (3) any action asserting a claim against us arising pursuant to any provision of the DGCL, our amended and restated certificate of incorporation or our amended and restated by-laws, (4) any action to interpret, apply, enforce or determine the validity of our amended and restated certificate of incorporation or our amended and restated bylaws or (5) any other action asserting a claim against us that is governed by the internal affairs doctrine; provided that, the exclusive forum provision will not apply to suits brought to enforce any liability or duty created by the Exchange Act or to any claim for which the federal courts have exclusive jurisdiction. Our amended and restated certificate of incorporation also provides that, unless we consent in writing to the selection of an alternative forum, the U.S. federal district courts shall be the exclusive forum for the resolution of any claims arising under the Securities Act. Any person or entity purchasing or otherwise acquiring any interest in shares of our capital stock shall be deemed to have notice of and to have consented to the provisions of our amended and restated certificate of incorporation described above. This choice of forum provision may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers or other employees, which may discourage such lawsuits against us and our directors, officers and employees.

Alternatively, if a court were to find these provisions of our amended and restated certificate of incorporation inapplicable to, or unenforceable in respect of, one or more of the specified types of actions or proceedings, we may incur additional costs associated with resolving such matters in other jurisdictions, which could adversely affect our business and financial condition.

If we cannot comply with Nasdaq's continued listing standards, our common stock could be delisted, which would harm our business, the trading price of our common stock, our ability to raise additional capital and the liquidity of the market for our common stock.

Our common stock is currently listed on The Nasdaq Global Select Market. To maintain the listing of our common stock on The Nasdaq Global Select Market, we are required to meet certain listing requirements, including related to the price of our common stock. Our common stock is currently closing below the minimum $1.00 bid price. If the bid price for our common stock continues to close below the minimum $1.00 bid price per share, we may risk not being in compliance with Nasdaq's requirements for continued listing. In such circumstances, to regain compliance, the bid price

for our common stock would need to close at $1.00 per share or more for a minimum of 10 consecutive business days, among other requirements. If we are unable to continue to meet Nasdaq's listing maintenance standards for any reason, our common stock could be delisted from The Nasdaq Global Select Market. To regain compliance, we would need to consider alternatives to resolve any listing deficiency, such as, subject to approval of our Board of Directors and stockholders, implementing a reverse stock split. However, there can be no assurance that a reverse stock split would be approved or would result in a sustained higher stock price that would allow us to meet the Nasdaq stock price listing requirements. If our common stock were delisted, we could seek to list our common stock on The Nasdaq Capital Market or trade our common stock on the OTC Markets. Listing on such other market or exchange could reduce the liquidity of our common stock and impede our ability to raise capital.

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

Use of Proceeds from the Sale of Registered Securities

On December 8, 2020, we closed our initial public offering in which we issued and sold 8,050,000 shares of our common stock, including 1,050,000 shares of common stock sold pursuant to the underwriters' full exercise of their option to purchase additional shares, at a public offering price of $18.00 per share, for aggregate gross proceeds of $144.9 million. All of the shares issued and sold in the IPO were registered under the Securities Act pursuant to a Registration Statement on Form S-1 (File No. 333-250070), which was declared effective by the SEC on December 3, 2020, and a Registration Statement on Form S-1 MEF (File No. 333-251111) filed pursuant to Rule 462(b) of the Securities Act.

The net offering proceeds to us, after deducting underwriting discounts and offering expenses payable by us of $13.1 million, were $131.8 million. No offering expenses were paid directly or indirectly to any of our directors or officers (or their associates) or persons owning 10.0% or more of any class of our equity securities or to any other affiliates. There has been no material change in our planned use of the balance of the net proceeds from the offering described in our final prospectus filed with the SEC pursuant to Rule 424(b)(4).

Item 3. Defaults upon Senior Securities

None.

Item 4. Mine Safety Disclosures

Not Applicable.

Item 5. Other Information

None.

Item 6. Exhibits

Exhibit number	Description of document
3.1	Fifth Amended and Restated Certificate of Incorporation of Sigilon Therapeutics, Inc. (incorporated by reference to Exhibit 3.1 to the Company's Current Report on Form 8-K filed with the SEC on December 8, 2020)
3.2	Amended and Restated Bylaws of Sigilon Therapeutics, Inc. (incorporated by reference to Exhibit 3.2 to the Company's Current Report on Form 8-K filed with the SEC on December 8, 2020)
3.3	Third Amended and Restated Investors' Rights Agreement, by and among Sigilon Therapeutics, Inc. and the investors party thereto, dated as of October 23, 2020 (incorporated by reference to Exhibit 4.2 to the Company's Registration Statement on Form S-1 (File No. 333-250070))

31.1*	Certification of Principal Executive Officer pursuant to Rule 13a-14(a) or Rule 15d-14(a) of 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 Rule 13a-14(a) or Rule 15d-14(a) of 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 and Principal Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002
101.INS	Inline XBRL Instance Document.
101.SCH	XBRL Taxonomy Extension Schema Document.
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document.
101.LAB	XBRL Taxonomy Extension Labels Linkbase Document.
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document.
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document.
104	Cover Page Interactive Data File (formatted as Inline XBRL and contained in Exhibit 101)

* Filed herewith

++ Portions of this exhibit (indicated by asterisks) have been redacted because they are both not material and the registrant customarily and actually treats such information as private or confidential.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

SIGILON THERAPEUTICS, INC.

By: /s/ Rogerio Vivaldi Coelho, M.D.
Rogerio Vivaldi Coelho, M.D.
President and Chief Executive Officer
(Principal Executive Officer)
Date: May 12, 2022

By: /s/ Josias Pontes
Josias Pontes
Senior Vice President, Acting Chief Financial Officer
(Principal Accounting Officer and Principal Financial Officer)
Date: May 12, 2022

Exhibit 31.1

Certification of Principal Executive Officer and Principal Financial Officer pursuant to Exchange Act Rules 13a-14(a) and 15d-14(a), as adopted pursuant to Section 302 of Sarbanes-Oxley Act of 2002

I, Rogerio Vivaldi Coelho, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q of Sigilon Therapeutics, Inc.;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:
    a. Designed such disclosure controls and procedures, or caused such disclosure controls and ... to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
    b. Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;
    c. Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
    d. Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report), that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
    a. All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
    b. Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: May 12, 2022 By: /s/ Rogerio Vivaldi Coelho, M.D.

Rogerio Vivaldi Coelho, M.D.
President and Chief Executive Officer
(Principal Executive Officer)

Exhibit 31.2

Certification of Principal Executive Officer and Principal Financial Officer pursuant to Exchange Act Rules 13a-14(a) and 15d-14(a), as adopted pursuant to Section 302 of Sarbanes-Oxley Act of 2002

I, Josias Pontes, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q of Sigilon Therapeutics, Inc.;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:
    a. Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
    b. Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;
    c. Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
    d. Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report), that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
    a. All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
    b. Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: May 12, 2022 By: /s/ Josias Pontes

Josias Pontes
Senior Vice President, Acting Chief Financial Officer
(Principal Accounting Officer and Principal Financial Officer)

Exhibit 32.1

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

In connection with this Quarterly Report on Form 10-Q of Sigilon Therapeutics, Inc. (the "Company") for the quarter ended March 31, 2022 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), each of the undersigned officers of the company, hereby certifies, pursuant to Section 1350 of Chapter 63 of Title 18, United States Code, that to the best of his knowledge:

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

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

Date: May 12, 2022 By: /s/ Rogerio Vivaldi Coelho, M.D.

Rogerio Vivaldi Coelho, M.D.
President and Chief Executive Officer
(Principal Executive Officer)

Date: May 12, 2022 By: /s/ Josias Pontes

Josias Pontes
Senior Vice President, Acting Chief Financial Officer
(Principal Accounting Officer and Principal Financial Officer)