UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-Q

(Mark One)

☒ **QUARTERLY REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES 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 _____

Commission File Number 001-41200

VIGIL NEUROSCIENCE, INC.

(Exact name of Registrant as specified in its Charter)

Delaware	**85-1880494**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
1 Broadway, 7th Floor, Suite 07-300 Cambridge, MA	**02142**
(Address of principal executive offices)	**(Zip Code)**

Registrant's telephone number, including area code: (857) 254-4445

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

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, par value $0.0001 per share	VIGL	The Nasdaq Global Select Market

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

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

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

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

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

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

The number of shares of Registrant's Common Stock outstanding as of April 30, 2022 was 28,266,815, par value $0.0001 per share.

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SUMMARY RISK FACTORS

We are subject to numerous risks and uncertainties, including those further described below in the section entitled "Risk Factors" in this Quarterly Report on Form 10-Q, that represent challenges that we face in connection with the successful implementation of our strategy and the growth of our business. In particular, the following considerations, among others, may offset our competitive strengths or have a negative effect on our business strategy, which could materially adversely affect our business, financial conditions, results of operations, future growth prospects, or cause a decline in the price of our common stock:

- We have a limited operating history, have incurred significant operating losses since our inception and expect to incur significant losses for the foreseeable future. We may never generate any revenue or become profitable, and, if we achieve profitability, we may not be able to sustain it.
- We will require additional financing to achieve our goals, and a failure to obtain this necessary capital when needed on acceptable terms, or at all, could force us to delay, limit, reduce or terminate our development programs, commercialization efforts or other operations.
- We have never successfully completed any clinical trials, and if we are unable to identify and advance therapeutic candidates through preclinical studies and clinical trials, obtain marketing approval and ultimately commercialize them, or experience significant delays in doing so, our business will be materially harmed.
- The results of preclinical studies are not necessarily predictive of the results of later preclinical studies and any clinical trials of our therapeutic candidates, and interim, topline and preliminary data from our preclinical studies and planned clinical trials that we announce or publish from time to time may change as more data become available and are subject to audit and verification procedures that could result in material changes in the final data.
- We may expend our limited resources to pursue a particular therapeutic candidate or indication, such as our initial focus on developing VGL101, and fail to capitalize on therapeutic candidates or indications that may be more profitable or for which there is a greater likelihood of success. As such, our business is highly dependent on the clinical advancement of our programs and is especially dependent on the success of our lead candidate, VGL101.
- We have concentrated a substantial portion of our research and development efforts on the treatment of neurodegenerative diseases, a field that has seen limited success in drug development. Further, our therapeutic candidates are based on new approaches, which makes it difficult to predict the time and cost of therapeutic candidate development and subsequently obtaining regulatory approval.
- We may encounter substantial delays in the commencement, enrollment or completion of our planned clinical trials, which could prevent us from receiving necessary regulatory approvals or commercializing any therapeutic candidates we develop on a timely basis, if at all.
- Use of our therapeutic candidates could be associated with side effects, adverse events or other properties or safety risks, which could delay or preclude approval, cause us to suspend or discontinue clinical trials, abandon a therapeutic candidate, limit the commercial profile of an approved label or result in other significant negative consequences that could severely harm our business, prospects, operating results and financial condition.
- Our therapeutic candidates are subject to extensive regulation and compliance, which is costly and time-consuming, and such regulation may cause unanticipated delays or prevent the receipt of the required approvals to commercialize our therapeutic candidates.
- We rely, and expect to continue to rely, on third parties to conduct some or all aspects of our product manufacturing, research and preclinical and clinical testing, and these third parties may not perform satisfactorily.
- If we are unable to obtain and maintain patent protection for our therapeutic programs and other proprietary technologies we develop, or if the scope of the patent protection obtained is not sufficiently broad, our competitors could develop and commercialize products and technology similar or identical to ours, and our ability to successfully commercialize our therapeutic programs and other proprietary technologies we may develop may be adversely affected.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Quarterly Report on Form 10-Q contains express or implied forward-looking statements that are based on our management's belief and assumptions and on information currently available to our management. Although we believe that the expectations reflected in these forward-looking statements are reasonable, these statements relate to future events or our future operational or financial performance, and involve known and unknown risks, uncertainties and other factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by these forward-looking statements. Forward-looking statements contained in this Quarterly Report on Form 10-Q include, but are not limited to, statements about:

- the initiation timing, progress, results and cost of VGL101 and our small molecule TREM2 agonists program, as well as our research and development programs and our current and future preclinical and clinical studies, including statements regarding the timing of initiation and completion of studies or trials and related preparatory work, the period during which the results of the trials will become available and our current and future programs;
- the application of our precision medicine approach to develop microglia-targeted therapies for patients with rare, genetically defined neurodegenerative diseases and subsequently advance into neurodegenerative diseases affecting larger patient populations;
- the expansion of our modality agnostic product pipeline to other microglial targets beyond TREM2;
- the ability of our preclinical studies and clinical trials to demonstrate safety and efficacy of our product candidates, as well as the beneficial characteristics, therapeutic effects and other positive results;
- our estimates of the number of patients that we will enroll and our ability to initiate, recruit and enroll patients in and conduct and successfully complete our clinical trials at the pace that we project;
- the ability to identify research and efficiently discover and develop product candidates;
- the timing, scope and likelihood of regulatory filings and approvals, including timing of INDs and final FDA approval of our current product candidates or any future product candidates;
- the timing, scope or likelihood of foreign regulatory filings and approvals;
- the scope of protection we are able to establish and maintain for intellectual property rights covering our product candidates and other product candidates we may develop, including the extensions of existing patent terms where available, the validity of intellectual property rights held by third parties, and our ability not to infringe, misappropriate or otherwise violate any third-party intellectual property rights;
- our ability to scale up our manufacturing and processing approaches to appropriately address our anticipated commercial needs, which will require significant resources
- the ability and willingness of our third-party strategic collaborators to continue research and development activities relating to our development candidates and product candidates;
- our ability to obtain funding for our operations necessary to complete further development and commercialization of our product candidates;
- our ability to commercialize our products, if approved;
- the pricing and reimbursement of our product candidates, if approved;
- the implementation of our business model, and strategic plans for our business, product candidates, and technology;
- estimates of our future expenses, revenues and capital requirements and our needs for additional financing;
- future agreements with third parties in connection with the development and commercialization of product candidates and any other approved product;
- the size and growth potential of the markets for our product candidates and our ability to serve those markets;
- our financial performance;
- the rate and degree of market acceptance of our product candidates;
- regulatory developments in the United States and foreign countries;
- our ability to attract and retain key scientific or management personnel;

- our ability to contract with third-party suppliers and manufacturers and their ability to perform adequately;
- our ability to produce our products or product candidates with advantages in turnaround times or manufacturing cost;
- the success of competing therapies that are or may become available;
- the impact of laws and regulations;
- developments relating to our competitors and our industry;
- the effect of the COVID-19 pandemic, including mitigation efforts and economic effects, on any of the foregoing or other aspects of our business operations, including but not limited to a negative impact on enrollment in our ongoing clinical trial as well as any other impacts on our existing and future clinical trials or our preclinical studies; and
- other risks and uncertainties, including those listed under the caption "Risk Factors."

In some cases, you can identify forward-looking statements by terminology such as "may," "should," "expects," "intends," "plans," "anticipates," "believes," "estimates," "predicts," "potential," "continue" or the negative of these terms or other comparable terminology. These statements are only predictions. You should not place undue reliance on forward-looking statements because they involve known and unknown risks, uncertainties, and other factors, which are, in some cases, beyond our control and which could materially affect results. All statements other than statements of historical facts are statements that could be deemed forward-looking statements. Factors that may cause actual results to differ materially from current expectations include, among other things, those listed above under "Summary of the Material Risks Associated with Our Business" and under the section titled "Risk Factors" and elsewhere in this Quarterly Report on Form 10-Q. If one or more of these risks or uncertainties occur, or if our underlying assumptions prove to be incorrect, actual events or results may vary significantly from those implied or projected by the forward-looking statements. No forward-looking statement is a guarantee of future performance. You should read this Quarterly Report on Form 10-Q and the documents that we reference in this Quarterly Report on Form 10-Q and have filed with the Securities and Exchange Commission, or the SEC, as exhibits hereto completely and with the understanding that our actual future results may be materially different from any future results expressed or implied by these forward-looking statements.

The forward-looking statements in this Quarterly Report on Form 10-Q represent our views as of the date of this Quarterly Report on Form 10-Q. We anticipate that subsequent events and developments will cause our views to change. However, while we may elect to update these forward-looking statements at some point in the future, we have no current intention of doing so except to the extent required by applicable 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.

This Quarterly Report on Form 10-Q also contains estimates, projections and other information concerning our industry, our business and the markets for our product candidates. Information that is based on estimates, forecasts, projections, market research or similar methodologies is inherently subject to uncertainties and actual events or circumstances may differ materially from events and circumstances that are assumed in this information. Unless otherwise expressly stated, we obtained this industry, business, market, and other data from our own internal estimates and research as well as from reports, research surveys, studies, and similar data prepared by market research firms and other third parties, industry, medical and general publications, government data and similar sources. While we are not aware of any misstatements regarding any third-party information presented in this Quarterly Report on Form 10-Q, their estimates, in particular as they relate to projections, involve numerous assumptions, are subject to risks and uncertainties and are subject to change based on various factors, including those discussed under the section titled "Risk Factors" and elsewhere in this Quarterly Report on Form 10-Q.

PART I—FINANCIAL INFORMATION

Item 1. Financial Statements.

VIGIL NEUROSCIENCE, INC.
CONDENSED CONSOLIDATED BALANCE SHEETS
(In thousands, except share and per share amounts)
(Unaudited)

	March 31, 2022	December 31, 2021
Assets		
Current assets:		
Cash and cash equivalents	$ 163,324	$ 91,420
Prepaid expenses and other current assets	7,101	6,063
Total current assets	170,425	97,483
Property and equipment, net	533	301
Operating lease right-of-use assets	725	882
Financing lease right-of-use assets	86	91
Restricted cash	927	927
Other assets	116	2,757
Total assets	$ 172,812	$ 102,441
Liabilities, Convertible Preferred Stock and Stockholders' Deficit		
Current liabilities:		
Accounts payable [(1)]	$ 2,713	$ 3,977
Accrued expenses and other current liabilities [(1)]	3,152	5,031
Operating lease liabilities	691	830
Financing lease liabilities	43	43
Total current liabilities	6,599	9,881
Operating lease liabilities, net of current portion	23	41
Finance lease liabilities, net of current portion	12	23
Total liabilities	6,634	9,945
Commitments and contingencies (Note 13)		
Series A convertible preferred stock, net of issuance costs, $0.0001 par value; 0 share authorized as of March 31, 2022 and 28,522,592 shares authorized as of December 31, 2021; 0 share issued and outstanding as of March 31, 2022 and 28,522,592 shares issued and outstanding as of December 31, 2021; liquidation preference of $0 and $72,647 as of March 31, 2022 and December 31, 2021, respectively	—	72,327
Series B convertible preferred stock, net of issuance costs, $0.0001 par value; 0 share authorized as of March 31, 2022 and 25,657,096 shares authorized as of December 31, 2021; 0 share issued and outstanding as of March 31, 2022 and 25,657,096 shares issued and outstanding as of December 31, 2021; liquidation preference of $0 and $90,000 as of March 31, 2022 and December 31, 2021, respectively	—	89,612
Stockholders' deficit:		
Undesignated preferred stock, $0.001 par value, 10,000,000 and 0 shares authorized as of March 31, 2022 and December 31, 2021; 0 share issued and outstanding at March 31, 2022 and December 31, 2021	—	—
Common stock, $0.0001 par value; 150,000,000 shares authorized at March 31, 2022 and 72,000,000 shares authorized at December 31, 2021; 28,311,138 shares issued as of March 31, 2022 and 1,748,879 shares issued as of December 31, 2021; and 28,266,815 shares outstanding as of March 31, 2022 and 1,724,950 shares outstanding as of December 31, 2021	3	—
Additional paid-in capital	253,338	2,386
Accumulated deficit	(87,163)	(71,829)
Total stockholders' equity (deficit)	166,178	(69,443)
Total liabilities, convertible preferred stock and stockholders' deficit	$ 172,812	$ 102,441

(1) Includes related party amounts of $69 (accrued expenses and other current liabilities) at March 31, 2022; $221 (accrued expenses and other current liabilities) at December 31, 2021 (see Note 12).

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

VIGIL NEUROSCIENCE, INC.
CONDENSED CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS
(In thousands, except share and per share amounts)
(Unaudited)

	Three Months Ended March 31,	
	2022	**2021**
Operating expenses:		
Research and development [(2)]	$ 10,365	$ 6,753
General and administrative	4,967	1,165
Total operating expenses	15,332	7,918
Loss from operations	(15,332)	(7,918)
Other income (expense):		
Change in fair value of the related party antidilution obligation	—	(252)
Change in fair value of Series A preferred stock tranche obligation	—	(21)
Interest income, net	2	2
Other income (expense), net	(4)	(2)
Total other expense, net	(2)	(273)
Net loss and comprehensive loss	$ (15,334)	$ (8,191)
Net loss per share attributable to common stockholders, basic and diluted	$ (0.58)	$ (5.46)
Weighted-average common shares outstanding, basic and diluted	26,660,246	1,499,843

(2) Includes related party amounts of $67 for the three months ended March 31, 2022, and $680 for the three months ended March 31, 2021 (see Note 12).

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

VIGIL NEUROSCIENCE, INC.
CONDENSED CONSOLIDATED STATEMENTS OF CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' EQUITY (DEFICIT)
(In thousands, except share amounts)
(Unaudited)

	Convertible Preferred Stock		Common Stock		Additional Paid-in	Accumulated	Total Stockholders'
	Shares	Amount	Shares	Amount	Capital	Deficit	Equity (Deficit)
Balances at December 31, 2020	18,707,126	$ 47,034	1,748,879	$ —	$ 263	$ (28,546)	$ (28,283)
Stock-based compensation expense	—	—	—	—	333	-	333
Net loss	—	—	—	—	-	(8,191)	(8,191)
Balances at March 31, 2021	18,707,126	$ 47,034	1,748,879	$ —	$ 596	$ (36,737)	$ (36,141)
Balances at December 31, 2021	54,179,688	$ 161,939	1,724,950	$ —	$ 2,386	$ (71,829)	$ (69,443)
Conversion of convertible preferred stock to common stock upon closing of initial public offering	(54,179,688)	(161,939)	19,536,870	2	161,937	—	161,939
Issuance of common stock from initial public offering, net of issuance costs of $10.0 million	—	—	7,000,000	1	87,985	—	87,986
Exercise of stock options	—	—	4,995	—	9	—	9
Stock-based compensation	—	—	—	—	1,021	—	1,021
Net loss	—	—	—	—	—	(15,334)	(15,334)
Balances at March 31, 2022	—	$ —	28,266,815	$ 3	$ 253,338	$ (87,163)	$ 166,178

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

VIGIL NEUROSCIENCE, INC.
CONDENSED CONSOLIDATED STATEMENTS OF CASH FLOWS
(In thousands)
(Unaudited)

	Three Months Ended March 31,	
	2022	**2021**
Cash flows from operating activities:		
Net loss	$ (15,334)	$ (8,191)
Adjustments to reconcile net loss to net cash used in operating activities:		
Stock-based compensation expense	1,021	333
Non-cash operating lease expense	219	—
Change in fair value of the related party antidilution obligation	—	252
Change in fair value of Series A preferred stock tranche obligation	—	21
Depreciation and amortization	18	—
Changes in operating assets and liabilities:		
Prepaid expenses and other current assets	(987)	490
Other non-current assets	(16)	—
Accounts payable	(1,339)	2,070
Accrued expenses and other current liabilities	(1,508)	262
Operating lease liabilities	(218)	—
Net cash used in operating activities	(18,144)	(4,763)
Cash flows from investing activities:		
Purchases of property and equipment	(142)	—
Net cash used in investing activities	(142)	—
Cash flows from financing activities:		
Proceeds from issuance of common stock upon initial public offering, net of offering costs	90,191	—
Payments of finance lease obligations	(10)	—
Proceeds from stock options exercised	9	—
Net cash provided by financing activities	90,190	—
Net increase in cash and cash equivalents	71,904	(4,763)
Cash, cash equivalents and restricted cash at beginning of period	92,347	24,151
Cash, cash equivalents and restricted cash at end of period	$ 164,251	$ 19,388
Supplemental disclosure of non-cash investing and financing activities:		
Conversion of Series A & Series B Preferred Stock to common stock, net of Issuance costs	$ 161,939	$ —
Deferred offering costs paid in the prior year	$ 1,887	$ —
Offering costs included in accounts payable and accrued expenses	$ 318	$ —
Right-of-use assets obtained in exchange for operating lease liabilities	$ 62	$ —
Other assets in accounts payable and accrued expenses	$ 94	$ —
Purchases of property and equipment included in accounts payable and accrued expenses	$ 102	$ —

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

1. Nature of the Business and Basis of Presentation

Vigil Neuroscience, Inc., together with its consolidated subsidiary, Vigil Neuroscience Securities Corporation ("Vigil" or the "Company"), is a microglia-focused company dedicated to improving the lives of patients, caregivers and families affected by rare and common neurodegenerative diseases by pursuing the development of disease-modifying therapeutics to restore the vigilance of microglia, the sentinel immune cells of the brain. The Company's initial focus is on developing a pipeline of therapeutic candidates that it believes will activate and restore microglia function, with an initial focus in genetically defined subpopulations. The Company was incorporated in the State of Delaware in June 2020 and is located in Cambridge, Massachusetts.

The Company is subject to risks and uncertainties common to early-stage companies in the biopharmaceutical industry, including, but not limited to, completing preclinical studies and clinical trials, the ability to raise additional capital to fund operations, obtaining regulatory approval for therapeutic candidates, market acceptance of products, competition from substitute products, protection of proprietary intellectual property, compliance with government regulations, the impact of the COVID-19 coronavirus, dependence on key personnel, reliance on third-party organizations and the clinical and commercial success of its therapeutic candidates. Even if the Company's development efforts are successful, it is uncertain when, if ever, the Company will realize significant revenue from product sales.

Reverse Stock Split

On December 30, 2021, the Company effected a one-for-2.7732 reverse stock split of its issued and outstanding shares of common stock and a proportional adjustment to the existing conversion ratios of each series of the Company's preferred stock (see Note 7). Accordingly, all share and per share amounts for all periods presented in the accompanying condensed consolidated financial statements and notes thereto have been adjusted retroactively, where applicable, to reflect this stock split and adjustment of the preferred stock conversion ratios.

Liquidity

The Company has evaluated whether there are certain 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 that the condensed consolidated financial statements are issued. As of March 31, 2022, the Company had cash and cash equivalents of $163.3 million and an accumulated deficit of $87.2 million. In January 2022, the Company completed its initial public offering ("IPO") of its common stock which resulted in net proceeds of $88.0 million. Although the Company has incurred recurring losses and expects to continue to incur losses for the foreseeable future, the Company expects that its cash and cash equivalents will be sufficient to fund current operations for at least the next twelve months from the issuance of these condensed consolidated financial statements.

The Company expects to seek additional funding through equity financings, government or private-party grants, debt financings or other capital sources, including collaborations with other companies or other strategic transactions. The Company may not be able to obtain financing on acceptable terms, or at all, and the Company may not be able to enter into collaborations or other arrangements. The terms of any financing may adversely affect the holdings or rights of the Company's stockholders.

If the Company is unable to obtain sufficient capital, the Company will be forced to delay, reduce or eliminate some or all of its research and development programs, product portfolio expansion or future commercialization efforts, which could adversely affect its business prospects, or the Company may be unable to continue operations. Although management continues to pursue these plans, there is no assurance that the Company will be successful in obtaining sufficient funding on terms acceptable to the Company to fund continuing operations, if at all.

The condensed consolidated financial statements have been prepared on a basis that assumes the Company will continue as a going concern and which contemplates the realization of assets and satisfaction of liabilities and commitments in the ordinary course of business.

Impact of the COVID-19 Coronavirus

In March 2020, the World Health Organization declared the outbreak of COVID-19 a global pandemic. The Company is subject to a number of risks associated with the COVID-19 global pandemic, including potential delays associated with the Company's ongoing preclinical studies and clinical trials. COVID-19 may have an adverse impact on the Company's operations, supply chains and

distribution systems or those of our third-party vendors and collaborators, and increase expenses, including as a result of impacts associated with preventive and precautionary measures that are being taken, such as restrictions on travel and border crossings, quarantine polices and social distancing. The Company and its third-party vendors and collaborators may experience disruptions in supply of items that are essential for its research and development activities. In addition, the spread of COVID-19 has disrupted global healthcare and healthcare regulatory systems, which could divert healthcare resources away from, or materially delay, U.S. Food and Drug Administration approval and approval by other health authorities worldwide with respect to its therapeutic candidates. Furthermore, the Company's clinical trials may be negatively affected by the COVID-19 outbreak. Site initiation, patient enrollment and patient follow-up visits may be delayed, for example, due to prioritization of hospital resources toward the COVID-19 outbreak, travel restrictions, the inability to access sites for initiation and monitoring, and difficulties recruiting or retaining patients in the Company's planned clinical trials. The emergence of additional variants, as well as reduced efficacy of vaccines over time and the possibility that a large number of people decline to get vaccinated or receive booster shots, creates inherent uncertainty as to the future of our business, our industry and the economy in general in light of the pandemic. Management cannot at this time predict the specific extent, duration, or full impact that the COVID-19 outbreak will have on the Company's financial condition, operations, and business plans for the year 2022 and beyond. If the Company does not successfully commercialize any of its therapeutic candidates, it will be unable to generate product revenue or achieve profitability.

Basis of Presentation

The accompanying condensed consolidated financial statements of Vigil are unaudited and have been prepared in accordance with accounting principles generally accepted in the United States of America ("GAAP") applicable to interim periods and, in the opinion of management, include all normal and recurring adjustments that are necessary to state fairly the results of operations for the reported periods. Any reference in these notes to applicable guidance is meant to refer to the authoritative GAAP as found in the Accounting Standards Codification ("ASC") and Accounting Standards Updates ("ASU") of the Financial Accounting Standards Board ("FASB"). Our condensed consolidated financial statements have also been prepared on a basis substantially consistent with, and should be read in conjunction with, our audited consolidated financial statements for the year ended December 31, 2021, which were included in our Annual Report on Form 10-K that was filed with the Securities and Exchange Commission on March 25, 2022. The year-end condensed consolidated balance sheet data was derived from our audited financial statements but does not include all disclosures required by GAAP. The results of our operations for any interim period are not necessarily indicative of the results of our operations for any other interim period or for a full fiscal year.

The accompanying condensed consolidated financial statements reflect the operations of the Company and its wholly-owned subsidiary. Intercompany balances and transactions have been eliminated in consolidation.

2. Summary of Significant Accounting Policies

The Company's significant accounting policies are disclosed in the audited consolidated financial statements for the year ended December 31, 2021, and notes thereto, which are included in the Company's Annual Report on Form 10-K that was filed with the Securities and Exchange Commission on March 25, 2022, or the 2021 Form 10-K. Since the date of those financial statements, there have been no material changes to Vigil's significant accounting policies except as noted below.

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 condensed consolidated financial statements, and the reported amounts of expenses during the reporting periods. Significant estimates and assumptions reflected in these condensed consolidated financial statements include, but are not limited to, research and development expenses and related prepaid or accrued costs and the valuation of common stock, Related Party Antidilution Obligation (as defined in Note 11) and Series A Preferred Stock Tranche Obligation. The Company bases its estimates on historical experience, known trends and other market-specific or 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.

Cash, Cash Equivalents and Restricted Cash

The Company considers all highly liquid investments with a remaining maturity when purchased of three months or less to be cash equivalents. Cash equivalents are reported at fair value. At March 31, 2022 and December 31, 2021, the Company's cash equivalents were in money market funds. As of each balance sheet date and periodically throughout the year, the Company has maintained balances in various operating accounts in excess of federally insured limits.

In connection with the Company's lease agreement entered into in September 2021 (see Note 13), the Company is required to maintain a certificate of deposit ("CD") of $0.9 million for the benefit of the landlord.

The following table provides a reconciliation of cash, cash equivalents and restricted cash in the unaudited condensed consolidated balance sheets that sum to the total of the amounts reported in the unaudited condensed consolidated statement of cash flows (in thousands):

	March 31, 2022	March 31, 2021
Cash and cash equivalents	$ 163,324	$ 19,388
Restricted cash, non-current	927	—
Total cash, cash equivalents and restricted cash	$ 164,251	$ 19,388

Property and Equipment

Property and equipment are stated at cost less accumulated depreciation. Depreciation is recognized using the straight-line method over the estimated useful life of each asset.

Costs for capital assets not yet placed into service are capitalized as construction-in-progress and depreciated once placed into service. Upon retirement or sale, the cost of assets disposed of and the related accumulated depreciation and amortization are removed from the accounts and any resulting gain or loss is included in loss from operations. Expenditures for repairs and maintenance that do no improve or extend the life of the respective assets are charged to expense in the period incurred.

The following is the summary of property and equipment and related accumulated depreciation as of March 31, 2022 (in thousands):

	Useful Life	March 31, 2022	December 31, 2021
Computer software and equipment	3 years	$ 16	$ 16
Furniture and fixtures	5 years	36	9
Lab equipment	5 years	192	192
Leasehold improvements	Lesser of (i) useful life or (ii) lease term	—	—
Construction in progress		317	99
Total property and equipment		561	316
Less: accumulated depreciation		(28)	(15)
Total property and equipment, net		$ 533	$ 301

Depreciation expense was $13 thousand during the three months ended March 31, 2022. The Company did not have any property and equipment during the three months ended March 31, 2021.

Recently Issued Accounting Pronouncements

From time to time, new accounting pronouncements are issued by the FASB or other standard setting bodies and adopted by the Company as of the specified effective date. The Company qualifies as an ''emerging growth company'' as defined in the Jumpstart Our Business Startups Act of 2012 and has elected not to ''opt out'' of the extended transition related to complying with new or revised accounting standards, which means that when a standard is issued or revised and it has different application dates for public and non-public companies, the Company can adopt the new or revised standard at the time non-public companies adopt the new or revised standard and can do so until such time that the Company either (i) irrevocably elects to ''opt out'' of such extended transition period or (ii) no longer qualifies as an emerging growth company. The Company may choose to early adopt any new or revised accounting standards whenever such early adoption is permitted for non-public companies.

In August 2020, the FASB issued ASU No. 2020-06, Debt*, Debt with Conversion and Other Options (Subtopic 470-20) and Derivatives and Hedging—Contracts in Entity's Own Equity (Subtopic 815-40): Accounting for Convertible Instruments and Contracts in an Entity's Own Equity*, which, among other things, provides guidance on how to account for contracts on an entity's own equity. This ASU simplifies the accounting for certain financial instruments with characteristics of liabilities and equity. Specifically, the ASU

eliminated the need for the Company to assess whether a contract on the entity's own equity (1) permits settlement in unregistered shares, (2) whether counterparty rights rank higher than shareholder's rights, and (3) whether collateral is required. In addition, the ASU requires incremental disclosure related to contracts on the entity's own equity and clarifies the treatment of certain financial instruments accounted for under this ASU on earnings per share. The ASU also simplifies the accounting for convertible instruments by removing the beneficial conversion feature and cash conversion feature separation models. This ASU may be applied on a full retrospective or modified retrospective basis. This ASU is effective for smaller reporting companies for fiscal years beginning after December 15, 2023 and all other public entities, this ASU is effective for fiscal years beginning after December 15, 2021. Early adoption permitted. The Company expects to adopt this ASU in fiscal year 2023. The Company does not currently expect the adoption to materially impact its financial position and results of operations.

3. Fair Value Measurements

The following table presents the Company's fair value hierarchy for its assets and liabilities items that are measured at fair value on a recurring basis as of March 31, 2022 and December 31, 2021, by level within the fair value hierarchy (in thousands):

	Fair Value Measurement at March 31, 2022 Using:			
	Level 1	Level 2	Level 3	Total
Assets:				
Cash equivalents (money market)	$ 67,944	$ —	$ —	$ 67,944
Restricted cash (non-current)	927	$ —	$ —	$ 927
	$ 68,871	$ —	$ —	$ 68,871

	Fair Value Measurement at December 31, 2021 Using:			
	Level 1	Level 2	Level 3	Total
Assets:				
Cash equivalents (money market)	$ 67,942	$ —	$ —	$ 67,942
Restricted cash (non-current)	927	$ —	$ —	$ 927
	$ 68,869	$ —	$ —	$ 68,869

The Company evaluates transfers between levels at the end of each reporting period. There were no transfers between Level 1, Level 2 or Level 3 for the three months ended March 31, 2022 and for the year ended December 31, 2021, respectively.

Related Party Antidilution Obligation

The Company was obligated to issue Series A convertible preferred stock with an antidilution provision as part of a license agreement with Amgen (see Note 11). The Related Party Antidilution Obligation is included within the Level 3 fair value hierarchy. The Related Party Antidilution Obligation was valued using a probability-weighted expected return method. The valuation model requires a variety of inputs, including the probability of occurrence of events that would trigger the issuance of additional shares, the expected timing of such events, the expected value of the contingently issuable equity upon occurrence of a triggering event and a discount rate. The Related Party Antidilution Obligation was remeasured on May 1, 2021, and December 31, 2020, with changes in fair value recognized within changes in fair value of the Related Party Antidilution Obligation in the consolidated statements of operations and comprehensive loss.

The significant unobservable inputs used in the valuation model to measure the Related Party Antidilution Obligation that are categorized within Level 3 of the fair value hierarchy, as of March 31, 2021 are as follows:

Expected term (years)	0.59
Risk-free rate	0.05 %
Probability of finance event occurring	90 %

At December 31, 2020, the Company had a $4.2 million liability related to the Related Party Antidilution Obligation. During the three months ended March 31, 2021, the Company recorded a $0.3 million increase in fair value of the Related Party Antidilution Obligation. On May 28, 2021, the Company completed the second closing pursuant to the Series A Convertible Preferred Stock Purchase Agreement which resulted in the Company raising net cash proceeds from financing activities in excess of the $45.0 million Related Party Antidilution Obligation cap. The second closing triggered the settlement of the remaining Related Party Antidilution Obligation, resulting in the issuance of 1,963,093 shares of Series A convertible preferred stock to Amgen with a fair value of $5.1 million.

Series A Preferred Stock Tranche Obligation

The Series A Preferred Stock Tranche Obligation was valued using a probability-weighted present value model. The valuation model considered the probability of closing the tranche, the estimated future value of the Series A convertible preferred stock to be issued at each closing and the investment required at each closing. Future values were converted to present value using a discount rate appropriate for probability-adjusted cash flows.

The significant unobservable inputs used in the valuation model to measure the Series A Preferred Stock Tranche Obligation that is categorized within Level 3 of the fair value hierarchy as of March 31, 2021 are as follows:

	March 31, 2021
Probability of meeting Series A milestones	90%
Time until Series A milestones (years)	0.59
Risk-free rate	0.05%
Expected value adjustment to Series A if second tranche milestones are not met	10%

The Related Party Antidilution Obligation and Series A Preferred Stock Tranche Obligation were settled in May 2021 (see Note 7).

The following table sets forth a rollforward of changes in the fair value of financial liabilities classified as Level 3 in the fair valued hierarchy (in thousands):

	Related Party Antidilution Obligation	Series A Preferred Stock Tranche Obligation	Total
Ending balance at December 31, 2020	$ 4,247	$ 303	$ 4,550
Change in fair value	252	21	273
Issuance of Series A preferred shares in partial settlement of related party antidilution obligation	—	—	—
Ending balance at March 31, 2021	$ 4,499	$ 324	$ 4,823

4. Prepaid Expenses and Other Current Assets

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

	March 31, 2022	December 31, 2021
Research and development	$ 4,924	$ 5,597
Business insurance	1,709	107
Other	468	359
Total	$ 7,101	$ 6,063

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
Research and development	$ 1,290	$ 1,422
Payroll and employee related	821	2,017
Professional fees	782	933
Deferred IPO	—	543
Other	259	116
Total	$ 3,152	$ 5,031

6. Stock-Based Compensation

2020 Equity Incentive Plan

The Company's 2020 Equity Incentive Plan (the "2020 Plan") provides for the Company to grant incentive stock options or non-qualified stock options, stock appreciation rights, restricted stock awards, restricted stock units, and other equity awards to employees, directors, and consultants of the Company. The 2020 Plan is administered by the Board or, at the discretion of the Board, by a committee of the Board. The Board may also delegate to one or more officers of the Company the power to grant awards to employees and certain officers of the Company. The exercise prices, vesting and other restrictions are determined at the discretion of the Board, or its committee or any such officer if so delegated.

Options under the 2020 Plan may be designated as incentive stock options or non-statutory stock options. The options granted under the 2020 Plan are either service-based options or performance-based options. As of March 31, 2022, 3,084,068 options were issued and outstanding under the 2020 Plan.

2021 Stock Option and Incentive Plan

On November 16, 2021, the Company's board of directors adopted, and on December 3, 2021 its stockholders approved, the 2021 Stock Option and Incentive Plan (the "2021 Plan"), which became effective on January 5, 2022, immediately preceding the date on which the registration statement for the Company's initial public offering was declared effective by the SEC. The 2021 Plan provides for the grant of incentive stock options, non-qualified stock options, stock appreciation rights, restricted stock awards, restricted stock units and other stock-based awards. The number of shares reserved for issuance under the 2021 Plan is initially equal to 3,145,281. In addition, the number of shares of the Company's common stock reserved for issuance under the 2021 Plan will automatically increase on the first day of each calendar year, beginning on January 1, 2023 and each January 1 thereafter, by an amount equal to the lesser of (i) five percent (5%) of the cumulative number of shares of common stock issued and outstanding on the immediately preceding December 31, or (ii) such lesser number of shares of common stock as determined by the compensation committee of the board of directors.

The shares of common stock underlying any awards under the 2021 Plan or the 2020 Plan that are forfeited, cancelled, held back upon exercise or settlement of an award to satisfy the exercise price or tax withholding, reacquired by us prior to vesting, satisfied without the issuance of stock, expire or are otherwise terminated will be added back to the shares of common stock available for issuance under the 2021 Plan.

In March of 2022, as part of the Company's annual grant of equity, the Company issued 802,145 stock options to employees. As of March 31, 2022, 839,345 options were issued and outstanding under the 2021 Plan.

2021 Employee Stock Purchase Plan

On November 16, 2021, the Company's board of directors adopted, and on December 3, 2021 its stockholders approved, the 2021 Employee Stock Purchase Plan (the ''2021 ESPP''), which became effective on January 5, 2022, immediately preceding the date on which the registration statement for the Company's initial public offering was declared effective by the SEC. A total of 286,127 shares of common stock were initially reserved for issuance under this plan. The number of shares of common stock that may be issued under the 2021 ESPP shall cumulatively increase beginning on January 1, 2023 and each January 1 thereafter through January 1, 2032, by the least of (A) 286,127 shares of common stock, (B) one percent (1%) of the cumulative number of shares of common stock issued and outstanding on the immediately preceding December 31 or (C) such lesser number of shares of common stock as determined by the administrator of the 2021 ESPP.

No stock-based compensation expense was recognized during the three months ended March 31, 2022 related to the 2021 ESPP.

Stock-Based Compensation Expense

The Company recorded stock-based compensation of $1.0 million, and $0.3 million during the three months ended March 31, 2022 and March 31, 2021, respectively. Stock-based compensation expense was classified as follows in the condensed consolidated statements of operations and comprehensive loss (in thousands):

	Three Months Ended March 31,	
	2022	2021
Research and development	$ 580	$ 121
General and administrative	441	212
Total stock-based compensation	$ 1,021	$ 333

At March 31, 2022, there was approximately $17.0 million unrecognized stock-based compensation expense related to unvested options, which is expected to be recognized over a weighted-average period of 3.28 years. At March 31, 2022, there was approximately $0.3 million unrecognized stock-based compensation expense related to unvested restricted stock, which is expected to be recognized over a weighted-average period of 2.09 years.

7. Preferred Stock

Convertible Preferred Stock

The Series A preferred stock and Series B preferred stock, described in more detail below, converted into 10,285,077 shares and 9,251,793 shares of common stock in January 2022 as part of our IPO.

Series A Convertible Preferred Stock and Series A Preferred Stock Tranche Obligation

On September 18, 2020, the Company entered into the Series A Convertible Preferred Stock Purchase Agreement with its initial investors committing to purchase an aggregate of $50.0 million in shares of Series A convertible preferred stock. At the initial closing, 9,815,467 shares of Series A convertible preferred stock were issued by the Company at a purchase price of $2.547 per share, for gross cash proceeds of $25.0 million. The gross proceeds were offset by $0.2 million of issuance costs and $0.2 million related to the Series A Preferred Stock Tranche Obligation, discussed below.

Included in the terms of the September 2020 Series A Convertible Preferred Stock Purchase Agreement were certain rights ("Series A Preferred Stock Tranche Obligation") granted to the investors who purchased the Series A convertible preferred stock in September 2020. The Series A Preferred Stock Tranche Obligation contingently obligated the investors to purchase, and the Company to sell, up to an aggregate of 7,852,373 shares of Series A convertible preferred stock at $2.547 per share upon the satisfaction of specified research and development milestones by the Company.

The Company concluded that the Series A Preferred Stock Tranche Obligation met the definition of a freestanding financial instrument, as the Series A Preferred Stock Tranche Obligation was legally detachable and separately exercisable from the Series A convertible preferred stock. Therefore, the Company allocated the proceeds from the September 2020 issuance between the Series A Preferred Stock Tranche Obligation and the Series A convertible preferred stock, including those issued in exchange for the SAFE. As the Series A convertible preferred stock is redeemable upon a deemed liquidation event at the election of the holder-controlled Board, and therefore outside of the control of the Company, the Series A Preferred Stock Tranche Obligation was classified as a liability and recorded at its fair value of $0.3 million at both inception and as of December 31, 2020. The Series A Preferred Stock Tranche Obligation was remeasured at fair value at each reporting period, with changes in fair value recorded in change in fair value of the Series A Preferred Stock Tranche Obligation in the condensed consolidated statements of operations and comprehensive loss (see Note 3).

On May 28, 2021, the Company issued 7,852,373 shares of its Series A convertible preferred stock at $2.547 per share, for which the Company received gross proceeds of $20.0 million, offset by issuance costs of $0.1 million. As a result of this issuance, the Series A Preferred Stock Tranche Obligation with a then fair value of approximately $0.3 million was settled and reclassified to Series A convertible preferred stock in the consolidated balance sheet.

Series B Convertible Preferred Stock Financing

On August 13, 2021, the Company issued 25,657,096 shares of its Series B convertible preferred stock at $3.5078 per share, for which the Company received gross proceeds of $90.0 million. Issuance costs were $0.4 million.

Upon issuance of each class of the Convertible Preferred Stock, the Company assessed the embedded conversion and liquidation features of the securities and determined that such features did not require the Company to separately account for these features. The Company also concluded that no beneficial conversion feature existed upon the issuance date of each class of the Convertible Preferred Stock or as of March 31, 2022 and December 31, 2021.

The holders of Convertible Preferred Stock had the followings rights and privileges:

Conversion

The holders of the Convertible Preferred Stock may convert, at any time, each share of the Convertible Preferred Stock into shares of common stock. In addition, upon either (a) the closing of the sale of shares of common stock to the public at a price of at least three times the Series A Original Issue Price (subject to adjustment) in an initial public offering with net proceeds to the Company of at least

$50.0 million or (b) the written consent of the holders of the outstanding shares of Convertible Preferred Stock, the Convertible Preferred Stock will automatically convert into common stock.

The conversion ratio of each series of the Convertible Preferred Stock is determined by dividing the Original Issuance Price of each series by the Conversion Price of each series. The Original Issuance Price per share is $2.547 for Series A convertible preferred stock and $3.5078 for Series B convertible preferred stock. The Conversion Price per share at issuance was $7.063 for Series A convertible preferred stock and $9.7278 for Series B convertible preferred stock, each subject to appropriate adjustment in the event of any stock dividend, stock split, combination or other similar recapitalization and other adjustments, including adjustment if common stock is issued for less than the Original Issue Price of each series of Convertible Preferred Stock. Accordingly, as of December 31, 2021, each share of each series of Convertible Preferred Stock was convertible into shares of common stock on a one-for-one basis.

8. Common Stock

Each share of common stock entitles the holder to one vote for each share of common stock held. Common stockholders are entitled to receive dividends, as may be declared by the Company's Board. During each of the three months ended March 31, 2022 and 2021, no dividends have been declared or paid.

Initial Public Offering

In January 2022, the Company completed its initial public offering ("IPO") of its common stock. In connection with its IPO, the Company issued and sold 7,000,000 shares of its common stock, at a price to the public of $14.00 per share. As a result of the IPO, the Company received $88.0 million in net proceeds, after deducting underwriting discounts and commissions and offering costs of $10.0 million.

Upon the closing of the IPO, 54,179,688 shares of outstanding convertible preferred stock were automatically converted into 19,536,870 shares of common stock, after the effect of the one-for-2.7732 reverse stock split, with the related carrying value of $161.9 million reclassified to common stock and additional paid-in capital. In connection with the IPO, the Company amended and restated its certificate of incorporation to change the authorized capital stock to 150,000,000 shares designated as common stock and 10,000,000 shares designated as preferred stock, all with a par value of $0.0001 per share.

The Company has reserved the following number of shares of common stock for the exercise of outstanding stock options and future issuance of stock-based awards.

	March 31, 2022	December 31, 2021
Common stock options	3,923,413	3,089,065
Shares available for issuance under the 2020 Plan	—	276,261
Shares available for issuance under the 2021 Plan	2,305,936	3,145,281
Shares available for issuance under the 2021 ESPP	286,127	286,127
Series A convertible preferred stock outstanding	—	10,285,087
Series B convertible preferred stock outstanding	—	9,251,793
Total common stock reserved for future issuance	6,515,476	26,333,614

9. Net Loss per Share

Basic and diluted net loss per common 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 attributable to common stockholders	$ (15,334)	$ (8,191)
Denominator:		
Weighted-average common shares outstanding, basic and diluted	26,660,246	1,499,843
Net loss per share attributable to common stockholders, basic and diluted	$ (0.58)	$ (5.46)

The Company's potentially dilutive securities have been excluded from the computation of diluted net loss per common share as the effect would be to reduce the net loss per common share. Therefore, the weighted-average number of common shares outstanding used to calculate both basic and diluted net loss per common share 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 common share for the periods indicated because including them would have had an anti-dilutive effect:

	Three Months Ended March 31,	
	2022	2021
Series A convertible preferred stock	—	6,745,679
Related party antidilution obligation	—	707,880
Options to purchase common stock – service based	3,712,784	1,022,000
Options to purchase common stock – performance based	210,629	229,019
Unvested restricted common stock	126,959	242,650
Total	4,050,372	8,947,228

10. Leases

In February 2021, the Company entered into an equipment lease with lease term of 24 months commencing in April 2021. The lease includes an option to purchase the equipment at fair market value at the end of the lease term.

In July 2021, the Company entered into a lease for laboratory space in Cambridge, Massachusetts, with an initial term of one year commencing in April 2021, with a month-to-month option to renew at the end of the initial lease term (see Note 12). At inception, the Company determined that it was reasonably certain that it would elect options to renew the lease through September 2022 and have included these renewal options into the initial determination of the lease term. In March 2021, the Company revised its estimated lease term with an estimated termination date of December 31, 2022.

In September 2021, the Company entered into a lease for laboratory and office space in Watertown, Massachusetts with an initial term of ten years, and a five-year renewal option at the end of the initial lease term. The monthly lease payment is approximately $0.2 million with annual escalation of approximately 3%. The lease includes a $3.7 million construction allowance. The lease is expected to commence in the second quarter of 2022 when the leased space is expected to be made available for the Company's use.

In October 2021, the Company entered into a lease for its corporate headquarters in Cambridge, Massachusetts with an initial term of 14 months. The monthly lease payment and security deposit are each approximately $49 thousand.

At March 31, 2022, the weighted-average remaining lease terms related to the finance and operating leases are 1.2 years and 0.7 years, respectively.

As the Company's operating leases did not provide an implicit rate, the Company used its incremental borrowing rate based on the information available in determining the present value of lease payments. The Company's incremental borrowing rate was based on the term of the lease, the economic environment of the lease and reflect the rate the Company would have had to pay to borrow on a secured basis. The weighted-average discount rates used at the time that the leases were evaluated were 5.20% for the finance leases and 6.34% for the operating leases.

11. Related Party License Agreement

Amgen, Inc.

In July 2020, the Company entered into an Exclusive License Agreement and Letter Agreement (collectively, the "Amgen Agreement") with Amgen, pursuant to which the Company has been granted an exclusive, royalty-bearing sublicensable license to certain intellectual property rights owned or controlled by Amgen, to commercially develop, manufacture, use, distribute and sell therapeutic products containing compounds that bind to Triggering Receptor Expressed on Myeloid Cells 2 ("TREM2").

As initial consideration for the license, the Company made a one-time, non-creditable, non-refundable upfront payment of $0.5 million. As additional consideration for the license, the Company is required to pay Amgen up to $80.0 million in the aggregate upon the achievement of specified regulatory milestones for the first monoclonal antibody agonist of TREM2 agonist ("mAb") product and the first small molecule TREM2 agonist product and aggregate milestone payments of up to $350.0 million upon the achievement of specific commercial milestones across all mAb products and small molecule products. No regulatory or commercial milestones have been achieved to date under the Amgen Agreement. The Company is also required to pay tiered royalties of low to mid single-digit percentages on annual net sales of the products covered by the license. In the event that the exploitation of a product is not covered by

a valid claim within the licensed patent rights, then the royalty rate with respect to the net sales shall be subject to a customary reduction by a certain percentage. The royalty term will terminate on a country-by-country basis on the later of (i) the expiration date of the last valid claim within the licensed patent rights, and (ii) the tenth (10th) anniversary of the first commercial sale of such product in such country. Further, the Company was required to reimburse Amgen for amounts it paid to its contract manufacturers on the Company's behalf. During the three months ended March 31, 2021, the Company incurred $0.7 million in contract manufacturing costs. No additional costs were incurred during the three months ended March 31, 2022. These costs are recognized as research and development expense over the period that the goods are provided, as applicable.

In addition to the cash consideration described above, the Company agreed to issue Series A convertible preferred stock to Amgen in an amount equal to 25% of the Company's capital stock on a fully diluted basis (the "Related Party Antidilution Obligation") until the Company has raised an aggregate of $45.0 million net cash proceeds from equity financings. The Company determined that the Related Party Antidilution Obligation was required to be recorded as a liability because it was a freestanding instrument that would require the Company to transfer assets to settle the obligation and it is indexed to an obligation to contingently redeem the Company's equity shares. Accordingly, the Company recognized the liability at fair value on the acquisition date and recognizes changes in the fair value of the anti-dilution rights at each subsequent reporting period in the change in fair value of the Related Party Antidilution Obligation in the consolidated statements of operations and comprehensive loss (see Note 3).

On September 18, 2020, the Company completed the first closing pursuant to the Series A Convertible Preferred Stock Purchase Agreement which triggered the Related Party Antidilution Obligation resulting in the issuance of 6,928,566 Series A convertible preferred stock to Amgen with a fair value of $17.5 million.

On May 28, 2021, the Company completed the second closing pursuant to the Series A Convertible Preferred Stock Purchase Agreement which resulted in the Company raising net cash proceeds from financing activities in excess of the $45.0 million Related Party Antidilution Obligation cap. Amgen received an additional 1,963,093 Series A convertible preferred stock with a fair value of $5.1 million.

As of March 31, 2022, Amgen owned approximately 11.34% of the Company's outstanding shares of capital stock.

Amounts paid with respect to goods provided by Amgen on the Company's behalf under the Amgen Agreement are recognized as research and development expense as such amounts are incurred. For the three months ended March 31, 2022 and 2021, the Company recognized $0 and $0.7 million, respectively, of expense in connection with goods provided by Amgen.

12. Related Party Transactions

Atlas

The Company entered into various lease agreements with Atlas Venture Fund XII, L.P., a principal stockholder of the Company, and incurred lease costs of less than $67 thousand for the three months ended March 31, 2022, and $16 thousand for the three months ended March 31, 2021. The lease payments are included in general and administrative expenses for office space and research and development expenses for lab space in the condensed consolidated statements of operations and comprehensive loss. The Company recorded an operating lease right-of-use asset and a lease liability for $0.2 million as of March 31, 2022. The right-of-use asset is included in operating lease right-of-use assets and the lease liability is included as an operating lease liability in the Company's condensed consolidated balance sheet as of March 31, 2022. As of March 31, 2022, the Company recognized $69 thousand in accrued expenses associated with the leases.

In September 2021, the Company terminated its short-term related party leases with Atlas Venture Fund XII, L.P. The effective termination date of the leases was in the fourth quarter of 2021.

Amgen, Inc.

Under the Amgen Agreement, the Company was obligated to issue shares of Series A convertible preferred stock to Amgen, a principal stockholder of the Company. Additionally, in consideration for the rights assigned and license conveyed under the Amgen Agreement, Amgen received upfront consideration in the form of Series A convertible preferred stock, and is entitled to receive milestone and royalty payments upon specified conditions and received payments from the Company for providing ongoing services under the agreement (see Note 11).

Expenses to reimburse Amgen's contract manufacturers incurred by the Company were $0 and $0.7 million during the three months ended March 31, 2022 and March 31, 2021, respectively. These costs are included in research and development expenses in the condensed consolidated statements of operations and comprehensive loss.

The Company did not have any amounts in accrued expenses and other current liabilities in the Company's condensed consolidated balance sheet as of March 31, 2022. As of December 31, 2021, $0.2 million was due to Amgen by the Company and was included in accruals in the consolidated balance sheet.

The Company did not have any amounts in prepaids as of March 31, 2022 and December 31, 2021, respectively.

13. Commitments and Contingencies

License Agreement

The Company entered into a license agreement with Amgen (see Note 11).

Letter of Credit

In September 2021, in connection with the Watertown, Massachusetts lease, the Company entered into a $0.9 million standby letter of credit which initially expires on September 10, 2022. The standby letter of credit will automatically renew for subsequent annual periods through December 2032. Remittance of funds from the letter of credit was not probable and the full amount was available as of September 2021. The Company did not recognize a liability in the condensed consolidated balance sheet.

Purchase Commitment

In November 2021, the Company entered into a statement of work ("SOW") with FUJIFILM Diosynth Biotechnologies Texas, LLC for $3.8 million under our existing master services agreement for the manufacturing of VGL101. If the Company terminates the SOW before completion, it may be required to pay fees ranging from 0% to 100%. The amount due upon an early termination depends on the length of time prior to the commencement of specific stages of the SOW. As of March 31, 2022, no significant work had begun. The SOW is expected to be incurred over approximately 2 years.

Contingencies

From time to time, the Company may have certain contingent liabilities that arise in the ordinary course of business. The Company accrues a liability for such matters when it is probable that future expenses will be incurred and can be reasonably estimated. As of March 31, 2022, the Company does not have any significant legal disputes that require a loss liability to be recorded.

401(k) Plan

The Company has a defined-contribution plan under Section 401(k) of the Internal Revenue Code of 1986 (the "401(k) Plan"). The 401(k) Plan covers all employees who meet defined minimum age and service requirements and allows participants to defer a portion of their annual compensation on a pre-tax basis. As currently established, the Company is not required to make, and to date has not made, any contributions to the 401(k) Plan.

Indemnification Agreements

In the ordinary course of business, the Company may provide indemnification of varying scope and terms to vendors, lessors, contract research organizations, 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 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 currently 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.

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

You should read the following discussion and analysis of our financial condition and results of operations together with the "Selected Consolidated Financial Data" section of this Quarterly Report on Form 10-Q (this "Quarterly Report") and our consolidated financial statements and related notes included elsewhere in this Quarterly Report. Some of the information contained in this discussion and analysis or set forth elsewhere in this Quarterly Report, including information with respect to our plans and strategy for our business and related financing includes forward-looking statements that involve risks and uncertainties. Many factors, including those factors set forth in the "Risk Factors" section of this Quarterly Report, may materially and adversely affect our actual results, which may differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis.

Overview

We are a microglia-focused company dedicated to improving the lives of patients, caregivers, and families affected by rare and common neurodegenerative diseases by pursuing the development of disease-modifying therapeutics to restore the vigilance of microglia. Microglia are the sentinel immune cells of the brain and play a critical role in maintaining central nervous system (CNS) health and responding to damage caused by disease. Leveraging recent research implicating microglial dysfunction in neurodegenerative diseases, we utilize a precision medicine approach to develop a pipeline of therapeutic candidates, initially addressing genetically defined patient subpopulations, that we believe will activate and restore microglial function. Our first therapeutic candidates are designed to activate Triggering Receptor Expressed on Myeloid Cells 2 (TREM2), a key microglial receptor protein that mediates responses to environmental signals in order to maintain brain health and whose dysfunction is linked to neurodegeneration.

We believe that each of the therapeutic candidates in our pipeline has the potential to be developed for multiple neurodegenerative diseases. Our precision medicine approach begins with rare, genetically defined diseases for which microglial dysfunction is believed to be a key driver of disease pathology and then utilizes findings from these efforts to inform expansion into larger and more common neurodegenerative diseases. Our strategy has the potential to mitigate downstream translational risk as we seek to advance our programs through early development and into the clinic. We believe this iterative, sequential approach is a key differentiator, potentially allowing us to generate clinical proof-of-concept (PoC) efficiently and leverage our initial development programs as well as research by others, in pursuing additional neurodegenerative disease opportunities.

Our lead candidate, VGL101, is a fully human monoclonal antibody (mAb) that is designed to activate TREM2. We are initially developing VGL101 for the treatment of adult-onset leukoencephalopathy with axonal spheroids and pigmented glia (ALSP), a rare, genetically defined, and fatal neurodegenerative disease caused by microglial dysfunction.

ALSP affects an estimated 10,000 people in the U.S., with about 1,000 to 2,000 new cases annually. ALSP has been diagnosed in countries around the world, with major clusters in North America (U.S. and Canada), Central and Northern Europe, and Asia. ALSP is caused by loss-of-function mutations in the Colony Stimulating Factor 1 Receptor (CSF1R), a receptor that shares a common downstream signaling pathway with TREM2. The therapeutic rationale for VGL101 is to compensate for CSF1R loss-of-function by activating TREM2. We have generated robust preclinical evidence that suggests TREM2 agonism can rescue CSF1R loss-of-function. We have completed dosing of the 20 mg/kg single ascending dose (SAD) cohort without any safety signals and are currently dosing the 20 mg/kg multiple ascending dose (MAD) cohort in our Phase 1 trial of VGL101 in healthy volunteers for ALSP. We continue to engage with the FDA regarding the partial clinical hold at doses above 20 mg/kg. Accordingly, we submitted data to the FDA from a 6-month GLP toxicology study in nonhuman primates in which we observed no adverse findings and Phase 1 SAD clinical data. We believe that 20 mg/kg is a clinically-relevant dose in ALSP.

We believe engagement with patients and the scientific and provider communities is central to our approach in rare neurodegenerative diseases. In September 2021, we began a natural history study of ALSP patients to better characterize the patient journey, inform our clinical trial design, and facilitate recruitment into our clinical trials. We also actively support a patient advocacy organization and have established the world's first patient-facing ALSP informational website to build disease awareness. In addition, we launched a global ALSP patient registry to further understand patient and caregiver journey, disease burden, and health economic outcomes.

In addition to VGL101 development in ALSP, we are planning to initiate a Phase 1b biomarker-based clinical trial with VGL101 for Alzheimer's disease (AD) in genetically defined populations of AD patients with or without the relevant TREM2 variants. We also intend to expand VGL101 development for the treatment of additional rare leukoencephalopathies and leukodystrophies in which microglia play an essential role, including cerebral adrenoleukodystrophy (cALD).

We are also developing a novel small molecule TREM2 agonist suitable for oral delivery to treat common neurodegenerative diseases associated with microglial dysfunction, with an initial focus on AD in genetically defined subpopulations. In the first quarter of 2022, we initiated IND-enabling studies for this program.

We believe our microglia focus, precision medicine approach, and pipeline, which spans multiple modalities, strongly position us to become a differentiated leader in the neurodegenerative therapeutic space.

Since our inception, we have devoted substantially all of our efforts to organizing and staffing our company, research and development activities, business planning, raising capital, building our intellectual property portfolio and providing general and administrative support for these operations. To date, we have funded our operations primarily through proceeds from our initial public offering of our common stock, the sale of shares of our convertible preferred stock and a Simple Agreement for Future Equity, or SAFE. As of March 31, 2022, we had $163.3 million of cash and cash equivalents. As of March 31, 2022, we raised aggregate gross proceeds of $238.0 million from the sale of equity securities as follows:

- During the period from June 22, 2020 (inception) to December 31, 2021, we raised $5.0 million gross proceeds from the SAFE which was subsequently converted to 1,963,093 shares of Series A convertible preferred stock, $45.0 million gross proceeds from the issuance of 17,687,840 shares of Series A convertible preferred stock at a purchase price of $2.547 per share, and $90.0 million gross proceeds from the issuance of 25,657,096 shares of Series B convertible preferred stock at $3.5078 per share. Costs associated with these issuances were approximately $0.6 million.
- During the three months ended March 31, 2022, we completed the initial public offering of our common stock, in which we issued an aggregate of 7,000,000 shares of common stock at a price of $14.00 per share, for gross cash proceeds of $98.0 million, before underwriting discounts and commissions. We received approximately $88.0 million in net proceeds, after deducting underwriting discounts, commissions and offering expenses. Based on our current operating plan, we believe that our existing cash and cash equivalents will be sufficient to fund our planned operating expenses and capital expenditure requirements into 2024.

We have incurred significant operating losses since the commencement of our operations. Our ability to generate product revenue sufficient to achieve profitability will depend heavily on the successful development and eventual commercialization of one or more of our current therapeutic candidates or any future therapeutic candidates. Our accumulated deficit was $71.8 million at December 31, 2021 and $87.2 million at March 31, 2022, respectively. We expect to continue to incur significant losses for the foreseeable future as we advance our current and future therapeutic candidates through preclinical and clinical development, continue to build our operations and transition to operating as a public company.

Our net losses may fluctuate significantly from period to period, depending on the timing of expenditures on our research and development activities. Our primary use of cash is to fund operating expenses, which consist primarily of research and development and general and administrative expenses. The timing of payment of these expenses has an effect on cash used to fund operating expenses, as reflected in the change in our outstanding accounts payable and accrued expenses.

We expect to continue to incur net operating losses for at least the next several years, and we expect our research and development expenses, general and administrative expenses, and capital expenditures will continue to increase. We expect our expenses and capital requirements will increase significantly in connection with our ongoing activities as we:

- continue our ongoing and planned research and development of our VGL101 and small molecule TREM2 agonist program;
- initiate preclinical studies and clinical trials for any additional therapeutic candidates that we may pursue in the future;
- expand our product pipeline based on TREM2 and other microglia targets across multiple therapeutic modalities, through internal discovery and development, or through strategic collaborations or alliances with academic organizations, pharmaceutical or biotechnology companies;
- seek regulatory approvals for any therapeutic candidates that successfully complete clinical trials;
- invest in capital equipment in order to expand our research and development activities;
- attract, hire and retain additional clinical, scientific, quality control, and manufacturing management and administrative personnel;
- add clinical, operational, financial and management information systems and personnel, including personnel to support our product development;
- develop, maintain, expand, protect and enforce our intellectual property portfolio, including patents, trade secrets and know-how;
- acquire or in-license other therapeutic candidates and technologies;
- expand our operations in the United States and to other geographies;

- incur additional legal, accounting, investor relations and other general and administrative expenses associated with operating as a public company; and
- establish a sales, marketing and distribution infrastructure, either ourselves or in partnership with others, to commercialize any therapeutic candidates, if approved.

We will not generate revenue from product sales unless and until we successfully complete clinical development and obtain regulatory approval for one or more of our therapeutic candidates. If we obtain regulatory approval for any of our therapeutic candidates, we expect to incur significant expenses related to product sales, marketing and distribution to the extent that such sales, marketing and distribution are not the responsibility of potential collaborators. We may also require additional capital to pursue in-licenses or acquisitions of other drug candidates. Further, we expect to incur additional costs associated with operating as a public company.

We also expect to increase the size of our administrative function to support the growth of our business. Our net losses may fluctuate significantly from quarter-to-quarter and year-to-year, depending on the timing of our clinical trials and our expenses related to other research and development activities.

As a result, we will require substantial additional funding to develop our therapeutic candidates and support our continuing operations. Until such time that we can generate significant revenue from product sales or other sources, we expect to finance our operations through the sale of equity, debt financings or other capital sources, which could include proceeds from potential collaborations, strategic partnerships or marketing, distribution, licensing or other strategic arrangements with third parties. We may be unable to raise additional funds or to enter into such agreements or arrangements on favorable terms, or at all. Our ability to raise additional funds may be adversely impacted by potential worsening global economic conditions and the recent disruptions to, and volatility in, the credit and financial markets in the United States and worldwide resulting from the ongoing COVID-19 pandemic and otherwise. If we fail to raise capital or enter into such agreements as, and when, needed, we may have to significantly delay, scale back or discontinue the development or commercialization of our therapeutic candidates or grant rights to develop and market therapeutic candidates that we would otherwise prefer to develop and market ourselves.

Our failure to obtain sufficient funds with acceptable terms could have a material adverse effect on our business, results of operations or financial condition, including requiring us to have to delay, reduce or eliminate our product development or future commercialization efforts. Because of the numerous risks and uncertainties associated with pharmaceutical product development, we are unable to accurately predict the amount of increased expenses or timing, or if we will be able to achieve or maintain profitability. If we fail to become profitable or are unable to sustain profitability on a continuing basis, then we may be unable to continue our operations at planned levels and be forced to reduce or terminate our operations. We cannot provide assurance that we will ever be profitable or generate positive cash flow from operating activities.

Impact of COVID-19 on Our Operations

In March 2020, the World Health Organization declared the outbreak of COVID-19 a global pandemic. We are subject to a number of risks associated with the COVID-19 global pandemic, including potential delays associated with our ongoing preclinical studies and clinical trials. COVID-19 may have an adverse impact on our operations, supply chains and distribution systems or those of our third-party vendors and collaborators, and increase expenses, including as a result of impacts associated with preventive and precautionary measures that are being taken, such as restrictions on travel and border crossings, quarantine polices and social distancing. We and our third-party vendors and collaborators may experience disruptions in supply of items that are essential for our research and development activities. In addition, the spread of COVID-19 has disrupted global healthcare and healthcare regulatory systems which could divert healthcare resources away from, or materially delay, FDA approval and approval by other health authorities worldwide with respect to our therapeutic candidates. Furthermore, our clinical trials may be negatively affected by the COVID-19 outbreak. Site initiation, patient enrollment and patient follow-up visits may be delayed, for example, due to prioritization of hospital resources toward the COVID-19 outbreak, travel restrictions, the inability to access sites for initiation and monitoring, and difficulties recruiting or retaining patients in our planned clinical trials. The emergence of additional variants, as well as reduced efficacy of vaccines over time and the possibility that a large number of people decline to get vaccinated or receive booster shots, creates inherent uncertainty as to the future of our business, our industry and the economy in general in light of the pandemic. We cannot at this time predict the specific extent, duration, or full impact that the COVID-19 outbreak will have on our financial condition and operations. If we do not successfully commercialize any of our therapeutic candidates, we will be unable to generate product revenue or achieve profitability.

Exclusive License Agreement with Amgen Inc.

In July 2020, we entered into an exclusive license agreement, or the Amgen Agreement, with Amgen Inc., or Amgen, pursuant to which we have been granted an exclusive, royalty-bearing license to certain intellectual property rights owned or controlled by Amgen, to commercially develop, manufacture, use, distribute and sell therapeutic products containing compounds that bind to TREM2. In addition, we are required to reimburse Amgen for amounts it paid to its contract manufacturers on our behalf. See Note 11 to the condensed consolidated financial statements appearing elsewhere in this Quarterly Report for more information on the Amgen Agreement.

As initial consideration for the license, we paid an upfront payment of $0.5 million and also recognized an obligation to issue shares of Series A convertible preferred stock with an antidilution provision, or the Related Party Antidilution Obligation. As Amgen reported in its Schedule 13G filed with the SEC on January 11, 2022, as of that date, Amgen owns approximately 11.3% of our outstanding shares of capital stock. As additional consideration for the license, we are required to pay Amgen up to $80.0 million in the aggregate upon the achievement of specified regulatory milestones for the first monoclonal antibody TREM2 agonist (mAb) product and the first small molecule TREM2 agonist product and aggregate milestone payments of up to $350.0 million upon the achievement of specific commercial milestones across all mAb products and small molecule products. No regulatory or commercial milestones have been achieved to date under the Amgen Agreement. We are also required to pay tiered royalties of low to mid single-digit percentages on annual net sales of the products covered by the license. In the event that the exploitation of a product is not covered by a valid claim within the licensed patent rights, then the royalty rate with respect to the net sales shall be subject to a customary reduction by a certain percentage. The royalty term will terminate on a country-by-country basis on the later of (i) the expiration date of the last valid claim within the licensed patent rights and (ii) the tenth (10^{th}) anniversary of the first commercial sale of such product in such country.

In connection with the license agreement, Amgen entered into certain stockholder agreements related to this investment. See "Certain Relationships and Related Party Transactions—Series A Preferred Stock Financings."

Components of Our Results of Operations

Operating Expenses

Our operating expenses since inception have consisted solely of research and development expenses and general and administrative expenses.

Research and Development

Research and development expenses consist of costs incurred for our research activities, including our discovery efforts and the development of our programs. These expenses include:

- employee related expenses, including salaries, related benefits, and stock-based compensation expense for employees engaged in research and development functions;
- expenses incurred in connection with the discovery, preclinical studies and clinical development of our VGL101 and small molecule TREM2 agonist program;
- expenses incurred under agreements with third parties, such as consultants, clinical investigators, contractors and contract research organizations, or CROs, that assist with (i) the preclinical studies and clinical development of VGL101 and (ii) identification of potential therapeutic candidates in our small molecule TREM2 agonist program;
- the cost of developing and scaling our manufacturing process and manufacturing therapeutic candidates for use in our research and preclinical studies, including under agreements with third parties, such as consultants, contractors, and contract manufacturing organizations, or CMOs; and
- other expenses incurred as a result of research and development activities.

Research and development expenses account for a significant portion of our operating expenses. We expense research and development costs as incurred. Nonrefundable advance payments for goods and services that will be used in future research and development activities are expensed when the activity has been performed or when the goods have been received rather than when the payment is made. When third-party service providers' billing terms do not coincide with our period-end, we are required to make estimates of our obligations to those third parties incurred in a given accounting period and record accruals at the end of the period. We base these estimates on our knowledge of the research and development programs, services performed for the period, past history for related activities and the expected duration of the third-party service contract, where applicable. If timelines or contracts are modified based upon changes in the scope of work to be performed, we modify our estimates of accrued expenses accordingly on a prospective basis. Actual results could differ from our estimates.

Our direct research and development expenses are tracked on a program-by-program basis and consist primarily of external costs, such as fees paid to CROs, CMOs, central laboratories and outside consultants in connection with our research and discovery, preclinical development, process development, manufacturing, clinical development, regulatory and quality activities. We do not allocate employee costs or facility expenses, including depreciation or other indirect costs, to specific programs because these costs are deployed across multiple programs. Our internal resources conduct our research and discovery activities and manage our preclinical development and process development, manufacturing and clinical development activities.

The table below summarizes our research and development expenses incurred by program:

	Three Months Ended March 31,	
	2022	2021
	($ in thousands)	
Direct, external research and development expenses by program:		
VGL101	$ 3,581	$ 3,605
Small molecule TREM2	2,606	1,103
Unallocated research and development expenses:		
External costs and other	882	686
Facilities, personnel-related, and other	3,296	1,359
Total research and development expenses	$ 10,365	$ 6,753

Research and development activities are central to our business model. Therapeutic candidates in later stages of clinical development generally have higher development costs than those in earlier stages, primarily due to the increased size and duration of later-stage clinical trials. As a result, we expect that our research and development expenses will increase substantially over the next several years as we expect to (i) advance VGL101 and our small molecule TREM2 agonist programs' initial clinical trials, (ii) develop VGL101 for other indications, including other rare leukodystrophies, and leukoencephalopathies, and (iii) expand our modality agnostic product pipeline to other microglia targets beyond TREM2.

The successful development and commercialization of our therapeutic candidates is highly uncertain. At this time, we cannot reasonably 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 therapeutic candidates. This uncertainty is due to the numerous risks and uncertainties associated with product development and commercialization, including the uncertainty of:

- the timing, design and successful completion of preclinical studies and clinical development activities;
- the sufficiency of our financial and other resources to complete the necessary preclinical studies and clinical trials;
- effective INDs or comparable foreign applications that allow commencement of our planned clinical trials or future clinical trials for any therapeutic candidates we may develop;
- successful enrollment and completion of clinical trials, including under the FDA's Good Clinical Practices, Good Laboratory Practices, and any additional regulatory requirements from foreign regulatory authorities;
- positive results from our future clinical trials that support a finding of safety and effectiveness and an acceptable risk-benefit profile in the intended populations;
- the receipt of regulatory marketing approvals from applicable regulatory authorities;
- the establishment of arrangements with third-party manufacturers for clinical supply and, where applicable, commercial manufacturing capabilities;
- the establishment, maintenance, defense and enforcement of patent, trademark, trade secret and other intellectual property protection or regulatory exclusivity for any therapeutic candidates we may develop;
- patient recruitment and enrollment;
- commercial launch of any therapeutic candidates we may develop, if approved, whether alone or in collaboration with others;
- acceptance of the benefits and use of our therapeutic candidates we may develop, including method of administration, if and when approved, by patients, the medical community and third-party payors;
- our ability to compete effectively with other therapies and treatment options;
- maintenance of a continued acceptable safety, tolerability and efficacy profile of any therapeutic candidates we may develop following approval;
- establishment and maintenance of healthcare coverage and adequate reimbursement by payors;
- our ability to establish new licensing or collaboration arrangements;
- the performance of our future collaborators, if any;

- development and timely delivery of commercial-grade drug formulations that can be used in our planned clinical trials and, if approved, for commercial launch;
- obtaining, maintaining, defending and enforcing patent claims and other intellectual property rights;
- launching commercial sales of our therapeutic candidates, if approved, whether alone or in collaboration with others; and
- maintaining a continued acceptable safety profile of the therapeutic candidates following approval.

Any changes in the outcome of any of these variables with respect to the development of our therapeutic candidates in preclinical and clinical development could mean a significant change in the costs and timing associated with the development of these therapeutic candidates. For example, if the FDA or another regulatory authority were to delay our planned start of clinical trials or require us to conduct clinical trials or other testing beyond those that we currently expect, or if we experience significant delays in enrollment in any of our planned clinical trials, we could be required to expend significant additional financial resources and time to complete clinical development of that therapeutic candidate. We may never obtain regulatory approval for any of our therapeutic candidates, and, even if we do, drug commercialization takes several years and millions of dollars in development costs.

General and Administrative

General and administrative expenses consist primarily of personnel expenses, including salaries, benefits and stock-based compensation expense, for personnel in executive, accounting, business development, legal, human resources and administrative functions. General and administrative expenses also include corporate facility costs not otherwise included in research and development expenses, depreciation and other expenses, which include direct or allocated expenses for rent and maintenance of facilities and insurance, not otherwise included in research and development expenses, as well as professional fees for legal, consulting, investor and public relations, accounting and audit services.

We expect that our general and administrative expenses will increase in the foreseeable future as we increase our headcount to support the continued research and development of our programs and the growth of our business. We also anticipate incurring additional expenses associated with operating as a public company, including increased expenses related to audit, legal, regulatory, compliance, director and officer insurance, investor and public relations and tax-related services associated with maintaining compliance with the rules and regulations of the Securities and Exchange Commission, or SEC, and standards applicable to companies listed on a national securities exchange, additional insurance expenses, investor relations activities and other administrative and professional services.

Other Income (Expense)

Change in Fair Value of Related Party Antidilution Obligation

Pursuant to the Amgen Agreement, we agreed to issue Amgen equity in an amount equal to 25% of our capital stock on a fully diluted basis until such time as we have raised an aggregate of $45.0 million in net cash proceeds from financing activities relating to dilutive transactions including the Related Party Antidilution Obligation. In September 2020, we completed the first closing pursuant to the Series A Convertible Preferred Stock Purchase Agreement, and as a result issued Amgen 6,928,566 shares of Series A convertible preferred stock such that Amgen's ownership represented 25% of the post-closing capitalization on a fully diluted basis. The Related Party Antidilution Obligation was separately exercisable from the Amgen Agreement and was classified as a liability and recorded at fair value in the consolidated balance sheet with a corresponding charge to research and development at inception of the license agreement in July of 2020. The Related Party Antidilution Obligation was remeasured at fair value at each reporting period, with changes in fair value recorded in change in fair value of Related Party Antidilution Obligation in the consolidated statement of operations and comprehensive loss. In September 2020, the Related Party Antidilution Obligation was partially settled through the issuance of 6,928,566 shares of Series A convertible preferred stock with a fair value of $17.5 million. In May 2021, we settled the remaining Related Party Antidilution Obligation in full with the second closing pursuant to the Series A Convertible Preferred Stock Purchase Agreement. Amgen received an additional 1,963,093 shares of Series A convertible preferred stock with a fair value of $5.1 million. These shares were subsequently converted into common stock in connection with the Company's IPO.

Change in Fair Value of Series A Preferred Stock Tranche Obligation

In September 2020, we entered into the Series A Convertible Preferred Stock Purchase Agreement and issued 9,815,467 shares of Series A convertible preferred stock at a purchase price of $2.547 per share, for gross cash proceeds of $25.0 million. The gross proceeds were offset by $0.2 million of issuance costs and $0.2 million related to the Series A Preferred Tranche Obligation. As part of the September 2020 Series A Convertible Preferred Stock Purchase Agreement, the investors were contingently obligated to purchase 7,852,373 additional shares of Series A convertible preferred stock at $2.547 per share upon the satisfaction of specified research and development milestones, collectively, the Series A Preferred Stock Tranche Obligation. The Series A Preferred Stock Tranche

Obligation was legally detachable and separately exercisable from the Series A convertible preferred stock. As such, we allocated the proceeds from the September 2020 issuance between the Series A Preferred Stock Tranche Obligation and the Series A convertible preferred stock. As the Series A convertible preferred stock is redeemable upon a deemed liquidation event at the election of the holder controlled Board, and therefore outside of the control of our company, the Series A Preferred Stock Tranche Obligation was classified as a liability and recorded at its fair value. The Series A Preferred Stock Tranche Obligation was remeasured at fair value at each reporting period, with changes in fair value recorded in change in fair value of Series A Preferred Stock Tranche Obligation in the condensed consolidated statement of operations and comprehensive loss.

Interest Income, net

Interest income, net consists of interest earned from our cash and cash equivalents and restricted cash. We expect our interest income will increase slightly as we invest the cash received from our sales of Series B preferred stock and the net proceeds from our IPO. Interest income was immaterial during the three months ended March 31, 2022, and March 31, 2021.

Other Expense, net

Other expense, net includes gains and losses from the remeasurement of foreign currency transactions into our functional currency. Other expense, net was immaterial during the three months ended March 31, 2022, and March 31, 2021.

Results of Operations

Three Months Ended March 31, 2022 Compared with Three Months Ended March 31, 2021

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

	Three Months Ended March 31,	
	2022	2021
	($ in thousands)	
Operating expenses:		
Research and development	$ 10,365	$ 6,753
General and administrative	4,967	1,165
Total operating expenses	15,332	7,918
Loss from operations	(15,332)	(7,918)
Other income (expense):		
Change in fair value of the related party antidilution obligation	—	(252)
Change in fair value of Series A preferred stock tranche obligation	—	(21)
Interest income	2	2
Other income (expense), net	(4)	(2)
Total other expense, net	(2)	(273)
Net loss and comprehensive loss	$ (15,334)	$ (8,191)

Research and Development Expenses

Research and development expenses were $10.4 million for the three months ended March 31, 2022, as compared to $6.8 million for the three months ended March 31, 2021. The increase of $3.6 million consisted primarily of the following:

- $1.9 million of facilities, personnel-related and other expenses, of which $1.5 million related to personnel-related costs, including salaries, bonuses, and other compensation-related costs, including stock-based compensation of $0.3 million
- $1.5 million of small molecule TREM2 agonist program expenses, including $0.8 million increase in lead optimization expenses;
- $0.6 million of other VGL101 program expenses

The increase in research and development expenses were partially offset by a $0.6 million in external manufacturing expenses due to timing of manufacturing runs of VGL101.

General and Administrative Expenses

General and administrative expenses were $5.0 million for the three months ended March 31, 2022, as compared to $1.2 million for the three months ended March 31, 2021. The increase of $3.8 million consisted primarily of the following:

- $1.4 million of professional fees, including legal, accounting and other expenses;
- $1.2 million of personnel-related costs, including salaries, bonuses, and other compensation-related costs, including stock-based compensation of $0.4 million; and
- $1.2 million of other headcount related expenses and costs associated with operating as a public company, including $0.5 million of Business Insurance

Change in Fair Value of Related Party Antidilution Obligation

The change in fair value of Related Party Antidilution Obligation was $0 for the three months ended March 31, 2022, as compared to $0.3 million for the three months ended March 31, 2021. This decrease of $0.3 million was related to the May 2021 settlement of the Related Party Antidilution Obligation associated with the Amgen Agreement. On September 18, 2020, we completed the first closing pursuant to the Series A Convertible Preferred Stock Purchase Agreement which triggered the partial settlement of the Related Party Antidilution Obligation resulting in the issuance of 6,928,566 shares of its Series A convertible preferred stock to Amgen. On May 28, 2021, we completed the second closing pursuant to the Series A Convertible Preferred Stock Purchase Agreement which resulted in our raising of net cash proceeds from financing activities in excess of the $45.0 million Related Party Antidilution Obligation cap. The second closing triggered the settlement of the remaining Related Party Antidilution Obligation, resulting in the issuance of 1,963,093 shares of Series A convertible preferred stock to Amgen with a fair value of $5.1 million.

Change in Fair Value of Series A Preferred Stock Tranche Obligation

The change in fair value of Series A Preferred Stock Tranche Obligation was $0 for the three months ended March 31, 2022 as compared to $21 thousand for the three months ended March 31, 2021. This decrease of $21 thousand related to the May 2021 settlement of the Series A Preferred Stock Tranche Obligation associated with the Series A Convertible Preferred Stock Purchase Agreement. In May 2021, we settled the Series A Tranche Obligation with the issuance of 7,852,373 shares of our Series A Convertible Preferred Stock.

Liquidity and Capital Resources

Sources of Liquidity

Since our inception, we have not generated any revenue from product sales and have incurred significant operating losses and negative cash flows from our operations. We expect to incur significant expenses and operating losses for the foreseeable future as we advance the clinical development of our therapeutic candidates. Since our inception through March 31, 2022, we have funded our operations with net proceeds from sales of our convertible preferred stock, issuance of our common stock from our initial public offering, and SAFE. As of March 31, 2022, we had cash and cash equivalents of $163.3 million.

In January 2022, we completed the initial public offering of our common stock, in which we issued an aggregate of 7,000,000 shares of common stock, at a price of $14.00 per share, for gross cash proceeds of $98.0 million, before underwriting discounts and commissions. We received approximately $88.0 million in net proceeds, after deducting underwriting discounts, commissions and offering expenses of $10.0 million.

Based on our current operating plan, we expect the net proceeds from our IPO, together with our existing cash, will be sufficient to fund our planned operating expenses and capital expenditure requirements into 2024.

Cash Flows

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

	Three Months Ended March 31,	
	2022	2021
	($ in thousands)	
Net cash used in operating activities	$ (18,144)	$ (4,763)
Net cash used by investing activities	(142)	—
Net cash provided by financing activities	90,190	—
Net increase in cash, cash equivalents and restricted cash	$ 71,904	$ (4,763)

Operating Activities

During the three months ended March 31, 2022, operating activities consisted primarily of our net loss of $15.3 million, partially offset by (i) $4.1 million of changes in operating assets and liabilities, (ii) $1.0 million stock-based compensation expense, and (iii) $0.2 million change in operating lease expenses. The net loss primarily consisted of $10.3 million of research and development expenses, and $5.0 million of general and administrative expenses.

During the three months ended March 31, 2021, operating activities consisted primarily of our net loss of $8.2 million, partially offset by (i) $0.3 million change in Related Party Antidilution Obligation, (ii) $2.8 million of changes in operating assets and liabilities and (iii) $0.3 million stock-based compensation expense. The net loss primarily consisted of $6.8 million of research and development expenses, $1.2 million of general and administrative expenses and a $0.3 million unfavorable change in fair value of Related Party Antidilution.

Investing Activities

During the three months ended March 31, 2022, net cash used by investing activities consisted of $0.1 million of purchases of property and equipment.

During the three months ended three months ended March 31, 2021, there was no net cash used by investing activities.

Financing Activities

During the three months ended March 31, 2022, net cash provided by financing activities consisted primarily of $88.0 million in net proceeds from the issuance of common stock upon initial public offering.

During the three months ended March 31, 2021, there was no net cash provided by financing activities.

Our primary uses of cash are to fund our research and development activities related to our VGL101 and small molecule TREM2 agonist program, hiring personnel, raising capital and providing general and administrative support for these operations.

We currently have no ongoing material financing commitments that are expected to affect our liquidity over the next five years, other than our lease obligations and a $0.9 million standby letter of credit we entered into in September 2021, in connection with a lease for laboratory and office space in Watertown, Massachusetts. The standby letter of credit expires in December 2032.

Funding Requirements

To date, we have not generated any revenue from product sales. We do not expect to generate revenue from product sales unless and until we successfully complete clinical development of, receive regulatory approval for, and commercialize, VGL101**,** and we do not know when, or if at all, that will occur. We expect our expenses and capital requirements to increase significantly in connection with our ongoing activities, particularly as we continue the research and development of, initiate clinical trials of, and seek marketing approval for our VGL101 and small molecule TREM2 agonist program. In addition, if we obtain regulatory approval for any of our therapeutic candidates, we expect to incur significant expenses related to product sales, marketing, and distribution to the extent that such sales, marketing and distribution are not the responsibility of potential collaborators. We may also require additional capital to pursue in-licenses or acquisitions of other drug candidates. Further, we expect to incur additional costs associated with operating as a public company. Accordingly, we will require substantial additional funding to develop our therapeutic candidates and support our continuing operations. If we are unable to raise capital when needed or on attractive terms, we would be forced to delay, reduce or eliminate our product development or future commercialization efforts.

Our future capital requirements will depend on many factors, including:

- the initiation, scope, progress, timing, results and costs of product discovery, preclinical studies and clinical trials for our therapeutic candidates or any future candidates we may develop;
- our ability to maintain our relationship with Amgen and any other key licensors or collaborators;
- the scope, prioritization and number of our research and development programs;
- the costs, timing and outcome of seeking and obtaining regulatory approvals from the FDA and comparable foreign regulatory authorities, including the potential for such authorities to require that we perform more preclinical studies or clinical trials than those that we currently expect or change their requirements on studies that had previously been agreed to;
- our ability to establish and maintain collaborations on favorable terms, if at all;
- the achievement of milestones or occurrence of other developments that trigger payments under any collaboration agreements we enter into;
- the extent to which we are obligated to reimburse, or entitled to reimbursement of, clinical trial costs under collaboration agreements, if any;
- the costs to establish, maintain, expand, enforce and defend the scope of our intellectual property portfolio, including preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims;
- the extent to which we acquire or in-license other therapeutic candidates and technologies;
- the costs of securing manufacturing arrangements for commercial production;
- the costs of establishing or contracting for sales and marketing capabilities if we obtain regulatory approvals to market our therapeutic candidates; and
- our need to implement additional internal systems and infrastructure, including financial and reporting systems.

Identifying potential therapeutic candidates and conducting preclinical studies 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 regulatory approval and commercialize our therapeutic candidates. In addition, our therapeutic candidates, if approved, may not achieve commercial success. Our commercial revenues, if any, will be derived from sales of products 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.

Until such time, if ever, as we can generate significant revenue from product sales or other sources, we expect to finance our operations through the sale of equity, debt financings, or other capital sources, which could include proceeds from potential collaborations, strategic partnerships or marketing, distribution, licensing or other similar arrangements with third parties. However, we may be unable to raise additional funds or enter into such agreements or arrangements on favorable terms, or at all. Market volatility resulting from the COVID-19 pandemic or other factors could also adversely impact our ability to access capital as and when needed. 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. Any future 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, selling or licensing our assets, making capital expenditures, declaring dividends or encumbering our assets to secure future indebtedness. Such restrictions could adversely impact our ability to conduct our operations and execute our business plan.

If we raise funds through 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 therapeutic candidates or to grant licenses on terms that may not be favorable to us. If we fail to raise capital or enter into such agreements as, and when, needed, we may have to significantly delay, scale back or discontinue the development or commercialization of our therapeutic candidates or grant rights to develop and market therapeutic candidates that we would otherwise prefer to develop and market ourselves. We expect our existing cash, and cash equivalents will enable us to fund our operating expenses and capital expenditure requirements into 2024 at which point we would need to obtain substantial additional funding in connection with our continuing operations.

Contractual Obligations and Commitments

In September 2021, we entered into a lease for laboratory and office space in Watertown, Massachusetts with an initial term of ten years, and a five-year renewal option at the end of the initial lease term. The monthly lease payment is approximately $0.2 million with annual escalation of approximately 3%. The lease includes a $3.7 million construction allowance. The lease is expected to commence in the second quarter of 2022 when the leased space is expected to be made available for use, as such this lease is not included in the table above given the commencement date.

In February 2021, we entered into a master services agreement with FUJIFILM Diosynth Biotechnologies UK Limited, FUJIFILM Diosynth Biotechnologies Texas, LLC, FUJIFILM Diosynth Biotechnologies U.S.A., Inc, and FUJIFILM Diosynth Biotechnologies Denmark ApS, or collectively, FUJIFILM. In November 2021, we entered into a statement of work with FUJIFILM for $3.8 million under our existing master services agreement for the manufacturing of VGL101. If we terminate the statement of work before completion, we may be required to pay fees ranging from 0% to 100%. The amount due upon an early termination depends on the length of time prior to the commencement of specific stages of the statement of work. As of March 31, 2022, no significant work had begun. The statement of work is expected to be incurred over approximately 2 years.

Apart from the contracts with payment commitments noted above, we have entered into contracts in the normal course of business with CROs, CMOs and other third parties for preclinical research studies and testing, clinical trials and manufacturing services. These contracts do not contain any minimum purchase commitments and are cancelable by us upon prior notice and, as a result, are not included in the table of contractual obligations and commitments above. Payments due upon cancellation consist only of payments for services provided and expenses incurred, including non-cancelable obligations of our service providers, up to the date of cancellation.

We may in the future incur potential royalty payments under license and collaboration agreements we have entered and will enter into with various entities pursuant to which we have in-licensed certain intellectual property, such as our exclusive license agreement with Amgen. Due to the uncertainty of the achievement and timing of the events requiring payment under these agreements, the amounts to be paid by us are not fixed or determinable at this time.

Critical Accounting Policies and Significant Judgments and Estimates

Our management's discussion and analysis of our financial condition and results of operations are based on our financial statements, which have been prepared in accordance with United States generally accepted accounting principles, or GAAP. The preparation of our financial statements and related disclosures requires us to make estimates and judgments that affect the reported amounts of assets, liabilities, expenses, and the disclosure of our contingent 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.

There have been no other material changes to the significant accounting policies previously disclosed in our Annual Report on Form 10-K for the fiscal year ended December 31, 2021.

Emerging Growth Company Status

The Jumpstart Our Business Startups Act of 2012, or JOBS, permits an "emerging growth company" such as us to take advantage of an extended transition to comply with new or revised accounting standards applicable to public companies until those standards would otherwise apply to private companies. We have elected not to "opt out" of such extended transition period, which means that when a standard is issued or revised and it has different application dates for public or private companies, we will adopt the new or revised standard at the time private companies adopt the new or revised standard and will do so until such time that we either (i) irrevocably elect to "opt out" of such extended transition period or (ii) no longer qualify as an emerging growth company. There are other exemptions and reduced reporting requirements provided by the JOBS Act that we are currently evaluating. For example, as an "emerging growth company," we are exempt from Sections 14A(a) and (b) of the Securities Exchange Act of 1934, as amended, which would otherwise require us to (1) submit certain executive compensation matters to shareholder advisory votes, such as "say-on-pay," "say-on-frequency," and "golden parachutes;" and (2) disclose certain executive compensation related items such as the correlation between executive compensation and performance and comparisons of our chief executive officer's compensation to our median employee compensation. We also intend to rely on an exemption from the rule requiring us to provide an auditor's attestation report on our internal controls over financial reporting pursuant to Section 404(b) of the Sarbanes-Oxley Act. We will continue to remain an "emerging growth company" until the earliest of the following: (1) the last day of the fiscal year following the fifth anniversary of the date of the completion of our IPO; (2) the last day of the fiscal year in which our total annual gross revenue is equal to or more than $1.07 billion; (3) the date

on which we have issued more than $1 billion in nonconvertible debt during the previous three years; or (4) the date on which we are deemed to be a large accelerated filer under the rules of the SEC.

Recently Issued Accounting Pronouncements

There have been no other material changes to the significant accounting policies previously disclosed in the Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2021.

Item 3. Quantitative and Qualitative Disclosures About Market Risk.

Information required by this Item is not applicable as we are electing scaled disclosure requirements available to Smaller Reporting Companies with respect to this Item.

Item 4. Controls and Procedures.

We have established 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) designed to ensure that information required to be disclosed in the reports that we file or submit under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms and is accumulated and communicated to management, including the principal executive officer (our Chief Executive Officer) and principal financial officer (our Chief Financial Officer), to allow timely decisions regarding required disclosure. In addition, the design of disclosure controls and procedures must reflect the fact that there are resource constraints and that management is required to apply judgment in evaluating the benefits of possible controls and procedures relative to their costs.

Evaluation of Disclosure Controls and Procedures

Our management, with the participation of our Chief Executive Officer and Chief Financial Officer, evaluated the effectiveness of our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act) as of March 31, 2022. 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. Our disclosure controls and procedures have been designed to provide reasonable assurance of achieving their objectives. Based on this evaluation, our Chief Executive Officer and Chief Financial Officer concluded that, as of March 31, 2022, our disclosure controls and procedures were not effective due to a material weakness in internal control over financial reporting relating to cut-off of certain general and administrative and research and development expenses. This material weakness resulted in immaterial adjustments to general and administrative expenses, research and development expenses and accrued expenses as of and for the year ending December 31, 2020, and as of and for each of the interim periods ending June 30, 2020 and September 30, 2020, all of which were recorded prior to the issuance of the interim and annual consolidated financial statements. Additionally, this material weakness could result in misstatements of the aforementioned account balances or disclosures that would result in a material misstatement to the annual or interim consolidated financial statements that would not be prevented or detected. Despite enhancements we implemented to our internal controls over financial reporting during fiscal year 2021 and continue to make, as the revised and enhanced controls need to be in operation for a sufficient period of time to ensure that the controls are operating as designed, management has concluded that the material weakness cannot be considered remediated as of March 31, 2022.

Notwithstanding the material weakness described in Management's Report on Internal Control Over Financial Reporting, our management has concluded that our condensed consolidated financial statements for the periods covered by and included in this Annual Report are prepared in accordance with accounting principles generally accepted in the United States ("GAAP") and fairly present, in all material respects, our financial position, results of operations and cash flows for each of the periods presented herein.

Changes in Internal Control Over Financial Reporting

No change in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) occurred during the three months ended 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 become involved in litigation or other legal proceedings. We are not currently a party to any litigation or legal proceedings that, in the opinion of our management, are probable to have a material adverse effect on our business. Regardless of outcome, litigation can have an adverse impact on our business, financial condition, results of operations and prospects because of defense and settlement costs, diversion of management resources and other factors.

Item 1A. Risk Factors.

Investing in our common stock involves a high degree of risk. You should consider carefully the risks and uncertainties described below, together with all of the other information in this Quarterly Report on Form 10-Q, including our financial statements and related notes and the "Management's Discussion and Analysis of Financial Condition and Results of Operations" section, before making an investment decision. These risks may materially and adversely affect our business, financial condition, results of operations and prospects. Additional risks and uncertainties that we are unaware of, or that we currently believe are not material, may also become important factors that affect us. In that event, the trading price of our common stock could decline, and you could lose part or all of your investment.

Risks Related to Our Limited Operating History, Business, and Financial Position

We have a limited operating history, have incurred significant operating losses since our inception and expect to incur significant losses for the foreseeable future. We may never generate any revenue or become profitable, and, if we achieve profitability, we may not be able to sustain it.

Biopharmaceutical product development is a highly speculative undertaking and involves a substantial degree of risk. We are a clinical-stage biopharmaceutical company with a limited operating history upon which you can evaluate our business and prospects. We commenced operations in 2020, and, to date, we have focused primarily on organizing and staffing our company, business planning, raising capital, identifying therapeutic candidates, establishing our intellectual property portfolio and conducting research and preclinical studies. As an organization, we have only recently initiated our first clinical trial and have not yet completed any clinical trials, obtained regulatory approvals, manufactured a commercial-scale product, or arranged for a third party to do so on our behalf, or conducted sales and marketing activities necessary for successful product commercialization. Consequently, any predictions made about our future success or viability are speculative.

We have incurred significant operating losses since our inception. We do not have any products approved for sale and have not generated any product revenue since our inception. If our therapeutic candidates are not successfully developed and approved, we may never generate any, or any significant revenue. Our net loss was $15.3 million for the three months ended March 31, 2022. As of March 31, 2022, we had an accumulated deficit of $87.2 million. Substantially all of our losses have resulted from expenses incurred in connection with our research and development programs and from general and administrative costs associated with our operations. All of our therapeutic candidates will require substantial additional development time and resources before we would be able to apply for or receive regulatory approvals and begin generating revenue from product sales. We expect to continue to incur losses for the foreseeable future, and we anticipate these losses will increase substantially as we continue our development of, seek regulatory approval for and potentially commercialize any of our therapeutic candidates.

To become and remain profitable, we must succeed in developing and eventually commercializing products that generate significant revenue. This will require us to be successful in a range of challenging activities, including identifying lead therapeutic candidates, discovering additional therapeutic candidates, conducting preclinical studies prior to submitting an IND, obtaining clearance for such IND, completing additional preclinical studies and clinical trials of our therapeutic candidates, obtaining regulatory approval for therapeutic candidates and manufacturing, marketing and selling any products for which we may obtain regulatory approval. We are only in the preliminary stages of most of these activities. We may never succeed in these activities and, even if we do, may never generate revenues that are significant enough to achieve profitability. In addition, we have not yet demonstrated an ability to successfully overcome many of the risks and uncertainties frequently encountered by companies in new and rapidly evolving fields, particularly in the biopharmaceutical industry. Because of the numerous risks and uncertainties associated with biopharmaceutical product development, we are unable to accurately predict the timing or amount of increased expenses or when, or if, we will be able to achieve profitability. 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 may have an adverse effect on the value of our company and could impair our ability to raise capital, expand our business, maintain our research and development efforts, diversify our therapeutic candidates or even continue our operations. A decline in the value of our company could also cause you to lose all or part of your investment.

Our limited operating history may make it difficult to evaluate our technology and industry and predict our future performance. Though several companies have conducted or are conducting studies involving neurodegenerative diseases for which microglia deficiency is a key driver of disease pathology, the relevance of those studies to the evaluation of therapeutic candidates developed using our precision medicine approach may be difficult to ascertain. Our short history as an operating company and novel therapeutic approach make assessments 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. Failure to address these risks successfully will cause our business to suffer. Similarly, we expect that our financial condition and operating results will fluctuate significantly from quarter to quarter and year to year due to a variety of factors, many of which are beyond our control. As a result, our stockholders should not rely upon the results of any quarterly or annual period as an indicator of future operating performance.

In addition, as an early-stage company, we will encounter unforeseen expenses, difficulties, complications, delays and other known and unknown circumstances. If we advance our therapeutic candidates, we will need to transition from a company with a research focus to a company capable of supporting clinical development and, if successful, commercial activities. We may fail in that transition.

We will require additional financing to achieve our goals, and failure to obtain this necessary capital when needed on acceptable terms, or at all, could force us to delay, limit, reduce or terminate our development programs, commercialization efforts or other operations.

The development of biopharmaceutical therapeutic candidates is capital-intensive. We expect our expenses to increase in connection with our ongoing and planned activities, particularly as we conduct preclinical studies of our development programs, initiate clinical trials for our therapeutic candidates and seek regulatory approvals for our current therapeutic candidates and any future therapeutic candidates we may develop. If we obtain regulatory approval for any of our therapeutic candidates, we also expect to incur significant commercialization expenses related to product manufacturing, marketing, sales and distribution. Because the outcome of any preclinical study or clinical trial is highly uncertain, we cannot reasonably estimate the actual amounts necessary to successfully complete the development and commercialization of our therapeutic candidates.

Furthermore, we expect to incur additional costs associated with operating as a public company. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. Failing to raise capital when needed or on attractive terms could force us to delay, reduce or eliminate our research and development programs or any future commercialization efforts.

We believe that the net proceeds from our IPO, together with our existing cash, cash equivalents and marketable securities, will enable us to fund our operations into 2024. We have based this estimate on assumptions that may prove to be wrong, and we could use our capital resources sooner than we currently expect. Our operating plans and other demands on our cash resources may change as a result of many factors currently unknown to us, and we may need to seek additional funds sooner than planned, through public or private equity or debt financings or other capital sources, including potentially collaborations, licenses and other similar arrangements. In addition, we may seek additional capital due to favorable market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. Attempting to secure additional financing may divert our management from our day-to-day activities, which may adversely affect our ability to develop our therapeutic candidates.

Our future capital requirements will depend on many factors, including, but not limited to:

- the type, number, scope, progress, expansions, results, costs and timing of our preclinical studies and clinical trials of the therapeutic candidates that we are pursuing or may choose to pursue in the future;
- the clinical development plans we establish for our therapeutic candidates;
- the costs and timing of manufacturing of our therapeutic candidates and commercial manufacturing if any therapeutic candidate is approved for sale;
- the costs of establishing and maintaining clinical and commercial supply for the development and manufacture of our therapeutic candidates;
- the costs, timing and outcome of regulatory review of our therapeutic candidates;
- the terms and timing of establishing and maintaining collaborations, licenses and other similar arrangements;
- the costs of obtaining, maintaining and enforcing our patents and other intellectual property rights;
- the costs associated with our efforts to enhance operational systems and hire additional personnel to satisfy our obligations as a public company, including enhanced internal control over financial reporting;
- the costs associated with hiring additional personnel and consultants as our preclinical and clinical activities increase;

- the achievement of milestones or occurrence of other developments that trigger payments under any collaboration agreements, if any;
- the costs and timing of establishing or securing sales and marketing capabilities if any therapeutic candidate is approved;
- regulatory approval and revenue, if any, received from commercial sales of our therapeutic candidates; and
- our ability to achieve sufficient market acceptance, coverage and adequate reimbursement from third-party payors and adequate market share and revenue for any approved products.

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.

Our operating results may fluctuate significantly, which makes our future operating results difficult to predict and could cause our operating results to fall below expectations or our guidance.

Our quarterly and annual operating results may fluctuate significantly in the future. From time to time, we may enter into license or collaboration agreements or strategic partnerships with other companies to gain access to new technologies, or to out-license our technologies. Any such agreement may include development funding and significant upfront and milestone payments and/or royalties, which may become an important source of our revenue. Under our exclusive license agreement with Amgen, for example, we are required to pay Amgen up to $80.0 million upon the achievement of specified regulatory milestones for the first mAb TREM2 agonist product, or mAb product, and first small molecule TREM2 agonist product, or small molecule product, upon achievement of specified regulatory milestones as well as aggregate milestone payments of up to $350.0 million upon achievement of specific commercial milestones across all such mAb products and small molecule products, and tiered royalties of low to mid single-digit percentages on annual net sales of the products covered by the license. These milestone payments may vary significantly from period to period and the variance could cause a significant fluctuation in our operating results from one period to the next.

In addition, we measure compensation cost for stock-based awards made to employees at the grant date of the award, based on the fair value of the award as determined by our board of directors, and recognize the cost as an expense over the employee's requisite service period. As the variables that we use as a basis for valuing these awards change over time, including, our underlying stock price and stock price volatility, the magnitude of the expense that we must recognize may vary significantly.

Furthermore, our operating results may fluctuate due to a variety of other factors, many of which are outside of our control and may be difficult to predict, including, but not limited to:

- the timing and outcomes of preclinical studies and clinical trials for VGL101 and any therapeutic candidates from our discovery programs, or competing therapeutic candidates;
- the timing and cost of, and level of investment in, research and development activities relating to our programs, which will change from time to time;
- the cost of manufacturing our current therapeutic candidates and any future therapeutic candidates, which may vary depending on the FDA, European Medicines Agency (EMA) or other comparable foreign regulatory authority guidelines and requirements, the quantity of production and the terms of our agreements with manufacturers;
- the timing and cost of meeting regulatory requirements established by the FDA or EMA or comparable foreign regulatory authorities;
- any delays in regulatory review or approval of VGL101 or therapeutic candidates from any of our discovery programs;
- the impact of the COVID-19 pandemic on the global economy, including causing or contributing to global supply chain disruption, price fluctuations, including increased costs for raw materials, and other significant economic effects;
- our ability to enroll patients in clinical trials and the timing of enrollment;
- expenditures that we will or may incur to acquire or develop additional therapeutic candidates and technologies or other assets;
- the need to conduct unanticipated preclinical studies or clinical trials or studies or trials that are larger, lengthier or more complex than anticipated;
- competition from existing and potential future products that compete with VGL101 or any of our discovery programs, and changes in the competitive landscape of our industry, including consolidation among our competitors or partners;

- the level of demand for any of our therapeutic candidates, if approved, which may fluctuate significantly and be difficult to predict;
- the risk/benefit profile, cost and reimbursement policies with respect to our therapeutic candidates, if approved, and existing and potential future products that compete with VGL101 or any of our discovery programs;
- our ability to commercialize VGL101 or therapeutic candidates from any of our discovery programs, if approved, inside and outside of the U.S., either independently or working with third parties;
- our ability to establish and maintain collaborations, licensing or other arrangements;
- potential unforeseen business disruptions that increase our costs or expenses;
- future accounting pronouncements or changes in our accounting policies; and
- the changing and volatile global economic and political environment.

The cumulative effect of these factors could result in large fluctuations and unpredictability in our quarterly and annual operating results. As a result, comparing our operating results on a period-to-period basis may not be meaningful. Investors should not rely on our past results as an indication of our future performance. This variability and unpredictability could also result in our failing to meet the expectations of industry or financial analysts or investors for any period. If our operating results fall below the expectations of analysts or investors or below any forecasts we may provide to the market, or if the forecasts we provide to the market are below the expectations of analysts or investors, the price of our common stock could decline substantially. Such a stock price decline could occur even when we have met any previously publicly stated guidance we may provide.

We have identified a material weakness in our internal control over financial reporting. If we are unable to remediate this material weakness, or if we identify additional material weaknesses in the future or otherwise fail to maintain effective internal control over financial reporting, we may not be able to accurately or timely report our financial condition or results of operations, which may adversely affect our business.

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 for external purposes in accordance with generally accepted accounting principles. Any failure to maintain effective internal control over financial reporting could cause us to fail to accurately or timely report our financial condition or results of operations to meet our reporting obligations.

We identified a material weakness in our internal control over financial reporting. A material weakness is a deficiency, or combination of deficiencies, in internal control over financial reporting, such that there is a reasonable possibility that a material misstatement of our annual or interim consolidated financial statements will not be prevented or detected on a timely basis. The Company did not design and maintain effective controls over the cut-off of certain general and administrative and research and development expenses. This material weakness resulted in immaterial adjustments to general and administrative expenses, research and development expenses and accrued expenses as of and for the year ending December 31, 2020, and as of and for each of the interim periods ending June 30, 2020 and September 30, 2020, all of which were recorded prior to the issuance of the interim and annual consolidated financial statements. Additionally, this material weakness could result in misstatements of the aforementioned account balances or disclosures that would result in a material misstatement to the annual or interim consolidated financial statements that would not be prevented or detected. Despite enhancements we implemented to date to our internal controls over financial reporting during fiscal year 2021 and continue to make, as the revised and enhanced controls need to be in operation for a sufficient period of time to ensure that the controls are operating as designed, management has concluded that the material weakness cannot be considered remediated as of March 31, 2022.

We cannot assure that the measures we have taken to date, and actions we may take in the future, will be sufficient to remediate the control deficiency that led to this material weakness in our internal control over financial reporting or that they will prevent or avoid potential future material weaknesses. In addition, neither our management nor an independent registered public accounting firm has performed an evaluation of our internal control over financial reporting because no such evaluation has been required. Had we or our independent registered public accounting firm performed an evaluation of our internal control over financial reporting, additional material weaknesses may have been identified. If we are unable to successfully remediate our existing or any future material weaknesses in our internal control over financial reporting, or we identify any additional material weaknesses, the accuracy and timing of our financial reporting may be adversely affected, potentially resulting in restatements of our consolidated financial statements; we may be unable to maintain compliance with securities law requirements regarding timely filing of periodic reports and applicable Nasdaq listing requirements; investors may lose confidence in our financial reporting; and our stock price may decline as a result.

If we are unable to design and maintain effective internal control over financial reporting in the future, investors may lose confidence in the accuracy and completeness of our financial reports and the market price of our common stock may decline.

Ensuring that we have adequate internal control over financial reporting 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 re-evaluated 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 for external purposes in accordance with generally accepted accounting principles. We have begun the process of documenting, reviewing and improving our internal control over financial reporting to comply with the Securities and Exchange Commission's (SEC) rules and regulations, which will require annual management assessment of the effectiveness of our internal control over financial reporting beginning with the Form 10-K for the year ending December 31, 2022.

Implementing any appropriate changes to our internal control over financial reporting 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 establishing and 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. If we fail to remediate our identified material weakness, or identify additional material weaknesses, in our internal control over financial reporting; if we are unable to comply with the requirements of the SEC's rules and regulations in a timely manner; or if we are unable to assert that our internal control over financial reporting is effective, investors may lose confidence in the accuracy and completeness of our financial reports and the market price of our common stock could decline, and we could also become subject to investigations by the stock exchange on which our common stock is listed, the SEC or other regulatory authorities, which could require additional financial and management resources.

Failure or security breaches of, loss or leakage of data from, or other disruptions in, our internal information technology systems, or those of our third-party CROs or other vendors, contractors or consultants, could result in a material disruption of our 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.

We are increasingly dependent upon information technology systems, infrastructure and data to operate our business. In the ordinary course of business, we collect, store and transmit confidential information (including but not limited to intellectual property, proprietary business information and personal information). We also have outsourced elements of our operations to third parties, and, as a result, we manage a number of third-party clinical research organizations (CROs), vendors, and other contractors and consultants who have access to our confidential information.

Despite the implementation of security measures, given their size and complexity and the increasing amounts of confidential information that they maintain, our internal information technology systems and those of our third-party CROs, vendors and other contractors and consultants are vulnerable to breakdown or other damage or interruption from service interruptions, system malfunction, natural disasters, terrorism, war and telecommunication and electrical failures, as well as security breaches from inadvertent or intentional actions by our employees, third-party CROs, vendors, contractors, consultants, business partners and/or other third parties, or from cyber-attacks by malicious third parties (including the deployment of harmful malware, ransomware, denial-of-service attacks, social engineering and other means to affect service reliability and threaten the confidentiality, integrity and availability of information), which may compromise our system infrastructure, or that of our third-party CROs, vendors and other contractors and consultants, or lead to data leakage. The risk of a security breach or disruption, particularly through cyber-attacks or cyber intrusion, including by computer hackers, foreign governments, and cyber terrorists, has generally increased as the number, intensity and sophistication of attempted attacks and intrusions from around the world have increased. Also, due to the COVID-19 pandemic, we have implemented a hybrid work model, enabling our employees to split time between working from the office and working from home. As a result, we may have increased cyber security and data security risks, due to increased use of home wi-fi networks and virtual private networks, as well as increased disbursement of physical machines. While we implement IT controls to reduce the risk of a cyber security or data security breach, there is no guarantee that these measures will be adequate to safeguard all systems, especially with an increased number of employees working remotely. The techniques used by cyber criminals change frequently, may not be recognized until launched and can originate from a wide variety of sources, including outside groups such as external service providers, organized crime affiliates, terrorist organizations or hostile foreign governments or agencies. Disruptions or security breaches resulting in a loss of, or damage to, our data or applications, or those of our third-party CROs, vendors and other contractors and consultants, or inappropriate disclosure of confidential or proprietary information, could generate liability and reputational damage and the further development and commercialization, if approved, of VGL101 or any future therapeutic candidates could be delayed. The costs related to significant security breaches or disruptions could be material and exceed the limits of the cybersecurity insurance we maintain against such risks. We may have limited recourse for disruptions or breaches of the information technology systems of our third-party CROs, vendors and other contractors and consultants, and we may have to expend significant resources to mitigate the impact of such an event, and to develop and implement protections to prevent future events of this nature from occurring.

Our data protection efforts and our investment in information technology do not preclude significant breakdowns, data leakages, breaches in our systems, or those of our third-party CROs, vendors and other contractors and consultants, or other cyber incidents that could have a material adverse effect upon our reputation, business, operations or financial condition. The loss of clinical trial data for VGL101 or any other therapeutic candidates could result in delays in our marketing approval efforts and significantly increase our costs to recover or reproduce the data.

Furthermore, security breaches or significant disruptions of our internal information technology systems or those of our third-party CROs, vendors and other contractors and consultants, could result in the loss, misappropriation and/or unauthorized access, use, or disclosure of, or the prevention of access to, confidential information (including trade secrets or other intellectual property, proprietary business information and personal information), which could result in financial, legal, business and reputational harm to us. For example, any such event that leads to unauthorized access, use, or disclosure of personal information, including personal information regarding our clinical trial subjects or employees, could harm our reputation directly, compel us to comply with federal and/or state breach notification laws and foreign law equivalents, subject us to mandatory corrective action, and otherwise subject us to liability under laws and regulations that protect the privacy and security of personal information, which could result in significant legal and financial exposure and reputational damages that could potentially have an adverse effect on our business.

A pandemic, epidemic or outbreak of an infectious disease, such as COVID-19, may materially and adversely affect our business and could cause a disruption to the development of our therapeutic candidates.

The ongoing COVID-19 pandemic has broadly affected the global economy, resulted in significant travel and work restrictions in many regions and has put a significant strain on healthcare resources. The ultimate extent of the impact of the COVID-19 pandemic on our business, financial condition and results of operations is highly uncertain and will depend on continued developments and actions taken by government authorities and businesses to contain or prevent the further spread of ongoing COVID-19 and its variants. The continuation of the worldwide COVID-19 pandemic may affect our ability to initiate and complete preclinical studies, delay the initiation of our planned clinical trials, disrupt regulatory activities or have other adverse effects on our business, results of operations, financial condition and prospects. In addition, the COVID-19 pandemic has adversely impacted economies worldwide and may continue to cause substantial disruption in the financial markets and global supply chains, all of which could adversely affect our business, operations and ability to raise funds to support our operations. While the increased prevalence of vaccinations and treatments have allowed for the partial reopening of the economy, the pandemic continues to be unpredictable. The emergence of additional variants, as well as reduced efficacy of vaccines over time and the possibility that a large number of people decline to get vaccinated or receive booster shots, creates inherent uncertainty as to the future of our business, our industry and the economy in general in light of the pandemic.

To date, we have not experienced a material financial impact or significant business disruptions, including with our vendors, or impairments of any of our assets as a result of the ongoing COVID-19 pandemic. We are following, and plan to continue to follow, recommendations from federal, state and local governments regarding workplace policies, practices and procedures. We have implemented temporary precautionary measures intended to help minimize the risk of the virus to our employees, including providing for social distancing, increased sanitization of our facilities, and providing access to rapid testing and personal protective equipment for our employees. We expect to continue to take actions as may be required or recommended by government authorities or as we determine are in the best interests of our employees and other business partners. We are continuing to monitor the potential impact of the COVID-19 pandemic, but even though many states within the U.S. are easing COVID-19 related restrictions, we cannot be certain what the overall impact of the ongoing COVID-19 pandemic will be on our business, financial condition, results of operations and prospects.

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

We are early in our development efforts. We have never successfully completed any clinical trials, and if we are unable to identify and advance therapeutic candidates through preclinical studies and small molecule clinical trials, obtain marketing approval and ultimately commercialize them, or experience significant delays in doing so, our business will be materially harmed.

We are early in our development efforts, and we have not yet demonstrated our ability to successfully complete any clinical trials, including large-scale, pivotal clinical trials, obtain regulatory approvals, manufacture a commercial scale product, or arrange for a third party to do so on our behalf, or conduct sales and marketing activities necessary for successful commercialization. We have invested substantially all of our research efforts to date in identifying potential therapeutic candidates and conducting preclinical studies. As an organization, we are in the process of conducting our first Phase 1 interventional clinical trial in healthy volunteers. Our lead therapeutic candidate, VGL101, is our only product candidate in Phase 1 clinical development for ALSP. We continue to engage with the FDA regarding the partial clinical hold at doses above 20 mg/kg. We initiated our Phase 1 trial in December 2021, and as of today, we have completed dosing of the 20 mg/kg SAD cohort without any safety signals observed and are currently dosing the 20 mg/kg MAD cohort. We believe that 20 mg/kg is a clinically-relevant dose in ALSP. In addition, we have a small molecule program that is in an earlier stage of development, for which we have not yet completed IND-enabling studies. We may never advance these or any future therapeutic candidates through IND-enabling studies or receive clearance from the FDA to commence clinical trials for our therapeutic 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 therapeutic 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.

As a general matter, commencing clinical trials in the U.S. is subject to acceptance by the FDA of an IND and finalizing the trial design based on discussions with the FDA and other regulatory authorities. For the FDA to accept an IND, we must complete toxicology and other preclinical studies pursuant to Good Laboratory Practices (GLPs), which may not be successful, or may take longer than we expect. The FDA may require us to complete additional preclinical studies or we may be required to satisfy other FDA requests prior to commencing clinical trials, and such requests may not currently be known or anticipated, which may cause the start of our first clinical trials to be delayed or prevent us from conducting clinical trials. Even after we receive and incorporate guidance from these regulatory authorities, the FDA or other regulatory authorities could disagree that we have satisfied their requirements to commence any clinical trial or change their position on the acceptability of our trial design or the clinical endpoints selected, which may require us to complete additional preclinical studies or clinical trials, impose stricter conditions than we currently expect or may prevent us from conducting clinical trials. There are equivalent processes and risks applicable to clinical trial applications in other countries, including countries in the European Union (EU).

The success of therapeutic candidates we may identify and develop will depend on many factors, including:

- timely and successful completion of preclinical studies, including toxicology studies, biodistribution studies and minimally efficacious dose studies in animals, where applicable, in accordance with FDA's GLPs and any additional regulatory requirements from foreign regulatory authorities;
- successful initiation, enrollment and completion of clinical trials, including under the FDA's Good Clinical Practices (GCPs) and any additional regulatory requirements from foreign regulatory authorities;
- positive results from our future clinical trials that support a finding of safety and effectiveness and an acceptable risk-benefit profile in the intended populations;
- sufficiency of our financial and other resources to complete the necessary preclinical studies and clinical trials;
- receipt of regulatory marketing approvals from applicable regulatory authorities;
- effective INDs or comparable foreign applications that allow commencement of our planned clinical trials or future clinical trials for any therapeutic candidates we may develop;
- establishment of arrangements with current Good Manufacturing Practice (cGMP) compliant third-party manufacturers for clinical supply and, where applicable, commercial manufacturing capabilities;
- establishment, maintenance, defense and enforcement of patent, trademark, trade secret and other intellectual property protection or regulatory exclusivity for any therapeutic candidates we may develop;
- patient recruitment, enrollment and retention;
- commercial launch of any therapeutic candidates we may develop, if approved, whether alone or in collaboration with others;
- acceptance of the benefits and use of our therapeutic candidates we may develop, including method of administration, if and when approved, by patients, the medical community and third-party payors;
- our ability to compete effectively with other therapies and treatment options;
- demonstration of an acceptable safety, tolerability and efficacy profile of any therapeutic candidates we may develop following approval; and
- establishment and maintenance of healthcare coverage and adequate reimbursement by payors.

If we do not succeed in one or more of these factors in a timely manner or at all, we could experience significant delays or an inability to successfully commercialize any therapeutic candidates we may develop, which would materially harm our business. If we are unable to advance our therapeutic candidates to clinical development, obtain regulatory approval and ultimately commercialize our therapeutic candidates, or experience significant delays in doing so, our business will be materially harmed.

We may expend our limited resources to pursue a particular therapeutic candidate or indication, such as our initial focus on developing VGL101, and fail to capitalize on therapeutic candidates or indications that may be more profitable or for which there is a greater likelihood of success. As such, our business is highly dependent on the clinical advancement of our programs and is especially dependent on the success of our lead candidate, VGL101.

One of our strategies is to identify and pursue clinical development of additional therapeutic candidates. Given our limited human capital and financial resources, we must focus on research programs and therapeutic candidates that we identify for specific indications. As a result, we may forego or delay pursuit of opportunities with other therapeutic candidates or for other indications that later prove to

have greater commercial potential. We are highly dependent on the success of the future clinical trials of VGL101, our lead therapeutic candidate, the outcomes of which are uncertain, to further develop our pipeline candidates for common neurodegenerative disease starting from patient segments with known genetic variations associated with microglial dysfunction. Because VGL101 is our first therapeutic candidate, if it encounters safety, efficacy, supply or manufacturing problems, developmental delays, regulatory or commercialization issues or other problems, the value of our pipeline could be greatly diminished and our development plans could be curtailed and our business would be significantly harmed.

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 therapeutic candidates for specific indications may not yield any commercially viable therapeutic candidates. If we do not accurately evaluate the commercial potential or target market for a particular therapeutic candidate or misread trends in the biopharmaceutical industry, in particular for neurodegenerative diseases, we may relinquish valuable rights to that therapeutic 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 therapeutic candidate.

At any time and for any reason, we may determine that one or more of our discovery programs or pre-clinical or clinical therapeutic candidates or programs does not have sufficient potential to warrant the allocation of resources toward such program or therapeutic candidate. Accordingly, we may choose not to develop a potential therapeutic candidate or elect to suspend, deprioritize or terminate one or more of our discovery programs or preclinical or clinical therapeutic candidates or programs. Suspending, deprioritizing or terminating a program or therapeutic candidate in which we have invested significant resources, means we will have expended resources on a program that will not provide a full return on our investment and may have missed the opportunity to have allocated those resources to potentially more productive uses, including existing or future programs or therapeutic candidates.

We have concentrated a substantial portion of our research and development efforts on the treatment of neurodegenerative diseases, a field that has seen limited success in drug development. Further, our therapeutic candidates are based on new approaches, which makes it difficult to predict the time and cost of therapeutic candidate development and subsequently obtaining regulatory approval.

We have focused our research and development efforts on therapeutic approaches for neurodegenerative diseases. Collectively, efforts by biopharmaceutical companies in the field of neurodegenerative diseases have seen limited success in drug development. No effective therapeutic options are available for patients with ALSP, and limited options exist for Alzheimer's disease and other neurodegenerative diseases. Our future success is highly dependent on the successful development of our therapeutic candidates for treating neurodegenerative diseases. Developing our therapeutic candidates for treatment of neurodegenerative diseases subjects us to a number of challenges, including demonstrating safety and efficacy and obtaining regulatory approval from the FDA and other regulatory authorities who have only a limited set of precedents to rely on.

We are pursuing a precision medicine approach to developing a broad range of therapeutics for neurodegenerative diseases. By targeting rare genetically defined neurodegenerative microgliopathies, our strategy is to advance our pipeline by reducing downstream translational risk, efficiently generating clinical PoM and PoC and expanding into multiple neurodegenerative indications where microglia-based therapeutics may have meaningful impact on disease progression and patient lives. This strategy may not prove to be successful. We cannot be sure that our approach will yield satisfactory therapeutic products that are safe and effective, scalable, or profitable.

We may conduct clinical trials that utilize an "open-label" trial, which are subject to various limitations that may exaggerate therapeutic effect or influence reporting of adverse events as patients in open-label clinical trials are aware when they are receiving treatment.

We may conduct clinical trials that utilize an "open-label" trial design. An "open-label" clinical trial is one where both the patient and investigator know whether the patient is receiving the investigational therapeutic candidate or an existing approved drug or placebo. Most typically, open-label clinical trials test only the investigational therapeutic candidate and sometimes may do so at different dose levels. Open-label clinical trials are subject to various limitations that may exaggerate any therapeutic effect as patients in open-label clinical trials are aware when they are receiving treatment. Open-label clinical trials may be subject to a "patient bias" where patients perceive their symptoms to have improved merely due to their awareness of receiving an experimental treatment. In addition, open-label clinical trials may be subject to an "investigator bias" where those assessing and reviewing the physiological outcomes of the clinical trials are aware of which patients have received treatment and may interpret the information of the treated group more favorably given this knowledge. On the other hand, patients who know that they are receiving an experimental treatment may expect and report negative outcomes, which may influence the reporting of adverse events during an open-label trial. The results from an open-label trial may not be predictive of future clinical trial results with any of our therapeutic candidates for which we include an open-label clinical trial when studied in a controlled environment with a placebo or active control.

We may fail to demonstrate safety and efficacy to the satisfaction of applicable regulatory authorities, which could prevent us from commercializing any therapeutic candidates we develop on a timely basis, if at all.

The risk of failure in developing therapeutic candidates is high. It is impossible to predict when or if any therapeutic candidate would prove effective or safe in humans or will receive regulatory approval. Before obtaining marketing approval from regulatory authorities for the sale of any therapeutic candidate, we must complete preclinical development, submit an IND or foreign equivalent to permit initiation of clinical studies, and then conduct extensive clinical trials to demonstrate the safety and efficacy of therapeutic candidates in humans. We initiated a first-in-human clinical trial for VGL101 in healthy volunteers in December 2021 and have identified a second rare microgliopathy, cALD, for which we plan to submit an IND amendment or additional IND, if required, to conduct a Phase 2 trial. We have limited experience as a company in preparing and submitting regulatory filings and have not previously submitted a new drug application (NDA), or a biologics license application (BLA), or other comparable foreign regulatory submission for any therapeutic candidate.

Before we can commence clinical trials for a therapeutic candidate, we must complete extensive preclinical testing and studies that support our INDs and other regulatory filings, as we did with our IND for VGL101 in ALSP. We cannot be certain of the timely identification of a therapeutic candidate or the completion or outcome of our preclinical testing and studies and cannot predict whether the FDA will accept our proposed clinical programs or whether the outcome of our preclinical testing and studies will ultimately support the further development of any therapeutic candidates. Conducting preclinical testing is a lengthy, time-consuming and expensive process. The length of time may vary substantially according to the type, complexity and novelty of the program, and often can be several years or more per program. As a result, we cannot be sure that we will be able to submit INDs for our preclinical programs on the timelines we expect, if at all, and we cannot be sure that submission of INDs will result in the FDA allowing clinical trials to begin.

Clinical trials are expensive, difficult to design and implement and can take many years to complete, and their outcome is inherently uncertain. A failure of one or more clinical trials can occur at any stage of testing, which may result from a multitude of factors, including, but not limited to, flaws in trial design, dose selection issues, patient enrollment criteria and failure to demonstrate favorable safety or efficacy traits. No therapeutic has been approved for the treatment of ALSP and the regulatory pathway for approval of a therapeutic for ALSP is uncertain. Given the lack of precedent, we may encounter difficulties in identifying and establishing clinical endpoints that FDA would consider clinically meaningful. Moreover, we have had limited interactions with the FDA and cannot be certain how many clinical trials of VGL101 or any other therapeutic candidates will be required or how such trials should be designed. Even after the FDA has received and commented on the design for our clinical trials, the agency may disagree with our clinical trial design and our interpretation of data from clinical trials, or may change the requirements for approval. Consequently, despite future regulatory interactions and advice, we may be unable to successfully and efficiently execute and complete necessary clinical trials in a way that leads to regulatory submission and approval of any of our therapeutic candidates. Additionally, because our initial target indications are rare diseases, we may face challenges identifying patients and enrolling clinical trials, which may delay or prevent completion of such trials. Clinical trials also may fail to demonstrate that our therapeutic candidates are safe for humans and effective for indicated uses. Successful completion of clinical trials is a prerequisite to submitting an NDA or BLA to the FDA or similar marketing applications to other regulatory authorities for each therapeutic candidate. Even if the clinical trials are successful, changes in marketing approval policies during the development period, changes in or the enactment or promulgation of additional statutes, regulations or guidance or changes in regulatory review for each submitted product application may cause delays in the approval or rejection of an application.

Other events that may prevent successful enrollment, initiation or timely completion of clinical development include:

- we may be unable to generate sufficient preclinical, toxicology or other *in vivo* or *in vitro* data to support the initiation of clinical trials;
- delays in reaching a consensus with regulatory authorities on trial design;
- delays in reaching agreement on acceptable terms with prospective CROs and clinical trial sites;
- delays in opening clinical trial sites or obtaining required institutional review board (IRB) or independent ethics committee approval, or the equivalent review groups for sites outside the U.S., at each clinical trial site;
- imposition of a clinical hold by regulatory authorities, including as a result of a serious adverse event or after an inspection of our clinical trial operations or trial sites;
- challenges identifying, enrolling and retaining participants in clinical trials;
- negative or inconclusive results observed in clinical trials, including failure to demonstrate statistical significance, safety, purity or potency, which could lead us, or cause regulators to require us, to conduct additional clinical trials or abandon product development programs;

- failure by us, any CROs we engage or any other third parties to adhere to clinical trial requirements and clinical trial protocols or to perform in accordance with the FDA's GCPs;
- failure by physicians to adhere to delivery protocols leading to variable results;
- delays in the testing, validation, manufacturing and delivery of any therapeutic candidates we may develop to the clinical sites, including delays by third parties with whom we have contracted to perform certain of those functions;
- failure of our third-party contractors to comply with regulatory requirements or to meet their contractual obligations to us in a timely manner, or at all;
- delays in having patients complete participation in a trial or return for post-treatment follow-up;
- issues with our clinical trial sites or patients dropping out of a trial;
- we may need to add new or additional clinical trial sites;
- selection of clinical endpoints that require prolonged periods of clinical observation or analysis of the resulting data;
- inability of selected endpoints to capture therapeutic benefit of the therapeutic candidate;
- occurrence of serious adverse events associated with the therapeutic candidate that are viewed to outweigh its potential benefits;
- occurrence of serious adverse events associated with a therapeutic candidate in development by another company, which are viewed to outweigh its potential benefits, and which may negatively impact the perception of our therapeutic candidate due to a similarity in technology or approach;
- changes in regulatory requirements and guidance that require amending or submitting new clinical protocols;
- the FDA or other regulatory authorities may require us to submit additional data such as long-term toxicology studies or impose other requirements before permitting us to initiate a clinical trial;
- changes in the legal or regulatory regimes domestically or internationally related to patient rights and privacy; or
- lack of adequate funding to continue the clinical trial.

We may encounter substantial delays in the commencement, enrollment or completion of our planned clinical trials, which could prevent us from receiving necessary regulatory approvals or commercializing any therapeutic candidates we develop on a timely basis, if at all.

We could encounter delays in our development plans when a clinical trial is suspended, placed on clinical hold or terminated by us, the IRBs of the institutions in which such trials are being conducted, or the FDA or other regulatory authorities or recommended for suspension or termination by the Data Safety Monitoring Board (DSMB) for such trial. A suspension or termination may be imposed due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA or other regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a product candidate or treatment, failure to establish or achieve clinically meaningful trial endpoints, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial. We continue to engage with the FDA regarding the partial clinical hold at doses above 20 mg/kg. Accordingly, we submitted data to the FDA from a 6-month GLP toxicology study in nonhuman primates in which we observed no adverse findings and Phase 1 SAD clinical data. We initiated our Phase 1 trial in December 2021, and as of today, we have completed dosing of the 20 mg/kg SAD cohort without any safety signals and are currently dosing the 20 mg/kg MAD cohort. We believe that 20 mg/kg is a clinically-relevant dose in ALSP. However, if changes in our understanding of the therapeutic concentrations of VGL101 necessitate exploration of doses above 20 mg/kg, and we are unable to reach agreement with the FDA to lift the partial clinical hold, we would be unable to complete our clinical trials of VGL101 in ALSP patients without delays in our clinical development plans and additional clinical development costs, which could impair our ability to obtain U.S. regulatory approval for VGL101.

Additionally, if the results of future clinical trials are inconclusive, we may be required to perform additional clinical trials to support approval. Many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of our therapeutic candidates.

Failure to locate and enroll a sufficient number of eligible patients to participate in clinical trials as required by the FDA or similar regulatory authorities outside the U.S. may delay or prevent us from initiating or continuing clinical trials fo25,657,096r our therapeutic candidates. Because the target patient populations for some of our therapeutic candidates, in particular for rare diseases such as the ones on which we are initially focused, are relatively small, it may be difficult to successfully identify patients for inclusion in clinical trials. This is especially important as we intend to offer to the volunteers of our natural history study enrollment in our planned interventional clinical trial in patients with ALSP and therefore any potential delays in enrollment could have adverse consequences for our planned clinical development program for VGL101.

In addition, we may experience delays or disruptions in the initiation of or enrollment in our planned clinical trials due to the COVID-19 pandemic and changes in local site or IRB policies, availabilities or changes of site staff, reprioritization of hospital resources, restricted access to healthcare professionals and testing sites and other containment measures or concerns among patients about participating in clinical trials during a pandemic. Furthermore, some of our competitors have ongoing clinical trials for therapeutic candidates that treat the same indications we plan to target with our therapeutic candidates, such as Alzheimer's disease and cALD, and may in the future initiate trials in our lead indication, ALSP. Accordingly, patients who would otherwise be eligible for our clinical trials may instead enroll in clinical trials of our competitors' therapeutic candidates. Patient enrollment and trial competition may be affected by other factors including:

- clinicians' and patients' perceived risks and benefits of the therapeutic candidate under trial, particularly therapeutic candidates developed using a novel and unproven therapeutic approach, such as VGL101, in relation to available or investigational drugs;
- clinicians' misdiagnosis of patients with existing neurodegenerative diseases in our targeted indications and our inability to recruit these patients successfully;
- design of the trial protocol;
- efforts to facilitate timely enrollment in clinical trials;
- eligibility and exclusion criteria;
- availability of competing therapies and clinical trials;
- severity of the disease or disorder under investigation;
- proximity and availability of clinical trial sites for prospective patients;
- ability to obtain and maintain patient consent;
- size of the patient population required for analysis of the trial's primary endpoints;
- ability to recruit clinical trial investigators with the appropriate competencies and experience;
- risk that enrolled patients will drop out before completion of the trial;
- performance of third party vendors, including CROs;
- patient referral practices of physicians; and
- ability to monitor patients adequately during and after treatment.

Our inability to identify patients appropriate for enrollment in our observational and interventional clinical trials, or to enroll a sufficient number of patients in such trials, would result in significant delays and could require us to abandon one or more clinical trials altogether. Enrollment delays in our clinical trials may result in increased development costs for our therapeutic candidates, which would cause the value of our company to decline and limit our ability to obtain additional financing. If we are unable to include symptomatic patients with the applicable genetic mutations and/or variations, this could limit our ability to seek participation in the FDA's expedited development programs, including breakthrough therapy designation and fast track designation, or otherwise to seek to accelerate clinical development and regulatory timelines.

Even if we are able to enroll a sufficient number of patients for our clinical trials, we may have difficulty retaining patients in our clinical trials. In our planned clinical trials that will include a placebo group, some of patients may perceive that they are not receiving the therapeutic candidate being tested, and they may decide to withdraw from our clinical trials to pursue other alternative therapies rather than continue the trial with the perception that they are receiving placebo. Difficulty enrolling or retaining a sufficient number of patients to conduct our clinical trials, may require us to delay, limit or terminate clinical trials, any of which would harm our business, financial condition, results of operations and prospects.

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

Use of our therapeutic candidates could be associated with side effects, adverse events or other properties or safety risks, which could delay or preclude approval, cause us to suspend or discontinue clinical trials, abandon a therapeutic candidate, limit the commercial profile of an approved label or result in other significant negative consequences that could severely harm our business, prospects, operating results and financial condition.

We have not yet completed interventional clinical trials of any of our therapeutic candidates, and our understanding of the clinical safety profile of these candidates is still limited. There may be serious adverse events or undesirable side effects related to our therapeutic candidates. To our knowledge, no approved products target TREM2 and no TREM2 agonists are in clinical development for ALSP. Moreover, it is impossible to predict when or if any therapeutic candidates we may develop will prove safe in humans. As is the case with biopharmaceuticals generally, it is likely that there may be side effects and adverse events associated with use of our therapeutic candidates. Results of our clinical trials could reveal a high and unacceptable severity and prevalence of side effects or unexpected characteristics. Undesirable side effects caused by our therapeutic candidates could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA or comparable foreign regulatory authorities. The drug-related side effects could affect patient recruitment or the ability of enrolled patients to complete the trial or result in potential product liability claims. Any of these occurrences may significantly harm our business, financial condition and prospects.

Further, clinical trials by their nature utilize a sample of the potential patient population. With a limited number of patients and limited duration of exposure, rare and severe side effects of our therapeutic candidates may only be uncovered with a significantly larger number of patients exposed to the therapeutic candidate. Any undesirable side effects or unexpected characteristics associated with our therapeutic candidates in clinical trials may lead us to elect to abandon their development or limit their development to more narrow uses or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective, which may limit the commercial expectations for the therapeutic candidate, if approved. We may also be required to modify our trial plans based on findings after we commence our clinical trials. Many compounds that initially showed promise in early-stage testing have later been found to cause side effects that prevented further development of the compound. In addition, regulatory authorities may draw different conclusions or require additional testing to confirm these determinations.

As we test our therapeutic candidates in larger, longer and more extensive clinical trials, or as the use of these therapeutic candidates becomes more widespread if they receive regulatory approval, illnesses, injuries, discomforts and other adverse events that were observed in earlier trials, as well as conditions that did not occur or went undetected in previous trials, may be reported. Any findings of such side effects later in development or following any approval may harm our business, financial condition and prospects significantly.

Patients treated with our therapeutics, if approved, may experience previously unreported adverse reactions, and the FDA or other regulatory authorities may ask for additional safety data as a condition of, or in connection with, our efforts to obtain approval of our therapeutic candidates.

If safety problems occur or are identified after our therapeutics reach the market, if any, we may make the decision or be required by regulatory authorities to amend the labeling of our therapeutics, recall our therapeutics or even withdraw approval for our therapeutics.

If there are safety concerns or serious adverse events associated with any therapeutic candidates we may develop, we may:

- be delayed in obtaining marketing approval for therapeutic candidates, if at all;
- obtain approval for indications or patient populations that are not as broad as intended or desired;
- obtain approval with labeling that includes significant use or distribution restrictions or safety warnings;
- be subject to changes in the way the product is administered;
- be required to perform additional clinical trials to support approval or be subject to additional post- marketing testing requirements;
- have regulatory authorities withdraw, or suspend, their approval of the product or impose restrictions on its distribution in the form of a modified risk evaluation and mitigation strategy (REMS);
- be subject to the addition of labeling statements, such as warnings or contraindications;
- be sued; or
- experience damage to our reputation.

Our therapeutic candidates are subject to extensive regulation and compliance, which is costly and time-consuming, and such regulation may cause unanticipated delays or prevent the receipt of the required approvals to commercialize our therapeutic candidates.

The clinical research, development, manufacturing, labeling, packaging, storage, record-keeping, advertising, promotion, import, export, marketing, distribution and adverse event reporting, including the submission of safety and other information, of our therapeutic candidates are subject to extensive regulation by the FDA in the U.S. and by comparable foreign regulatory authorities in foreign markets. In the U.S., we are not permitted to market our therapeutic candidates until we receive regulatory approval from the FDA. The process of obtaining regulatory approval is expensive, often takes many years following the commencement of clinical trials and can vary substantially based upon the type, complexity and novelty of the therapeutic candidates involved, as well as the target indications and patient population. Approval policies or regulations may change, and the FDA has substantial discretion in the drug approval process, including the ability to delay, limit or deny approval of a therapeutic candidate for many reasons. Despite the time and expense invested in clinical development of therapeutic candidates, regulatory approval is never guaranteed. Neither we nor any current or future collaborator is permitted to market any of our therapeutic candidates in the U.S. until we receive approval from the FDA.

The FDA or comparable foreign regulatory authorities can delay, limit or deny approval of a therapeutic candidate for many reasons, including:

- we or any of our current or future collaborators may be unable to demonstrate that a therapeutic candidate is safe and effective, and that therapeutic candidate's clinical and other benefits outweigh its safety risks;
- serious and unexpected drug-related side effects may be experienced by participants in our clinical trials or by individuals using drugs similar to our therapeutic candidates;
- such authorities may disagree with the design or implementation of our or our current or future collaborators' clinical trials;
- negative or ambiguous results from our clinical trials or results may not meet the level of statistical significance required by the FDA or comparable foreign regulatory agencies for approval;
- such authorities may not accept clinical data from trials which are conducted at clinical facilities or in countries where the standard of care is potentially different from that of the U.S.;
- such authorities may disagree with our interpretation of data from preclinical studies or clinical trials;
- such authorities may not agree that the data collected from clinical trials of our therapeutic candidates are acceptable or sufficient to support the submission of an NDA or BLA or other submission or to obtain regulatory approval in the U.S. or elsewhere, and such authorities may impose requirements for additional preclinical studies or clinical trials;
- such authorities may disagree regarding the formulation, labeling and/or the specifications of our therapeutic candidates;
- approval may be granted only for indications that are significantly more limited than what we apply for and/or with other significant restrictions on distribution and use;
- such authorities may find deficiencies in the manufacturing processes, approval policies or facilities of our third-party manufacturers with which we or any of our current or future collaborators contract for clinical and commercial supplies;
- regulations of such authorities may significantly change in a manner rendering our or any of our potential future collaborators' clinical data insufficient for approval; or
- such authorities may not accept a submission due to, among other reasons, the content or formatting of the submission.

With respect to foreign markets, approval procedures vary among countries and, in addition to the foregoing risks, may involve additional product testing, administrative review periods and agreements with pricing authorities. In addition, events raising questions about the safety of certain marketed biopharmaceuticals may result in increased cautiousness by the FDA and comparable foreign regulatory authorities in reviewing new drugs based on safety, efficacy or other regulatory considerations and may result in significant delays in obtaining regulatory approvals. Any delay in obtaining, or inability to obtain, applicable regulatory approvals would prevent us or any of our potential future collaborators from commercializing our therapeutic candidates.

The results of preclinical studies are not necessarily predictive of the results of later preclinical studies and any clinical trials of our therapeutic candidates, and interim, topline and preliminary data from our preclinical studies and planned clinical trials that we announce or publish from time to time may change as more data become available and are subject to audit and verification procedures that could result in material changes in the final data.

The results from preclinical studies of a therapeutic candidate may not predict the results of later preclinical studies and any clinical trials of the therapeutic candidate. Therapeutic candidates in later stages of clinical trials may fail to show the desired safety and efficacy characteristics despite having progressed through preclinical studies and initial clinical trials. In particular, while we have conducted certain preclinical studies of VGL101 and other potential therapeutic candidates, we do not know whether VGL101 or the other potential therapeutic candidates will perform in future clinical trials as they have performed in prior preclinical studies. The positive results we have observed for our therapeutic candidates in early, GLP and non-GLP preclinical studies, animal and *in vitro* models may not be predictive of our future clinical trials in humans. This may be a result of technical challenges unique to that program or due to biology risk, which is unique to every program. As we progress our programs through clinical development, there may be new technical challenges that arise that cause an entire program to fail. Furthermore, for some indications that we are pursuing there are no animal models that adequately mirror the human disease to predict any level of positive results. Unexpected observations or toxicities observed in these studies, or in IND-enabling studies for any of our other development programs, could delay clinical trials for VGL101 or our other development programs.

From time to time, we may publicly disclose interim, preliminary or topline data from our preclinical studies and planned clinical trials, which are 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. 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. Additionally, interim, topline or preliminary 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, topline or interim data and final data could significantly harm our business prospects.

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 therapeutic candidate or product and the value of our company in general. A number of companies in the biopharmaceutical and biotechnology industries have suffered significant setbacks in clinical development even after achieving promising results in earlier studies, and companies that have believed their therapeutic candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain FDA approval. In addition, the information we choose to publicly disclose regarding a particular study or clinical trial will be based on what is typically extensive information, and you or others may not agree with what we determine is the material or otherwise appropriate information to include in our disclosure, and any information we determine not to disclose may ultimately be deemed significant with respect to future decisions, conclusions, views, activities or otherwise regarding a particular product, therapeutic candidate or our business. If the topline 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 therapeutic candidates may be harmed, which could harm our business, operating results, prospects or financial condition.

We may not be successful in our efforts to expand our pipeline of therapeutic candidates.

We believe the central role that microglia play in sensing and coordinating the response to tissue damage and disease provides therapeutic opportunities for many neurodegenerative diseases, either through TREM2 activation or potentially other microglia targets. Over time, we plan to expand our pipeline, either through internal discovery and development, or through strategic collaborations or alliances with academic organizations, pharmaceutical or biotechnology companies.

Although our research and development efforts to date have resulted in a pipeline of potential programs and therapeutic candidate, we may not be able to identify other microglia targets and develop therapeutic candidates. We may also pursue opportunities to acquire or in-license additional businesses, technologies or therapeutic candidates, form strategic alliances or create joint ventures with third parties to complement or augment our existing business. However, we may not be able to identify any therapeutic candidates for our pipeline through such acquisition or in-license.

Even if we are successful in continuing to build and expand our pipeline, the potential therapeutic candidates that we identify may not be suitable for clinical development. For example, they may be shown to have harmful side effects or other characteristics that indicate that they are unlikely to be drugs that will be successful in clinical trials or receive marketing approval and achieve market acceptance. If we do not successfully develop and commercialize therapeutic candidates, we will not be able to obtain drug revenues in future periods, which likely would result in significant harm to our financial position and adversely affect our stock price.

Clinical trial and product liability lawsuits against us could divert our resources, could cause us to incur substantial liabilities and could limit commercialization of any therapeutic candidates we may develop.

We will face an inherent risk of clinical trial and product liability exposure related to the testing of any therapeutic candidates we may develop in clinical trials, and we will face an even greater risk if we commercially sell any products that we may develop. The future use of therapeutic candidates by us in clinical trials, and the sale of any approved products in the future, may expose us to liability claims. These claims might be made by patients that use the product, healthcare providers, pharmaceutical companies or others selling such products. If we cannot successfully defend ourselves against claims that our therapeutic candidates or products caused injuries, we will incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- decreased demand for any therapeutic candidates we may develop;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial participants and inability to continue clinical trials;
- initiation of investigations by regulators;
- significant costs to defend any related litigation;
- substantial monetary awards to trial participants or patients;
- product recalls, withdrawals or labeling, marketing or promotional restrictions;
- loss of revenue;
- exhaustion of any available insurance and our capital resources;
- decline in our stock price;
- reduced resources of our management to pursue our business strategy; and
- the inability to commercialize any therapeutic candidates we may develop.

We will need to increase our insurance coverage if we expand our clinical trial activities and if we commence commercialization of any therapeutic candidates. Insurance coverage is increasingly expensive. We may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise. If and when coverage is secured, our insurance policies may also have various exclusions and we may be subject to a product liability claim for which we have no coverage.

Even if our agreements with any future corporate collaborators entitle us to indemnification against losses, such indemnification may not be available or adequate should any claim arise, nor would such indemnity insulate us from potential reputational damage. If a successful clinical trial or product liability claim or series of claims is brought against us for uninsured liabilities or in excess of insured liabilities, our assets may not be sufficient to cover such claims and our business operations could be impaired.

We may develop our current or future therapeutic candidates in combination with other therapies, which would expose us to additional risks.

We may develop our current or potential future therapeutic candidates in combination with one or more currently approved therapies or therapies in development. Even if any of our current or future therapeutic candidates were to receive marketing approval or be commercialized for use in combination with other existing therapies, we would continue to be subject to the risks that the FDA, EMA or other comparable foreign regulatory authorities could revoke approval of the therapy used in combination with any of our therapeutic candidates, or safety, efficacy, manufacturing or supply issues could arise with these existing therapies, which could affect the status of our product candidates used in combination with these therapies. In addition, it is possible that in the future, existing therapies with which our therapeutic candidates are then approved for use could themselves fall out of favor or be relegated to later lines of treatment. This could result in the need to identify other combination therapies for our therapeutic candidates or our own products being removed from the market or being less successful commercially.

We may also evaluate our current or future therapeutic candidates in combination with one or more other therapies that have not yet been approved for marketing by the FDA, EMA or comparable foreign regulatory authorities. We will not be able to market and sell any therapeutic candidate in combination with any such unapproved therapies that do not ultimately obtain marketing approval.

Furthermore, we cannot be certain that we will be able to obtain a steady supply of such therapies for use in developing combinations with our therapeutic candidates on commercially reasonable terms or at all. Any failure to obtain such therapies for use in clinical development and the expense of purchasing therapies in the market may delay our development timelines, increase our costs

and jeopardize our ability to develop our therapeutic candidates as commercially viable therapies. If the FDA, EMA or other comparable foreign regulatory authorities do not approve or withdraw their approval of these other therapies, or if safety, efficacy, commercial adoption, manufacturing or supply issues arise with the therapies we choose to evaluate in combination with any of our current or future therapeutic candidates, we may be unable to obtain approval of or successfully market any one or all of the current or future therapeutic candidates we develop. Additionally, if the third-party providers of therapies or therapies in development used in combination with our current or future therapeutic candidates are unable to produce sufficient quantities for clinical trials or for commercialization of our current or future therapeutic candidates, or if the cost of combination therapies are prohibitive, our development and commercialization efforts would be impaired, which would have an adverse effect on our business, financial condition, results of operations and growth prospects.

Where appropriate, we plan to secure approval from the FDA, EMA or comparable foreign regulatory authorities through the use of expedited approval pathways, such as accelerated approval. If we are unable to obtain such approvals, we may be required to conduct additional preclinical studies or clinical trials beyond those that we contemplate, which could increase the expense of obtaining, and delay the receipt of, necessary marketing approvals. Even if we receive accelerated approval from the FDA, EMA or comparable regulatory authorities, if our confirmatory trials do not verify clinical benefit, or if we do not comply with rigorous post-marketing requirements, the FDA, EMA or such other regulatory authorities may seek to withdraw the accelerated approval.

Where possible, we plan to pursue accelerated development strategies in areas of high unmet need. We may seek an accelerated approval pathway for our one or more of our therapeutic candidates from the FDA, EMA or comparable foreign regulatory authorities. Under the accelerated approval provisions in the Federal Food, Drug, and Cosmetic Act, and the FDA's implementing regulations, the FDA may grant accelerated approval to a therapeutic candidate designed to treat a serious or life- threatening condition that provides meaningful therapeutic benefit over available therapies upon a determination that the therapeutic candidate has an effect on a surrogate endpoint or intermediate clinical endpoint that is reasonably likely to predict clinical benefit. The FDA considers a clinical benefit to be a positive therapeutic effect that is clinically meaningful in the context of a given disease, such as irreversible morbidity or mortality. For the purposes of accelerated approval, a surrogate endpoint is a marker, such as a laboratory measurement, radiographic image, physical sign, or other measure that is thought to predict clinical benefit, but is not itself a measure of clinical benefit. An intermediate clinical endpoint is a clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit. The accelerated approval pathway may be used in cases in which the advantage of a new drug over available therapy may not be a direct therapeutic advantage, but is a clinically important improvement from a patient and public health perspective. If granted, accelerated approval is usually contingent on the sponsor's agreement to conduct, in a diligent manner, additional post-approval confirmatory studies to verify and describe the drug's clinical benefit. If such post-approval studies fail to confirm the drug's clinical benefit, the FDA may withdraw its approval of the drug.

Prior to seeking accelerated approval, we would seek feedback from the FDA, EMA or comparable foreign regulatory authorities and would otherwise evaluate our ability to seek and receive such accelerated approval. There can be no assurance that after our evaluation of the feedback and other factors we will decide to pursue or submit an NDA or BLA for accelerated approval or any other form of expedited development, review or approval. Similarly, there can be no assurance that after subsequent feedback from the FDA, EMA or comparable foreign regulatory authorities, we will continue to pursue or apply for accelerated approval or any other form of expedited development, review or approval, even if we initially decide to do so. Furthermore, if we decide to submit an application for accelerated approval, there can be no assurance that such application will be accepted or that any approval will be granted on a timely basis, or at all. The FDA, EMA or other comparable foreign regulatory authorities could also require us to conduct further studies prior to considering our application or granting approval of any type, including, for example, if other products are approved via the accelerated pathway and subsequently converted by FDA to full approval. A failure to obtain accelerated approval or any other form of expedited development, review or approval for our therapeutic candidate would result in a longer time period to commercialization of such therapeutic candidate, could increase the cost of development of such therapeutic candidate and could harm our competitive position in the marketplace. Moreover, even if we are able to obtain accelerated approval for any of our therapeutic candidates, there is no guarantee that post-approval studies will be able to confirm the clinical benefit, which could cause FDA to withdraw our approval.

We may seek fast track designation, breakthrough therapy designation, priority review and/or orphan drug designation from the FDA or similar designations from other regulatory authorities for one or more of our therapeutic candidates. Even if one or more of our therapeutic candidates receive any of these designations, we may be unable to obtain or maintain the benefits associated with such designation.

The FDA has established various designations to facilitate more rapid and efficient development and approval of certain types of drugs. Such designations include fast track designation, breakthrough therapy designation, priority review and orphan drug designation. Fast track designation is designed to facilitate the development and expedite the review of therapies for serious conditions that fill an unmet medical need. Programs with fast track designation may benefit from early and frequent communications with the FDA, potential priority review and the ability to submit a rolling application for regulatory review. Fast track designation applies to both the therapeutic

candidate and the specific indication for which it is being studied. If any of our therapeutic candidates receive fast track designation but do not continue to meet the criteria for fast track designation, or if our clinical trials are delayed, suspended or terminated, or put on clinical hold due to unexpected adverse events or issues with clinical supply or due to other issues, we will not receive the benefits associated with the fast track program. Fast track designation alone does not guarantee qualification for the FDA's priority review procedures.

A breakthrough therapy, on the other hand, is defined as a drug or biologic that is intended, alone or in combination with one or more other drugs or biologics, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the drug or biologic may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints. For therapeutic candidates that have been designated as breakthrough therapies, interaction and communication between the FDA and the sponsor of the trial can help to identify the most efficient path for clinical development while minimizing the number of patients placed in ineffective control regimens. Designation as a breakthrough therapy is within the discretion of the FDA, and drugs designated as breakthrough therapies by the FDA may also be eligible for other expedited approval programs, including accelerated approval and priority review. Even if one or more of our therapeutic candidates qualify as breakthrough therapies pursuant to FDA standards, the FDA may later decide that the product no longer meets the conditions for qualification. Thus, even though we may seek breakthrough therapy designation for one or more of our current or future therapeutic candidates, there can be no assurance that we will receive breakthrough therapy designation.

Even in the absence of obtaining fast track and/or breakthrough therapy designations, a sponsor can seek priority review at the time of submitting a marketing application. The FDA may designate a product for priority review if it is a product that treats a serious condition and, if approved, would provide a significant improvement in safety or effectiveness when compared with other available therapies. Significant improvement may be illustrated by evidence of increased effectiveness in the treatment of a condition, elimination or substantial reduction of a treatment-limiting adverse reaction, documented enhancement of patient compliance that may lead to improvement in serious outcomes, or evidence of safety and effectiveness in a new subpopulation. A priority review designation is intended to direct overall attention and resources to the evaluation of such applications, and to shorten the FDA's goal for taking action on a marketing application from ten months to six months. Priority review designation may be rescinded if a product no longer meets the qualifying criteria.

Regulatory authorities in some jurisdictions, including the U.S. and the EU, may also designate drugs for relatively small patient populations as orphan drugs. Under the Orphan Drug Act, the FDA may designate a therapeutic candidate as an orphan drug if it is a drug intended to treat a rare condition, which is generally defined as a patient population of fewer than 200,000 individuals annually in the U.S., or a patient population greater than 200,000 in the U.S. where there is no reasonable expectation that the cost of developing the drug will be recovered from sales in the U.S. In the EU, the EMA's Committee for Orphan Medicinal Products (COMP) evaluates orphan drug designation to promote the development of products that are intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition affecting not more than five in 10,000 persons in the EU. In the U.S., orphan drug designation entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages and user-fee waivers, and it may entitle the therapeutic to exclusivity in the U.S. and the EU. Regulatory authorities may not grant our requests for orphan designation, or may require submission of additional data before making such determination. For example, we submitted a request for orphan drug designation of VGL101 in May 2021, and FDA has requested clinical or additional *in vivo* animal data to facilitate the agency's review of this request. Even if we obtain orphan drug designation for a therapeutic candidate, we may not be able to obtain or maintain orphan drug exclusivity for that therapeutic candidate.

If any of our programs or therapeutic candidates receive fast track, breakthrough therapy, priority review, or orphan drug designation by the FDA or similar designations by other regulatory authorities, there is no assurance that we will receive any benefits from such programs or that we will continue to meet the criteria to maintain such designation. Even if we obtain such designations, we may not experience a faster development process, review or approval compared to conventional FDA procedures. A fast track, breakthrough therapy, priority review, or orphan drug designation does not ensure that a therapeutic candidate will receive marketing approval or that approval will be granted within any particular timeframe. In addition, the FDA may withdraw any such designation if it believes that the designation is no longer supported by data from our clinical development program.

Risks Related to Our Reliance on Third Parties

We may be required to make significant payments under our license agreement with Amgen Inc. for certain TREM2 agonists, and, if we breach our license agreement with Amgen related to these TREM2 agonists, we could lose the ability to continue the development and commercialization of TREM2 agonists.

In July 2020, we acquired an exclusive, royalty-bearing license to certain intellectual property rights owned or controlled by Amgen, to commercially develop, manufacture, use, distribute and sell therapeutic products containing compounds that bind to TREM2 (the Amgen Agreement). Under the Amgen Agreement, in consideration for the license, we made an upfront payment of $500,000 and

also issued 6,928,566 shares of our Series A preferred stock to Amgen at the time of the initial closing with a subsequent 1,963,093 shares of our Series A preferred stock issued at the time of the milestone closing. As additional consideration for the license, we are required to pay Amgen up to $80.0 million in the aggregate upon the achievement of specified regulatory milestones for the first monoclonal antibody TREM2 agonist (mAb) product and the first small molecule TREM2 agonist product and aggregate milestone payments of up to $350.0 million upon the achievement of specific commercial milestones across all such mAb products and small molecule products. No regulatory or commercial milestones have been achieved to date under the license agreement. We are also required to pay tiered royalties of low to mid single-digit percentages on annual net sales of the products covered by the license. If milestone or other non-royalty obligations become due, we may not have sufficient funds available to meet our obligations, which will materially adversely affect our business operations and financial condition. For more information on the terms of the license agreement with Amgen, see Note 11 to the condensed consolidated financial statements appearing elsewhere in this Quarterly Report.

We are dependent on patents, know-how and proprietary technology in-licensed from Amgen. Our commercial success depends upon our ability to develop, manufacture, market and sell our therapeutic candidate or any future therapeutic candidates and use our and our licensor's proprietary technologies without infringing the proprietary rights of third parties. Amgen may have the right to terminate the license agreement in full in the event we materially breach or default in the performance of any of the obligations under the license agreement. A termination of the license agreement with Amgen could result in the loss of significant rights and could harm our ability to develop and commercialize our therapeutic candidates.

Disputes may also arise between us and Amgen, as well as any future potential licensors, regarding intellectual property subject to a license agreement, including:

- the scope of rights granted under the license agreement and other interpretation-related issues;
- whether and the extent to which our technology and processes infringe on intellectual property of the licensor that is not subject to the licensing agreement;
- our right to sublicense patent and other rights to third parties under collaborative development relationships;
- our diligence obligations with respect to the use of the licensed technology in relation to our development and commercialization of our therapeutic candidate and what activities satisfy those diligence obligations; and
- the ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our licensors and us and our partners.

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

In addition, the Amgen Agreement under which we currently license intellectual property is complex, and certain provisions 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 increase what we believe to be our financial or other obligations under the Amgen Agreement, either of which could have a material adverse effect on our business, financial condition, results of operations, and prospects. For example, under the Amgen Agreement, Amgen shall have the right to terminate the agreement if we are deemed to have directly or indirectly conducted, enabled or participated in any distracting program (as defined in the Amgen Agreement), and do not elect to add the program to the agreement. There could be disagreements on whether a certain program would be considered as a distracting program. Moreover, if disputes over intellectual property that we have licensed prevent or impair our ability to maintain our current licensing arrangement on commercially acceptable terms, we may be unable to successfully develop and commercialize the affected therapeutic candidates, which could have a material adverse effect on our business, financial conditions, results of operations, and prospects.

We are generally also subject to all of the same risks with respect to protection of intellectual property that we license, as we are for intellectual property that we own, which are described below. If we or our licensors fail to adequately protect this intellectual property, our ability to commercialize products could suffer.

We rely, and expect to continue to rely, on third parties to conduct some or all aspects of our product manufacturing, research and preclinical and clinical testing, and these third parties may not perform satisfactorily.

We do not expect to independently conduct all aspects of our product manufacturing, research and preclinical and clinical testing. We currently rely, and expect to continue to rely, on third parties with respect to many of these items, including contract manufacturing organizations (CMOs) for the manufacturing of any therapeutic candidates we test in preclinical or clinical development, as well as CROs for the conduct of our preclinical testing and research and CROs for the conduct of our planned clinical trials. For instance, VGL101 is a monoclonal antibody and is produced from a recombinant cell line only by permitted CMOs as set forth in the Amgen

Agreement, the replacement of which would need to be approved by Amgen. We have established non-exclusive relationships with these CMOs for the manufacturing of VGL101 drug substance and drug product, and other third parties for testing, fill finish, and packaging and labeling. Any of these third parties may terminate their engagements with us at any time. A need to enter into alternative arrangements could delay our product development activities. Delays in CMO production of VGL101 drug substance or drug product would delay our ability to conduct and complete clinical trials.

Our reliance on these third parties for research and development activities will reduce our control over these activities but will not relieve us of our responsibility to ensure compliance with all required regulations and study protocols. For example, for therapeutic candidates that we develop and commercialize on our own, we will remain responsible for ensuring that each of our IND-enabling studies and clinical trials are conducted in accordance with the study plan and protocols. Moreover, the FDA requires us to comply with GLPs for preclinical studies intended to support INDs and applications for marketing authorization, and with GCPs 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 GCP requirements through periodic inspections of trial sponsors, clinical investigators and trial sites. We also are required to register applicable clinical trials and post the results of completed clinical trials on a government-sponsored database, ClinicalTrials.gov within specified timeframes. Failure to do so can result in fines, adverse publicity and civil and criminal sanctions.

Although we depend heavily on these parties, we control only certain aspects of their activity and therefore, we cannot be assured that these third parties will adequately perform all of their contractual obligations to us in compliance with regulatory and other legal requirements and our internal policies and procedures. Nevertheless, we are responsible for ensuring that each of our studies is conducted in accordance with the applicable protocol, legal, regulatory and scientific standards, and our reliance on third parties does not relieve us of our regulatory responsibilities. If we or any of our CROs or other third parties, including trial sites, fail to comply with applicable GLPs or GCPs, the preclinical and clinical data generated in our preclinical studies and clinical trials may be deemed unreliable and the FDA, EMA or comparable foreign regulatory authorities may require us to suspend, place on clinical hold or terminate these trials or require us to perform additional preclinical studies or clinical trials before approving our marketing applications. We cannot assure you that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our clinical trials complies with GCP regulations, or that applicable preclinical studies comply with GLPs. In addition, our clinical trials must be conducted with product produced under conditions that comply with the FDA's current Good Manufacturing Practices (cGMP). Our failure to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process.

Although we intend to design the clinical trials for any therapeutic candidates we may develop, 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. We expect to have to negotiate budgets and contracts with CROs and trial sites, which may result in delays to our development timelines and increased costs. In addition, any third parties conducting our clinical trials will not be our employees, and except for remedies available to us under our agreements with such third parties, we cannot control whether or not they devote sufficient time and resources to our clinical programs. If these CROs, and any other third parties we engage do not perform preclinical studies and future clinical trials in a satisfactory manner, if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols, or if they breach their obligations to us or fail to comply with regulatory requirements, the development, regulatory approval and commercialization of any therapeutic candidates we may develop may be delayed, we may not be able to obtain regulatory approval and commercialize our therapeutic candidates or our development programs may be materially and irreversibly harmed. If we are unable to rely on preclinical and clinical data collected by our CROs and other third parties, we could be required to repeat, extend the duration of or increase the size of any preclinical studies or clinical trials we conduct and this could significantly delay commercialization and require greater expenditures.

These third parties may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical trials or other product development activities, which could affect their performance on our behalf. If these third parties 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 or regulatory requirements or for other reasons, our clinical trials may be extended, delayed or terminated and we may not be able to complete development of, obtain regulatory approval of or successfully commercialize our therapeutic candidates. As a result, our financial results and the commercial prospects for our therapeutic candidates would be harmed, our costs could increase and our ability to generate revenue could be delayed.

Our failure or any failure by these third parties to comply with these regulations, including to implement and maintain adequate standard operating procedures in order to comply, or to recruit a sufficient number of patients may require us to repeat clinical trials, which would delay the regulatory approval process. Moreover, our business may be implicated if any of these third parties violates federal or state fraud and abuse or false claims laws and regulations or healthcare privacy and security laws.

For any violations of laws and regulations during the conduct of our preclinical studies and clinical trials, we could be subject to warning letters or enforcement action that may include civil penalties up to and including criminal prosecution.

If any of our relationships with these third-party CROs or others terminate, we may not be able to enter into arrangements with alternative CROs or other third parties or to do so on commercially reasonable terms. 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 begins work. As a result, delays may occur, which can materially impact our ability to meet our desired clinical development timelines. 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. If third parties do not successfully carry out their contractual duties, meet expected deadlines or conduct our studies in accordance with regulatory requirements or our stated study plans and protocols, we will not be able to complete, or may be delayed in completing, the preclinical studies and clinical trials required to support future IND submissions and approval of any therapeutic candidates we may develop.

We are dependent on third-party vendors to provide certain licenses, products and services and our business and operations, including clinical trials, could be disrupted by problems with or challenges faced by our significant third-party vendors.

We engage a number of third-party suppliers and service providers to supply critical goods and services, such as contract research services, contract manufacturing services and information technology services. Disruptions to the business, financial stability or operations of these suppliers and service providers, including due to strikes, labor disputes or other disruptions to the workforce, for instance, if, as a result of the COVID-19 pandemic, employees are not able to come to work, or to their willingness and ability to produce or deliver such products or provide such services in a manner that satisfies the requirements put forth by the authorities, or in a manner that satisfies our own requirements, could affect our ability to develop and market our future therapeutic candidates on a timely basis. If these suppliers and service providers were unable or unwilling to continue to provide their products or services in the manner expected, or at all, we could encounter difficulty finding alternative suppliers. Even if we are able to secure appropriate alternative suppliers in a timely manner, costs for such products or services could increase significantly. Additionally, with the approval and manufacturing prevalence of COVID-19 vaccines, the resultant demand for vaccines and potential for manufacturing facilities and materials to be commandeered under the Defense Production Act of 1950, or equivalent foreign legislation, may make it more difficult to obtain materials or manufacturing slots for the products needed for our clinical trials, which could lead to delays in these trials. Any of these events could adversely affect our results of operations and our business.

We depend, and may continue to depend on single-source suppliers for some of the components and materials used in the therapeutic candidates we are developing.

We depend, and may continue to depend, on single-source suppliers for some of the components and materials used in the therapeutic candidates we are developing. For example, we currently rely on a master services agreement with FUJIFILM (as defined in "Management's Discussion and Analysis of Financial Condition and Results of Operations") pursuant to which FUJIFILM is the sole provider to us of certain research, development, testing and manufacturing services for certain of our product candidates, including VGL101 (the FUJIFILM Agreement). In the event the FUJIFILM Agreement is terminated, our ability to meet the desired clinical development timelines may be materially impacted and our business will be implicated. We cannot ensure that these suppliers or service providers will remain in business, have sufficient capacity or supply to meet our needs or that they will not be purchased by one of our competitors or another company that is not interested in continuing to work with us. Our use of single-source suppliers of raw materials, components, key processes and finished goods could expose us to several risks, including disruptions in supply, price increases or late deliveries. There are, in general, relatively few alternative sources of supply for substitute components. These vendors may be unable or unwilling to meet our future demands for our clinical trials or commercial sale. Establishing additional or replacement suppliers for these components, materials and processes could take a substantial amount of time and it may be difficult to establish replacement suppliers who meet regulatory requirements. Any disruption in supply from any single- source supplier or service provider could lead to supply delays or interruptions which would damage our business, financial condition, results of operations and prospects.

If we have to switch to a replacement supplier, the manufacture and delivery of any therapeutic candidates we may develop could be interrupted for an extended period, which could adversely affect our business. Establishing additional or replacement suppliers, if required, may not be accomplished quickly. If we are able to find a replacement supplier, the replacement supplier would need to be qualified and may require additional regulatory authority approval, which could result in further delay. While we seek to maintain adequate inventory of the single source components and materials used in our therapeutics, any interruption or delay in the supply of components or materials, or our inability to obtain components or materials from alternate sources at acceptable prices in a timely manner, could impair our ability to meet the demand for our investigational medicines.

We may enter into collaborations, licenses and other similar arrangements with third parties for the research, development and commercialization of certain of the therapeutic candidates we may develop. If any such arrangements are not successful, we may not be able to capitalize on the market potential of those therapeutic candidates.

We may seek third-party collaborators for the research, development and commercialization of certain of the therapeutic candidates we may develop. If we enter into any such arrangements with any third parties, we will likely have limited control over the amount and timing of resources that our partners dedicate to the development or commercialization of any therapeutic candidates we may seek to develop with them. Our ability to generate revenues from these arrangements will depend on the ability of such collaborators to successfully perform the functions assigned to them in these arrangements. We cannot predict the success of any arrangement that we enter into.

Collaborations involving our research programs or any therapeutic candidates we may develop pose numerous risks to us, including the following:

- collaborators may not pursue development and commercialization of any therapeutic candidates we may develop 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 programs, preclinical studies or clinical trials, provide insufficient funding for programs, preclinical studies or clinical trials, stop a preclinical study or clinical trial or abandon a therapeutic candidate, repeat or conduct new clinical trials or require a new formulation of a therapeutic candidate for clinical testing;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with any therapeutic candidates we may develop 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 may be acquired by a third party having competitive products or different priorities, causing the emphasis on our product development or commercialization program under such collaboration to be delayed, diminished or terminated;
- collaborators would have significant discretion in determining the efforts and resources that they will apply to these collaborations;
- collaborators may not perform their obligations as expected;
- collaborators with marketing and distribution rights to one or more products may not commit sufficient resources to the marketing and distribution of such product or products;
- 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;
- if a collaborator of ours is involved in a business combination, the collaborator might deemphasize or terminate the development or commercialization of any therapeutic candidate licensed to it by us;
- our collaborators' business or operations could be disrupted due to the ongoing COVID-19 pandemic or other reasons outside of our control, which could have an adverse impact on their development and commercialization efforts or the prospects of our collaboration;
- disputes may arise between the collaborators and us that result in the delay or termination of the research, development, or commercialization of any therapeutic candidates we may develop or that result in costly litigation or arbitration that diverts management attention and resources;
- we may lose certain valuable rights under certain circumstances, 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 therapeutic candidates we may develop; and
- collaboration agreements may not lead to development or commercialization of therapeutic candidates in the most efficient manner or at all.

If our collaborations do not result in the successful development and commercialization of therapeutic candidates, or if one of our collaborators terminates its agreement with us, we may not receive any future research funding or milestone or royalty payments pursuant to the collaboration arrangement. If we do not receive the funding we expect under these agreements, our development of therapeutic candidates could be delayed, and we may need additional resources to develop therapeutic 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.

Furthermore, all of the risks relating to product development, regulatory approval and commercialization described in this Quarterly Report 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 therapeutic candidates we or our collaborators may develop, 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.

Risks Related to Our Intellectual Property

If we are unable to obtain and maintain patent protection for our therapeutic programs and other proprietary technologies we develop, or if the scope of the patent protection obtained is not sufficiently broad, our competitors could develop and commercialize products and technology similar or identical to ours, and our ability to successfully commercialize our therapeutic programs and other proprietary technologies we may develop may be adversely affected.

Our success depends in large part on our ability to obtain and maintain patent protection in the U.S. and other countries with respect to our therapeutic programs and other proprietary technologies we may develop. In order to protect our proprietary position, we have filed and intend to file additional patent applications in the U.S. and abroad relating to our therapeutic programs and other proprietary technologies we may develop; however, there can be no assurance that any such patent applications will issue as granted patents or that a granted patent will provide sufficient coverage for our therapeutic programs. If we are unable to obtain or maintain patent protection with respect to our therapeutic programs and other proprietary technologies we may develop, our business, financial condition, results of operations and prospects could be materially harmed.

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. 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 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 U.S. and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. Therefore, we cannot be certain that we or our licensors were the first to make the inventions claimed in any of our owned or 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. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. Our patent applications may not result in patents being issued which protect our therapeutic programs and other proprietary technologies we may develop or which effectively prevent others from commercializing competitive technologies and products. In particular, our ability to stop third parties from making, using, selling, offering to sell, or importing products that infringe our intellectual property will depend in part on our success in obtaining and enforcing patent claims that cover all of our technology, inventions and improvements. We do not currently have issued patents in the U.S. or other major

markets that cover all of our technology or therapeutic candidates. With respect to both licensed and company-owned intellectual property, we cannot be sure that patents will be granted with respect to any of our pending patent applications or with respect to any patent applications filed by us in the future. Moreover, even issued patents do not provide us with the right to practice our technology in relation to the commercialization of our therapeutics. The area of patent and other intellectual property rights in biotechnology is an evolving one with many risks and uncertainties, and third parties may have blocking patents that could be used to prevent us from commercializing our patented therapeutic candidates and practicing our proprietary technology. Our issued patent as well as patents that may issue in the future that we own or in-license may be challenged, invalidated, or circumvented, which could limit our ability to stop competitors from marketing related products or limit the length of the term of patent protection that we may have for our therapeutic candidates. Furthermore, our competitors may independently develop similar technologies.

Additionally, issuance of a patent is not conclusive as to its inventorship, scope, validity, or enforceability and our patents may be challenged in the courts or patent offices in the U.S. and abroad. We may be subject to a third-party pre-issuance submission of prior art to the U.S. Patent and Trademark Office (USPTO) or in other jurisdictions, or become involved in opposition, derivation, revocation, reexamination, post-grant and *inter partes* review, or other similar proceedings challenging our patent rights. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate or render unenforceable, our patent rights, allow third parties to commercialize our therapeutic programs and other proprietary technologies we may develop and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize products without infringing third-party patent rights. Such proceedings also may result in substantial cost and require significant time from our scientists and management, even if the eventual outcome is favorable to us.

In addition, if the breadth or strength of protection provided by our patents and patent applications is threatened, regardless of the outcome, it could dissuade companies from collaborating with us to license, develop or commercialize current or future therapeutic candidates.

Our rights to develop and commercialize our therapeutic candidates are subject in part to the terms and conditions of a license granted to us by a third party. If we fail to comply with our obligations under our intellectual property license agreement, license agreements that we enter into in the future, or otherwise experience disruptions to our business relationships with our current or any future licensors, we could lose intellectual property rights that are important to our business.

We are and expect to continue to be reliant upon third-party licensors for certain patent and other intellectual property rights that are important or necessary to the development of our therapeutic programs, eventual therapeutic candidates, and proprietary technologies. For example, we rely on the Amgen Agreement for a license to technologies necessary for our monoclonal antibody TREM2 agonist program, including VGL101 and related molecules, intellectual property and manufacturing know-how, and our small molecule agonist program, including a portfolio of approximately 1,000 compounds. The Amgen Agreement imposes, and we expect that any future license agreement will impose, specified diligence, milestone payment, royalty, commercialization, development and other obligations on us and require us to meet development timelines, or to exercise diligent or commercially reasonable efforts to develop and commercialize licensed products, in order to maintain the licenses.

Furthermore, our licensors have, or may in the future have, the right to terminate a license if we materially breach the agreement and fail to cure such breach within a specified period or in the event we undergo certain bankruptcy events. In spite of our best efforts, our current or any future licensors might conclude that we have materially breached our license agreements and might therefore terminate the license agreements. If our license agreements are terminated, we may lose our rights to develop and commercialize therapeutic candidates and technology, lose patent protection, experience significant delays in the development and commercialization of our therapeutic candidates and technology, and incur liability for damages. If these in-licenses are terminated, or if the underlying intellectual property fails to provide the intended exclusivity, our competitors or other third parties could have the freedom to seek regulatory approval of, and to market, products and technologies identical or competitive to ours and we may be required to cease our development and commercialization of certain of our therapeutic candidates and technology. In addition, we may seek to obtain additional licenses from our licensors and, in connection with obtaining such licenses, we may agree to amend our existing licenses in a manner that may be more favorable to the licensors, including by agreeing to terms that could enable third parties, including our competitors, to receive licenses to a portion of the intellectual property that is subject to our existing licenses and to compete with any therapeutic candidates we may develop and our technology. Any of the foregoing could have a material adverse effect on our competitive position, business, financial condition, results of operations and prospects.

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

- the scope of rights granted and obligations imposed under the license agreement and other interpretation-related issues;
- our or our licensors' ability to obtain, maintain and defend intellectual property and to enforce intellectual property rights against third parties;

- the extent to which our technology, therapeutic candidates and processes infringe, misappropriate or otherwise violate the intellectual property of the licensor that is not subject to the license agreement;
- the sublicensing of patent and other intellectual property rights under our license agreements;
- our diligence, development, regulatory, commercialization, financial or other obligations under the license agreement 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 current or future licensors and us and our partners; and
- the priority of invention of patented technology.

In addition, any current or future license agreements to which we are a party, including our license agreement with Amgen, are likely to be 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 diligence, development, regulatory, commercialization, financial or other obligations under the relevant agreement. In addition, if disputes over intellectual property that we have licensed or any other dispute related to our license agreements prevent or impair our ability to maintain our current license agreements on commercially acceptable terms, we may be unable to successfully develop and commercialize the affected therapeutic candidates and technology. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations and prospects.

License agreements we may enter into in the future may be non-exclusive. Accordingly, third parties may also obtain non-exclusive licenses from such licensors with respect to the intellectual property licensed to us under such license agreements. Accordingly, these license agreements may not provide us with exclusive rights to use such licensed patent and other intellectual property rights, or may not provide us with exclusive rights to use such patent and other intellectual property rights in all relevant fields of use and in all territories in which we may wish to develop or commercialize our technology and any therapeutic candidates we may develop in the future.

Moreover, if some of our in-licensed patent and other intellectual property rights in the future become subject to third party interests such as co-ownership and we are unable to obtain an exclusive license to such third-party co-owners' interest, in such patent and other intellectual property rights, the third-party co-owners may be able to license their rights to other third parties, including our competitors, and our competitors could market competing products and technology. Additionally, we or our licensors may need the cooperation of any such co-owners of our licensed patent and other intellectual property rights in order to enforce them against third parties, and such cooperation may not be provided to us or our licensors.

Additionally, there could be instances where we may not have complete control over the preparation, filing, prosecution, maintenance, enforcement and defense of patents and patent applications that we license from third parties. In such instances, it is possible that our licensors' filing, prosecution and maintenance of the licensed patents and patent applications, enforcement of patents against infringers or defense of such patents against challenges of validity or claims of enforceability may be less vigorous than if we had conducted them ourselves, and accordingly, we cannot be certain that these patents and patent applications will be prepared, filed, prosecuted, maintained, enforced and defended in a manner consistent with the best interests of our business. If our licensors fail to file, prosecute, maintain, enforce and defend such patents and patent applications, or lose rights to those patents or patent applications, the rights we may license may be reduced or eliminated, our right to develop and commercialize any of our technology and any therapeutic candidates we may develop that are the subject of such licensed rights could be adversely affected and we may not be able to prevent competitors or other third parties from making, using and selling competing products.

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

Filing, prosecuting, maintaining, enforcing and defending patents and other intellectual property rights on our technology and any therapeutic candidates we may develop in all jurisdictions throughout the world would be prohibitively expensive, and accordingly, our intellectual property rights in some jurisdictions outside the U.S. could be less extensive than those in the U.S. In some cases, we or our licensors may not be able to obtain patent or other intellectual property protection for certain technology and therapeutic candidates outside the U.S. In addition, the laws of some foreign jurisdictions do not protect intellectual property rights to the same extent as federal and state laws in the U.S. Consequently, we and our licensors may not be able to obtain issued patents or other intellectual property rights covering any therapeutic candidates we may develop and our technology in all jurisdictions outside the U.S. and, as a result, may not be able to prevent third parties from practicing our and our licensors' inventions in all countries outside the U.S., or from selling or importing products made using our inventions in and into the U.S. or other jurisdictions. For example, third parties may use our technologies in jurisdictions where we and our licensors have not pursued and obtained patent or other intellectual property protection to develop their own products and, further, may export otherwise infringing, misappropriating or violating products to territories where we have patent or other intellectual property protection, but enforcement is not as strong as that in the U.S.

Additionally, many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain jurisdictions, 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, misappropriation or other violation of our patent and other intellectual property rights or marketing of competing products in violation of our intellectual property rights generally. Proceedings to enforce our or our licensors' patent and other 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 patent and other intellectual property rights 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 or our licensors may not prevail in any lawsuits that we or our licensors initiate and, if we or our licensors prevail, the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

Many jurisdictions also have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties, and, many jurisdictions limit the enforceability of patents against government agencies or government contractors. In these jurisdictions, the patent owner may have limited remedies, which could materially diminish the value of such patents. 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.

Issued patents covering therapeutic candidates we may develop could be found invalid or unenforceable if challenged in court or before administrative bodies in the U.S. or abroad.

Our owned and licensed patent rights may be subject to priority, validity, inventorship and enforceability disputes. If we or our licensors are unsuccessful in any of these proceedings, such patent rights may be narrowed, invalidated or held unenforceable. The foregoing could have a material adverse effect on our business, financial condition, results of operations and prospects.

For example, if we or one of our licensors initiate legal proceedings against a third party to enforce a patent covering any of our therapeutic candidates or our technology, the defendant could counterclaim that the patent is invalid or unenforceable. In patent litigation in the U.S., defendant counterclaims alleging invalidity or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness, lack of written description or non-enablement. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld information material to patentability from the USPTO, or made a misleading statement, during prosecution. Third parties also may raise similar claims before administrative bodies in the U.S. or abroad, even outside the context of litigation. Such mechanisms include re-examination, interference proceedings, derivation proceedings, post grant review, *inter partes* review and equivalent proceedings such as opposition, invalidation and revocation proceedings in foreign jurisdictions. Such proceedings could result in the revocation or cancellation of or amendment to our patents in such a way that they no longer cover one or more of our therapeutic candidates or our technology or no longer prevent third parties from competing with any therapeutic candidates we may develop or our technology. The outcome following legal assertions of invalidity and unenforceability is unpredictable. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a distraction to management and other employees. With respect to the validity question, for example, we cannot be certain that there is no invalidating prior art, of which the patent examiner and we or our licensing partners were unaware during prosecution. If a third party were to prevail on a legal assertion of invalidity or unenforceability, we could lose at least part, and perhaps all, of the patent protection on one or more of our therapeutic candidates or technology. Such a loss of patent protection could have a material adverse effect on our business, financial condition, results of operations and prospects.

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 will be due to be paid to the USPTO and various government patent agencies outside of the U.S. over the lifetime of our owned or licensed patents and applications. The USPTO and various non-U.S. government agencies require compliance with several procedural, documentary, fee payment and other similar provisions during the patent application process. In some cases, an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with the applicable rules. There are situations, however, in which non-compliance can result in abandonment or lapse of the patent or patent application, resulting in a partial or complete loss of patent rights in the relevant jurisdiction. In such an event, potential 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 U.S. or worldwide could diminish the value of patents in general, thereby impairing our ability to protect any therapeutic candidates we may develop and our technology.

Changes in either the patent laws or interpretation of patent laws in the U.S. and worldwide, including patent reform legislation such as the Leahy-Smith America Invents Act (the Leahy-Smith Act), could increase the uncertainties and costs surrounding the prosecution of any owned or in-licensed patent applications and the maintenance, enforcement or defense of any current in-licensed issued patents and issued patents we may own or in-license in the future. The Leahy-Smith Act includes a number of significant changes to U.S. patent law. These changes include provisions that affect the way patent applications are prosecuted, redefine prior art, provide more efficient and cost-effective avenues for competitors to challenge the validity of patents, and enable third-party submission of prior art to the USPTO during patent prosecution and additional procedures to attack the validity of a patent at USPTO-administered post-grant proceedings, including post-grant review, *inter partes* review, and derivation proceedings. Assuming that other requirements for patentability are met, prior to March 2013, in the U.S., the first to invent the claimed invention was entitled to the patent, while outside the U.S., the first to file a patent application was entitled to the patent. After March 2013, under the Leahy- Smith Act, the U.S. transitioned to a first-to-file system in which, assuming that the other statutory requirements for patentability are met, the first inventor to file a patent application will be entitled to the patent on an invention regardless of whether a third party was the first to invent the claimed invention. As such, the Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of patents to issue based on our in-licensed patent applications and issued patents we may own or in-license in the future, all of which could have a material adverse effect on our business, financial condition, results of operations and prospects.

The Leahy-Smith Act also includes a number of significant changes that may affect patent litigation. These include additional procedures to attack the validity of a patent by USPTO administered post-grant proceedings, 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 U.S. 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 unpatentable 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 review patentability of our patent claims that would not have been invalidated if first challenged by the third party as a defendant in a district court action. Therefore, the Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our owned or in-licensed patent applications and the enforcement or defense of our owned or in-licensed issued patents, all of which could have a material adverse effect on our business, financial condition, results of operations, and prospects.

In addition, the patent positions of companies in the development and commercialization of biologics and pharmaceuticals are particularly uncertain. 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. As one example, in the case *Assoc. for Molecular Pathology v. Myriad Genetics, Inc.*, the U.S. Supreme Court held that certain claims to DNA molecules are not patentable simply because they have been isolated from surrounding material. Moreover, in 2012, the USPTO issued a guidance memo to patent examiners indicating that process claims directed to a law of nature, a natural phenomenon or a naturally occurring relation or correlation that do not include additional elements or steps that integrate the natural principle into the claimed invention such that the natural principle is practically applied and the claim amounts to significantly more than the natural principle itself should be rejected as directed to patent-ineligible subject matter. 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 have a material adverse effect on our patent rights and our ability to protect, defend and enforce our patent rights in the future.

If we do not obtain patent term extension and data exclusivity for any therapeutic candidates we may develop, our business may be harmed.

Depending upon the timing, duration and specifics of any FDA marketing approval of any therapeutic candidates we may develop and our technology, our U.S. patent or one or more U.S. patents that may issue in the future based on a patent application that we license or may own may be eligible for limited patent term extension under Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent extension term of up to five years as compensation for patent term lost during the FDA regulatory review process. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, only one patent may be extended and only those claims covering the approved product, a method for using it or a method for manufacturing it may be extended. The application for the extension must be submitted prior to the expiration of the patent for which extension is sought and within 60 days of FDA approval. A patent that covers multiple products for which approval is sought can only be extended in connection with one of the approvals. However, we may not be granted an extension because of, for example, failing to exercise due diligence during the testing phase or regulatory review process, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents or otherwise failing to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. In addition, to the extent we wish to pursue patent term extension based on a patent that we in-license from a third party, we would need the cooperation of that third party. If we are unable to obtain patent term extension or the term of any such extension is less than we request, our competitors may obtain approval of competing products following our patent expiration, and our revenue could be reduced. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations and prospects.

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

We or our licensors may be subject to claims that former employees, collaborators or other third parties have an interest in our owned or in-licensed patent rights, 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 therapeutic candidates or technology. Litigation may be necessary to defend against these and other claims challenging inventorship or our or our licensors' ownership of our owned or in-licensed patent rights, trade secrets or other intellectual property. If we or our licensors fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of or right to use intellectual property that is important to any therapeutic candidates we may develop or our technology. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations and prospects.

We may not be successful in obtaining necessary rights to a therapeutic candidate we may develop through acquisitions and in-licenses.

We currently own or exclusively license intellectual property rights covering certain aspects of our therapeutic programs. Other pharmaceutical companies and academic institutions may also have filed or are planning to file patent applications potentially relevant to our business. In order to avoid infringing these third-party patents, we may find it necessary or prudent to obtain licenses to such patents 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 our therapeutic programs and other proprietary technologies we may develop. The licensing or acquisition of third-party intellectual property rights is a competitive area, and several more established companies may pursue strategies to license or acquire third party intellectual property rights that we may consider attractive or necessary. These established companies may have a competitive advantage over us due to their size, capital resources and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. 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 therapeutic candidate, which could have a material adverse effect on our business, financial condition, results of operations and prospects.

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

Some of our employees, consultants and advisors are currently or were previously employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although we try to ensure that our employees, consultants and 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 used or disclosed intellectual property, including trade secrets or other proprietary information, of any such individual's current or former employer. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to our management.

In addition, while it is our policy to require our employees and contractors who may be involved in the conception or development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who, in fact, conceives or develops intellectual property that we regard as our own. The assignment of intellectual property rights may not be self-executing, or the assignment agreements may be breached, and we may be forced to bring claims against third parties, or defend claims that they may bring against us, to determine the ownership of what we regard as our intellectual property. Such claims could have a material adverse effect on our business, financial condition, results of operations and prospects.

Third-party claims of intellectual property infringement, misappropriation or other violations against us or our collaborators may prevent or delay the development and commercialization of our therapeutic programs and other proprietary technologies we may develop.

Our commercial success depends in part on our ability to avoid infringing, misappropriating and otherwise violating the patents and other intellectual property rights of third parties. There is a substantial amount of complex litigation involving patents and other intellectual property rights in the biotechnology and pharmaceutical industries, as well as administrative proceedings for challenging patents, including interference, derivation and reexamination proceedings before the USPTO or oppositions and other comparable proceedings in foreign jurisdictions. As discussed above, recently, due to changes in U.S. law referred to as patent reform, new procedures including *inter partes* review and post-grant review have also been implemented. As stated above, this reform adds uncertainty to the possibility of challenge to our patents in the future.

Numerous U.S. and foreign issued patents and pending patent applications owned by third parties exist in the fields in which we are commercializing or plan to commercialize our therapeutic programs and in which we are developing other proprietary technologies. As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our therapeutic programs and commercializing activities may give rise to claims of infringement of the patent rights of others. We cannot assure you that our therapeutic programs and other proprietary technologies we may develop will not infringe existing or future patents owned by third parties. We may not be aware of patents that have already been issued and that a third party, for example, a competitor in the fields in which we are developing our therapeutic programs, might assert as infringed by us. It is also possible that patents owned by third parties of which we are aware or patents that may issue in the future from patent applications owned by third parties of which we are aware, but which we do not believe we infringe or that we believe we have valid defenses to any claims of patent infringement, could be found to be infringed by us, such as in connection with one or more of our therapeutic candidates. In addition, because patent applications can take many years to issue, and the scope of any patent claims that may ultimately issue are difficult to predict, there may be currently pending patent applications that may later result in issued patents that we may infringe and that, as a result, could harm our business.

In the event that any third party claims that we infringe their patents or that we are otherwise employing their proprietary technology without authorization and initiates litigation against us, even if we believe such claims are without merit, a court of competent jurisdiction could hold that such patents are valid, enforceable and infringed by us. In this case, the holders of such patents may be able to block our ability to commercialize the infringing products or technologies unless we obtain a license under the applicable patents, or until such patents expire or are finally determined to be held invalid or unenforceable. Such a license may not be available on commercially reasonable terms or at all. Even if we are able to obtain a license, the license would likely obligate us to pay license fees or royalties or both, and the rights granted to us might be nonexclusive, which could result in our competitors gaining access to the same intellectual property. If we are unable to obtain a necessary license to a third-party patent on commercially reasonable terms, we may be unable to commercialize the infringing products or technologies or such commercialization efforts may be significantly delayed, which could in turn significantly harm our business.

Defense of infringement claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of management and other employee resources from our business, and may impact our reputation. In the event of a successful claim of infringement against us, we may be enjoined from further developing or commercializing the infringing products or technologies. In addition, we may have to pay substantial damages, including treble damages and attorneys' fees for willful infringement, obtain one or more licenses from third parties, pay royalties and/or redesign our infringing products or technologies, which may be impossible or require substantial time and monetary expenditure. In that event, we would be unable to further develop and commercialize our therapeutic candidate or technologies, which could harm our business significantly. Further, we cannot predict whether any required license would be available at all or whether it would be available on commercially reasonable terms. We could be prevented from commercializing a product, or be forced to cease some aspect of our business operations, if, as a result of actual or threatened patent infringement claims, we are unable to enter into licenses on acceptable terms.

We may in the future pursue invalidity proceedings with respect to third-party patents. The outcome following legal assertions of invalidity is unpredictable. Even if resolved in our favor, these legal proceedings may cause us to incur significant expenses, and could distract 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, it could have a substantial adverse effect on the price of our common stock. Such proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing or distribution activities. If we do not prevail in the patent proceedings the third parties may assert a claim of patent infringement directed at our therapeutic candidates.

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

Third parties, such as a competitor, may infringe our patent rights. In an infringement proceeding, a court may decide that a patent owned by us is invalid or unenforceable or may refuse to stop the other party from using the invention at issue on the grounds that the patent does not cover the technology in question. In addition, our patent rights may become involved in inventorship, priority or validity disputes. To counter or defend against such claims can be expensive and time-consuming. An adverse result in any litigation proceeding could put our patent rights at risk of being invalidated or interpreted narrowly. 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.

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. 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.

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. Our efforts to enforce or protect our proprietary rights related to trademarks, trade names, domain name 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 prospects.

We may not be successful in obtaining or maintaining necessary rights to product components and processes for our development pipeline through acquisitions and in-licenses.

The growth of our business may depend in part on our ability to acquire, in-license or use third-party proprietary rights. For example, our therapeutic candidates may require specific formulations to work effectively and efficiently, we may develop therapeutic candidates containing our compounds and pre-existing pharmaceutical compounds, or we may be required by the FDA or comparable foreign regulatory authorities to provide a companion diagnostic test or tests with our therapeutic candidates, any of which could require us to obtain rights to use intellectual property held by third parties. We may be unable to acquire or in-license any compositions, methods of use, processes or other third-party intellectual property rights from third parties that we identify as necessary or important to our business operations. In addition, we may fail to obtain any of these licenses at a reasonable cost or on reasonable terms, if at all. Were that to happen, we may need to cease use of the compositions or methods covered by those third-party intellectual property rights, and may need to seek to develop alternative approaches that do not infringe on those intellectual property rights, which may entail additional costs and development delays, even if we were able to develop such alternatives, which may not be feasible.

We, our collaborators and our service providers may be subject to a variety of privacy and data security laws and contractual obligations, which could increase compliance costs and our failure to comply with them could subject us to potentially significant fines or penalties and otherwise harm our business.

We maintain a large quantity of sensitive information, including confidential business and patient health information in connection with our preclinical studies, and are subject to laws and regulations governing the privacy and security of such information. The global data protection landscape is rapidly evolving, and we may be affected by or subject to new, amended or existing laws and regulations in the future, including as our operations continue to expand or if we operate in foreign jurisdictions. These laws and regulations may be subject to differing interpretations, which adds to the complexity of processing personal data. Guidance on implementation and compliance practices are often updated or otherwise revised.

In the U.S., there are numerous federal and state privacy and data security laws and regulations governing the collection, use, disclosure and protection of personal information, including health information privacy laws, security breach notification laws and consumer protection laws. Each of these laws is subject to varying interpretations and is constantly evolving. By way of example, the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, imposes privacy and security requirements and breach reporting obligations with respect to individually identifiable health information upon “covered entities” (health plans, health care clearinghouses and certain health care providers), and their respective business associates (individuals or entities that create, received, maintain or transmit protected health information in connection with providing a service for or on behalf of a covered entity). Entities that are found to be in violation of HIPAA may be subject to significant civil, criminal and administrative fines and penalties and/or additional reporting and oversight obligations. Even when HIPAA does not apply, failing to take appropriate steps to keep consumers’ personal information secure may constitute unfair acts or practices in or affecting commerce in violation of Section 5(a) of the Federal Trade Commission Act (the FTCA), 15 U.S.C § 45(a). The FTC expects a company’s data security measures to be reasonable and appropriate in light of the sensitivity and volume of consumer information it holds, the size and complexity of its business and the cost of available tools to improve security and reduce vulnerabilities. Individually identifiable health information is considered sensitive data that merits stronger safeguards.

In addition, certain state laws govern the privacy and security of health information in certain circumstances, some of which are more stringent than HIPAA and many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts. For example, California enacted the California Consumer Privacy Act of 2018 (CCPA), which took effect on January 1, 2020 and became enforceable by the California Attorney General on July 1, 2020, and broadly defines personal information. The CCPA creates new individual privacy rights for consumers (as that term is broadly defined) and places increased privacy and security obligations on entities handling personal data of consumers or households. The CCPA requires covered companies to provide certain disclosures to California consumers about its data collection, use and sharing practices, provide such consumers with ways to opt-out of certain sales or transfers of personal information, provides for civil penalties for violations, and allows for a new private right of action for data breaches that has resulted in an increase in data breach litigation. Many aspects of the CCPA, including the expansion of the consumer rights granted therein under the California Privacy Rights Act (CPRA), and its interpretation remain unclear. As such, its full impact on our business and operations remains uncertain. Additionally, comprehensive privacy laws akin to the CCPA have recently been passed in Virginia and Colorado, and it is quite possible that other U.S. states will follow suit. New privacy and data security laws have been proposed in more than half of the states in the U.S. and in the U.S. Congress. The existence of comprehensive privacy laws in different states in the country will make our compliance obligations more complex and costly.

As we conduct studies with subjects from outside of the U.S., we may be subject to additional, more stringent privacy laws in other jurisdictions. Most notably, in the EU, in May 2018, a new privacy regime, the General Data Protection Regulation, the GDPR, took effect in the European Economic Area, the EEA. The GDPR governs the collection, use, disclosure, transfer or other processing of personal data of European persons. Among other things, the GDPR imposes new requirements regarding the security of personal data and notification of data processing obligations to the competent national data processing authorities, changes the lawful bases on which personal data can be processed, expands the definition of personal data and requires changes to informed consent practices, as well as more detailed notices for clinical trial subjects and investigators. In addition, the GDPR increases the scrutiny of transfers of personal data from clinical trial sites located in the EEA to the U.S. and other jurisdictions that the European Commission does not recognize as having "adequate" data protection laws, and imposes substantial fines for breaches and violations (up to the greater of €20 million or 4% of our consolidated annual worldwide gross revenue).

Moreover, the United Kingdom leaving the EU could also lead to further legislative and regulatory changes. In addition, further to the U.K.'s exit from the EU on January 31, 2020, the GDPR ceased to apply in the U.K. at the end of the transition period on December 31, 2020. However, as of January 1, 2021, the U.K.'s European Union (Withdrawal) Act 2018 incorporated the U.K. GDPR into U.K. law. The U.K. GDPR and the U.K. Data Protection Act 2018 set out the U.K.'s data protection regime. Non-compliance with the U.K. GDPR may result in monetary penalties of up to £17.5 million or 4% of worldwide revenue, whichever is higher.

As these privacy, data protection and data security laws continue to evolve, we may be required to make changes to our business, including by taking on more onerous obligations in our contracts, limiting our storage, transfer and processing of data and, in some cases, limiting our activities in certain locations. Changes in these laws may also increase our potential exposure through significantly higher potential penalties for non-compliance. In addition, due to the uncertainty and potentially conflicting interpretations of these laws, it is possible that such laws and regulations may be interpreted and applied in a manner that is inconsistent from one jurisdiction to another and may conflict with other rules or our practices. Any failure or perceived failure by us to comply with applicable laws or satisfactorily protect personal information could result in governmental enforcement actions, litigation, or negative publicity, any of which could inhibit our ability to grow our business.

Organizations are also increasingly subject to a wide variety of sophisticated attacks on their networks, systems and endpoints, including the theft and subsequent misuse of employee credentials, denial-of-service attacks, ransomware attacks, business email compromises, malware, viruses, and social engineering (including phishing). The techniques used to obtain unauthorized access or to sabotage systems, networks, or physical facilities in which data is stored or through which data is transmitted change frequently and generally are not identified until they are launched against a target. We and our third party service providers may be unable to anticipate these techniques or to implement adequate preventative measures.

Compromise of our data security or of third parties with whom we do business, failure to prevent or mitigate the loss of personal or business information and delays in detecting or providing prompt notice of any such compromise or loss could disrupt our operations, harm our reputation, subject us to litigation, government action or other additional costs and liabilities that could adversely affect our business, financial condition and operating results. Any reputational damage resulting from breach of our security measures could create distrust of our company. In addition, our insurance coverage may not be adequate to cover costs, expenses and losses associated with such events, and in any case, such insurance may not cover all of the types of costs, expenses and losses we could incur to investigate, respond to and remediate a security breach. As a result, we may be required to expend significant additional resources to protect against the threat of these disruptions and security breaches or to alleviate problems caused by such disruptions or breaches, including costs to deploy additional personnel and protection technologies, train employees, and engage third-party experts and consultants, which could materially and adversely affect our business, financial condition and results of operations.

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:

- others may be able to make products that are similar to our therapeutic candidate or utilize similar technology but that are not covered by the claims of the patents that we license or may own;
- we might not have been the first to make the inventions covered by our current or future patent applications;
- we might not have been the first to file patent applications covering our inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights;
- it is possible that our current or future patent applications will not lead to issued patents;
- any patent issuing from our current or future patent applications may be held invalid or unenforceable, including as a result of legal challenges by our competitors or other third parties;
- our competitors or other third parties 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 may not develop additional proprietary technologies that are patentable;
- the patents of others may harm our business; and
- we may choose not to file for patent protection in order to maintain certain trade secrets or know-how, and a third party may subsequently file a patent application covering such intellectual property.

Risks Related to Government Regulation

Even if we obtain regulatory approval for any of our therapeutic candidates, we will still face extensive and ongoing regulatory requirements and obligations, which may result in significant additional expense, and any therapeutic candidates, if approved, may face future development and regulatory difficulties.

Any therapeutic candidate for which we obtain marketing approval will be subject to extensive and ongoing requirements of and review by the FDA and other regulatory authorities, including requirements related to the manufacturing processes, post-approval clinical data, labeling, packaging, distribution, adverse event reporting, storage, recordkeeping, export, import, and advertising and promotional activities for such product, among other things. These requirements include submissions of safety and other post-marketing information and reports, establishment registration and drug listing requirements, continued compliance with cGMP requirements relating to manufacturing, quality control, quality assurance, and corresponding maintenance of records and documents, compliance with applicable product tracking and tracing requirements, requirements regarding the distribution of samples to physicians and recordkeeping and GCP requirements for any clinical trials that we conduct post-approval.

Even if marketing approval of a therapeutic candidate is granted, the approval may be subject to limitations on the indicated uses for which the therapeutic candidate may be marketed or to the conditions of approval, including a requirement to implement a REMS. If a therapeutic candidate receives marketing approval, the accompanying label may limit the approved indicated use of the product, which could limit sales of the product. The FDA may also require costly post-marketing studies or clinical trials and surveillance to monitor the safety or efficacy of a product. The FDA closely regulates the post-approval marketing and promotion of drugs to ensure drugs are marketed only for the approved indications and in accordance with the provisions of the approved labeling. The FDA imposes stringent restrictions on manufacturers' communications regarding off-label use, and if we market our products for uses beyond their approved indications, we may be subject to enforcement action for off-label marketing. Violations of the Federal Food, Drug, and Cosmetic Act, relating to the promotion of prescription drugs, may lead to FDA enforcement actions and investigations alleging violations of federal and state healthcare fraud and abuse laws, as well as state consumer protection laws.

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

- restrictions on manufacturing such products;
- restrictions on the labeling or marketing of products;
- restrictions on product distribution or use;

- requirements to conduct post-marketing studies or clinical trials;
- issuance of warning letters or untitled letters;
- refusal to approve pending applications or supplements to approved applications that we submit;
- recalls or market withdrawals of products;
- fines, restitution, or disgorgement of profits or revenues;
- suspension or termination of ongoing clinical trials;
- suspension or withdrawal of marketing approvals;
- refusal to permit the import or export of our products;
- product seizure; or
- injunctions, consent decrees, or the imposition of civil or criminal penalties.

Obtaining and maintaining marketing approval or commercialization of our therapeutic candidates in the U.S. does not mean that we will be successful in obtaining marketing approval of our therapeutic candidates in other jurisdictions. Failure to obtain marketing approval in foreign jurisdictions would prevent any therapeutic candidates we may develop from being marketed in such jurisdictions, which, in turn, would materially impair our ability to generate revenue.

In order to market and sell any therapeutic candidates we may develop in the EU and many other foreign jurisdictions, we must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. The approval procedure varies among countries and can involve additional testing. The time required to obtain approval may differ substantially from that required to obtain FDA approval.

To obtain a marketing authorization for a product in the EU, an applicant must submit a marketing authorization application either under a centralized procedure administered by the EMA, or one of the procedures administered by competent authorities in the EU Member States (decentralized procedure, national procedure or mutual recognition procedure). We anticipate that the centralized procedure will be mandatory for the product candidates we are developing. The centralized procedure provides for the grant of a single marketing authorization by the European Commission that is valid throughout the EU, and in the additional Member States of the European Economic Area (Iceland, Liechtenstein and Norway).

Under the centralized procedure, the EMA's Committee for Human Medicinal Products, or CHMP, is responsible for conducting the initial assessment of a product and for several post-authorization and maintenance activities, such as the assessment of modifications or extensions to an existing marketing authorization. The maximum timeframe for the evaluation of a marketing authorization application under the centralized procedure by the EMA is 210 days, excluding clock stops, when additional written or oral information is to be provided by the applicant in response to questions asked by the CHMP. Clock stops may extend the timeframe of evaluation of an application considerably beyond 210 days. Where the CHMP gives a positive opinion, it provides the opinion together with supporting documentation to the European Commission, who makes the final decision to grant a marketing authorization, which is issued within 67 days of receipt of the EMA's recommendation. Accelerated evaluation might be granted by the CHMP in exceptional cases, when a medicinal product is expected to be of major public health interest, particularly from the viewpoint of therapeutic innovation. If the CHMP accepts such request, the time limit of 210 days will be reduced to 150 days, excluding clock stops, but it is possible that the CHMP can revert to the standard time limit for the centralized procedure if it considers that it is no longer appropriate to conduct an accelerated assessment.

The regulatory approval process outside the U.S. generally includes all of the risks associated with obtaining FDA approval. In addition, in many countries outside the U.S., it is required that the product be approved for reimbursement before the product can be approved for sale in that country. We may not obtain approvals from regulatory authorities outside the U.S. on a timely basis, if at all. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one regulatory authority outside the U.S. does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA. We may 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.

Our relationships with healthcare providers, patients and third-party payors are subject to applicable anti-kickback, fraud and abuse and other healthcare laws and regulations, which could expose us to significant penalties, including criminal sanctions, civil penalties, exclusion from government healthcare programs, contractual damages, reputational harm and diminished profits and future earnings.

Although we do not currently have any drugs on the market, our current and future operations are subject to additional healthcare statutory and regulatory requirements and enforcement by the federal government and the states and foreign governments in which we conduct our business. Healthcare providers and third-party payors will play a primary role in the recommendation and prescription of VGL101 and future therapeutic candidates for which we obtain marketing approval. Our 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 research as well as market, sell and distribute VGL101 and future therapeutic candidates for which we obtain marketing approval. Restrictions under applicable federal and state healthcare laws and regulations, include the following:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons or entities from knowingly and willfully soliciting, receiving, offering or paying any remuneration (including any kickback, bribe or rebate), directly or indirectly, overtly or covertly, in cash or in kind, to induce, or in return for, the purchase, lease, order, arrangement, or recommendation of any good, facility, item or service for which payment may be made, in whole or in part, under a federal healthcare program, such as the Medicare and Medicaid programs. A person or entity does not need to have actual knowledge of the federal Anti-Kickback Statute or specific intent to violate it to have committed a violation. Violations are subject to civil and criminal fines and penalties for each violation, plus up to three times the remuneration involved, imprisonment, and exclusion from government healthcare programs. In addition, the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal False Claims Act or federal civil money penalties;
- the federal civil and criminal false claims laws and civil monetary penalty laws, such as the federal False Claims Act, which impose criminal and civil penalties and authorize civil whistleblower or qui tam actions, against individuals or entities for, among other things: knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent; knowingly making, using or causing to be made or used, a false statement of record material to a false or fraudulent claim or obligation to pay or transmit money or property to the federal government or knowingly concealing or knowingly and improperly avoiding or decreasing an obligation to pay money to the federal government. Manufacturers can be held liable under the federal False Claims Act even when they do not submit claims directly to government payors if they are deemed to "cause" the submission of false or fraudulent claims. The federal False Claims Act also permits a private individual acting as a "whistleblower" to bring actions on behalf of the federal government alleging violations of the federal False Claims Act and to share in any monetary recovery;
- HIPAA, which created new federal criminal statutes that prohibit a person from knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or obtain, by means of false or fraudulent pretenses, representations or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program, regardless of the payor (e.g., public or private) and knowingly and willfully falsifying, concealing or covering up by any trick or device a material fact or making any materially false, fictitious, or fraudulent statements or representations in connection with the delivery of, or payment for, healthcare benefits, items or services 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;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, or HITECH and their respective implementing regulations, including the Final Omnibus Rule published in January 2013, which impose requirements on certain covered healthcare providers, health plans, and healthcare clearinghouses as well as their respective business associates, independent contractors or agents of covered entities, that perform services for them that involve the creation, maintenance, receipt, use, or disclosure of, individually identifiable health information relating to the privacy, security and transmission of individually identifiable health information. HITECH also created new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorneys' fees and costs associated with pursuing federal civil actions. In addition, there may be additional federal, state and non-U.S. laws which govern the privacy and security of health and other personal information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts;
- the U.S. Physician Payments Sunshine Act and its implementing regulations, which requires certain manufacturers of drugs, devices, biologics and medical supplies that are reimbursable under Medicare, Medicaid, or the Children's Health Insurance Program, with specific exceptions, to report annually to the Centers for Medicare & Medicaid Services information related to certain payments and other transfers of value to physicians, nurse practitioners, certified nurse anesthetists, physician assistants, clinical nurse specialists, and certified nurse midwives as well as teaching hospitals. Manufacturers are also required to disclose ownership and investment interests held by physicians and their immediate family members;

- federal government price reporting laws, which require us to calculate and report complex pricing metrics in an accurate and timely manner to government programs; and
- federal consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm customers.

Additionally, we are subject to state and foreign equivalents of each of the healthcare laws and regulations described above, among others, some of which may be broader in scope and may apply regardless of the payor. Many U.S. states have adopted laws similar to the federal Anti-Kickback Statute and False Claims Act, and may apply to our business practices, including, but not limited to, research, distribution, sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental payors, including private insurers. In addition, some states have passed laws that require pharmaceutical companies to comply with the April 2003 Office of Inspector General Compliance Program Guidance for Pharmaceutical Manufacturers and/or the Pharmaceutical Research and Manufacturers of America's Code on Interactions with Healthcare Professionals. Several states also impose other marketing restrictions or require pharmaceutical companies to make marketing or price disclosures to the state and require the registration of pharmaceutical sales representatives. State and foreign laws, including for example the European Union General Data Protection Regulation, which became effective May 2018 also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts. There are ambiguities as to what is required to comply with these state requirements and if we fail to comply with an applicable state law requirement we could be subject to penalties. Finally, there are state and foreign laws governing the privacy and security of health information, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

The scope and enforcement of these laws is uncertain and subject to rapid change in the current environment of healthcare reform, especially in light of the lack of applicable precedent and regulations. Federal and state enforcement has led to a number of investigations, prosecutions, convictions and settlements in the healthcare industry. Ensuring that our internal operations and future business arrangements with third parties comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices do not comply with current or future statutes, regulations, agency guidance or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of the laws described above or any other governmental laws and regulations that may apply to us, we may be subject to significant penalties, including administrative, civil and criminal penalties, damages, fines, disgorgement, the exclusion from participation in federal and state healthcare programs, reputational harm, and the curtailment or restructuring of our operations, as well as additional reporting obligations and oversight if we become subject to a corporate integrity agreement or other agreement to resolve allegations of non-compliance with these laws. Further, defending against any such actions can be costly and time consuming, and may require significant financial and personnel resources. Therefore, even if we are successful in defending against any such actions that may be brought against us, our business may be impaired. If any of the physicians or other providers or entities with whom we expect to do business are found to not be in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs and individual imprisonment. If any of the above occur, our ability to operate our business and our results of operations could be adversely affected.

We are subject to certain U.S. and certain foreign anti-corruption, anti-money laundering, export control, sanctions and other trade laws and regulations. We can face serious consequences for violations.

U.S. and foreign anti-corruption, anti-money laundering, export control, sanctions and other trade laws and regulations prohibit, among other things, companies and their employees, agents, CROs, legal counsel, accountants, consultants, contractors and other partners from authorizing, promising, offering, providing, soliciting or receiving directly or indirectly, corrupt or improper payments or anything else of value to or from recipients in the public or private sector. Violations of these laws can result in substantial criminal fines and civil penalties, imprisonment, the loss of trade privileges, debarment, tax reassessments, breach of contract and fraud litigation, reputational harm and other consequences. We have direct or indirect interactions with officials and employees of government agencies or government- affiliated hospitals, universities and other organizations. We also expect our non-U.S. activities to increase over time. We expect to rely on third parties for research, preclinical studies and clinical trials and/or to obtain necessary permits, licenses, patent registrations and other marketing approvals. We can be held liable for the corrupt or other illegal activities of our personnel, agents or partners, even if we do not explicitly authorize or have prior knowledge of such activities.

Any violations of the laws and regulations described above may result in substantial civil and criminal fines and penalties, imprisonment, the loss of export or import privileges, debarment, tax reassessments, breach of contract and fraud litigation, reputational harm and other consequences.

Healthcare legislative reform discourse and potential or enacted measures may have a material adverse impact on our business and results of operations and legislative or political discussions surrounding the desire for and implementation of pricing reforms may adversely impact our business.

Payors, whether domestic or foreign, or governmental or private, are developing increasingly sophisticated methods of controlling healthcare costs and those methods are not always specifically adapted for new technologies such as gene therapy and therapies addressing rare diseases such as those we are developing. In both the U.S. and certain foreign jurisdictions, there have been a number of legislative and regulatory changes to the health care system that could impact our ability to sell our products profitably. In particular, in 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively, the ACA, was enacted, which, among other things, subjected biologic products to potential competition by lower-cost biosimilars; addressed a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected; increased the minimum Medicaid rebates owed by most manufacturers under the Medicaid Drug Rebate Program; extended the Medicaid Drug Rebate program to utilization of prescriptions of individuals enrolled in Medicaid managed care organizations; subjected manufacturers to new annual fees and taxes for certain branded prescription drugs; created a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% (increased to 70% pursuant to the Bipartisan Budget Act of 2018, effective as of January 1, 2019) point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D; and provided incentives to programs that increase the federal government's comparative effectiveness research.

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

In addition, other legislative and regulatory changes have been proposed and adopted in the U.S. since the ACA was enacted:

- On August 2, 2011, the U.S. Budget Control Act of 2011, among other things, included aggregate reductions of Medicare payments to providers of 2% per fiscal year. These reductions went into effect on April 1, 2013 and, due to subsequent legislative amendments to the statute, will remain in effect through 2030, with the exception of a temporary suspension from May 1, 2020 through March 31, 2022 due to the COVID-19 pandemic. Following the temporary suspension, a 1% payment reduction will occur beginning April 1, 2022 through June 30, 2022, and the 2% payment reduction will resume on July 1, 2022.
- On January 2, 2013, the U.S. American Taxpayer Relief Act of 2012 was signed into law, which, among other things, further reduced Medicare payments to several types of providers.
- On April 13, 2017, Centers for Medicare & Medicaid Services, or CMS, an agency within the U.S. Department of Health and Human Services, published a final rule that gives states greater flexibility in setting benchmarks for insurers in the individual and small group marketplaces, which may have the effect of relaxing the essential health benefits required under the ACA for plans sold through such marketplaces.
- On May 30, 2018, the Right to Try Act, was signed into law. The law, among other things, provides a federal framework for certain patients to access certain investigational new drug products that have completed a Phase 1 clinical trial and that are undergoing investigation for FDA approval. Under certain circumstances, eligible patients can seek treatment without enrolling in clinical trials and without obtaining FDA permission under the FDA expanded access program. There is no obligation for a pharmaceutical manufacturer to make its drug products available to eligible patients as a result of the Right to Try Act.
- On May 23, 2019, CMS published a final rule to allow Medicare Advantage Plans the option of using step therapy for Part B drugs beginning January 1, 2020.
- On December 20, 2019, former President Trump signed into law the Further Consolidated Appropriations Act (H.R. 1865), which repealed the Cadillac tax, the health insurance provider tax, and the medical device excise tax. It is impossible to determine whether similar taxes could be instated in the future.

Additionally, there has been increasing legislative and enforcement interest in the U.S. with respect to drug pricing practices. Specifically, there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several U.S. Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, and review the relationship between pricing and manufacturer patient programs.

At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing.

We expect that the ACA, as well as other healthcare reform measures that may be adopted in the future, may result in additional reductions in Medicare and other healthcare funding, more rigorous coverage criteria, lower reimbursement, and new payment methodologies. This could lower the price that we receive for our products. Any denial in coverage or reduction in reimbursement from Medicare or other government-funded programs may result in a similar denial or reduction in payments from private payors, which may prevent us from being able to generate sufficient revenue, attain profitability or commercialize our products. It is not clear how other future potential changes to the ACA will change the reimbursement model and market outlook for our current and future therapeutic candidates.

The commercial success of our therapeutic candidates will depend upon the degree of market acceptance of such therapeutic candidates by physicians, patients, healthcare payors and others in the medical community.

Our therapeutic candidates may not be commercially successful. Even if any of our therapeutic candidates receive regulatory approval, they may not gain market acceptance among physicians, patients, healthcare payors or the medical community. The commercial success of any of our current or future therapeutic candidates will depend significantly on the broad adoption and use of the resulting product by physicians and patients for approved indications. The degree of market acceptance of our therapeutics will depend on a number of factors, including:

- demonstration of clinical efficacy and safety compared to other more-established products;
- the indications for which our therapeutic candidates are approved;
- the limitation of our targeted patient population and other limitations or warnings contained in any labeling required by the FDA or comparable foreign regulatory authorities;
- acceptance of a new drug for the relevant indication by healthcare providers and their patients;
- the pricing and cost-effectiveness of our therapeutics, as well as the cost of treatment with our therapeutics in relation to alternative treatments and therapies;
- our ability to obtain and maintain sufficient third-party coverage and adequate reimbursement from government healthcare programs, including Medicare and Medicaid, private health insurers and other third-party payors;
- the willingness of patients to pay all, or a portion of, out-of-pocket costs associated with our therapeutics in the absence of sufficient third-party coverage and adequate reimbursement;
- any restrictions on the use of our therapeutics, and the prevalence and severity of any adverse effects;
- potential product liability claims;
- the timing of market introduction of our therapeutics as well as competitive drugs;
- the effectiveness of our or any of our current or potential future collaborators' sales and marketing strategies; and
- unfavorable publicity relating to the product.

If any therapeutic candidate is approved but does not achieve an adequate level of acceptance by physicians, hospitals, healthcare payors or patients, we may not generate sufficient revenue from that product and may not become or remain profitable. Our efforts to educate the medical community and third-party payors regarding the benefits of our therapeutics may require significant resources and may never be successful.

Even if we are able to commercialize our therapeutic candidates, the products may not receive coverage and adequate reimbursement from third-party payors in the U.S. and in other countries in which we seek to commercialize our products, which could harm our business.

In the U.S. and markets in other countries, patients generally rely on third-party payors to reimburse all or part of the costs associated with their treatment. Adequate coverage and reimbursement from governmental healthcare programs, such as Medicare and Medicaid, and commercial payors is critical to new product acceptance. Our ability to successfully commercialize our therapeutic candidates will depend in part on the extent to which coverage and adequate reimbursement for these products and related treatments will be available from government health administration authorities, private health insurers and other organizations. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow us to establish or maintain pricing sufficient to realize a sufficient return on our investment. Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels.

There is also significant uncertainty related to the insurance coverage and reimbursement of newly approved products and coverage may be more limited than the purposes for which the medicine is approved by the FDA or comparable foreign regulatory authorities. In the U.S., the principal decisions about reimbursement for new medicines are typically made by the CMS. CMS decides whether and to what extent a new medicine will be covered and reimbursed under Medicare and private payors tend to follow CMS to a substantial degree.

Factors payors consider in determining reimbursement are based on whether the 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.

Net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the U.S. Increasingly, third-party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. We cannot be sure that reimbursement will be available for any therapeutic candidate that we commercialize and, if reimbursement is available, the level of reimbursement. In addition, many pharmaceutical manufacturers must calculate and report certain price reporting metrics to the government, such as average sales price, or ASP, and best price. Penalties may apply in some cases when such metrics are not submitted accurately and timely. Further, these prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs.

In addition, in some foreign countries, the proposed pricing for a drug must be approved before it may be lawfully marketed. The requirements governing drug pricing vary widely from country to country. For example, the European Union provides options for its Member States to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. To obtain reimbursement or pricing approval, some of these countries may require the completion of clinical trials that compare the cost effectiveness of a particular therapeutic candidate to currently available therapies. A Member State may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any of our therapeutic candidates. Historically, products launched in the European Union do not follow price structures of the U.S. and generally prices tend to be significantly lower.

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

We are subject to numerous foreign, federal, state and local environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations involve the use of hazardous and flammable materials, including chemicals and biological materials. Our operations also produce hazardous waste products. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources, including any available insurance.

In addition, our leasing and operation of real property may subject us to liability pursuant to certain of these laws or regulations. Under existing U.S. environmental laws and regulations, current or previous owners or operators of real property and entities that disposed or arranged for the disposal of hazardous substances may be held strictly, jointly and severally liable for the cost of investigating or remediating contamination caused by hazardous substance releases, even if they did not know of and were not responsible for the releases.

We could incur significant costs and liabilities which may adversely affect our financial condition and operating results for failure to comply with such laws and regulations, including, among other things, civil or criminal fines and penalties, property damage and personal injury claims, costs associated with upgrades to our facilities or changes to our operating procedures, or injunctions limiting or altering our operations. Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with our storage or disposal of biological, hazardous or radioactive materials.

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

Legislation or other changes in U.S. tax law could adversely affect our business and financial condition.

The rules dealing with U.S. federal, state, and local income taxation are constantly under review by persons involved in the legislative process and by the Internal Revenue Service and the U.S. Treasury Department. Changes to tax laws (which changes may have retroactive application) could adversely affect us or holders of our common stock. In recent years, many changes have been made to applicable tax laws and changes are likely to continue to occur in the future.

Future changes in tax laws could have a material adverse effect on our business, cash flow, financial condition or results of operations. It cannot be predicted whether, when, in what form, or with what effective dates, new tax laws may be enacted, or regulations and rulings may be enacted, promulgated or issued under existing or new tax laws, which could result in an increase in our or our stockholders' tax liability or require changes in the manner in which we operate in order to minimize or mitigate any adverse effects of changes in tax law or in the interpretation thereof. We urge investors to consult with their legal and tax advisers regarding the implications of potential changes in tax laws on an investment in our common stock.

Our ability to use our U.S. net operating loss carryforwards and certain other U.S. tax attributes may be limited.

Our ability to use our U.S. federal and state net operating losses to offset potential future taxable income and related income taxes that would otherwise be due is dependent upon our generation of future taxable income, and we cannot predict with certainty when, or whether, we will generate sufficient taxable income to use all of our net operating losses.

Under the TCJA, as amended by the CARES Act, unused U.S. federal net operating losses generated for tax years beginning after December 31, 2017 are not subject to expiration and may be carried forward indefinitely. Such U.S. federal net operating losses generally may not be carried back to prior taxable years, except that, net operating losses generated in 2018, 2019 and 2020 may be carried back to each of the five tax years preceding the tax years of such losses. Additionally, for taxable years beginning after December 31, 2020, the deductibility of such U.S. federal net operating losses is limited to 80% of our taxable income in any future taxable year. In addition, both our current and our future unused U.S. federal net operating losses and tax credits may be subject to limitations under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended (the Code), if we undergo an "ownership change," generally defined as a greater than 50 percentage point change (by value) in a corporation's equity ownership by certain stockholders over a rolling three-year period. We may have experienced such ownership changes in the past, and we may experience ownership changes in the future as a result of subsequent shifts in our stock ownership, some of which are outside our control. Our net operating losses and tax credits may also be impaired or restricted under state law. Our ability to utilize our net operating loss carryforwards could be limited by an "ownership change" as described above, which could result in increased tax liability to us.

Risks Related to Employee Matters and Managing our Growth

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

We are highly dependent on the expertise of our executive officers. Although we have entered into employment agreements and/or offer letters with our executive officers, each of them may terminate their employment with us at any time. Our industry has experienced a high rate of turnover in recent years. Our ability to compete in the highly competitive pharmaceuticals industry depends upon our

ability to attract, retain and motivate highly skilled and experienced personnel with scientific, clinical, regulatory, manufacturing and management skills and experience. We conduct our operations in the Cambridge, MA area, a region that is home to many other pharmaceutical companies as well as many academic and research institutions, resulting in fierce competition for qualified personnel. We may not be able to attract or retain qualified personnel in the future due to the intense competition for a limited number of qualified personnel among pharmaceutical companies. Many of the other pharmaceutical companies against which we compete have greater financial and other resources, different risk profiles and a longer history in the industry than we do. Our competitors may provide higher compensation, more diverse opportunities and/or better opportunities for career advancement. Any or all of these competing factors may limit our ability to continue to attract and retain high quality personnel, which could negatively affect our ability to successfully develop and commercialize our therapeutic candidates and to grow our business and operations as currently contemplated.

To induce valuable employees to remain at our company, in addition to salary, benefits, and cash incentives, we have provided stock options that vest over time. The value to employees of stock options that vest over time may be significantly affected by movements in our stock price that are beyond our control and may at any time be insufficient to counteract more lucrative offers from other companies. Despite our efforts to retain valuable employees, members of our management, scientific and development teams may terminate their employment with us on short notice. For example, employment of our key employees is at-will, which means that any of our employees could leave our employment at any time, with or without notice.

In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us.

We will need to grow our size and capabilities, and as a result, we may encounter difficulties in managing our growth, which could disrupt our operations.

As of April 30, 2022, we had 46 full-time employees. We expect to experience significant growth in the number of our employees and the scope of our operations, particularly in the areas of clinical development, clinical operations, manufacturing, regulatory affairs and, if any of our therapeutic candidates receives marketing approval, sales, marketing and distribution. We are continuing our efforts to recruit and hire the necessary employees to support our planned operations in the near term. However, competition for qualified employees among companies in the biotechnology and biopharmaceutical industry is intense, and no assurance can be given that we will be able attract, hire, retain and motivate the highly skilled employees that we need. Future growth will impose significant added responsibilities on members of management, including identifying, recruiting, integrating, maintaining and motivating additional employees and managing our internal development efforts effectively, while complying with our contractual obligations to contractors and other third parties. Our future financial performance and our ability to commercialize our product candidates, if approved, will depend, in part, on our ability to effectively manage any future growth, and our management may also have to divert a disproportionate amount of its attention away from day-to-day activities in order to devote a substantial amount of time to managing these growth activities.

To manage our anticipated future growth, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. Due to our limited financial resources and the limited experience of our management team in managing a company with such anticipated growth and potentially with developing sales, marketing and distribution infrastructure, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. The expansion of our operations may lead to significant costs and may divert our management and business development resources.

If we are not able to effectively manage growth and expand our organization, we may not be able to successfully implement the tasks necessary to further develop and commercialize VGL101, our other pipeline therapeutic candidates or any future therapeutic candidates and, accordingly, may not achieve our research, development and commercialization goals.

Our employees and independent contractors, including principal investigators, CROs, consultants and vendors, may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements.

We are exposed to the risk that our employees and independent contractors, including principal investigators, CROs, consultants and vendors may engage in misconduct or other illegal activity. Misconduct by these parties could include intentional, reckless and/or negligent conduct or disclosure of unauthorized activities to us that violate: (i) the laws and regulations of the FDA and other similar regulatory requirements, including those laws that require the reporting of true, complete and accurate information to such authorities, (ii) manufacturing standards, including cGMP requirements, (iii) federal and state data privacy, security, fraud and abuse and other healthcare laws and regulations in the U.S. and abroad or (iv) laws that require the true, complete and accurate reporting of financial information or data. Activities subject to these laws also involve the improper use or misrepresentation of information obtained in the course of clinical trials, the creation of fraudulent data in our preclinical studies or clinical trials or illegal misappropriation of drug

product, which could result in regulatory sanctions and cause serious harm to our reputation. It is not always possible to identify and deter misconduct by employees and other third parties, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations. In addition, we are subject to the risk that a person or government could allege such fraud or other misconduct, even if none occurred. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business and financial results, including, without limitation, the imposition of significant civil, criminal and administrative penalties, damages, monetary fines, disgorgements, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, imprisonment, contractual damages, reputational harm, diminished profits and future earnings, additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws and curtailment of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

We face significant competition, and if our competitors develop technologies or therapeutic candidates more rapidly than we do or their technologies are more effective, our business and our ability to develop and successfully commercialize products may be adversely affected.

The biotechnology and pharmaceutical industry is characterized by rapidly changing technologies, significant competition and a strong emphasis on intellectual property. These characteristics also apply to the development and commercialization of treatments in neurodegenerative diseases, including AD. While we believe that our focus, expertise, scientific knowledge and intellectual property provide us with competitive advantages, we face competition from several different sources, including large and small biopharmaceutical companies, academic research institutions, government agencies and public and private research organizations, that conduct research, seek patent protection, and establish collaborative arrangements for research, development, manufacturing and commercialization.

No products have been approved to treat ALSP, and we are not aware of any in clinical development other than VGL101. Academics have investigated the use of hematopoietic stem cell transplantation in a small number of ALSP patients, however, we believe this modality has limited benefits and several key limitations.

We are aware of one company, bluebirdbio, Inc., which received marketing approval for SKYSONA™ (elivaldogene autotemcel) in July 2021 in the European Union for a cALD treatment. In October 2021, the company announced it will withdraw its regulatory marketing authorization for SKYSONA™ from the European Union. In the U.S., development of elivaldogene autotemcel was put on clinical hold in August 2021 following a report that one treated patient developed myelodysplastic syndrome (MDS), a type of blood cancer. Two additional cases of MDS have been subsequently reported. In December 2021, bluebirdbio announced that the FDA has accepted its BLA for elivaldogene autotemcel for cALD. As of March 2022, a second company, Minoryx Therapeutics, Inc. is developing a small molecule therapeutic for the treatment of cALD in a Phase 2/3 trial.

Currently, there is a few other companies that are in the early stages of developing TREM2 agonists for the treatment of AD. We consider our direct competitors to be Alector, Inc. and its corporate partner, AbbVie Inc., Denali Therapeutics, Inc. and its corporate partner, Takeda Pharmaceutical Company, Cognyxx Pharmaceuticals, Inc. and Muna Therapeutics, Inc.

There are several existing treatments marketed today for the treatment of AD, which primarily provide symptomatic relief. Notably, Biogen Inc., received FDA accelerated approval for a product based on reduction of amyloid beta plaques, a biomarker that may predict a reduction in clinical decline; continued approval may require demonstration of disease-modifying benefits. Other pharmaceutical and biotechnology companies are pursuing disease-modifying treatments for AD and other common neurodegenerative disorders by seeking to modulate a range of targets. Companies pursuing microglia-targeted therapeutics include Janssen Pharmaceuticals, Inc., Alector Inc., Denali Therapeutics, Inc., Elixiron Therapeutics, Inc., Muna Therapeutics, Inc., Cognyxx Pharmaceuticals, Inc., and CAMP4 Therapeutics Corporation, Inc.

Many of our competitors have significant financial, technical, manufacturing, marketing, sales and supply resources or experience. These competitors also compete with us in recruiting qualified scientific and management personnel as well as establishing clinical trial sites and patient registration for clinical trials, and in acquiring new technologies. If we successfully obtain approval for any therapeutic candidate, we will face competition based on many different factors, including the safety and effectiveness of our therapeutics, the ease with which our therapeutics can be administered, the timing and scope of regulatory approvals for these products, the availability and cost of manufacturing, marketing and sales capabilities, price, reimbursement coverage and patent position. Competing products could present superior treatment alternatives, including by being more effective, safer, more convenient, less expensive or marketed and sold more effectively than any products we may develop. Competitive products or technological approaches may make any products we develop obsolete or noncompetitive before we recover the expense of developing and commercializing our therapeutic candidates. If we are unable to compete effectively, our opportunity to generate revenue from the sale of the therapeutics we may develop could be adversely affected.

Risks Related to Ownership of Our Common Stock

If securities or industry analysts do not publish research or reports, or if they publish adverse or misleading research or reports, regarding us, our business or our market, our stock price and trading volume could decline.

The trading market for our common stock will be influenced by the research and reports that securities or industry analysts publish about us, our business or our market. If few securities or industry analysts commence coverage of us, our stock price could be negatively impacted. In the event we obtain securities or industry analyst coverage, if any of the analysts who cover us issue adverse or misleading research or reports regarding us, our business model, our intellectual property, our stock performance or our market, or if our operating results fail to meet the expectations of analysts, our stock price would likely decline. If one or more of these analysts cease coverage of us or fail to publish reports on us regularly, we could lose visibility in the financial markets, which in turn could cause our stock price or trading volume to decline.

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

As widely reported, global credit and financial markets have experienced extreme volatility and disruptions in the past several years, most recently due to the COVID-19 pandemic, including severely diminished liquidity and credit availability, declines in consumer confidence, declines in economic growth, increases in unemployment rates and uncertainty about economic stability. There can be no assurance that further deterioration in credit and financial markets and confidence in economic conditions, whether due to the evolving effects of the COVID-19 pandemic or otherwise, will not occur. Our general business strategy may be adversely affected by any such economic downturn, volatile business environment or continued unpredictable and unstable market conditions. If the current equity and credit markets deteriorate, or do not improve, it may make any necessary debt or equity financing more difficult, more costly, and more dilutive.

Failure to secure necessary financing in a timely manner and on favorable terms could have a material adverse event on our growth strategy, financial performance and stock price and could require us to delay or abandon clinical development plans. In addition, there is a risk that one or more of our current service providers, manufacturers and other partners may not survive these difficult economic times, which could directly affect our ability to attain our operating goals on schedule and on budget. Our stock price may decline due in part to the volatility of the stock market and the general economic downturn.

Our principal stockholders and management own a significant percentage of our stock and will be able to exert significant control over matters subject to stockholder approval.

Our executive officers, directors, holders of 5% or more of our capital stock and their respective affiliates beneficially owned approximately 78% of our outstanding voting stock as of April 30, 2022.

These stockholders, acting together, may be able to impact matters requiring stockholder approval. For example, they may be able to impact elections of directors, amendments of our organizational documents or approval of any merger, sale of assets or other major corporate transaction. This may prevent or discourage unsolicited acquisition proposals or offers for our common stock that investors may feel are in their best interest as one of our stockholders. The interests of this group of stockholders may not always coincide with each investor's interests or the interests of other stockholders and they may act in a manner that advances their best interests and not necessarily those of other stockholders, including seeking a premium value for their common stock, and might affect the prevailing market price for our common stock.

Future sales and issuances of our common stock or rights to purchase common stock, including pursuant to our 2021 Plan, could result in additional dilution of the percentage ownership of our stockholders and could cause our stock price to fall.

We expect that significant additional capital may be needed in the future to continue our planned operations, including conducting clinical trials, commercialization efforts, expanded research and development activities and costs associated with operating a public company. To raise capital, we may sell common stock, convertible securities or other equity securities in one or more transactions at prices and in a manner we determine from time to time. If we sell common stock, convertible securities or other equity securities, investors may be materially diluted by subsequent sales. Such sales may also result in material dilution to our existing stockholders, and new investors could gain rights, preferences and privileges senior to the holders of our common stock. Pursuant to our 2021 Stock Option and Grant Plan (2021 Plan), our management is authorized to grant stock options to our employees, directors and consultants. If the number of shares reserved under our 2021 Plan is increased pursuant to the terms of the 2021 Plan, our stockholders may experience additional dilution, which could cause our stock price to fall. 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 administrator of the 2021 Plan is authorized to exercise its discretion to effect the repricing of stock options and stock appreciation rights and there may be adverse consequences to our business if the administrator of the 2021 Plan exercises such discretion.

Pursuant to our 2021 Plan, we are authorized to grant equity awards, including stock options and stock appreciation rights, to our employees, directors and consultants. The compensation committee is the administrator of the 2021 Plan and is authorized to exercise its discretion to reduce the exercise price of stock options or stock appreciation rights or effect the repricing of such awards. Although we do not anticipate needing to exercise this discretion in the near term, or at all, if the administrator of the 2021 Plan were to exercise such discretion without seeking prior stockholder approval, certain proxy advisory firms or institutional investors may be unsupportive of such actions and publicly criticize our compensation practices, and proxy advisory firms may recommend an "against" or "withhold" vote for members of our compensation committee. In addition, if we are required to hold an advisory vote on named executive officer compensation (known as the "say-on-pay" vote) at the time of, or subsequent to, any such repricing, it is likely that proxy advisory firms would issue an "against" recommendation on our say on pay vote and institutional investors may not be supportive of our say-on-pay vote. If proxy advisory firms or institutional investors are successful in aligning their views with our broader stockholder base and we are required to make changes to the composition of our board and its committees, or if we need to make material changes to our compensation and corporate governance practices, our business might be disrupted and our stock price might be negatively impacted. Even if we are able to successfully rationalize the exercise of such discretionary power, defending against any "against" or "withhold" recommendation for members of our compensation committee, any "against" recommendation on our say on pay vote or public criticism could be distracting to management, and responding to such positions from such firms or investors, even if remedied, can be costly and time-consuming.

In addition, if the administrator of the 2021 Plan does determine to reprice stock options or stock appreciation rights, even absent negative reactions from proxy advisory firms and institutional investors, and we could incur significant costs, including accounting and administrative costs and attorneys' fees. We may also be required to recognize incremental compensation expense as such result of a repricing. These actions could cause our stock price to decrease and experience periods of increased volatility, which could result in material adverse consequences to our business.

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

We do not have any committed external source of funds or other support for our development and commercialization efforts, and we cannot be certain that additional funding will be available on acceptable terms, or at all. Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through equity offerings, debt financings, or other capital sources, including potential collaborations, licenses and other similar 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. Any future 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, selling or licensing our assets, making capital expenditures, declaring dividends or encumbering our assets to secure future indebtedness. Such restrictions could adversely impact our ability to conduct our operations and execute our business plan.

As a result of our recurring losses from operations and recurring negative cash flows from operations, there is uncertainty regarding our ability to maintain liquidity sufficient to operate our business effectively. If we raise additional funds through future collaborations, licenses and other similar arrangements, we may have to relinquish valuable rights to our future revenue streams, research programs or therapeutic candidates, or grant licenses on terms that may not be favorable to us and/or that may reduce the value of our common stock. If we are unable to raise additional funds through equity or debt financings or other arrangements when needed or on terms acceptable to us, we would be required to delay, limit, reduce, or terminate our product development or future commercialization efforts or grant rights to develop and market therapeutic candidates that we would otherwise prefer to develop and market ourselves. 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.

We are an "emerging growth company" and a smaller reporting company, and we cannot be certain if the reduced reporting requirements applicable to emerging growth companies and smaller reporting companies will 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 (JOBS Act). For as long as we continue to be an emerging growth company, we intend to take advantage of exemptions from various reporting requirements that are applicable to other public companies that are not emerging growth companies, including:

- being permitted to provide only two years of audited financial statements, in addition to any required unaudited interim financial statements, with correspondingly reduced "Management's Discussion and Analysis of Financial Condition and Results of Operations" disclosure in our Annual Report on Form 10-K;
- not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002, as amended (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 in our Annual Report on Form 10-K and our periodic reports and proxy statements; and
- exemptions from the requirements of holding nonbinding advisory stockholder votes on executive compensation and stockholder approval of any golden parachute payments not previously approved.

Under the JOBS Act, emerging growth companies can also delay adopting new or revised accounting standards until such time as those standards apply to private companies. We have elected to avail ourselves of this exemption from new or revised accounting standards and, therefore, will not be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies. As a result, our financial statements may not be comparable to companies that comply with the new or revised accounting pronouncements as of public company effective dates.

We will remain an emerging growth company until the earliest to occur of: (i) the last day of the fiscal year in which we have more than $1.07 billion in annual revenue; (ii) the date we qualify as a "large accelerated filer," with at least $700.0 million of equity securities held by non-affiliates; (iii) the date on which we have issued more than $1.0 billion in non-convertible debt securities during the prior three-year period; and (iv) the last day of the fiscal year ending after the fifth anniversary of our initial public offering.

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 continue to take advantage of many of the same exemptions from disclosure requirements, including not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act and reduced disclosure obligations regarding executive compensation in our Annual Report on Form 10-K and our periodic reports and proxy statements. 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 price may be more volatile.

We do not intend to pay dividends on our common stock so any returns will be limited to the value of our stock.

We have never declared or paid any cash dividends on our common stock. We currently anticipate that we will retain future earnings for the development, operation and expansion of our business and do not anticipate declaring or paying any cash dividends for the foreseeable future. Any return to stockholders will therefore be limited to any appreciation in the value of their stock.

Anti-takeover provisions in our certificate of incorporation and bylaws and Delaware law might discourage, delay or prevent a change in control of our company or changes in our management and, therefore, depress the market price of our common stock.

Our third amended and restated certificate of incorporation and our amended and restated bylaws, contain provisions that could depress the market price of our common stock by acting to discourage, delay or prevent a change in control of our company or changes in our management that the stockholders of our company may deem advantageous. These provisions, among other things:

- a board of directors divided into three classes serving staggered three-year terms, such that not all members of the board will be elected at one time;
- a prohibition on stockholder actions through written consent, which requires that all stockholder actions be taken at a meeting of our stockholders;

- a requirement that special meetings of stockholders be called only by the board of directors acting pursuant to a resolution approved by the affirmative vote of a majority of the directors then in office;
- advance notice requirements for stockholder proposals and nominations for election to our board of directors;
- a requirement that no member of our board of directors may be removed from office by our stockholders except for cause and, in addition to any other vote required by law, upon the approval of not less than two-thirds of all outstanding shares of our voting stock then entitled to vote in the election of directors;
- a requirement of approval of not less than two-thirds of all outstanding shares of our voting stock to amend any bylaws by stockholder action or to amend specific provisions of our certificate of incorporation; and
- the authority of the board of directors to issue preferred stock on terms determined by the board of directors without stockholder approval and which preferred stock may include rights superior to the rights of the holders of common stock.

In addition, Section 203 of the General Corporation Law of the State of Delaware (DGCL) prohibits a publicly-held Delaware corporation from engaging in a business combination with an interested stockholder, generally a person which together with its affiliates owns, or within the last three years has owned, 15% of our voting stock, for a period of three years after the date of the transaction in which the person became an interested stockholder, unless the business combination is approved in a prescribed manner.

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

Our bylaws designate certain courts as the sole and 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 bylaws provide that, unless we consent in writing to an alternative forum, the Court of Chancery of the State of Delaware will be the sole and exclusive forum for any state law claims for (i) any derivative action or proceeding brought on our behalf, (ii) any action asserting a claim of breach of, or a claim based on, fiduciary duty owed by any of our current or former directors, officers, and employees to us or our stockholders, (iii) any action asserting a claim arising pursuant to any provision of the Delaware General Corporation Law, our certificate of incorporation or our bylaws (including the interpretation, validity or enforceability thereof), or (iv) any action asserting a claim that is governed by the internal affairs doctrine, in each case subject to the Court of Chancery having personal jurisdiction over the indispensable parties named as defendants therein (Delaware Forum Provision). The Delaware Forum Provision will not apply to any causes of action arising under the Securities Act or the Exchange Act. Our amended and restated bylaws further provide that, unless we consent in writing to the selection of an alternative forum, the United States District Court for the District of Massachusetts shall be the sole and exclusive forum for resolving any complaint asserting a cause or causes of action arising under the Securities Act (Federal Forum Provision). In addition, our amended and restated bylaws provide that any person or entity purchasing or otherwise acquiring any interest in shares of our common stock is deemed to have notice of and consented to the foregoing provisions; provided, however, that stockholders cannot and will not be deemed to have waived our compliance with the federal securities laws and the rules and regulations thereunder.

The Delaware Forum Provision and the Federal Forum Provision in our amended and restated bylaws may impose additional litigation costs on stockholders in pursuing any such claims. Additionally, the forum selection clauses in our amended and restated bylaws may limit our stockholders' ability to bring a claim in a forum that they find favorable for disputes with us or our directors, officers or employees, which may discourage such lawsuits against us and our directors, officers and employees even though an action, if successful, might benefit our stockholders. In addition, while the Delaware Supreme Court ruled in March 2020 that federal forum selection provisions purporting to require claims under the Securities Act be brought in federal court were "facially valid" under Delaware law, there is uncertainty as to whether other courts will enforce our Federal Forum Provision. If the Federal Forum Provision is found to be unenforceable, we may incur additional costs associated with resolving such matters. The Federal Forum Provision may also impose additional litigation costs on stockholders who assert that the provision is not enforceable or invalid. The Court of Chancery of the State of Delaware and the federal district courts of the U.S. may also reach different judgments or results than would other courts, including courts where a stockholder considering an action may be located or would otherwise choose to bring the action, and such judgments may be more or less favorable to us than our stockholders.

General Risk Factors

We may be subject to securities litigation, which is expensive and could divert management attention.

The market price of our common stock may be volatile and, in the past, companies that have experienced volatility in the market price of their stock have been subject to securities class action litigation. We may be the target of this type of litigation in the future. Securities litigation against us could result in substantial costs and divert our management's attention from other business concerns, which could seriously harm our business.

We will incur increased costs as a result of operating as a public company, and our management will devote substantial time to related compliance initiatives.

As a public company, we are subject to the reporting requirements of the Securities Exchange Act of 1934, as amended (Exchange Act), the Sarbanes-Oxley Act, the Dodd-Frank Wall Street Reform and Protection Act, as well as rules adopted, and to be adopted, by the SEC and Nasdaq. Our management and other personnel need to devote a substantial amount of time to these compliance initiatives. Moreover, we expect these rules and regulations to substantially increase our legal and financial compliance costs and to make some activities more time-consuming and costly, which will increase our operating expenses. For example, we expect these rules and regulations to make it more difficult and more expensive for us to obtain director and officer liability insurance and we may be required to incur substantial costs to maintain sufficient coverage, particularly in light of recent cost increases related to coverage. We cannot accurately predict or estimate the amount or timing of additional costs we may incur to respond to these requirements. The impact of these requirements could also make it more difficult for us to attract and retain qualified persons to serve on our board of directors, our board committees or as executive officers.

In addition, as a public company we are required to incur additional costs and obligations in order to comply with SEC rules that implement Section 404 of the Sarbanes-Oxley Act. Under these rules, beginning with our second annual report on Form 10-K after we become a public company, we will be required to make a formal assessment of the effectiveness of our internal control over financial reporting, and once we cease to be an emerging growth company, we may be required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. To achieve compliance with Section 404 within the prescribed period, we will be engaging in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to continue to dedicate internal resources, potentially engage outside consultants and adopt a detailed work plan to assess and document the adequacy of our internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are designed and operating effectively, and implement a continuous reporting and improvement process for internal control over financial reporting.

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

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

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

The market price of our common stock may be volatile, and investors could lose all or part of their investment.

The trading price of our common stock is likely to be highly volatile and subject to wide fluctuations in response to various factors, some of which we cannot control. The stock market in general, and pharmaceutical and biotechnology companies in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies.

Broad market and industry factors may negatively affect the market price of our common stock, regardless of our actual operating performance. In addition to the factors discussed in this "Risk Factors" section and elsewhere in this Quarterly Report, these factors include:

- the timing and results of INDs, preclinical studies and clinical trials of our therapeutic candidates or those of our competitors;
- the success of competitive products or announcements by potential competitors of their product development efforts;

- our decision to initiate a clinical trial, not to initiate a clinical trial or to terminate an existing clinical trial;
- any delay in our regulatory filings for our therapeutic candidates and any adverse development or perceived adverse development with respect to the applicable regulatory authority's review of such filings;
- adverse developments concerning our potential future in-house manufacturing facilities or CMOs;
- regulatory actions with respect to our therapeutics or therapeutic candidates or our competitors' products or therapeutic candidates;
- actual or anticipated changes in our growth rate relative to our competitors;
- the size and growth of our initial target markets;
- unanticipated serious safety concerns related to the use of our therapeutic candidates;
- regulatory or legal developments in the U.S. and other countries;
- developments or disputes concerning patent applications, issued patents or other proprietary rights;
- significant lawsuits, including patent or stockholder litigation;
- publication of research reports about us or our industry, or positive or negative recommendations or withdrawal of research coverage by securities analysts;
- the recruitment or departure of key personnel;
- announcements by us or our competitors of significant acquisitions, strategic collaborations, joint ventures, collaborations or capital commitments;
- actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts;
- fluctuations in the valuation of companies perceived by investors to be comparable to us;
- market conditions in the pharmaceutical and biotechnology sector;
- changes in the structure of healthcare payment systems;
- share price and volume fluctuations attributable to inconsistent trading volume levels of our shares;
- our failure to meet the estimates and projections of the investment community or that we may otherwise provide to the public;
- announcement or expectation of additional financing efforts;
- sales of our common stock by us, our insiders or our other stockholders;
- expiration of market stand-off or lock-up agreements;
- the impact of any natural disasters or public health emergencies, such as the COVID-19 pandemic;
- general economic, political, industry and market conditions; and
- other events or factors, many of which are beyond our control.

The realization of any of the above risks or any of a broad range of other risks, including those described in this "Risk Factors" section, could have a dramatic and adverse impact on the market price of our common stock.

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

Recent Sales of Unregistered Securities

None.

Use of Proceeds from Registered Securities

On January 6, 2022, the SEC declared effective our registration statement on Form S-1 (File No. 333-261230), as amended, filed in connection with our IPO, or the Registration Statement. Pursuant to the Registration Statement, we registered the offer and sale of 7,000,000 shares of our common stock with a proposed maximum aggregate offering price of approximately $136,850,000. Morgan Stanley & Co. LLC and Jefferies LLC acted as representatives of the underwriters for the offering. On January 11, 2022, we issued and sold 7,000,000 shares of our common stock at a price to the public of $14.00 per share. Upon completion of the IPO on January 11, 2022, we received net proceeds of approximately $91.1 million, after deducting underwriting discounts and commissions, but before deducting offering costs payable by us of $3.1 million. No payments for such expenses were made directly or indirectly to (i) any of our officers or directors or their associates, (ii) any persons owning 10% or more of any class of our equity securities or (iii) any of our affiliates.

We are holding a significant portion of the balance of the net proceeds in a variety of capital preservation investments, including money market funds, short-term investment-grade, interest bearing instruments and U.S. government securities. There has been no material change in the planned proceeds from our IPO, as described in our final prospectus filed with the SEC on January 10, 2022 pursuant to Rule 424(b) under the Securities Act.

The offering terminated after the sale of all securities registered pursuant to the Registration Statement. There has been no material change in the expected use of the net proceeds from our IPO as described in the final prospectus dated January 6, 2022 and filed with the SEC on January 10, 2022, pursuant to Rule 424(b)(4) (File No. 333-261230) of the Securities Act.

Item 3. Defaults Upon Senior Securities.

Not Applicable.

Item 4. Mine Safety Disclosures.

Not Applicable.

Item 5. Other Information.

None.

Item 6. Exhibits

Furnish the exhibits required by Item 601 of Regulation S-K (§ 229.601 of this chapter).

Exhibit Number	Description
3.1	Third Amended and Restated Certificate of Incorporation of the Registrant ((incorporated by reference to Exhibit 3.1 to the Registrant's Form 8-K (File No. 001-41200) filed on January 11, 2022).
3.2	Amended and Restated Bylaws of the Registrant. (incorporated by reference to Exhibit 3.2 to the Registrant's Form 8-K (File No. 001-41200) filed on January 11, 2022).
4.1	Specimen Common Stock Certificate (incorporated by reference to Exhibit 4.1 of the Registrant's Registration Statement on Form S-1/A (File No. 333-261230) filed on January 3, 2022).
10.1	2021 Stock Option and Incentive Plan and form of award agreements thereunder (incorporated by reference to Exhibit 10.2 of the Registrant's Registration Statement on Form S-1/A (File No. 333-261230) filed on January 3, 2022).
10.2	2021 Employee Stock Purchase Plan (incorporated by reference to Exhibit 10.3 of the Registrant's Registration Statement on Form S-1/A (File No. 333-261230) filed on January 3, 2022).
10.3	Form of Indemnification Agreement between the Registrant and each of its directors and executive officers (incorporated by reference to Exhibit 10.4 of the Registrant's Registration Statement on Form S-1/A (File No. 333-261230) filed on January 3, 2022).
10.4	Senior Executive Cash Incentive Bonus Plan (incorporated by reference to Exhibit 10.5 of the Registrant's Registration Statement on Form S-1 (File No. 333-261230) filed on November 19, 2021).
10.5	Form of Executive Employment Agreement (incorporated by reference to Exhibit 10.6 of the Registrant's Registration Statement on Form S-1 (File No. 333-261230) filed on November 19, 2021).
10.6	Non-Employee Director Compensation Policy (incorporated by reference to Exhibit 10.7 of the Registrant's Registration Statement on Form S-1 (File No. 333-261230) filed on November 19, 2021).
31.1*	Certification of Principal Executive Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
31.2*	Certification of Principal Financial Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
32.1**	Certification of Principal Executive Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
32.2**	Certification of Principal Financial Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
101.INS*	Inline XBRL Instance Document – the instance document does not appear in the Interactive Data File because XBRL tags are embedded within the Inline XBRL document.
101.SCH*	Inline XBRL Taxonomy Extension Schema Document
101.CAL*	Inline XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF*	Inline XBRL Taxonomy Extension Definition Linkbase Document
101.LAB*	Inline XBRL Taxonomy Extension Label Linkbase Document
101.PRE*	Inline XBRL Taxonomy Extension Presentation Linkbase Document
104*	Cover Page Interactive Data File (embedded within the Inline XBRL document)

* Filed herewith.

** The certifications furnished in Exhibit 32.1 and Exhibit 32.2 hereto are deemed to accompany this Quarterly Report on Form 10-Q and will not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended. Such certifications will not be deemed to be incorporated by reference into any filings under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended, except to the extent that the Registrant specifically incorporates it by reference.

SIGNATURES

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

Vigil Neuroscience, Inc.

Date: May 12, 2022 By: /s/ Ivana Magovčević-Liebisch

Ivana Magovčević-Liebisch, PhD, JD
President and Chief Executive Officer
(Principal Executive Officer)

Date: May 12, 2022 By: /s/ Jennifer Ziolkowski

Jennifer Ziolkowski
Chief Financial Officer
(Principal Financial and Accounting Officer)

Exhibit 31.1

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

I, Ivana Magovčević-Liebisch , certify that:

(1) I have reviewed this quarterly report on Form 10-Q of Vigil Neuroscience, Inc.;

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

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

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

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

(b) (Paragraph omitted pursuant to SEC Release Nos. 33-8238/34-47986 and 33-8392/34-49313);

(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/ Ivana Magovčević-Liebisch
Ivana Magovčević-Liebisch
President and Chief Executive Officer

(Principal Executive Officer)

Exhibit 31.2

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

I, Jennifer Ziolkowski, certify that:

(1) I have reviewed this quarterly report on Form 10-Q of Vigil Neuroscience, Inc.;

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

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

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

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

(b) (Paragraph omitted pursuant to SEC Release Nos. 33-8238/34-47986 and 33-8392/34-49313);

(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/ Jennifer Ziolkowski
Jennifer Ziolkowski
Chief Financial Officer

(Principal Financial Officer)

Exhibit 32.1

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

In connection with the Quarterly Report on Form 10-Q of Vigil Neuroscience, Inc. (the "Company") for the period ended March 31, 2022 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I certify, pursuant to 18 U.S.C. § 1350, as adopted pursuant to § 906 of the Sarbanes-Oxley Act of 2002, that:

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

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

Date: May 12, 2022

By: /s/ Ivana Magovčević-Liebisch
Ivana Magovčević-Liebisch
President and Chief Executive Officer

(Principal Executive Officer)

Exhibit 32.2

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

In connection with the Quarterly Report on Form 10-Q of Vigil Neuroscience, Inc. (the "Company") for the period ended March 31, 2022 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I certify, pursuant to 18 U.S.C. § 1350, as adopted pursuant to § 906 of the Sarbanes-Oxley Act of 2002, that:

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

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

Date: May 12, 2022

By: /s/ Jennifer Ziolkowski
Jennifer Ziolkowski
Chief Financial Officer

(Principal Financial Officer)