UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-K

(Mark One)

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

For the fiscal year ended December 31, 2021

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

Securities registered pursuant to Section 12(g) of the Act: **None**

Indicate by check mark if the Registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. YES ☐ NO ☒

Indicate by check mark if the Registrant is not required to file reports pursuant to Section 13 or 15(d) of the Act. YES ☐ NO ☒

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 has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report. ☐

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

The Registrant was not a public company as of the last business day of its most recently completed second fiscal quarter and therefore cannot calculate the aggregate market value of the voting and non-voting common equity held by non-affiliates as of such date.

The number of shares of Registrant's Common Stock outstanding as of February 28, 2022 was 28,266,815.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's proxy statement for the 2022 annual meeting of stockholders to be filed pursuant to Regulation 14A within 120 days after the registrant's fiscal year ended December 31, 2021, are incorporated by reference in Part III of this Form 10-K.

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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 Annual Report on Form 10-K, 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 Annual Report on Form 10-K 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 Annual Report on Form 10-K 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 Annual Report on Form 10-K. 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 Annual Report on Form 10-K and the documents that we reference in this Annual Report on Form 10-K 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 Annual Report on Form 10-K represent our views as of the date of this Annual Report on Form 10-K. 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 Annual Report on Form 10-K.

This Annual Report on Form 10-K 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 Annual Report on Form 10-K, 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 Annual Report on Form 10-K.

PART I

Item 1. Business.

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. Our lead candidate, VGL101, is a fully human monoclonal antibody (mAb) that is designed to activate TREM2. In November 2021, the FDA cleared our Investigational New Drug application (IND) for VGL101 in ALSP at doses up to 20 mg/kg, with a partial clinical hold on doses higher than 20 mg/kg. We do not believe the partial clinical hold will have a material impact on our current clinical development plans and timelines for our clinical trial in ALSP. We initiated our first-in-human Phase 1 clinical trial with VGL101 in healthy volunteers in December 2021 and as of today, we have completed dosing of the 20 mg/kg SAD (single ascending dose) cohort without any safety signals and initiated the 20 mg/kg MAD (multiple ascending dose) cohort. We expect to announce topline data in the second half of 2022. 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. We intend to expand development of VGL101 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. The initial focus of our novel small molecule TREM2 agonist program is for the treatment of Alzheimer's disease (AD) in genetically defined subpopulations. In the first quarter of 2022, we initiated IND-enabling studies for this program and expect to file an IND in 2023. 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.

Microglia sense signals in the brain, maintain homeostasis, and coordinate signal-specific downstream responses to clear pathogens and cellular debris that can evolve into disease-inducing agents. Homeostatic microglia transition to a neuroprotective disease-associated microglia (DAM) phenotype that maintains the anti-inflammatory CNS environment and removes protein clumps (misfolded protein aggregates that can form plaques) and cellular debris that accumulate in the brains of patients with neurodegenerative diseases and during normal aging. Microglial dysfunction, including the failure to transition to the DAM phenotype, is linked to a range of rare and common neurodegenerative diseases, including leukoencephalopathies, leukodystrophies, AD (particularly genetically defined AD subpopulations), and frontotemporal dementia (FTD). Preclinical data generated by third parties also support the modulation of microglia as a potential therapeutic approach in a variety of CNS diseases in the absence of a clear genetic link to microglial dysfunction such as Parkinson's disease (PD) and Multiple Sclerosis (MS).

TREM2 acts as a sensor to detect cellular debris, lipids, and other damage signals. The receptor's normal function is required for microglial transition to the neuroprotective DAM phenotype. TREM2's protective role in neurodegenerative diseases was discovered through genome-wide association studies (GWAS). Multiple third party studies in animal models and in humans have shown that TREM2 deficiency is a likely driver of neurodegeneration, and we believe such studies provide a compelling rationale for therapeutically activating TREM2 signaling to treat neurodegenerative diseases.

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.

We are executing on this approach with our lead pipeline candidate, VGL101, by initially focusing on the treatment of ALSP. ALSP affects an estimated 10,000 people in the U.S., with about 1,000 to 2,000 new cases annually. ALSP has been

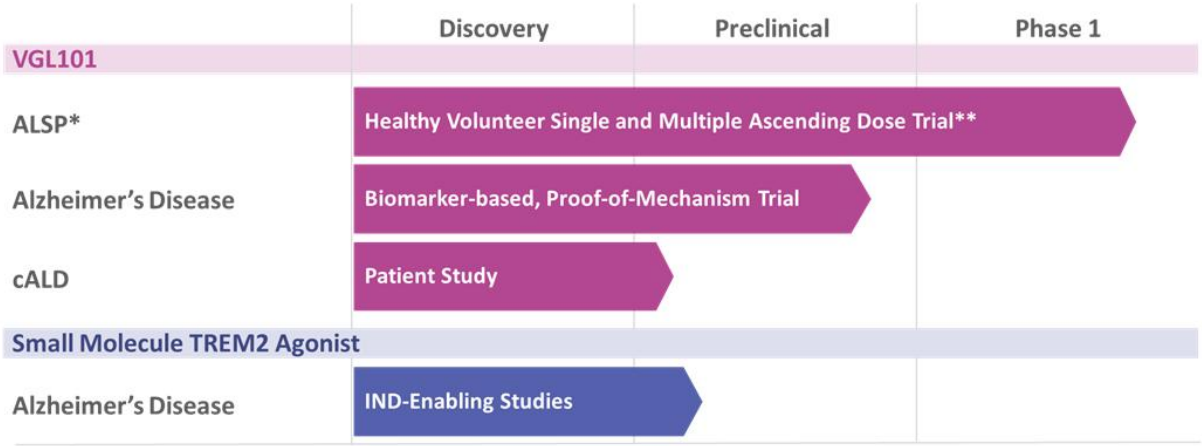
diagnosed in countries around the world, with major clusters in North America (U.S. and Canada), Central and Northern Europe, and Asia. ALSP is caused by loss-of-function mutations in the Colony Stimulating Factor 1 Receptor (CSF1R), a receptor that shares a common downstream signaling pathway with TREM2. 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.

Engagement with our stakeholders, including patients and 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 actively support a patient advocacy organization and have created a strong global network of key opinion leaders (KOLs), centers of excellence, and genetic counseling practices that each treat ALSP patients and work with families affected by the disease. We have also established the world's first patient-facing ALSP informational website to build disease awareness and recently we launched a global ALSP patient registry to further understand patient and caregiver journey, disease burden, and health economic outcomes.

Beyond VGL101, we are developing a novel small molecule TREM2 activator (agonist) for the treatment of AD. GWAS have shown that a specific mutation in a *TREM2* variant (R47H) has one of the strongest associations with the development of AD, second in magnitude only to that associated with the apolipoprotein E4 (*ApoE4*) genotype. Our strategy in AD is to initially target genetically defined AD subpopulations with microglia dysregulation including those carrying *TREM2* and other variants. As a first step, we plan to conduct a Phase 1b biomarker-based proof-of-mechanism trial with VGL101 in these AD subpopulations. We expect the VGL101 Phase 1b data to inform the target patient population and design for future larger studies in AD that evaluate the safety and efficacy of our small molecule.

AD is the most common cause of dementia affecting an estimated 6.2 million patients in the U.S. alone as well as their families and caregivers**.** The cost of care for people with AD to our healthcare system is substantial. According to the Alzheimer's Association, the aggregate cost of AD and other dementias is expected to be $355 billion in 2021, and this number could increase to as much as $1.1 trillion by 2050.

The following table highlights our preclinical and clinical programs.



** Additional non-interventional observational Natural History Study in ALSP is ongoing*

*** The healthy volunteer single and multiple ascending dose trial is a first-in-human Phase 1 clinical trial, principally to evaluate VGL101's safety and tolerability. The trial, depending on the safety and tolerability results, is expected to provide a basis for conducting subsequent clinical trials in ALSP, AD, and cALD patients.*

Over time, we plan to expand our pipeline, either through internal discovery and development, or through strategic collaborations or alliances with academic organizations or pharmaceutical or biotechnology companies.

Our Business Strategy

Our goal is to be a leader in the development and commercialization of microglia-targeted, disease-modifying therapeutics that slow or halt progression of a range of rare and common neurodegenerative diseases. Key elements of our business strategy are to:

- **Apply 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 initial indications we are pursuing are rare diseases that have strong genetic, mechanistic, and biochemical associations with microglial dysfunction. We believe these associations provide a strong rationale for potential intervention with microglia-targeted therapies. By focusing on these known relationships, we believe we may mitigate downstream translational risk as we seek to advance our programs through early development and into the clinic. We expect this approach will allow us to identify biologically and clinically relevant biomarkers and to generate PoC efficiently. We plan to apply the specific learnings from these studies to pursue the development of our therapeutic candidates in other neurodegenerative disease indications with broader patient populations.
- **Advance our lead therapeutic candidate, VGL101, a mAb TREM2 agonist, for the treatment of ALSP and other rare leukoencephalopathies and leukodystrophies.** We are currently developing VGL101, our fully human mAb that is highly selective for TREM2, for the treatment of ALSP. We believe there is strong genetic, molecular, and cellular evidence implicating microglial dysfunction and signaling deficiency in ALSP, which we believe could be correctable through TREM2 activation. In November 2021, the FDA cleared our IND for VGL101 in ALSP at doses up to 20 mg/kg, with a partial clinical hold on doses higher than 20 mg/kg. We do not believe the partial clinical hold will have a material impact on our current clinical development plans and timelines for our clinical trial in ALSP. We initiated our first-in-human Phase 1 clinical trial with VGL101 in healthy volunteers in December 2021 and as of today, we have completed dosing of the 20 mg/kg SAD cohort without any safety signals and initiated the 20 mg/kg MAD cohort in our Phase 1 trial. We expect to announce topline data from the Phase 1 trial in the second half of 2022. Assuming our Phase 1 trial progresses on our expected timeline, our FDA discussions proceed as currently planned, and we identify an acceptable dose as part of the Phase 1 trial, we believe we can initiate our interventional studies in ALSP in the second half of 2022. We plan to leverage various target engagement and therapeutic biomarkers to evaluate the biology and clinical activity of VGL101. Target engagement biomarkers, such as IP-10, the soluble versions of the Colony Stimulating Factor 1 Receptor (sCSF1R) and TREM2 (sTREM2), are designed to assess VGL101's ability to bind to TREM2 and generate a biological result, such as increased or decreased levels of a protein specifically resulting from TREM2 activation. Such studies aim to establish proof of mechanism (PoM). We believe disease biomarkers, such as changes in the neurofilament light protein (NfL) levels in serum or cerebrospinal fluid, and magnetic resonance imaging (MRI) for white matter lesion changes, are potential indicators of therapeutic response and in human studies, may support demonstration of PoC. We also plan to submit a protocol to the FDA under our open IND to conduct a Phase 1b biomarker-based, PoM clinical trial with VGL101 in genetically defined AD patients with or without the relevant *TREM2* variants, expected to begin in the second half of 2022. We may seek to expand the development of VGL101 for use in additional rare leukoencephalopathies and leukodystrophies where microglia play an essential role, including cALD, for which we plan to submit an IND amendment or additional IND, if required, to conduct a Phase 2 clinical trial in the first half of 2023 following the completion of the VGL101 Phase 1 clinical trial in healthy volunteers. This class of diseases is also characterized by increased permeability of the blood brain barrier, which we expect will facilitate the passage of VGL101 from the bloodstream into the brain.

- **Develop a novel, orally-available, small molecule TREM2 agonist for the treatment of more common neurodegenerative diseases, beginning with genetically defined subpopulations of AD patients.** Peer reviewed literature suggests a strong genetic association between certain *TREM2* variants and the development and progression of AD. We believe our precision medicine approach will enable us to identify subpopulations of AD patients who are most likely to benefit from treatment with a small molecule TREM2 agonist. We plan to begin the work of selecting genetically defined subpopulations to evaluate in our small molecule program by studying microglial modulation with VGL101. As mentioned above, in the second half of 2022, we also plan to conduct a Phase 1b biomarker-based, PoM clinical trial with VGL101 in genetically defined AD patients with or without the relevant *TREM2* variants. Data from these and other studies will inform the selection of the patient population for a Phase 2 clinical trial with a small molecule candidate designed to evaluate efficacy and safety. In preclinical studies conducted to date, the small molecule compounds we are developing have demonstrated encouraging CNS penetration and physiochemical properties that we believe make them suitable for oral delivery. We believe that an orally-available small molecule therapeutic may have meaningful clinical and commercial advantages in large chronic indications, especially when treatment is administered in the outpatient setting. In the first quarter of 2022, we initiated IND-enabling studies for this program and expect to file an IND application in 2023.
- **Expand our modality-agnostic product pipeline to other microglial targets beyond TREM2.** Given the central role that microglia play in maintaining brain health, we plan to explore targets beyond TREM2 for the development of therapeutics that modulate microglial activity across multiple modalities for the treatment of additional neurodegenerative diseases. We plan to regularly evaluate opportunities to expand and diversify our pipeline either through internal discovery and development, or through strategic collaborations or alliances with academic organizations or pharmaceutical or biotechnology companies.
- **Engage the stakeholder community including patients, advocacy groups, and clinical leaders**. Support of the stakeholder community is an integral part of our mission to bring microglia-targeted therapeutics to patients with neurodegenerative diseases. Early and ongoing engagement increases our understanding of the patient journey, helps build disease awareness, and facilitates recruitment of patients and clinicians to participate in clinical trials. For example, we actively support the first and only ALSP patient organization, Sisters' Hope Foundation, and launched the world's first patient-facing ALSP informational website, to increase ALSP awareness, engage with and support patients, the clinical community, and other relevant stakeholders. We recently launched a global ALSP patient registry to further understand patient and caregiver journey, disease burden, and health economic outcomes. Beyond developing an ALSP KOL network and forming our Patient and Caregiver Advisory Council (PCAC), we have also partnered with larger leukodystrophy and rare disease umbrella organizations, such as United Leukodystrophy Foundation, National Organization for Rare Diseases (NORD), Global Genes, the Every Life Foundation, and the European Leukodystrophy Association.

Microglia and Their Role in CNS Health and Neurodegeneration

Microglia are the sentinel immune cells of the brain and play a critical role in maintaining CNS health, or homeostasis, and responding to damage caused by disease. In recent years, the scientific community's understanding of microglia's role in brain health and neurodegeneration has advanced markedly. A 2020 review in the journal *Science*, for example, highlighted microglia's "fundamental role" as "governors of neuronal function and homeostasis in the adult brain." In their homeostatic state, microglia monitor for potential damage. Microglia sense multiple types of signals in the brain, including those generated by infection, cell death and breakdown, and replacement of myelin (sheaths of protein and fat that insulate axon fibers that turn over as part of normal brain physiology). Homeostatic microglia transition to a DAM phenotype and then coordinate signal-specific downstream responses, such as potentiation of microglial survival and proliferation, activation of microglial phagocytosis (cellular debris removal by innate immune cells), removal of unneeded neural connections (axonal pruning) to maintain synaptic health, and stimulation of microglial lysosomal function, and lipid and cholesterol metabolism.

Recent studies have shown that DAM possess neuroprotective disease-preventing effects. DAM are not associated with any specific primary cause of disease pathology or disease etiology, but rather display a protective phenotype that maintains the anti-inflammatory CNS environment and removes protein clumps and cellular debris that accumulate in the brains of patients with neurodegenerative diseases and during normal aging. Microglia maintain homeostasis in healthy areas of the brain by preventing accumulation of debris resulting from normal brain maintenance and thus preventing initiation of neuroinflammation and neuropathology. For example, in AD animal model studies, DAM congregate and form a protective barrier at sites of neuroinflammatory lesions and around neurotoxic plaques, which are aggregates of ß-amyloid protein.

The essential role played by microglia in maintaining brain health is exemplified by diseases of the white matter, such as leukoencephalopathies and leukodystrophies. In these diseases, microglial dysfunction directly affects neuronal function and

white matter integrity. White matter consists of bundles of axon fibers wrapped in myelin sheaths that project from neurons and transmit signals across the brain. The bundles of myelin sheaths appear white and together are called white matter. Debris from the maintenance and regeneration of myelin sheaths must be cleared away by DAM to prevent inflammation and subsequent neurodegeneration. Microglial dysfunction and the resulting build-up of inflammatory myelin debris in these diseases leads to destruction of the white matter and the breakdown of the blood brain barrier, which can allow disruptive infiltration of inflammatory cells that further drive disease progression. Therefore, we believe treatments that prevent long term microglial dysfunction could prevent failure of the blood brain barrier and the resulting devastating inflammation that leads to neurodegeneration.

In more common neurodegenerative diseases such as AD, evidence suggests that microglia dysfunction is present in genetically defined subpopulations. Similar to leukoencephalopathies and leukodystrophies, failure of microglia to remove debris, in this case protein clumps, is believed to lead to degeneration of vulnerable neuronal subtypes. Restoring microglial function could prevent the expansion of ß-amyloid plaque and slow down the neurodegenerative process in these subpopulations.

Our initial focus on microglia and microglia-targeted therapeutics is based on research linking microglia to both rare and common neurodegenerative diseases that either result from genetic mutations or are associated with genetic variations. These conditions include leukoencephalopathies and leukodystrophies, a set of rare, mainly genetic disorders affecting neurons and white matter, such as ALSP, cALD, Krabbe, MLD, as well as genetic subpopulations of AD carrying variants affecting microglial function. Due to their multiple functions, microglia are also implicated in other CNS diseases, including AD, FTD, MS, PD, amyotrophic lateral sclerosis (ALS), and certain rare epilepsies.

Genomic analyses have shown that genetic mutations or variations that affect microglial physiology predispose individuals to neuroimmune dysfunction and neurodegeneration. As a result, the brain’s immune function, orchestrated by microglia, deteriorates, and subsequently fails to carry out critical activities, which include:

- clearing pathological neurodegenerative protein aggregates, such as those that accumulate in AD, to prevent accumulation and subsequent neuroinflammation;
- providing metabolic and functional support to maintain healthy nerve cells;
- regulating connections between nerve cells;
- removing white matter debris to prevent inflammation; and
- maintaining blood brain barrier integrity and regulating neurovascular function.

As illustrated in Figure 1 below, diseases colored in green represent our current focus areas, while diseases colored in purple represent potential future therapeutic opportunities for modulating microglial function.

Figure 1: Neurodegenerative Diseases Linked to Microglial Function and U.S. Prevalence Estimates

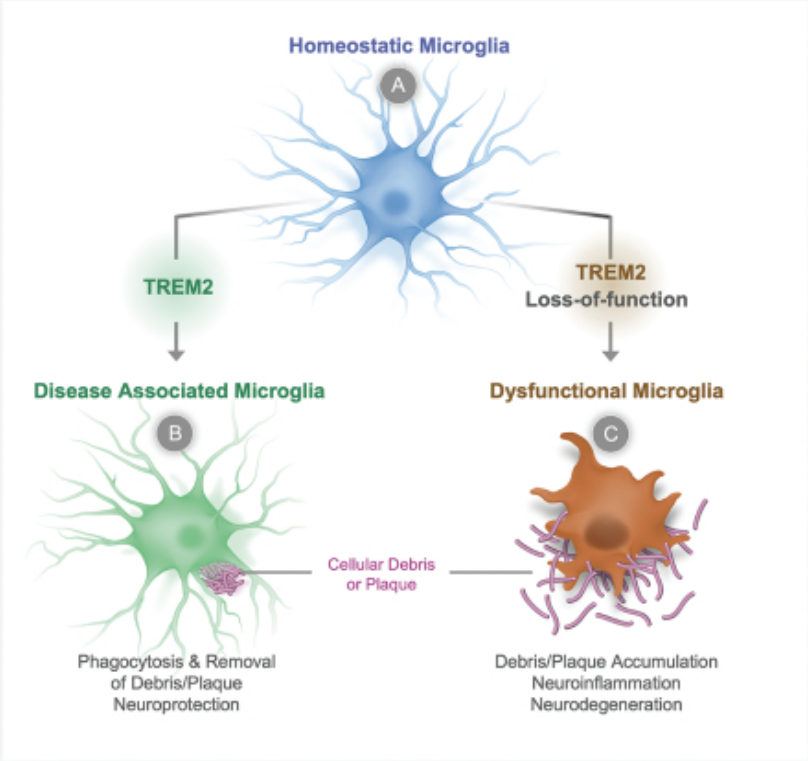
**Lennox-Gastaut & Dravet Syndromes (i.e., rare epilepsies).*

TREM2: Our Initial Therapeutic Target

Our most advanced therapeutic programs are aimed at developing activators of TREM2, a membrane spanning receptor expressed specifically on microglia in the brain. TREM2 is essential for microglia's homeostatic maintenance functions and response to inflammatory CNS damage in various disease states. TREM2 acts like a sensor to detect cellular damage in the brain, such as from dead neurons and myelin debris (cellular debris), and protein clumps that form plaques. Once TREM2 encounters and binds to such damage, TREM2 mediates signals for the microglia to respond appropriately, for example, by transitioning to DAM, migrating to sites of damage, clearing away debris through phagocytosis, and acting as a barrier to

prevent further damage (Figure 2). In preclinical studies across multiple neurodegenerative conditions, it has been shown that the transition from homeostatic microglia to fully activated DAM requires activation of the TREM2 receptor.

Figure 2: TREM2 Receptor Activation is Required for Homeostatic Microglia to Transition to DAM



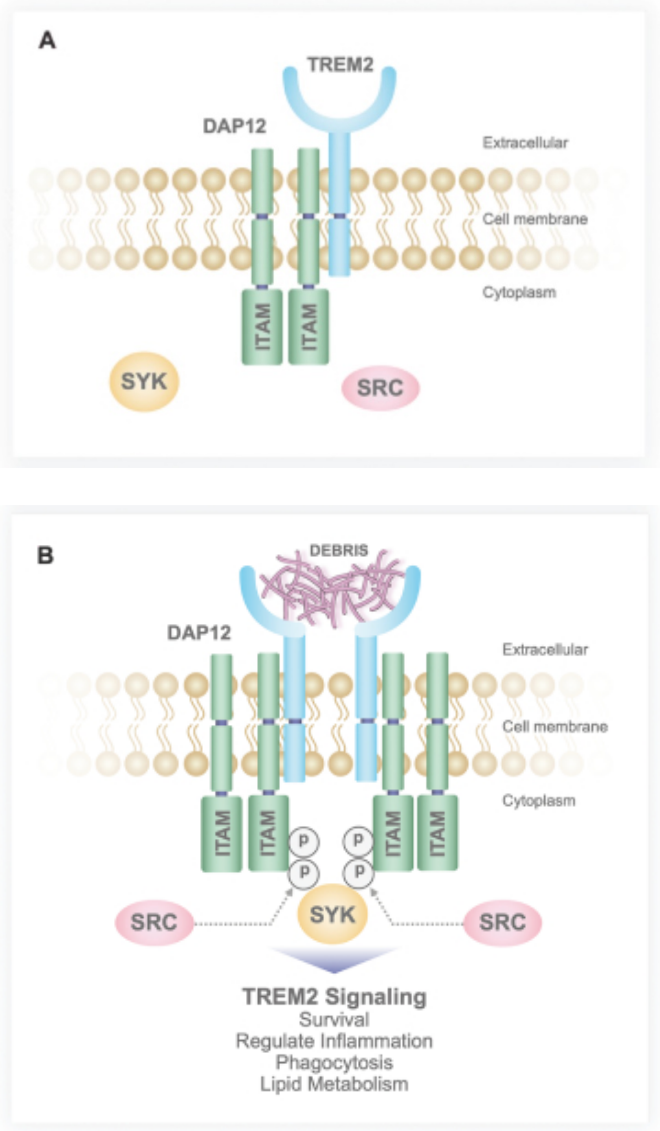
A. Homeostatic microglia sense debris. **B.** Microglia transitions to DAM through binding of cellular debris to TREM2, leading to debris removal. **C**. TREM2 loss-of-function results in dysfunctional microglia, unable to transition to DAM, leading to accumulation of cellular debris, neuroinflammation, and subsequent neurodegeneration.

TREM2's protective role in neurodegenerative disease was discovered through GWAS. This finding was confirmed and extended through transgenic animal studies and single cell RNA sequencing analyses. TREM2 signals through an associated protein complex, which triggers a cascade of biochemical changes that maintain microglial homeostasis and promote microglial migration to sites of injury, activate phagocytosis, and promote cell survival and proliferation.

Figure 3A below shows the TREM2 receptor and the key components of the associated protein complex, including a membrane protein called DNAX-activating protein of 12 kilodaltons (DAP12), which is associated with TREM2, and consists of an intracellular region, called ITAM, and intracellular proteins called SRC and SYK. As shown in Figure 3B, when adjacent TREM2 receptors recognize and bind to damage-associated materials, such as cell debris, the TREM2 receptors cluster. This triggers the phosphorylation, defined as a molecular modification involving addition of a phosphate group, of DAP12 at its ITAM region by SRC. Each phosphorylated ITAM region then binds to SYK, which relays the receptor signals within the cell.

SYK also becomes phosphorylated after binding to relay the signal for initiating biochemical changes in the cell to promote microglial survival, proliferation, migration, and phagocytosis, and regulate inflammation and lipid metabolism.

Figure 3: TREM2 is an Environmental Sensor, Which Binds to Damage- or Infection-associated Materials, such as Cell Debris, Triggering its Activation



Multiple clinical trials have shown that TREM2 deficiency is a driver of neurodegeneration, and we believe such studies provide a compelling rationale for therapeutically activating TREM2 signaling to treat neurodegenerative diseases. Loss-of-function mutations of TREM2, such as those associated with AD and other neurodegenerative diseases, disrupt signaling through reduced binding to brain debris and reduced TREM2 levels at the cell surface. The following findings further support the link between TREM2 loss-of-function and disease:

- The importance of TREM2 in the CNS and its involvement in microglial dysfunction comes directly from a devastating human genetic disease called Nasu-Hakola disease (NHD). NHD is an autosomal recessive disorder, caused by a defect in two gene copies, that renders the receptor non-functional due to *TREM2* or *DAP12* mutations. Clinically, NHD is characterized by a rapidly progressive and fatal adult-onset leukodystrophy with a predominantly cognitive phenotype directly caused by microglial dysfunction.

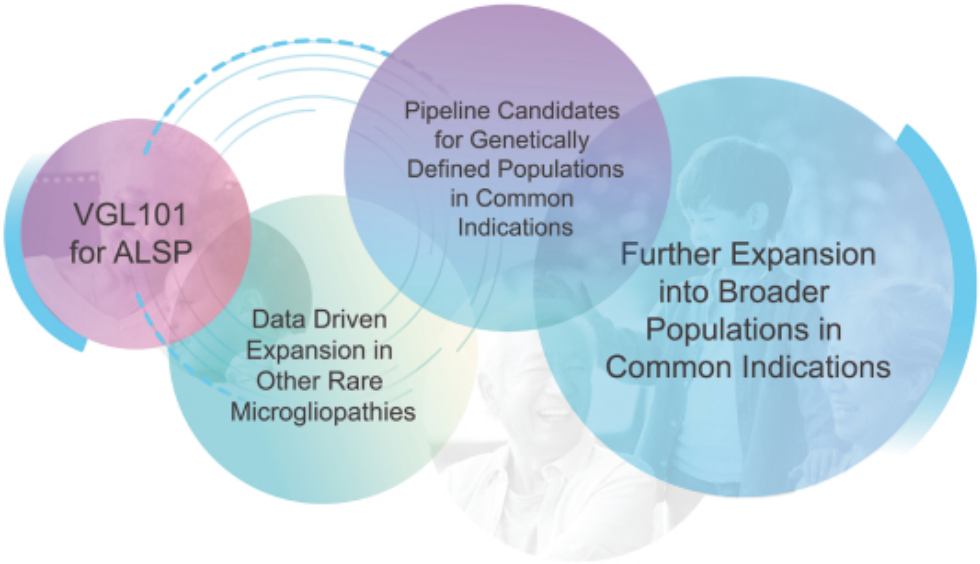
- *TREM2* loss-of-function variants are associated with several neurodegenerative diseases, FTD, ALS, and AD. For example, GWAS have shown that a specific mutation in a *TREM2* variant (R47H) has one of the strongest associations with the development of AD, second in magnitude only to that associated with the apolipoprotein E4 (*ApoE4*) genotype.
- Functionally, *TREM2* mutations drive disease pathology in multiple animal studies, such as studies for AD, stroke, MS, and other white matter diseases. For example, in an AD mouse study, microglial inactivation via *TREM2* deletion enhanced the spreading of both pathological ß-amyloid and tau proteins.

In our preclinical studies to date, we have not observed any adverse effects resulting from TREM2 agonism. Data in animal studies for AD and other neurodegenerative diseases suggest that chronic treatment with a TREM2 agonist has the potential to ameliorate AD pathology. To our knowledge, no association has been established between gain-of-function mutations for *TREM2* and any disease.

Our Precision Medicine Approach to Development

We are pursuing a precision medicine approach to developing a broad range of therapeutics for neurodegenerative diseases. We believe that each of the drugs in our pipeline can be developed for multiple neurodegenerative diseases, some of which have very large patient populations. Our development strategy, as shown in Figure 4 below, is to begin with rare, genetically defined diseases for which microglial dysfunction is a key driver of disease pathology and to use findings from these efforts to inform expansion into larger and more common neurodegenerative indications. We believe this iterative, sequential approach is a key differentiator which will help reduce downstream translational risk and potentially allow us to generate clinical PoC efficiently and leverage our initial development programs as well as research by others in pursuing additional neurodegenerative disease opportunities. We also believe we are differentiated by developing both large molecule (i.e., injectable) antibodies as well as small molecule (i.e., orally available) drugs.

Figure 4: Our Development Strategy



We are executing on this approach with our lead pipeline candidate, VGL101, which is initially being developed for the treatment of ALSP. ALSP has strong genetic, mechanistic, and biochemical associations with microglial dysfunction. The understanding of the genetic defect, the molecular pathway deficit, the potential for TREM2 agonism to mitigate the deficit, and the availability of both target engagement and disease biomarkers, serve to increase our confidence in our efforts to rapidly achieve clinical PoC for VGL101 for this disease. We believe the significant unmet need and lack of approved therapies in ALSP have the potential to enable a more efficient clinical development path to PoC and regulatory approval, if these trials are successful.

We plan to leverage our work in ALSP to target other rare leukoencephalopathies and leukodystrophies, such as cALD. We also plan to evaluate VGL101 in certain genetically defined patient segments of more common neurodegenerative diseases for which TREM2 and/or microglial dysfunction is believed to be a key driver of disease pathology, such as AD.

We are developing an orally-available small molecule that we believe may have potential clinical and commercial advantages, including ease of administration, improved treatment compliance, and use in outpatient settings. We believe our small molecule TREM2 agonist could be particularly impactful for treating diseases with larger patient populations.

We expect to apply learnings from our VGL101 program to inform development of our small molecule TREM2 agonist program in larger and more common neurodegenerative indications. For example, we expect the VGL101 program will provide insights into the mechanism of action and pharmacology of TREM2 agonism, relevant biomarkers as well as help us identify the appropriate patient populations for TREM2 agonist therapies.

Our Product Development Programs

We currently have two programs aimed at developing microglia-targeted TREM2 agonists for the treatment of neurodegenerative diseases:

- VGL101: A fully human monoclonal antibody, or mAb, targeting human TREM2 for the treatment of rare microgliopathies. We are initially developing VGL101 for the treatment of patients with ALSP, a rare, genetically defined, and fatal neurogenerative disease caused by microglial dysfunction. In multiple preclinical *in vitro* and *in vivo* studies, VGL101 specifically and potently activated TREM2, thereby targeting cells expressing human TREM2 to initiate the cascade of downstream signaling that modulates the neuroprotective and homeostatic functions of microglia. In September 2021, we began a non-interventional natural history study of ALSP patients. In November 2021, the FDA cleared our IND for VGL101 in ALSP at doses up to 20 mg/kg, with a partial clinical hold on doses higher than 20 mg/kg. We do not believe the partial clinical hold will have a material impact on our current clinical development plans and timelines for our clinical trial in ALSP. We initiated our first-in-human Phase 1 clinical trial with VGL101 in healthy volunteers in December 2021 and as of today, we have completed dosing of the 20 mg/kg SAD cohort without any safety signals and initiated the 20 mg/kg MAD cohort. We expect to announce topline data in the second half of 2022. Assuming our Phase 1 trial progresses on our expected timeline, our FDA discussions proceed as currently planned, and we identify an acceptable dose as part of the Phase 1 trial, we believe we can initiate our interventional studies in ALSP in the second half of 2022. We have also 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 clinical trial in the first half of 2023, following the completion of the VGL101 Phase 1 clinical trial in healthy volunteers. We also plan to submit a protocol amendment to the FDA under our open IND to conduct a Phase 1b biomarker-based, proof-of-mechanism clinical trial of VGL101, expected to begin in the second half of 2022, in genetically defined AD patients with or without the relevant *TREM2* variants to inform subsequent clinical trials with our small molecule agonist.
- A novel, orally available, small molecule TREM2 agonist for common neurodegenerative diseases that are linked to microglial dysfunction. We are initially developing this program for the treatment of genetically defined subpopulations of AD patients. Compounds in our lead series have been observed to be highly CNS penetrant after oral dosing, and similar to VGL101, are specific, potent activators of TREM2. In the first quarter of 2022, we initiated IND-enabling studies for this program and expect to file an IND application in 2023. In addition, we have ongoing screening efforts that have resulted in the discovery of a second series that is built around a different chemical core structure than the lead series. Our second series is currently in the early lead optimization stage.

VGL101

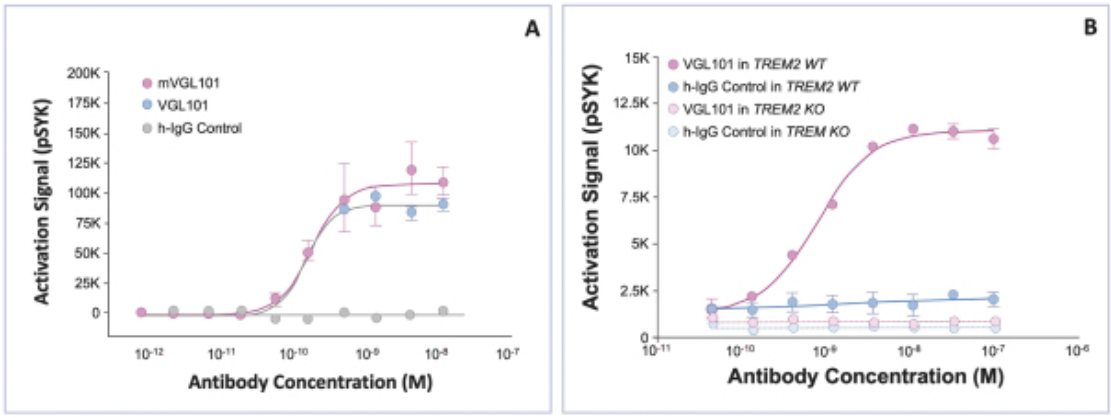
Our lead candidate, VGL101, is a fully human mAb targeting human TREM2 that was designed to minimize unwanted immune responses and engineered to prevent mediating cellular toxicity.

In multiple preclinical *in vitro* and *in vivo* studies, VGL101 has demonstrated target engagement with TREM2. VGL101 specifically and potently activated TREM2, thereby targeting cells expressing human TREM2 to initiate the cascade of downstream signaling that modulates the neuroprotective and homeostatic functions of microglia.

In *in vitro* studies in human embryonic kidney (HEK) cells engineered with human TREM2 and its receptor partner, DAP12, VGL101 activated TREM2, as measured by phosphorylation of SYK (pSYK) in a dose dependent manner at very low concentrations (i.e., sub-nanomolar levels, below $1X10^{-9}M$) (Figure 5A). Additionally, mVGL101, an engineered version of

VGL101 that minimizes immunogenicity in mice, showed comparable TREM2 agonist activity as VGL101. VGL101 also activated wild-type TREM2 ("*TREM2 WT*") in human microglia cultures and did not demonstrate any activity in microglia without TREM2 ("*TREM2 KO*"; Figure 5B).

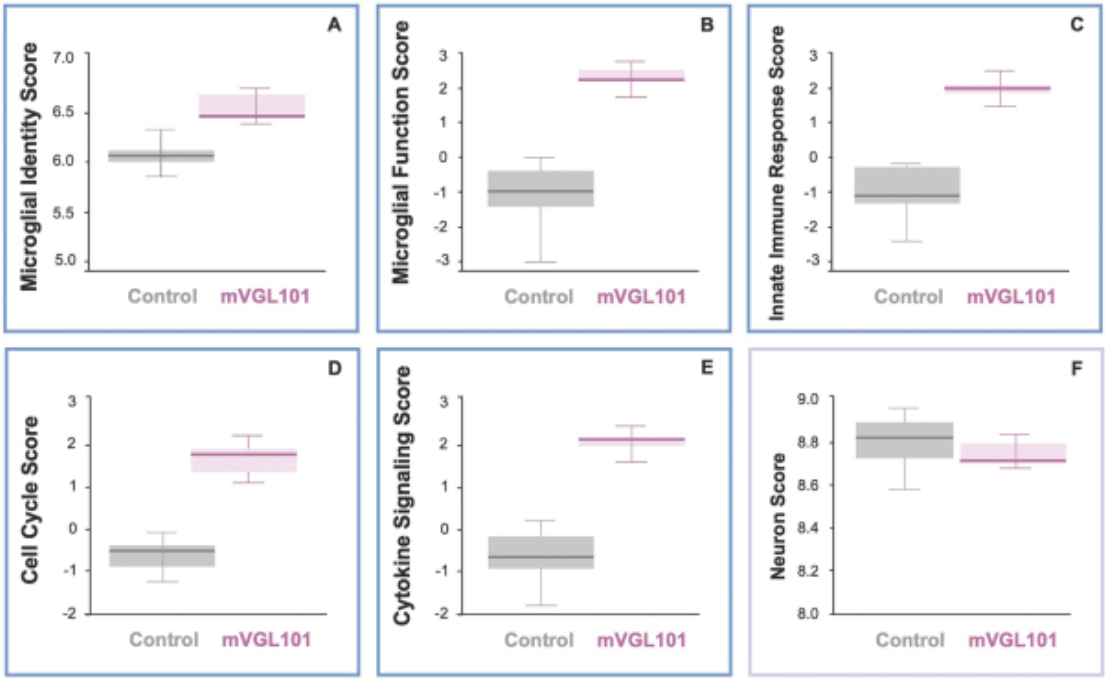
Figure 5: VGL101 Activated TREM2 in *In Vitro* Studies of HEK Cells and Human Microglia



Activation Signal (pSYK): measurement of phosphorylation level of SYK; VGL101 Concentration: molar concentration (M) of VGL101 on a logarithmic scale – $1x10^{-12}$M, $1x10^{-11}$M, $1X10^{-10}$M, $1X10^{-9}$M, $1X10^{-8}$M, $1X10^{-7}$M; $1X10^{-6}$M; h-IgG Control: immunoglobulin G acting as negative control: TREM2 WT; wild-type TREM2 gene: TREM2 KO; TREM2 gene removed or knocked out

To validate target engagement, we conducted studies through the genetic engineering of mice in which the human *TREM2* gene was "knocked in" to replace the mouse *Trem2* gene homolog. Figure 6 below shows that a systemically administered mVGL101 dose increased brain expression of genes associated with microglial identity (homeostatic genes; Figure 6A), microglial function (Figure 6B), innate immune response (neuroprotection genes, Figure 6C), cell cycle (proliferation genes; Figure 6D), and cytokine signaling (neuroprotection genes; Figure 6E) without affecting the gene expression in other cell types found in the brain, specifically neurons (Figure 6F) and astrocytes. Therefore, following systemic administration, mVGL101 has been demonstrated to reach the brain, engage human TREM2, and activate microglia to increase gene programs that define normal functioning states related to damage surveillance, response to damage sensing, and neuroprotection.

Figure 6: A Single Dose of mVGL101 Increased the Expression of Genes Associated with Microglial Identity, Microglial Function, Innate Immune Response Cell Cycle and Cytokine Signaling Without Affecting the Gene Expression in Neurons

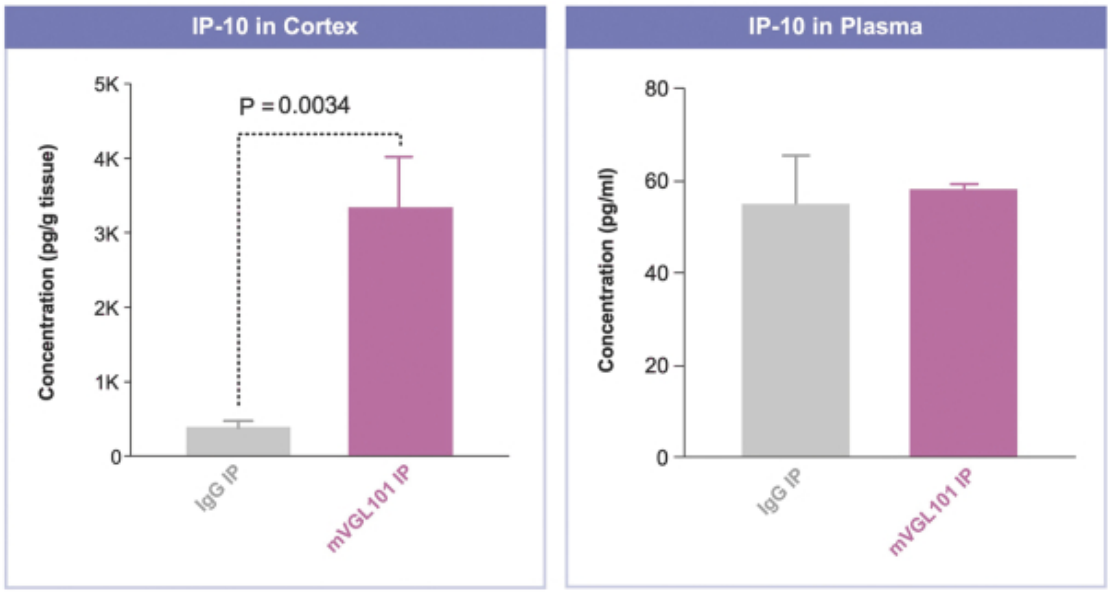


Y-axes—reflect the level of gene expression changes based on analyses comparing total brain RNA (gene transcripts) isolated from negative control (antibody without TREM2 binding) and mVGL101-treated mice: A: "Microglial Identity Score"—gene expression associated with microglial identity; B: "Microglial Function Score"—gene expression associated with microglial activation; C: "Innate Immune Response Score"—gene expression associated with innate immunity and neuroprotection; D: "Cell Cycle Score"— gene expression associated with cell cycle and proliferation; E: "Cytokine Signaling Score" —gene expression associated with cytokine signaling and neuroprotection; F: "Neuron Score" – gene expression associated with neuronal identity.

In a separate set of experiments designed to confirm target engagement in the CNS, the intraperitoneal (IP) administration of mVGL101 in mice resulted in increased levels in the brain of IP-10, a cytokine secreted only by microglia following TREM2 activation. As shown in Figure 7, mVGL101 did not increase IP-10 levels in plasma, further confirming that target engagement

was localized to the CNS alone. We believe this finding suggests that VGL101 administration is unlikely to result in undesirable, off-target effects outside of the brain.

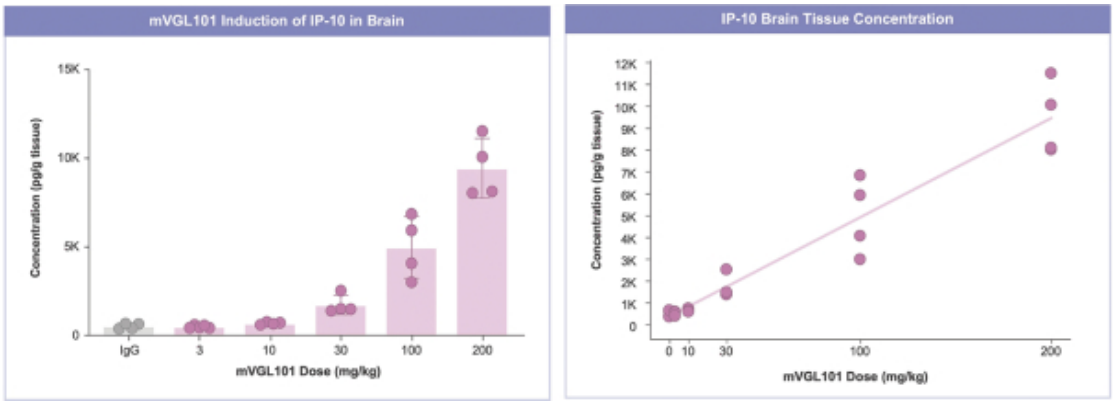
Figure 7: mVGL101 Productively Activated Microglia in Human *TREM2* Knock-in Mice without Peripheral Effects



Concentration (pg/g tissue): concentration of IP-10 protein (pg) per gram of cortical homogenate; Concentration (pg/ml): concentration of IP-10 protein (pg) per milliliter of plasma; IgG IP—intraperitoneal administration of immunoglobulin G as a negative control; mVGL101 IP—intraperitoneal administration of mVGL101 in a single dose of 100 mg/kg. The IP-10 level for mVGL101 in the Cortex group was determined to be statistically different than that for IgG control with a P value < 0.01.

In addition, we have conducted single ascending dose studies in mice with mVGL101. As shown in Figure 8, these studies demonstrated that the administration of mVGL101 produced dose-dependent increases of IP-10 in the brain.

Figure 8: mVGL101 Dose-dependent CNS Induction of IP-10 (left) and Linearity of mVGL101 Dose-dependent CNS Induction of IP-10 (right)

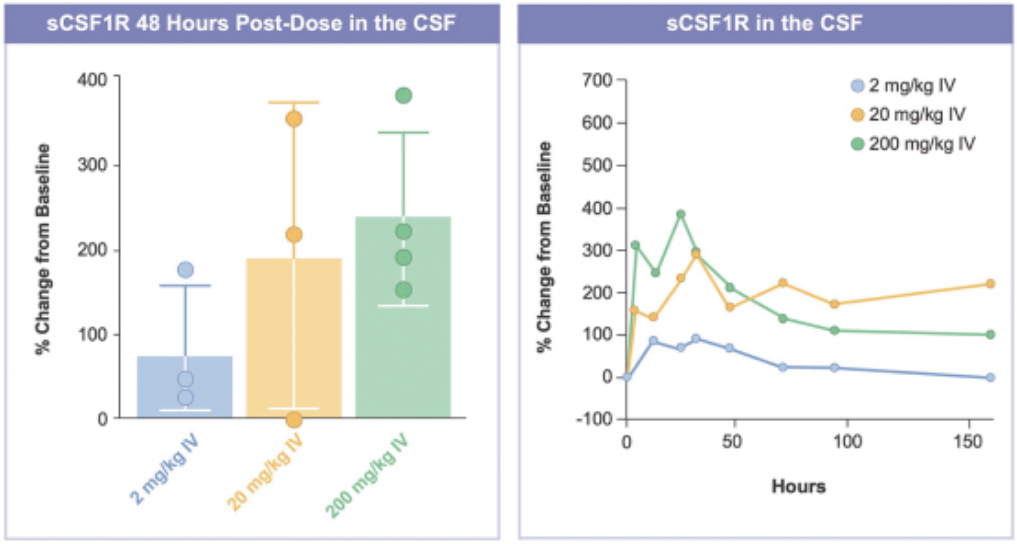


Concentration (pg/g tissue): concentration of IP-10 (pg) per gram of cortical homogenate.

The ability of a therapeutic to cross the blood-brain barrier to reach its target within the brain is critical to neurodegenerative disease drug development and can be a challenge for large molecules such as antibodies. In non-human primates (NHP), we demonstrated that VGL101 was able to penetrate the blood brain barrier at levels in line with those typically observed in prior NHP studies of currently marketed antibody drugs. In the same study, we further demonstrated TREM2 target engagement, showing an increase in levels of sCSF1R over baseline in the cerebrospinal fluid (CSF). This increase in sCSF1R persisted in the CSF for more than six days (150 hours), as shown in Figure 9. We believe that this data, taken together with other preclinical data, suggests that VGL101 can achieve therapeutically relevant concentrations in the brain.

In addition, leukodystrophies, and leukoencephalopathies such as ALSP, are characterized by blood brain barrier disruption, which increases its permeability in areas where the disease is active. We believe such disruption has the potential to facilitate entry of VGL101 from the bloodstream into the brain to targeted areas of active neuro-inflammatory lesions in these diseases.

Figure 9: Increase in sCSF1R (left) and Sustainable Increase (right) in the CSF Following VGL101 Administration in NHP

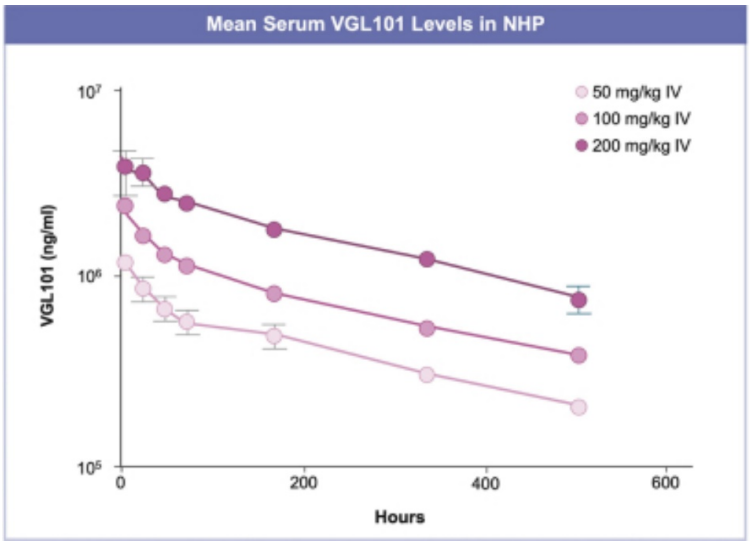


Percentage Change from Baseline: change in levels of sCSF1R in the CSF expressed as a percentage of baseline levels.

The pharmacokinetics of VGL101 have been characterized in NHP (Figure 10). Based on these data, the predicted serum half-life in humans is 21 days, which we believe supports monthly intravenous (IV) dosing in patients. In this study, VGL101 was administered intravenously at 3 dose levels, 50 mg/kg, 100 mg/kg, and 200 mg/kg. Blood samples were obtained from

each NHP at multiple timepoints after VGL101 administration to monitor the change in systemic VGL101 levels and calculate a half-life for the drug candidate. The data from these experiments will inform the projected dose level for human clinical trials.

Figure 10: The Pharmacokinetics of VGL101 in NHP Show Predicted Serum Half-life in Humans is 21 Days



The safety profile of VGL101 was assessed in a six-month repeat-dose toxicology study in NHPs. Administration of VGL101 once weekly via IV injection to cynomolgus monkeys at dose levels of 50 mg/kg, 100 mg/kg, and 200 mg/kg was well tolerated, with no adverse VGL101 related findings observed. Based on these results, the no-observed-adverse-effect level was considered to be 200 mg/kg/day.

Our First VGL101 Indication—ALSP

ALSP is a rare, inherited, autosomal dominant neurological disease with high penetrance. Because ALSP is autosomal dominant, the disease requires a mutation in only one of two gene copies in order to develop. It is caused by a mutation of the *CSF1R* gene and affects approximately 10,000 people in the U.S., with an estimated incidence of 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 was only recently recognized as a distinct disease in 2012. Initial symptoms of the disease, at times, resemble other neurodegenerative disorders, such as FTD, leading to misdiagnoses. Therefore, we believe the published prevalence figures may underrepresent the ALSP patient population. With the recent availability of genetic testing for *CSF1R* mutations and disease awareness-building efforts by us and patient advocacy groups, including the global ALSP patient registry, we expect the number of diagnoses to increase.

The disease generally presents in adults in their forties, is diagnosed through genetic testing for *CSF1R* mutations and established clinical/radiologic criteria, and is characterized by cognitive dysfunction, neuropsychiatric symptoms, and motor impairment. These devastating symptoms typically exhibit rapid progression and those affected have an average life expectancy of approximately six to seven years following symptom onset.

To our knowledge, there are no approved products for ALSP, and beyond VGL101, there are none in clinical development. Academic investigators have tried hematopoietic stem cell transplantation in a small number of patients. In a published report on seven patients followed for a median period of 11 months, although the investigators reported some improvements, all patients experienced some level of disease progression as well as MRI lesion progression with three patients experiencing graft versus host disease and one death in addition to other side effects. Off-label use of symptomatic treatments (e.g. anti-Parkinsonian drugs) appear to provide minimal benefit to patients with ALSP.

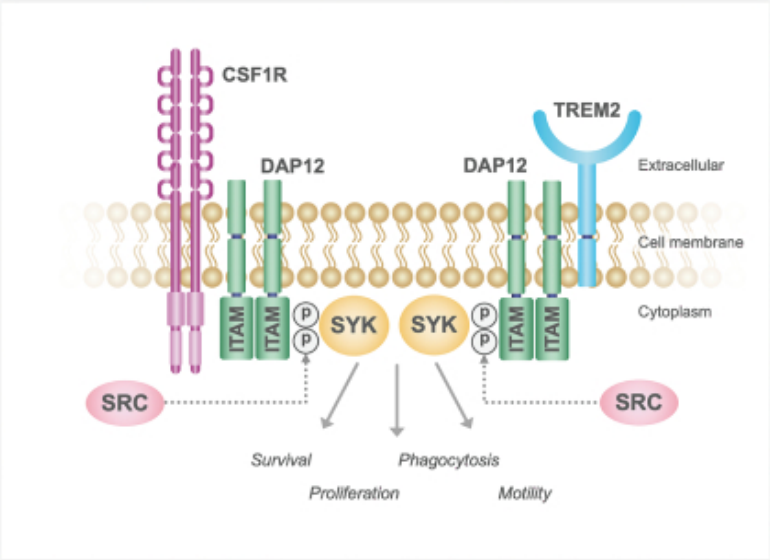
ALSP is caused by loss-of-function mutations in the *CSF1R* gene, which lead to microglial dysfunction. *CSF1R*+/- microglia, which lack one copy of functional or wild-type *CSF1R*, fail to perform homeostatic functions, such as phagocytosis and removal of myelin debris, as well as maintenance of synaptic health by axonal pruning. This microglial dysfunction leads to loss of oligodendrocytes, as well as axonal damage, manifesting as demyelination, axonal spheroids, and a devastating

neurodegenerative and neuroinflammatory phenotype. ALSP patients experience both microglial loss and dysfunction in the white matter regions of the brain. As disease progression accelerates, the blood brain barrier function becomes compromised and peripheral immune cells infiltrate into the brain, contributing to the pro-inflammatory pathophysiology of ALSP.

Treatment Rationale for VGL101

We believe that VGL101 has the potential to be a treatment for ALSP because CSF1R and TREM2 share a common downstream signaling pathway. As shown in Figure 11 below, both cell surface receptors transmit their biological effects, including cell survival and proliferation signals, through the same signaling partner, DAP12/SYK.

Figure 11: CSF1R and TREM2 Share a Common Signaling Pathway

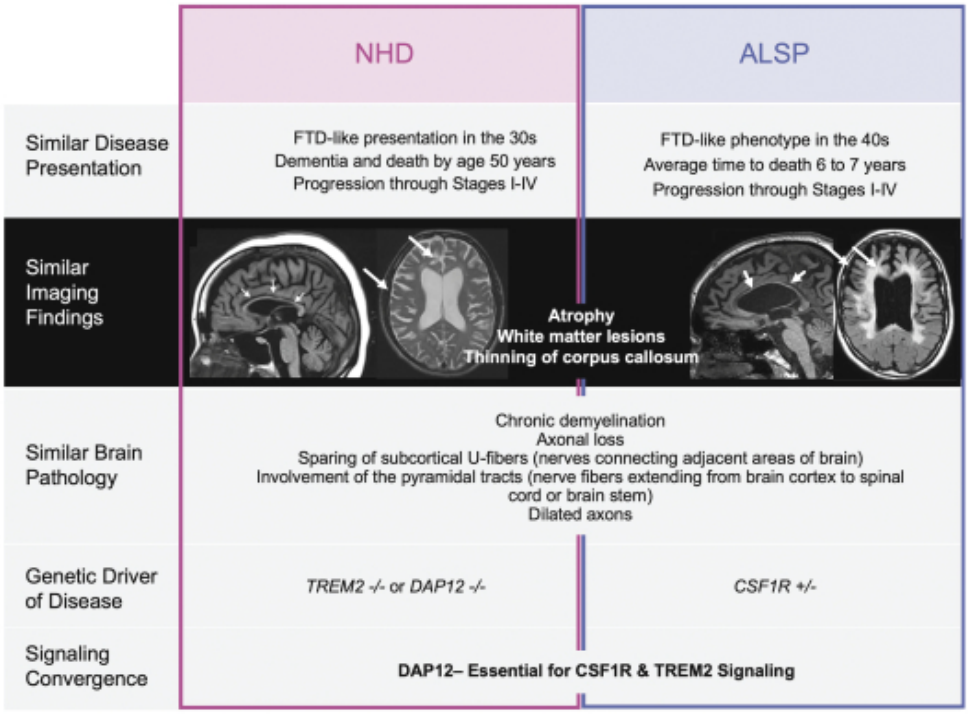


TREM2's signaling for phagocytosis and cell motility is also transmitted through DAP12/SYK. The upstream biology of CSF1R and TREM2 is distinct, with CSF1R responding to either of two growth factors, CSF1 and IL34, a cytokine that elicits its activity by binding to CSF1R, for cell survival, proliferation, and differentiation, while TREM2 is activated by a broad array of damage-associated cellular debris, as part of its sensor function.

VGL101 is designed to increase signaling through DAP12/SYK to compensate for CSF1R loss-of-function by mitigating microglial dysfunction. Human genetics have demonstrated the impact of deficient signaling through TREM2 or DAP12/SYK in the rare, fatal genetic disease, NHD, which is caused by mutations in *TREM2* or *DAP12*, resulting in the complete loss of their signaling function. As seen in Figure 12 below, the disease presentation, imaging findings, and brain pathology of ALSP and NHD are similar, highlighting that converging, dysfunctional biochemical pathways produce similar pathobiology. For example, both NHD and ALSP are fatal, rapidly progressing disorders that produce FTD-like symptoms that first appear in the thirties in the case of NHD, and forties for ALSP. Both are characterized by chronic loss of myelin and loss of axons, nerve

fibers that transmit electrical signals away from nerve cells and which are the primary constituents of white matter. The white matter brain lesions resulting from both diseases have a similar distribution as shown by the arrows in Figure 12.

Figure 12: *TREM2* and *CSF1R* Mutations Result in Diseases with Similar Pathology

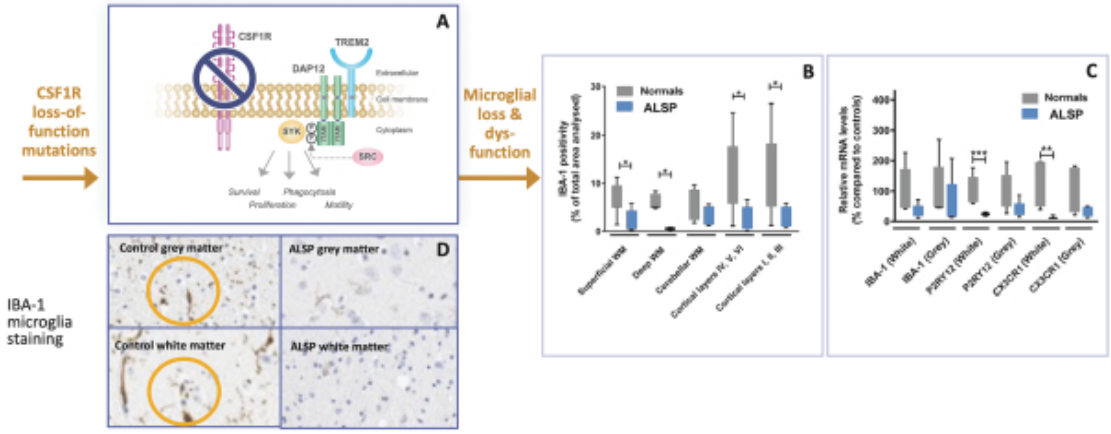


Bianchin et al, Nat Rev Neurol. 2010. Coomans, C., et al. Acta Neurologica Belgica. 2018, Konno et al, Neurology 2018. Oyanagi et al, Brain Pathol. 2017

Mutations in *CSF1R* that result in the development of ALSP cause the loss of proper receptor signaling, reducing microglia cell numbers and impairing their activity in several of the affected white matter and cortical regions. As seen in Figure 13B below, brain tissue from ALSP patients showed a reduction in the number of microglia as compared with normal tissue, as measured by a microglial marker, IBA-1. Brain tissue from ALSP patients also showed decreased levels of microglial-specific RNA transcripts compared with healthy tissue, as evidenced by the downregulation of key microglial homeostatic genes such as *IBA-1, P2RY12* and *CX3CR1* (Figure 13C). Several academic groups have demonstrated the loss of microglia (decreased staining for IBA-1 positive cells) in the grey and white matter regions of ALSP brain tissue, implicating ALSP as a

primary microgliopathy (Figure 13D). Additionally, microglia exhibiting an elongated shape, which are indicative of a DAM phenotype, are absent in the brain tissue of ALSP patients.

Figure 13: CSF1R Mutations Lead to Microglial Loss and Dysfunction in ALSP

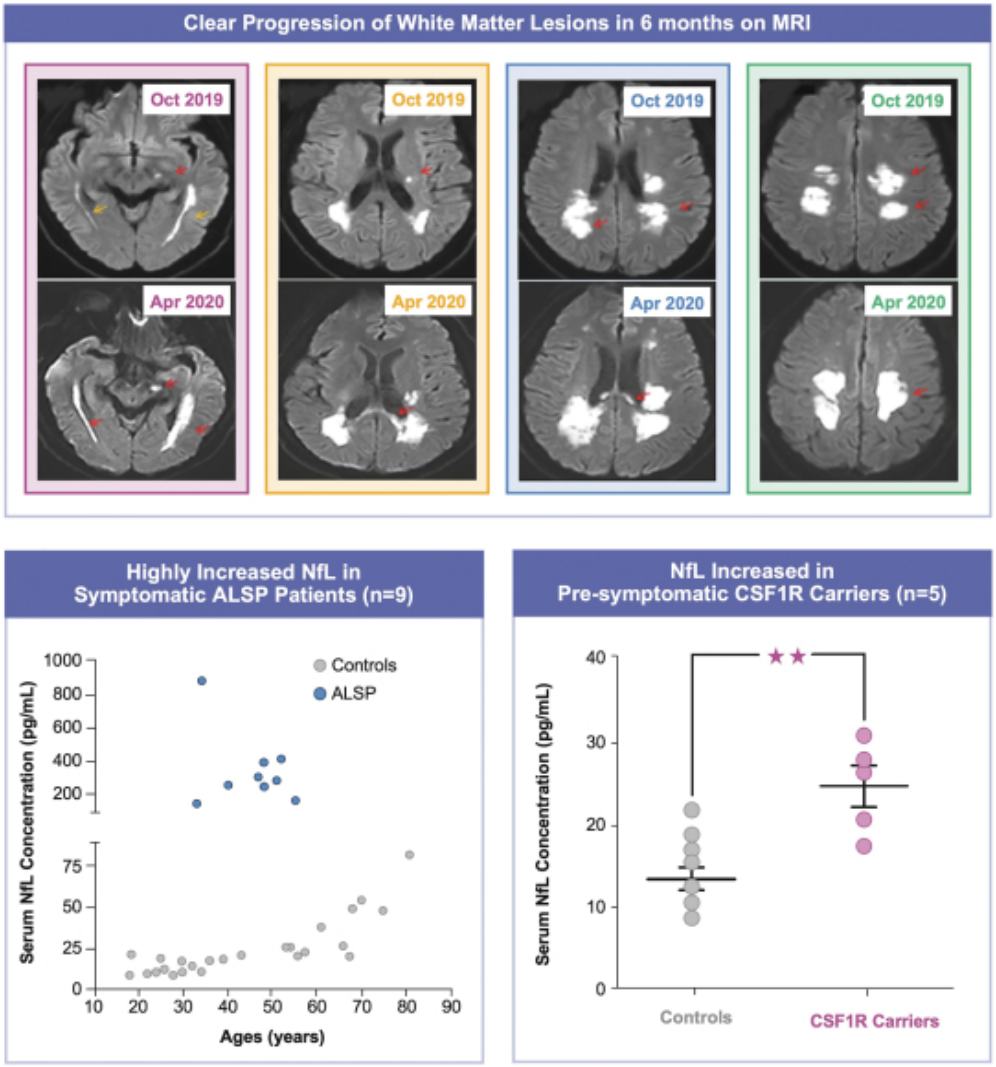


A: CSF1R receptor signaling deficient due to loss-of-function mutations. B: y-axis ("IBA-1 positivity (% of total are analyzed)") - quantification of levels of IBA-1 stained cells (indicative of microglia); x-axis: various layers of brain cortex, WM- white matter. C: y-axis ("Relative mRNA levels (% compared to controls)") - quantification of expression levels of various genes reflected along the x-axis; x-axis: "White"- brain white matter region, "Grey"- brain grey matter region. D: immunohistochemical staining of ALSP and control brain tissues: brown staining represents IBA-1 positive cells (microglia). B, C and D are adapted from Kempthorne et al. Acta Neuropathologica. 2020.

As seen below in Figure 14, we believe that there are quantifiable, disease-associated biomarkers which correlate with disease progression and could be used to detect treatment effects in ALSP clinical trials. These include MRI of brain lesions, which appear to correlate with disease progression, and fluid biomarkers such as NfL, an axonal protein, for which detection in the blood or CSF is quantitatively indicative of white matter degeneration. Deep phenotype maps based on digital sensing technologies of ALSP patients could capture therapeutic responsiveness to any experimental treatment paradigms in the future. We believe the change in NfL levels from baseline is a potential therapeutic biomarker. NfL protein levels in the CSF have been shown to be more than 30-fold higher in ALSP patients than in age-matched controls and approximately 14-fold higher in serum. Serum NfL protein levels have been reported to be significantly higher, approximately two-fold, in young pre-symptomatic *CSF1R* mutation carriers than age-matched healthy subjects. To our knowledge, the magnitude of NfL increase in the serum and CSF of ALSP patients is higher than in any other neurodegenerative disease described to date. We believe that these robust NfL levels will make them readily quantifiable with lower variability than has been observed in other clinical programs, with changes from baseline levels indicative of a therapeutic response. By contrast, patients with AD, ALS, FTD, MS, Lewy body dementia, and progressive supranuclear palsy have been shown to have CSF NfL levels approximately 2.3-fold, 7.2-fold, 3-fold, 2.1-fold, 2.8-fold, and 3.5-fold higher than healthy controls, respectively.

We believe that the availability of such biomarkers and their relation to disease progression will provide us with early indicators of VGL101's therapeutic response and in human studies may support demonstration of PoC. Along with the high unmet need in the disease, we believe the availability of these quantifiable biomarkers make ALSP an attractive initial indication for VGL101.

Figure 14: ALSP Has Disease Biomarkers That Can Be Used in Clinical Development Including MRI (Top Panel) and NfL (Bottom Panel)

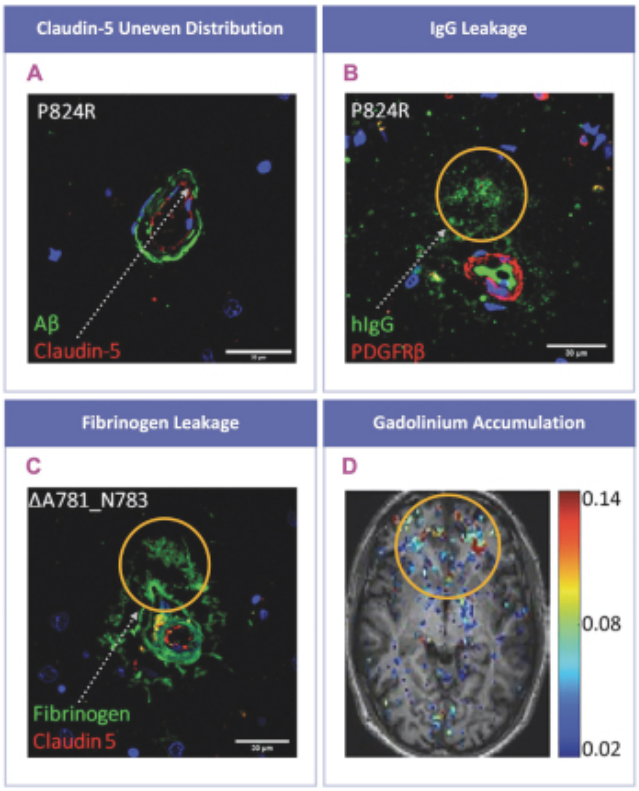


Oyanagi et al, Brain Pathol. 2017; Lakshmanan et al, Neurol Genet, 2017. Hayer et al, Neurology 2018. Kang et al. Radiol Case Rpts 2019; Huang et al. BMC Neurology 2021.

The compromised blood-brain barrier (BBB) of patients with ALSP is observable on histopathology and MRI. BBB disruption in human ALSP brain tissue is evidenced in histopathology images showing uneven distribution of claudin-5 (Figure 15A, punctate red staining), indicating the breakdown of tight junction function at the BBB. The compromised BBB results in leakage of large biological molecules such as IgG (Figure 15B, diffused green staining) and fibrinogen (Figure 15C, diffused green staining) from the bloodstream into the brain tissue (areas outside the circle-like structures near the center of the images) that do not typically occur in healthy individuals. The overall effects of a disrupted BBB are evidenced by MRI showing

gadolinium accumulation in the frontal cortex regions of ALSP patients (Figure 15D, different colored signals indicating levels of accumulation), which coincides with the regions of white matter degeneration during disease progression. We believe this increased BBB permeability in ALSP has the potential to increase brain exposure of large biological molecules such as VGL101 in the areas of active inflammation, which may restore microglial function and BBB integrity in these areas through TREM2 agonism.

Figure 15: Loss of CSF1R Activity in ALSP Reduced Blood Brain Barrier Integrity and Led to Increased Large Biological Molecule Permeability



A – C: Immunohistochemical staining of ALSP post-mortem brain tissue; P824R and ΔA781_N783 are loss-of-function mutations in CSF1R. A: "Aß"- amyloid-beta staining (green); "Claudin-5"- claudin-5 staining (red); uneven punctate staining pattern denoted by arrow indicates breakdown of tight junction function (tight junctions are multiprotein complexes of the BBB whose function is to seal the bloodstream from the brain and prevent leakage of proteins and other soluble material into the brain). B: "hIgG"- human immunoglobulin G staining (green); leakage of hIgG into brain tissue indicated by diffused staining pattern and denoted by arrow and circle; "PDGFRß"- platelet-derived growth factor receptor beta staining (red). C: "Fibrinogen"- fibrinogen staining (green); leakage of fibrinogen into brain tissue indicated by diffused staining pattern and denoted by arrow and circle; "Claudin-5"- claudin-5 staining (red); uneven punctate staining pattern indicates breakdown of tight junction function. D: T1-weighted dynamic contrast-enhanced MRI of an ALSP patient with the ΔA781_N783 CSF1R variant; colormetric scale indicates levels of gadolinium accumulation as an indicator of BBB permeability; grey lines in lower right corner of A, B and C represent the scale of the figure – length of line is 30 µM. Delaney et al. EMBO Mol Med 2021.

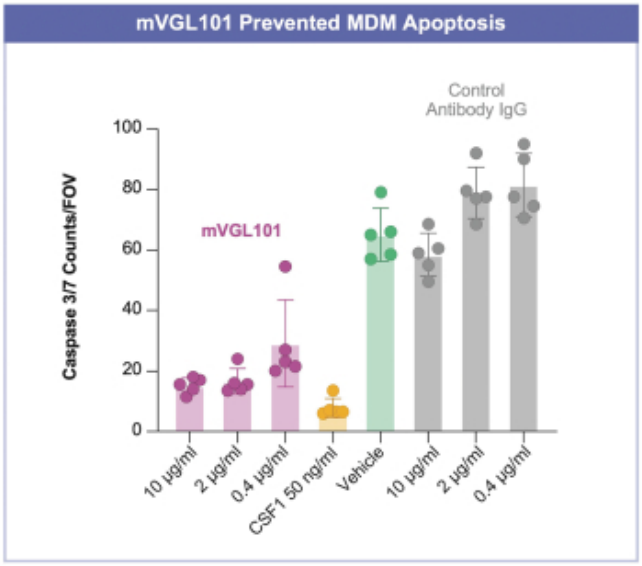
We have demonstrated PoM in *in vitro* studies that model CSF1R loss-of-function in ALSP. For these studies, we used a system for differentiation of macrophages, which are innate immune cells outside of the brain that have similar functions as microglia. We established human monocyte-derived macrophage (MDM) culture systems using monocytes, immature

pre-macrophage cells isolated from human blood, that are dependent on the growth factor CSF1 for survival and differentiation into more mature cells. In the first study illustrated in Figures 16A and 16B below, we observed that VGL101 rescued cultured differentiating monocytes cells from depletion of CSF1.

In this study, monocytes were co-cultured with CSF1 to induce differentiation into macrophages via DAP12/SYK signaling. When CSF1 is removed from the culture, the cells die by a process called apoptosis or programmed cell death, mimicking CSF1R loss-of-function. When mVGL101 was used to mediate DAP12/SYK signaling through TREM2 activation, and thus compensate for the missing CSF1, the cells survived. Specifically, as shown in Figure 16A, the levels of apoptosis markers (Caspase 3/7) in cultures treated with mVGL101 are similar to those of the CSF1-treated culture, whereas the levels for cultures treated with vehicle and control antibody are markedly higher.

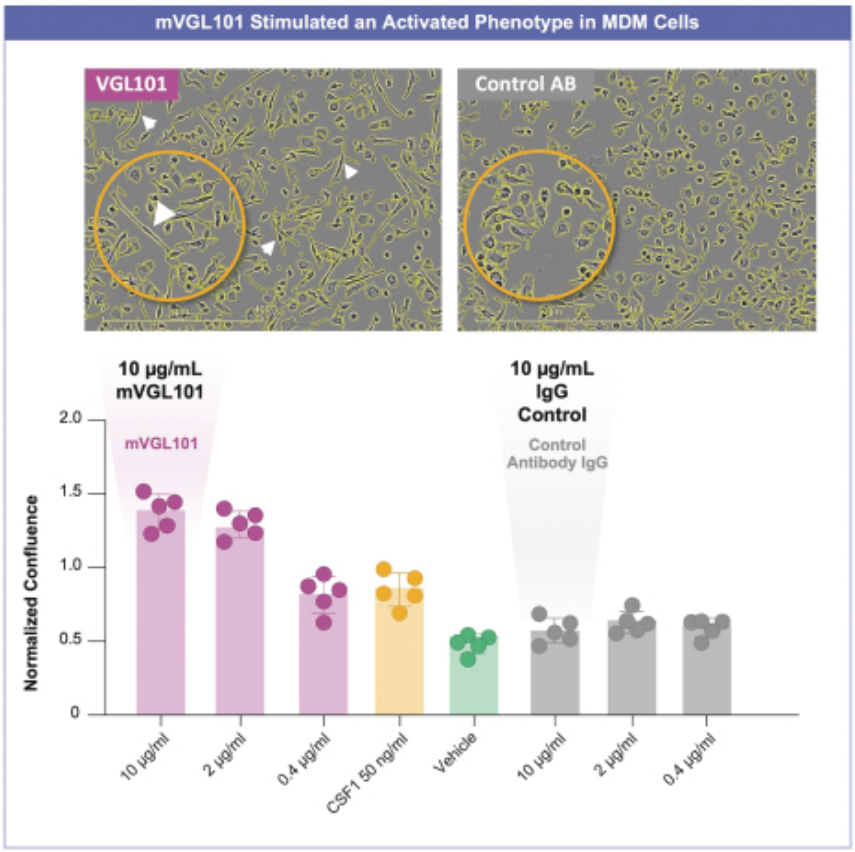
mVGL101 also enabled the transition to the MDM activated phenotype, as demonstrated both by the increased confluence, a measure of cell shape changes based on the area occupied by cells within a field of view, and by the motility of mVGL101-treated cells as compared to those treated with the control antibody, as shown in the Figure 16B below. The macrophage differentiation transition induced by mVGL101 was demonstrated by monitoring cell shape and cell motility changes using microscopic video image captures (Figure 16B) and video, respectively. These images show that the mVGL101-treated cultures contained numerous elongated cells that are transitioning to a more mature state (characterized by elongated cell processes), while the negative control treated cells remained spheroid and without elongated processes. The videos of these cultures over 48 hours showed that mVGL101 treated cultures contained numerous motile cells that migrate across the field of view indicating TREM2-mediated activation. No activation was observed in the control antibody cultures.

Figure 16A: TREM2 Agonism Mediated by mVGL101 Compensated for CSF1R Loss-of-Signaling and Prevented Apoptosis of MDM, Providing *In Vitro* PoM for CSF1R Deficiency in ALSP



Caspase3/7 Counts/FOV: Number of Cells Staining Positive for Activated Caspase 3/7 within a Field of View (FOV).

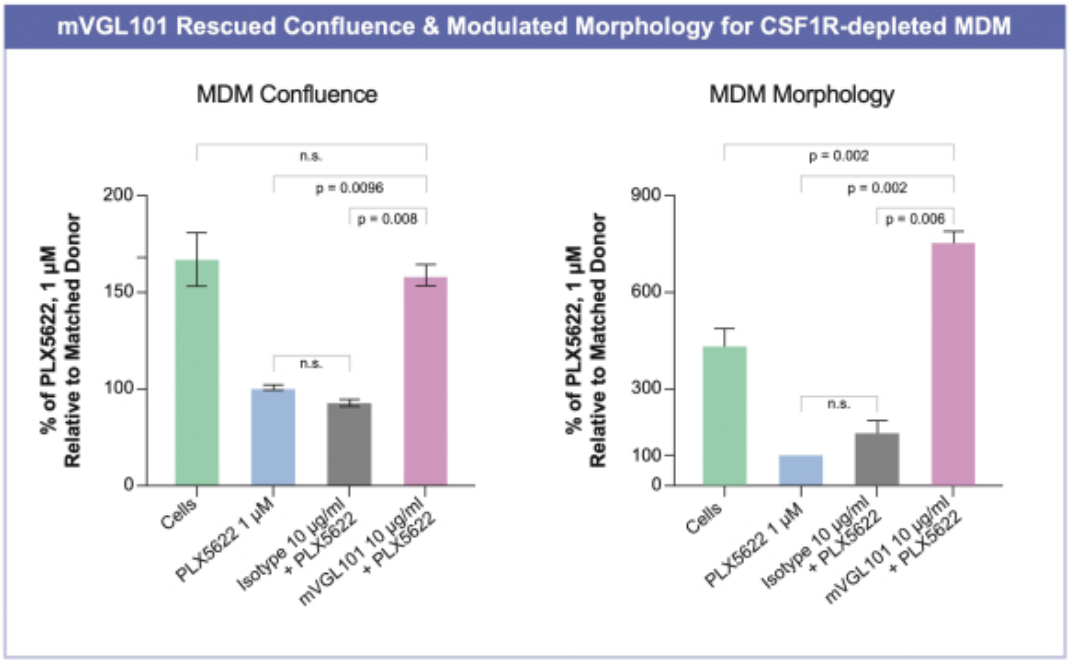
Figure 16B: mVGL101 Stimulated a Transition to an Activated Phenotype in MDM Cells and Induced a Morphology Indicative of a Transition to a Motile and Phagocytic State (White Arrowhead) Indicating an Increased Ability to Clear Debris from Dead and Dying Cells



In the second study illustrated in Figures 17A and 17B, we demonstrated mVGL101 rescue of CSF1R deficiency using PLX5622, a highly selective CSF1R inhibitor. MDM cells treated with PLX5622 alone displayed significantly reduced confluence, impaired ability to differentiate, and a dysfunctional microscopic phenotype compared to untreated cells. These changes are similar to what was observed with CSF1 withdrawal in the first experiment described above. Treatment of the PLX5622-treated cultures with mVGL101 rescued the cells from CSF1R inhibition and supported survival, as measured by an

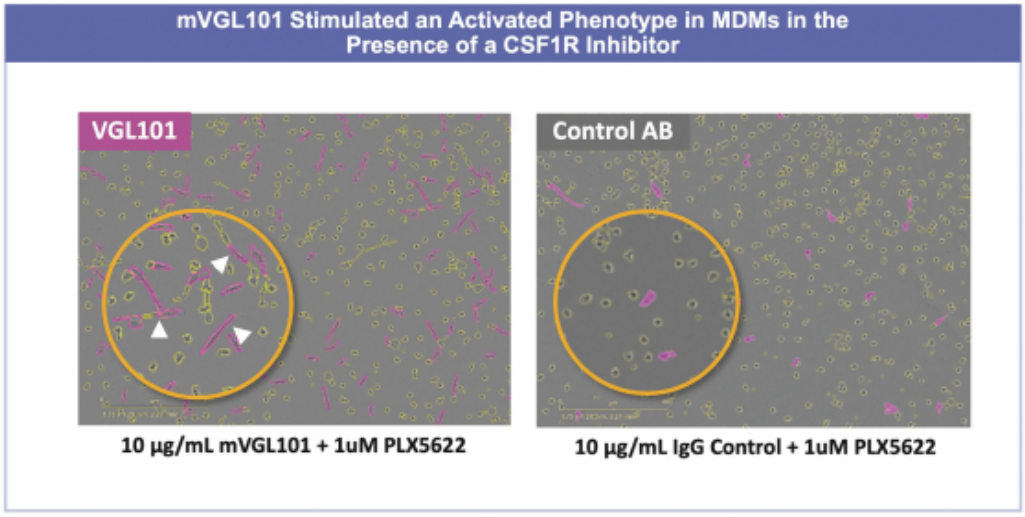
automated confluence algorithm (Figure 17A) and promoted morphological changes toward an elongated and motile phenotype, as measured by microscopic quantification of cell shape (Figure 17B), consistent with an activated cell type.

Figure 17A: **mVGL101 Rescued Confluence and Modulated Morphology for CSF1R-Depleted MDM**



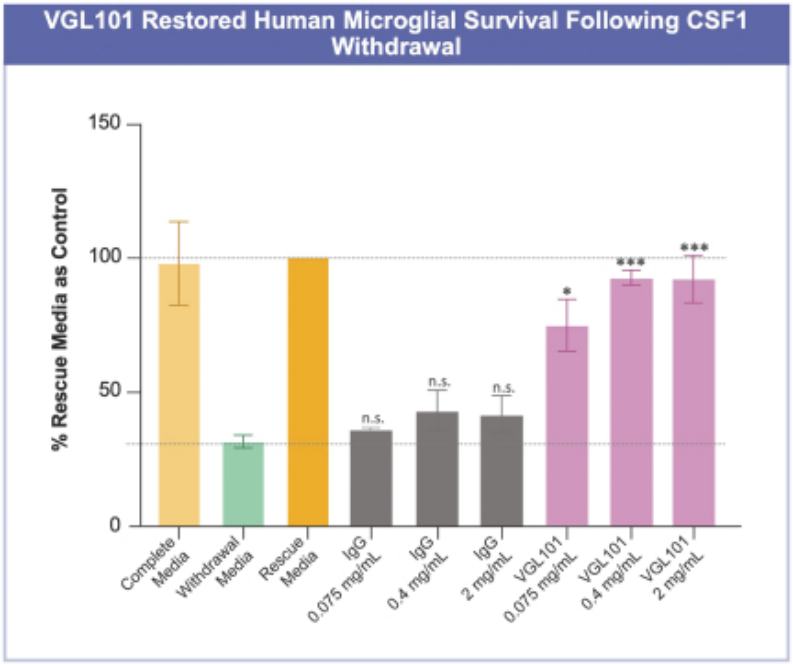
Percentage of PLX5622, 1 µM Relative to Matched Donor: Level of MDM Confluence (left) or Morphological Changes (right) Expressed as a Percentage of Untreated Cells from a Matched Donor; n.s. – not statistically significant.

Figure 17B: mVGL101 Stimulated a Productively Activated Phenotype in MDMs in the Presence of a CSF1R Inhibitor



In another *in vitro* study, we demonstrated that VGL101 compensated for CSF1 withdrawal in maintaining survival of microglia, thereby supporting our hypothesis that VGL101 can improve microglia survival under CSF1R-deficient conditions. In this study, withdrawal of CSF1 reduced microglia survival, similar to that observed in our MDM culture study. Treatment with VGL101 restored microglia survival in a dose-dependent manner to levels similar to that observed with CSF1-treated culture.

Figure 18: VGL101 Restored Human Microglial Survival Following CSF1 Withdrawal



*Y-axis ("% Rescue Media as Control"): survival of microglia culture based on levels of adenosine triphosphate generation, a measure of cell metabolism, compared to that observed with Rescue Media; X-axis – Complete Media: cell culture media containing CSF1 at 25 ng/mL and IL34 at 100 ng/mL; Withdrawal Media: Complete Media without CSF1 and IL34; Rescue Media: Withdrawal Media with CSF1 and IL34 added back in at 25 ng/mL and 100 ng/mL, respectively; IgG: immunoglobulin G control; n.s. – not statistically significant vs Withdrawal Media; * - adjusted p-value < 0.05 vs Withdrawal Media;*** - adjusted p-value < 0.001 vs Withdrawal Media*

We have not employed available *in vivo* CSF1R-deficient mouse models to support the case for clinical development of VGL101 in ALSP because we believe these models do not adequately recapitulate human disease. Additionally, the available *CSF1R+/-* mouse models have low penetrance (approximately 50 percent) and do not display symptoms for 12-18 months after birth, which make the model very challenging to utilize.

Clinical Development Plan

In September 2021, we began a non-interventional natural history study of ALSP patients. In November 2021, the FDA cleared our IND for VGL101 in ALSP at doses up to 20 mg/kg, with a partial clinical hold on doses higher than 20 mg/kg. We do not believe the partial clinical hold will have a material impact on our current clinical development plans and timelines for our clinical trial in ALSP. We initiated our first-in-human Phase 1 clinical trial with VGL101 in healthy volunteers in December 2021 and as of today, we have completed dosing of the 20 mg/kg SAD cohort without any safety signals and initiated the 20 mg/kg MAD cohort. We expect to announce topline data from the Phase 1 trial in the second half of 2022. Assuming our Phase 1 trial progresses on our expected timeline, our FDA discussions proceed as currently planned, and we identify an acceptable dose as part of the Phase 1 trial, we believe we can initiate our interventional studies in ALSP in the second half of 2022. We have also 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 clinical trial in the first half of 2023 following the completion of the VGL101 Phase 1 clinical trial in healthy volunteers. We also plan to submit a protocol amendment to the FDA under our open IND to conduct a Phase 1b biomarker-based, PoM clinical trial of VGL101, expected to begin in the second half of 2022, in genetically defined AD patients with or without the relevant *TREM2* variants to inform subsequent clinical trials with our small molecule agonist.

- ***Natural History Study:*** We began this study in September 2021 with the objectives of further understanding the phenotype and natural course of the disease, the patient journey and treatment paradigm, as well as further developing, and evaluating biomarkers and potential clinical outcome measures. One of the most important objectives for the natural history study is to serve as a potential synthetic control arm which will function as a comparator group in our interventional trial. Patients who participate in our natural history study may also participate in our interventional clinical trials.
- ***First-In-Human Phase 1 Trial:*** This clinical trial is designed as a dose escalating (single and multiple ascending dose (SAD/MAD)) trial of VGL101 in healthy volunteers, including subjects of various ethnic backgrounds. This trial is designed to evaluate safety and tolerability as well as measure biomarkers to confirm target engagement such as sCSF1R, sTREM2 and induced microglial factors found in CSF. This trial will provide a foundation for clinical trials of VGL101 in patients with ALSP as well as with other neurodegenerative disorders. We submitted our IND for the Phase 1 trial in October 2021 and received clearance from the FDA to initiate dosing of healthy volunteers in our Phase 1 SAD/MAD clinical trial at doses up to 20 mg/kg. The SAD portion of the Phase 1 trial includes four cohorts, and the MAD portion of the trial includes one cohort that would be dosed after successful completion of the four SAD cohorts. Prior to dosing patients in additional cohorts, we will be required to resolve a partial clinical hold placed by the FDA on doses higher than 20 mg/kg. Following our response to the FDA's initial request for information, as communicated in the agency's partial clinical hold letter, we received an updated letter from the FDA requesting additional non-clinical data. We expect to resubmit a response to the FDA in the second quarter of 2022 with new data including from our 6-month GLP toxicology study in nonhuman primates and Phase 1 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 initiated the 20 mg/kg MAD cohort. We do not believe the partial clinical hold will have a material impact on our current clinical development plans and timelines for our clinical trial in ALSP. We expect to announce topline data from the Phase 1 trial in the second half of 2022. Pending safety results of the Phase 1 trial and discussions with the FDA, we plan to evaluate VGL101 in a Phase 2/3 trial at doses up to 20 mg/kg based on our current dosing rationale for VGL101.
- ***Phase 2/3 Clinical Trial:*** We plan to begin a seamless Phase 2/3 trial in ALSP patients, assuming our Phase 1 trial progresses on our expected timeline, our FDA discussions proceed as currently planned, and we identify an acceptable dose as part of the Phase 1 trial. The Phase 2 portion of that trial could begin as early as the second half of 2022. Our clinical development plan is based on pre-IND interactions with the FDA during which we provided information regarding the devastating nature of ALSP, the prevalence of the disease and our proposed development plan. Based on this information, the FDA suggested we consider a seamless Phase 2/3 trial design as part of our clinical development plan to support a BLA.

The Phase 2 part of the trial would be a PoC trial with the objectives of:

- evaluating the safety and tolerability of VGL101 in patients with ALSP;
- evaluating the pharmacokinetics of VGL101 in patients with ALSP;
- assessing fluid, such as NfL, and imaging, such as MRI, biomarkers of disease progression in patients with ALSP; and
- demonstrating fluid and brain imaging biomarker efficacy.

In addition, we plan to generate data from VGL101 clinical trials to inform our TREM2 small molecule agonist program for AD. Following successful completion of our Phase 1 SAD/MAD trial in healthy volunteers, we plan to conduct early human translational work with VGL101 in AD to evaluate the effect of TREM2 agonism in microglia modulation in genetically defined AD subpopulations and compare them with a non-carrier cohort. Towards that end, we are targeting submission of a protocol to the FDA under our open ALSP IND to conduct a Phase 1b biomarker-based, PoM trial. Although VGL101 and our small molecule TREM2 agonists are different modalities with different product profiles, both of them have been shown to elicit similar effects on TREM2 agonism. We expect our PoM trial of VGL101in AD to inform the target patient population and design for future larger studies that evaluate the safety and efficacy of our small molecule agonist. We are currently conducting feasibility studies to identify AD patients carrying genetic variants associated with microglial dysfunction and have initiated protocol preparation for our Phase 1b biomarker trial, which we expect to begin in the second half of 2022. We believe this

approach will help reduce translational risk and optimize the selection of the initial patient population recruited for our small molecule program.

Patient Engagement and Recruitment

We have created a strong global network of KOLs, centers of excellence, and genetic counseling practices that each treat ALSP patients and work with families affected by the disease. These span all geographies but are mainly focused in areas where ALSP clusters have been identified (North America, Europe, and Asia).

We have launched the world's first patient-facing ALSP informational website and actively support the first and only patient advocacy organization dedicated to ALSP, the Sisters' Hope Foundation. Strong partnerships with patient organizations like Sisters' Hope Foundation enable us to learn in real-time as more patients are diagnosed with ALSP. In partnership with Sisters' Hope Foundation, we recently launched a global ALSP patient registry to further understand patient and caregiver journey, disease burden, and health economic outcomes. We have also partnered with genetic testing companies to increase disease awareness and help with patient engagement for upcoming clinical trials.

We are also partnering with a larger leukodystrophy umbrella organization, the United Leukodystrophy Foundation, as well as rare disease umbrella organizations such as NORD, Global Genes, the Every Life Foundation, and the European Leukodystrophy Association, to provide disease education and raise awareness of ALSP.

We have formed a PCAC consisting of members who can provide a well-rounded patient and caregiver perspective. Members of the PCAC include a patient who has received a transplant, an asymptomatic patient, a parent of a patient, a caregiver, and a genetic counselor. The PCAC will offer guidance on elements of the patient experience to help us embed the patient voice into the clinical infrastructure to support patient identification, recruitment, and retention.

We play a central role in the development of an ALSP KOL network to support global collaboration. We intend for this organized KOL network to focus on streamlining and building consensus around disease status definitions and disease measurement tools, as well as working on ways to educate neurologists to recognize and test for the relevant gene mutation.

To date, through these efforts, we have identified a significant number of symptomatic, pre-symptomatic, and asymptomatic carriers of *CSF1R* mutations, which we anticipate will facilitate recruitment into our clinical program.

Indication Expansion in Rare Leukodystrophies

According to the National Institute of Neurological Diseases and Stroke, leukodystrophies include more than 50 rare, genetic disorders that selectively affect the CNS' white matter, and are typically caused by defects that affect its generation, maintenance, and repair. Collectively, they afflict approximately 99,000 people in the U.S.

We plan to pursue additional indications in this space, where a breakdown of healthy microglial function acts as either a driver or a contributor to the neurodegenerative process. Operationally, our decisions are informed by the availability of translational tools, overall disease profile, medical need and clinical development tractability, competition, and commercial feasibility. From a mechanistic perspective, our approach is to initially target indications which TREM2 agonists can potentially address.

We have identified several white matter diseases as potential therapeutic opportunities that share similar characteristics with ALSP and appear to be driven by either peroxisomal or lysosomal deficits (Table 1). These disorders include cALD, MLD, and Krabbe. Our hypothesis is that we can restore microglial function resulting from loss-of-function mutations with TREM2 agonists in these diseases.

Table 1: Additional Leukodystrophies for Potential Pipeline Expansion

	Epidemiology	Genetics	Pathology	Unmet Medical Need	Diagnosis	Treatment
cALD	**Rare** **~7-8K in U.S. & EU**	***ABCD1* mutations**	**Progressive cerebral inflammatory neurodegeneration**	**Significant** **Vegetative state: 2 yrs** **Death: 10 yrs**	**Blood test** **Newborn screening**	**No approved tx** **HSCT in limited pts**
MLD	Rare ~2-8K in U.S. & EU	*ASA* and *PSAP* mutations	Progressive cerebral inflammatory neurodegeneration	Significant Infantile form – rapid progression	Clinical/Imaging Genetic screening	No approved tx HSCT in limited pts
Krabbe	Rare ~1/100K newborns in U.S.	*GALC* mutations	Progressive cerebral inflammatory neurodegeneration	Significant Infantile form – rapid progression	Enzymatic testing Limited newborn screening	No approved tx HSCT in limited pts

HSCT: Hematopoietic stem cell transplantation.

We have selected cALD as the first follow-on indication because microglial dysfunction in this disease is more thoroughly defined than it is in other indications. cALD is the severe, progressive neurodegenerative form of X-linked adrenoleukodystrophy (X-ALD), a rare metabolic disorder affecting the microglia. The birth prevalence of X-ALD is estimated at one in 3,878 males in a study on newborn screening for this disease in 2017.

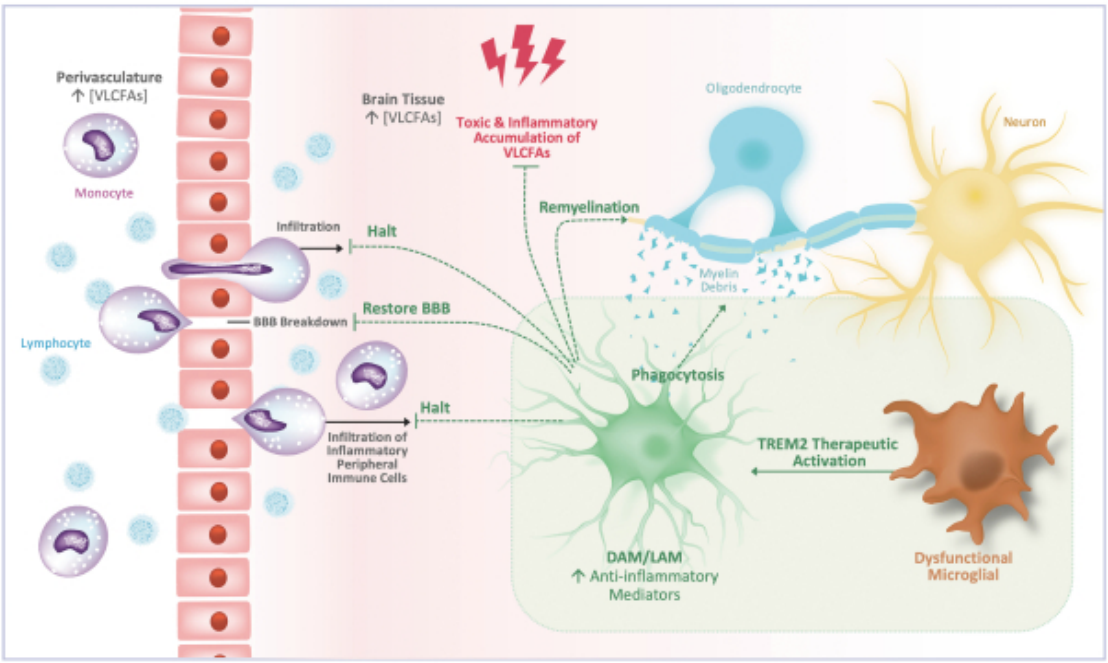
Approximately 37-47% of males diagnosed with ALD will progress to cerebral ALD with a majority in their childhood and adolescent years. A smaller number of adult men with adrenomyeloneuropathy (AMN), the slowly progressive adult form of x-ALD, will also develop cALD. cALD is characterized by progressive cerebral demyelination and inflammation in the white matter of the brain leading to a rapidly progressive neurologic decline and resulting in severe loss of neurologic function and death in most untreated patients.

Specifically, cALD is caused by loss-of-function mutations in the *ABCD1* gene, which encodes a transporter protein for very long chain fatty acids (VLCFAs) into peroxisomes, intracellular organelles critical for lipid metabolism. As illustrated in Figure 19, *ABCD1* loss-of-function mutations result in toxic and inflammatory accumulation of VLCFAs and lead to oxidative stress, as well as energetic and functional microglial deficits resulting in inflammation, increased myelin debris, axonal injury and BBB breakdown. ABCD1 is highly expressed in microglia where ABCD1-deficiency leads to well-described microglial dysfunction.

Figure 19 also illustrates our hypothesis on VGL101's ability to reverse microglial dysfunction caused by ABCD1 mutations by activating the TREM2 pathway to transition microglia to DAM and lipid associated microglia (LAM), microglia associated with lipid debris removal. The resulting DAM and LAM may promote proliferation, survival, and ability to maintain an anti-inflammatory environment, while enhancing phagocytosis of myelin debris, enabling remyelination and reducing VLCFA accumulation. We believe VGL101-mediated TREM2 agonism may also have beneficial effects on the BBB and could halt the infiltration of inflammatory leukocytes into the brain.

We plan to submit an IND amendment or additional IND, if required, to begin a Phase 2 clinical trial in cALD in the first half of 2023, following the completion of the VGL101 Phase 1 clinical trial in healthy volunteers. We believe patient availability to participate in our clinical trial will be facilitated by expanded newborn genetic screening in the U.S., disease awareness, endpoint qualification and the mature nature of patient advocacy efforts.

Figure 19: cALD is a Microglial-modulated Leukodystrophy Caused by Peroxisomal Deficiency, Potentially Addressable by TREM2 Agonism



Pink area illustrates the involvement of microglia in cALD and green area/arrows illustrate our hypothesis of mechanism of action of TREM2 agonism as a potential therapeutic strategy; LAM - lipid-associated microglia; ↑ [VLCFAs] - increase in VLCFA concentrations.

Small Molecule TREM2 Agonists for the Treatment of Neurodegenerative Diseases

We are advancing our novel, orally-available, small molecule TREM2 agonist for the treatment of more common neurodegenerative diseases, beginning with genetically defined AD populations associated with *TREM2* gene variants. An orally available and highly CNS penetrant small molecule has many potential clinical and commercial advantages in large chronic indications, including ease of administration and use in outpatient settings. We also intend to explore the potential of our small molecule agonist for the general AD population, if clinical data support this approach.

Our Small Molecule TREM2 Agonist Program

We have in-licensed more than 1,000 small molecule TREM2 agonist compounds resulting from a robust hit-to-lead and lead optimization program. Expanding on this program, we have synthesized more than 500 additional compounds.

We have demonstrated in preclinical studies that compounds in our lead series are highly selective, potent activators of TREM2, and which we believe are highly CNS penetrant to facilitate blood brain barrier crossing after oral dosing. In addition, we have ongoing screening efforts that have resulted in the discovery of a second series with a different chemical core structure than the lead series. Our second series is currently in the early lead optimization stage.

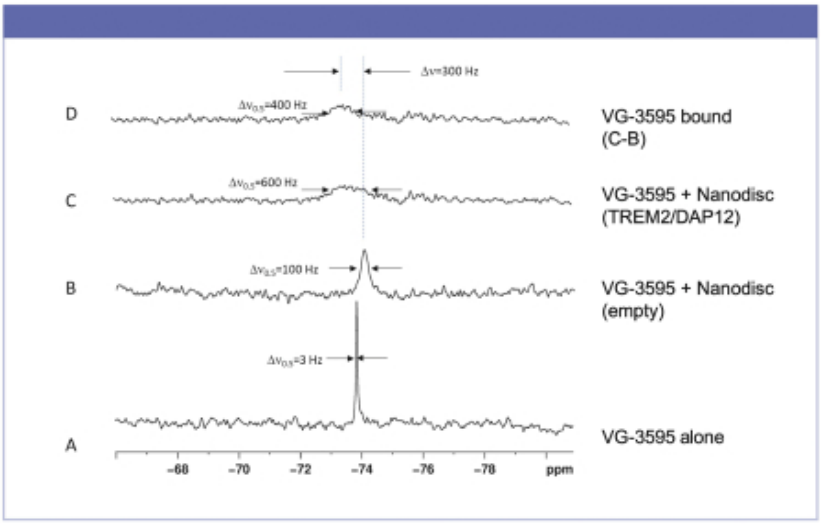
We believe the physical and chemical attributes of the small molecule candidates in our lead series make them promising for further drug development, including solubility, permeability, and oral bioavailability. Based on our analysis, preliminary safety screening with the compounds in our lead series in standard assays has not identified any major off target binding, genetic toxicity, as measured by the Ames assay, cardiac toxicity, as measured by a human cardiac receptor assay, called hERG, or

drug metabolism issues, as measured by liver metabolism assays, known as cytochrome P450 (CYP) induction and time dependent cytochrome P450 inhibition (CYP TDI). In the first quarter of 2022, we initiated IND-enabling studies for this program and expect to file an IND application in 2023.

Data collected from single oral dose studies in human *TREM2* knock-in mice have shown that our prototypical small molecule TREM2 agonists recapitulated many of the gene expression changes and much of the *IP-10* induction mediated by a single dose of VGL101.

In vitro experiments have been conducted with membrane-like structures, called nanodiscs, into which TREM2 and DAP12 have been engineered. Direct binding between a radioisotope-labeled prototype small molecule compound VG-3595 and the membrane associated TREM2 is determined using nuclear magnetic resonance (NMR) analyses. Figure 20 below shows NMR data from a series of experiments which, taken together, indicated that VG-3595 directly bound TREM2-containing nanodiscs with high affinity. The NMR data for VG-3595 incubated with an empty nanodisc (B) is subtracted from the NMR data for VG-3595 incubated with TREM2/DAP12 loaded nanodiscs (C), and the difference represents specifically bound VG-3595 (D).

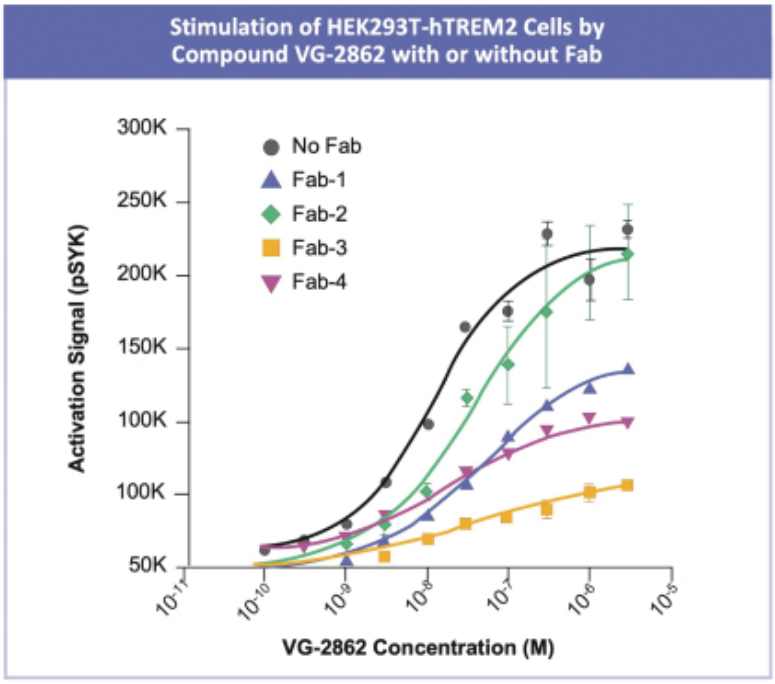
Figure 20: Small Molecule TREM2 Agonist Target Engagement with TREM2 Confirmed *In Vitro*



In other experiments using engineered cell lines overexpressing human TREM2 and human DAP12 for the binding target, we have shown that antibody fragments (Fabs) that bind to TREM2, but cannot trigger TREM2 activation, inhibited small molecule mediated TREM2 activation by another prototype TREM2 agonist compound, VG-2862 (Figure 21). Taken together,

we believe the NMR binding data and the antibody fragment competition data are encouraging evidence for direct interactions between our prototype small molecule TREM2 agonists and TREM2.

Figure 21: Anti-TREM2 Fabs Inhibit Small Molecule Agonist Activity

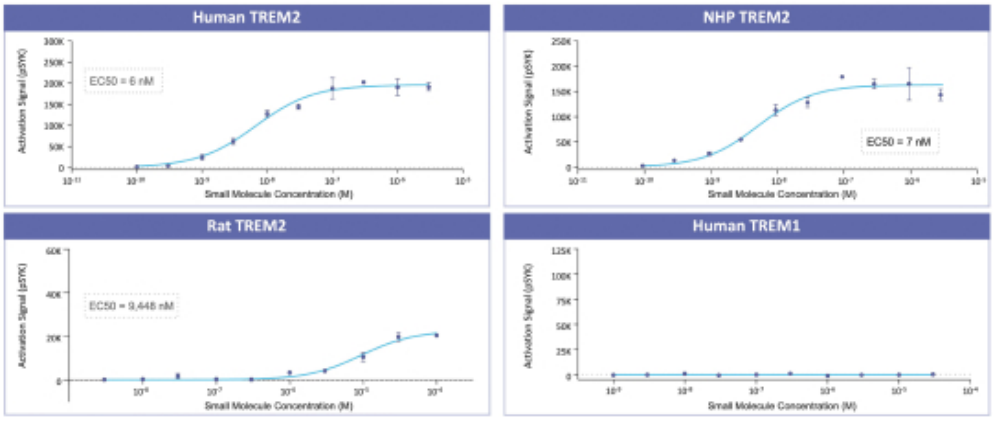


Activation Signal (pSYK): Measurement of Phosphorylation Level of SYK; VG-2862 Concentration: Molar Concentration (M) of VG-2862 on a Logarithmic Scale: $1x10^{-11}$M, $1X10^{-10}$M, $1X10^{-9}$M, $1X10^{-8}$M, $1X10^{-7}$M, $1X10^{-6}$M, $1X10^{-5}$M; No Fab: no Fab added; Fab 1-4: Fab 1 to 4 added.

We have demonstrated the selectivity of prototype small molecules in experiments comparing HEK cells engineered with either human TREM2 or human TREM1, both of which use the adaptor DAP12 for downstream signaling. In these studies, prototype TREM2 agonists generated a SYK activation signal in cells expressing human TREM2 but not in cells expressing

human TREM1, as shown in Figure 22 below. Additionally, as shown in Figure 22, we demonstrated our prototype small molecules had high selectivity for human and NHP TREM2 over rat TREM2.

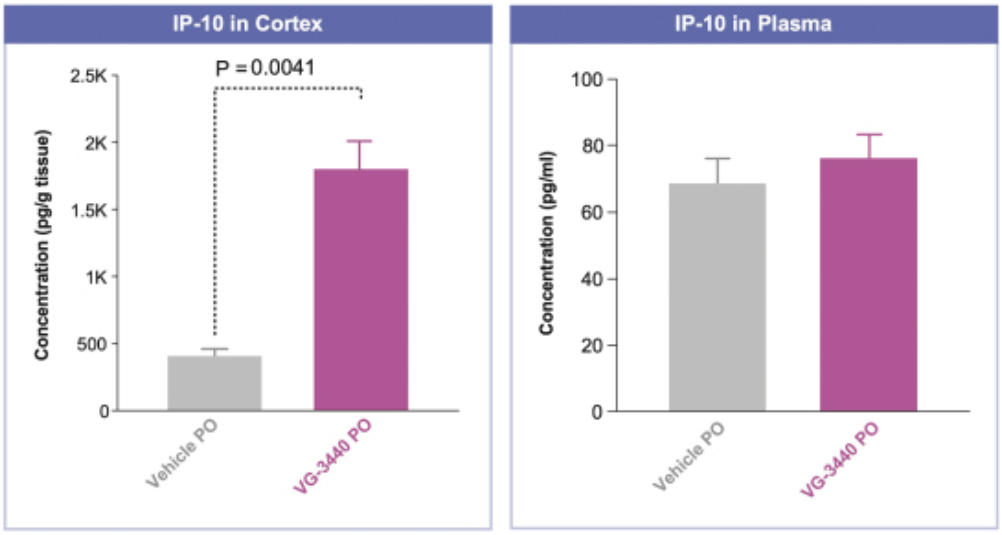
Figure 22: Small Molecule Agonist is Selective for human and NHP TREM2



y-axis: Activation Signal (pSYK) - Measurement of SYK Phosphorylation Level. x-axis: Small Molecule Concentration - Molar Concentration (M) of prototype small molecule TREM2 agonist on a Logarithmic Scale ($1x10^{-11}$M, $1X10^{-10}$M, $1X10^{-9}$M, $1X10^{-8}$M, $1X10^{-7}$M, $1X10^{-6}$M, $1X10^{-5}$M, $1X10^{-4}$M). EC50 - Concentration of a compound where 50% of its maximal effect (SYK phosphorylation) is observed.

We have also conducted *in vivo* studies in human *TREM2* knock-in mice analogous to those shown above for VGL101. Oral dosing with a prototype small molecule agonist (VG-3440) demonstrated increases in the microglial biomarker, IP-10, in the brain after 24 hours. There were no increases in plasma IP-10 concentrations, indicating selective microglia targeting in the brain (Figure 23).

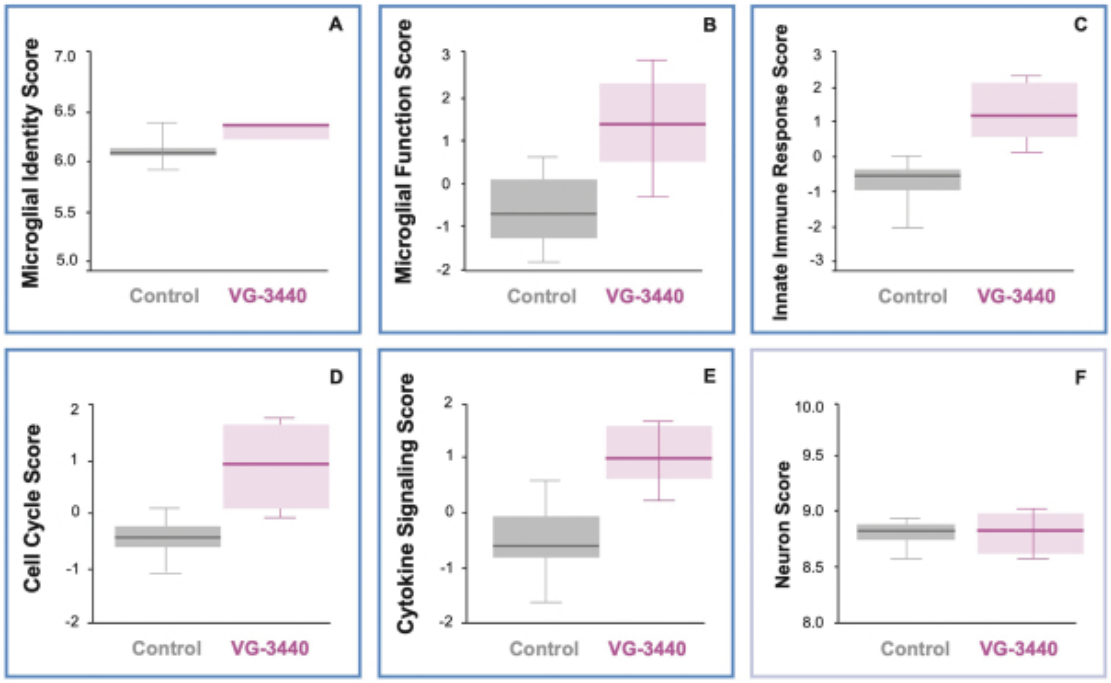
Figure 23: Prototype Small Molecule TREM2 Agonist Productively Activated Microglia in Human *TREM2* Knock-in Mice without Peripheral Effects



Concentration (pg/g tissue): Concentration of IP-10 Protein (pg) Per Gram of Cortical Homogenate; Concentration (pg/ml): Concentration of IP-10 protein (pg) Per Milliliter of Plasma; Vehicle PO—Oral Administration (PO—per os) of Inactive Compound; VG-3440 PO: Oral Administration of Prototype Small Molecule TREM2 at 50 mg/kg in Two Doses. The IP-10 level for VG-3440 in Cortex group was determined to be statistically different than that for the Vehicle with a P value < 0.01.

In the human *TREM2* knock-in mouse model, we demonstrated that our prototype small molecule TREM2 agonists selectively increased the expression of genes related to microglial identity, microglial function, innate immune response, cell cycle (proliferation genes), and cytokine signaling (neuroprotection genes) in a similar manner to what we have demonstrated for VGL101, as shown in Figure 24 below. There was no increase in either neuronal or astrocytic gene expression following dosing with the small molecule TREM2 agonist, further demonstrating microglia-specific targeting through TREM2. Therefore, similar to VGL101, our small molecule TREM2 agonist prototype, VG-3440, reached the brain, engaged its target, human TREM2, and activated microglia to increase gene programs that define normal functioning states related to damage surveillance, response to damage sensing, and neuroprotection.

Figure 24: VG-3440 Increased the Expression of Genes Associated with Microglial Identity, Microglial Function, Innate Immune Response, Cell Cycle, and Cytokine Signaling, Without Affecting the Gene Expression in Neurons



y-axes – reflect the level of gene expression changes based on analyses comparing total brain RNA (gene transcripts) isolated from negative control (antibody without TREM2 binding) and mVGL101-treated mice. A: "Microglial Identity Score"—gene expression associated with microglial identity. B: "Microglial Function Score"—gene expression associated with microglial activation. C: "Innate Immune Response Score"—gene expression associated with innate immunity and neuroprotection. D: "Cell Cycle Score"—gene expression associated with cell cycle and proliferation. E: "Cytokine Signaling Score"—gene expression associated with cytokine signaling and neuroprotection. F: "Neuron Score"—gene expression associated with neuronal identity; VG-3340 orally administered at 50 mg/kg in 2 doses

Overview of Alzheimer's Disease

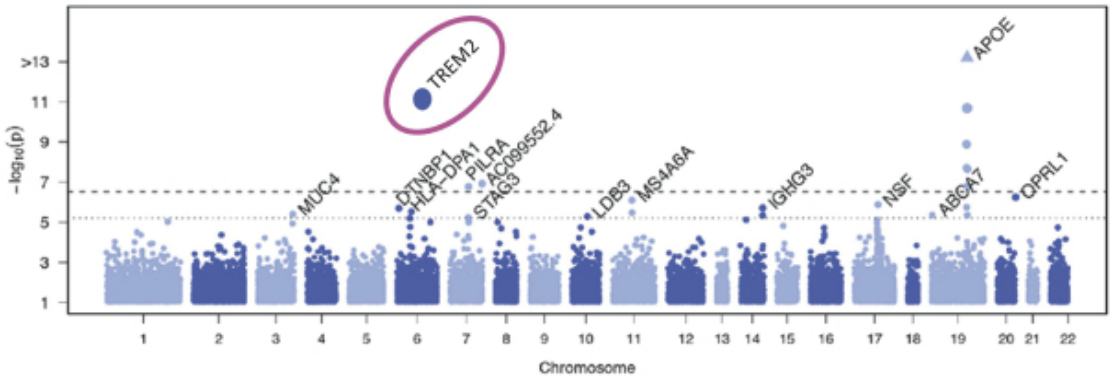
AD is the most common cause of dementia, a general term for the loss of memory and other cognitive abilities severe enough to interfere with daily life. AD accounts for 60-80% of dementia cases, and the majority of people with AD are aged 65 and older. A progressive disease, AD usually presents with mild memory loss and progresses to include disorientation, loss of initiative or judgment, difficulty with self-care, behavioral problems, and general mental decline. People aged 65 and older survive an average of four to eight years after diagnosis, with some living as long as 20 years. These data reflect the slow, uncertain progression of the disease, which is the sixth-leading cause of death in the U.S.

The Alzheimer's Association estimates that 6.2 million people in the U.S. are living with AD in 2021. By 2050, this number is projected to rise to nearly 13 million. The costs of health care and long-term care for people with AD to our healthcare system are substantial. According to the Alzheimer's Association, the aggregate cost of AD and other dementias is expected to be $355 billion in 2021, and this number could increase to as much as $1.1 trillion by 2050.

TREM2 in Alzheimer's Disease

Loss-of-function *TREM2* variants occur in seven to eight percent of the AD population and are linked to both disease progression and worsened patient outcomes. Several genetic variants in *TREM2* have emerged from GWAS (Figure 25) that significantly increase AD risk by two- to four- fold, an increase in risk comparable to that associated with having one copy of *ApoE4*. The most common and most well-studied *TREM2* variant known to increase the risk of AD is the R47H variant. The R47H variant, which represents two to three percent of the AD population, has been reported to triple AD risk in GWAS and is associated with a 23% more rapid progression of dementia compared with non-variant carriers. Other *TREM2* variants have also been implicated as risk factors for developing AD, including R62H, L211P, and R136Q, all of which are loss-of-function variants.

Figure 25: Exome Sequencing Based GWAS Identified *TREM2* Mutations as an AD Risk Factor



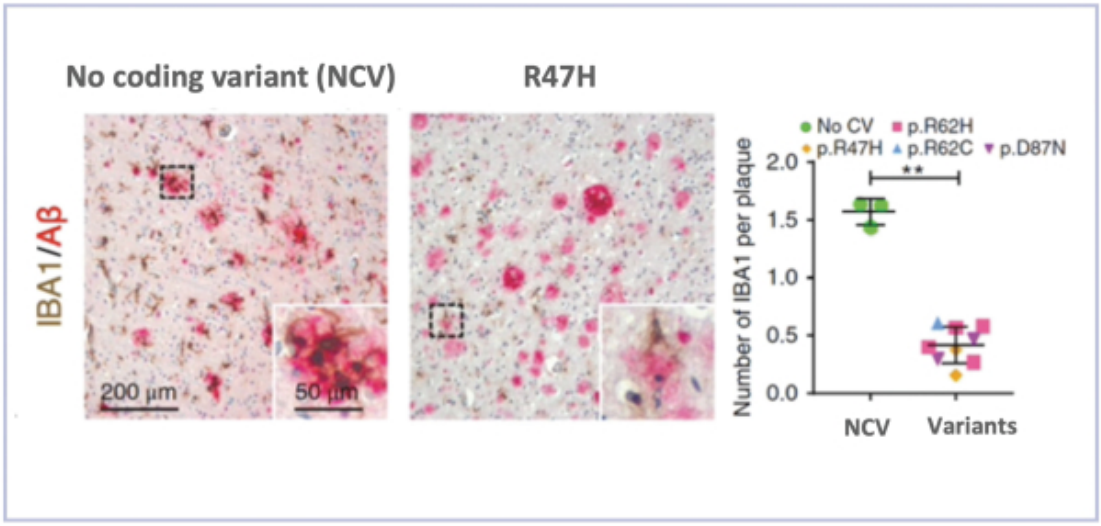
Y-axis – reflects the level of significance for each corresponding gene and its association for the risk of developing AD. The larger the y-axis number (negative logarithmic scale for p) for a gene the more significant it is as a genetic AD risk factor. The dotted line indicates a threshold of $p < 6.1 \times 10^{-6}$ and the dashed line indicates a threshold of p < 3.1 × 10–7. Bis et al. Mol Psychiatry 2020.

Our understanding of the role of microglial dysfunction in plaque development in AD is based on the observation that normally functioning microglia reduce levels of toxic amyloid plaques in the brain, while increasing the number of inert, dense core plaques. In addition, normal TREM2 function is required to prevent AD-associated tau protein aggregates from forming. AD models have shown that TREM2 plays a protective role throughout all stages of disease progression.

In AD patients carrying the R47H *TREM2* variant, the number of microglia associated with amyloid-ß plaques is reduced, indicating a defect in responding to damage signals from plaque, as illustrated in Figure 26. The graph on the right indicates a 3-fold reduction of IBA-1-staining cells (microglia) between R47H TREM2 carrier patients and normal TREM2 patients. R47H TREM2 patient brains also showed reduced barrier function around neurotoxic amyloid-ß compared with normal TREM2 AD patient brains, seen as reduced clustering of IBA-1-staining cells around amyloid-ß plaques ("R47H" versus "No coding variant

(NCV)" in the brain histopathology images). R47H *TREM2* AD patients also experienced more rapid disease progression and a greater number of co-morbidities, such as a neuropathological protein accumulation, called -synucleinopathy.

Figure 26: Impaired Microglia Clustered Around Aß Plaques with TREM2 Coding Variants

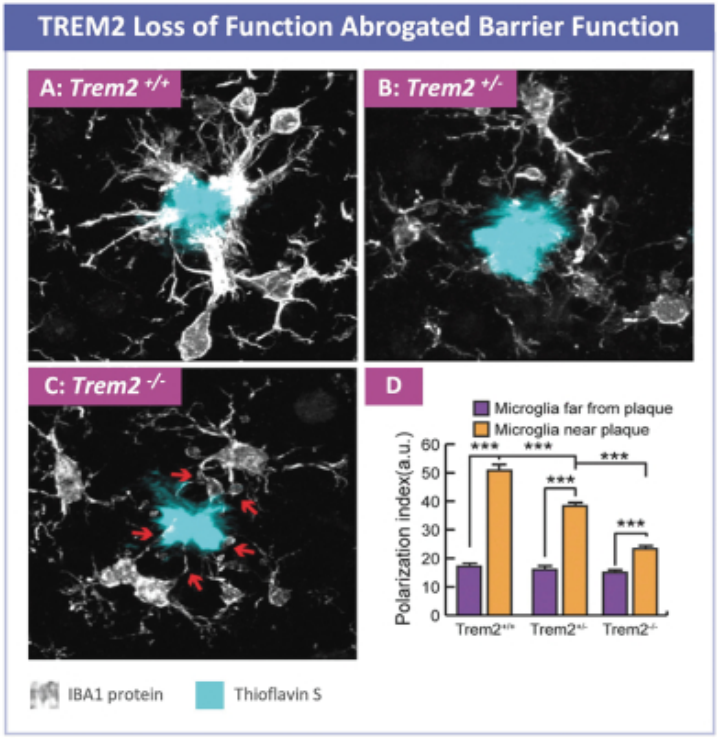


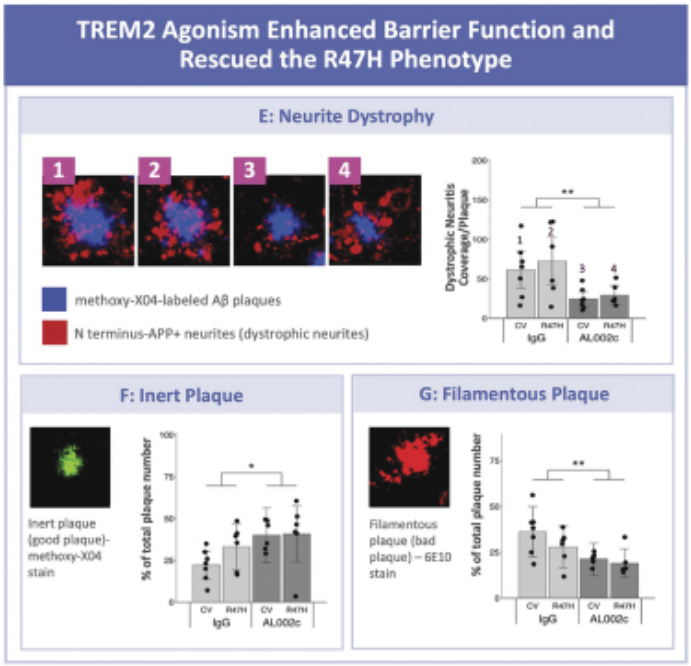
Immunohistochemical staining of brain tissue: IBA1/Aß - IBA1 staining in brown and amyloid-ß staining in magenta. Graph quantifies the number of IBA1-stained cells (indicative of microglia) per amyloid-ß plaque for patients with normal TREM2 ("NCV") (green circles) and TREM2 variants ("Variants"), including R47H (orange diamonds), R62H (pink squares), R62C (blue triangles) and D87N (purple triangles). Parhizkar et al. Nat Neurosci. 2019.

The impaired barrier function with R47H TREM2 and *Trem2* knock-out is further demonstrated in an AD mouse model which induces AD neuropathology such as amyloid-ß plaques and neuronal dysfunction (Figure 27). Microglia (white) from *Trem2* knock-out mice failed to form a protective barrier around amyloid-ß plaque (blue) to reduce regional amyloid neurotoxicity, compared to control (*Trem2*+/+) mice (Figures 27 A and C). These microglia showed a *Trem2* dosage effect in their ability to form a protective barrier around amyloid-ß plaque, as seen in Figure 27D which shows the allelic reduction in *Trem2* and the stepwise decrease in microglia around plaques. The barrier defect in microglia from R47H TREM2 mice is correlated with increased neuritic dystrophy (abnormal nerve processes; red staining in Photograph 2 in Figure 27E), with increased filamentous, neurotoxic amyloid-ß plaques (red staining in Figure 27G) and with relatively reduced inert, non-neurotoxic plaque (green staining in Figure 27F). This pathobiology is thought to be due to defective responses to damage signals caused by reduced TREM2-ligand interactions and an inability of microglia to convert to the DAM state. The

neuropathology induced in this AD mouse model, which is more enhanced with R47H TREM2 due to its reduction of function (as compared to CV TREM2), was ameliorated by treatment with a TREM2 agonist antibody (graphs in Figure 27 E – G).

Figure 27: TREM2 Promoted Barrier Function and Reduced Toxic Filamentous Plaque



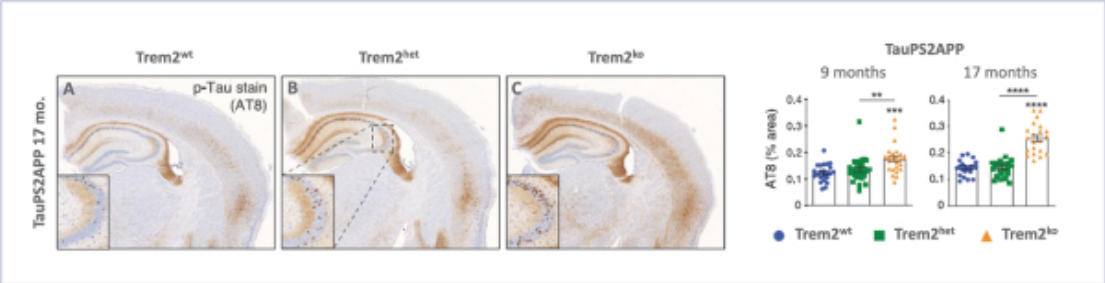


*A – C: Immunohistochemical staining of IBA1 (white, indicative of microglia) and thioflavin-S (blue, indicative of amyloid-ß plaques) in brain tissue of AD mouse model (5XFAD). C: red arrows indicate inability of microglia to move toward and surround (i.e. polarize) the plaque. D: quantification of ability of microglia to polarize around plaques ("Polarization index") in arbitrary units ("a.u.") for various Trem2 genetic backgrounds, ***: p<0.001. E: photographs 1 – 4: immunohistochemical staining of amyloid-ß plaques (blue) and dystrophic neurites (red) in AD mouse model (5XFAD) carrying different human TREM2 genes: 1 – common variant (CV) TREM2 treated with control immunoglobulin G (IgG); 2 – R47H TREM2 treated with IgG; 3 – CV TREM2 treated with AL002c; 4 – R47H TREM2 treated with AL002c; graph shows quantification of number of dystrophic neurites covering each plaque for photographs 1 – 4, **- p<0.01; F and G: photographs show representative inert (good, green staining for methoxy-X04) and filamentous (bad; red staining for 6E10) amyloid-ß plaques and their respective contribution to overall plaque number in different TREM2 backgrounds (CV or R47H) treated with IgG or AL002c, *- p<0.05; **- p<0.01. A – D: Yuan et al Neuron 2016; E – G: Wang et al J Exp Med 2020.*

As shown in Figure 28 below, AD model mice carrying *Trem2*+/+ (Figure 27A, $Trem2^{wt}$), Trem2+/- (Figure 28B, $Trem2^{het}$), or *Trem2*-/- (Figure 28C, $Trem2^{ko}$) alleles demonstrated stepwise reduction of *Trem2* levels that were correlated with increased neuropathology, as measured by tau accumulation (Figures 28B and C, brown stained dots with the graph quantifying the differences in tau accumulation), and with amyloid-ß pathology in the brains of mice. These results provide strong evidence that TREM2 restrains the accumulation of tau in the presence of amyloid-ß pathology. The failure of *Trem2*-/- microglia to restrain tau accumulation is thought to be driven by their inability to transition to the neuroprotective TREM2-dependent DAM state. We believe TREM2 agonism has the potential to provide therapeutic benefit against tau accumulation, which is believed to occur in the later stages of AD.

We believe the robust body of experimental and genetic evidence points to TREM2 as a key modulator of amyloidosis and tauopathy, and that activating TREM2 has potential to provide disease modifying benefit to those living with AD.

Figure 28: TREM2 Restrained the Enhancement of Tau Accumulation



*TauPS2APP: mouse with PS2APP transgene and mutant tau gene; p-Tau - phosphorylated tau protein; AT8 - antibody detecting p-Tau and used for immunohistochemical staining of p-Tau in a brown color; wt - wild type; het - heterozygous; ko - knockout; graph shows the percentage of a defined area covered by AT8-staining cells for various Trem2 genetic backgrounds; **: p<0.01; ***: p<0.001; ****: p<0.0001. Lee et al Neuron 2021.*

Our Small Molecule TREM2 Agonist Clinical Strategy

Our strategy in AD is to follow a precision medicine approach that first establishes the role of TREM2-mediated microglial dysregulation in the pathogenesis of AD within certain genetically defined patient subpopulations, which includes *TREM2* and other variants. Following successful completion of our Phase 1 SAD/MAD trial in healthy volunteers, we plan to conduct early human translational work with VGL101 in AD to evaluate the effect of TREM2 agonism in microglia modulation in genetically defined AD subpopulations and compare them with a non-carrier cohort. Towards that end, we are targeting submission of a protocol to the FDA under our open ALSP IND to conduct a Phase 1b biomarker-based, PoM trial. Although VGL101 and our small molecule TREM2 agonists are different modalities with different product profiles, both of them have been shown to elicit similar effects on TREM2 agonism. The trial is intended to inform the target patient population and design for future larger studies that evaluate the safety and efficacy of our small molecule agonist. We are currently conducting feasibility studies to identify AD patients carrying genetic variants associated with microglial dysfunction and have initiated protocol preparation for our Phase 1b biomarker-based, PoM trial, which we expect will begin in the second half of 2022. We believe this approach will reduce translational risk and optimize the selection of the initial patient population recruited for our small molecule program.

Competition

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 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 are 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., recently received FDA accelerated approval for a product based on reduction of ß-amyloid 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.

Exclusive License Agreement with Amgen Inc.

In July 2020, we entered into an exclusive license agreement with Amgen Inc., 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 particular, we have been granted licenses under patents filed in both the United States and foreign jurisdictions that are owned or controlled by Amgen, including an exclusive license under certain patents claiming compounds that bind to TREM2. Our exclusively licensed patents include, but are not limited to, patents claiming the composition of TREM2 agonist compounds and methods of using the same.

Pursuant to the terms of the license agreement, we must use commercially reasonable efforts to develop, manufacture, gain marketing authorization and commercialize at least one mAb product and at least one small molecule product in each of several major market territories. In addition, Amgen provided us, at its expense, consulting support in connection with the transfer of the licensed materials and the exploitation of the products. We are also entitled to sublicense the rights granted to us under the license agreement.

As initial consideration for the license, we paid 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 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 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. 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.

The license agreement expires upon the expiration of the last-to-expire royalty term for the products in the territory. Upon expiration of the license agreement, the licenses granted to us will be considered fully paid-up, irrevocable and non-exclusive. Either we or Amgen may terminate the license agreement if the other party commits a material breach of the agreement or defaults in the performance thereunder and fails to cure that breach within 90 days after written notice is provided or in the event of bankruptcy, insolvency, dissolution or winding up. Amgen has the right to terminate the license agreement in full upon written notice to us in the event we, our affiliates or sublicensees, directly challenge the patentability, enforceability or validity of any licensed patents, unless, in the event of a sublicensee challenge, we terminate the sublicense within 60 days' notice. Amgen has the right to terminate the license agreement in the event we do not elect to treat a distracting product (as defined in the license agreement) as a newly added product under the license agreement. We shall have the right to terminate the license agreement if we conclude, due to scientific, technical, regulatory or commercial reasons, that the exploitation of the products is no longer commercially practicable.

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

Master Services Agreement with FUJIFILM

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, pursuant to which FUJIFILM provides research, development, testing and manufacturing services of certain of our product candidates, which are or will be designated as programs pursuant to scope of work agreements. The fees for such services are set out in each scope of work agreement. We may pay additional fees in consideration for certain research and development and technical consultancy services in relation to the procurement, testing and management of consumables; subcontracted work (including delivery of material to and from such subcontractors); process-specific equipment (including installation and qualification thereof); modifications; and special waste.

Either party may terminate the FUJIFILM Agreement by giving three months written notice to the other party, provided there are no uncompleted programs existing at the date such notice is given, or upon material breach that the breaching party cannot cure, does not cure within sixty (60) days if a breach for payment, or otherwise does not commence and diligently pursue a remedy within 60 days. Each scope of work will continue until the earlier of (i) the date the specified in the scope of work, or if no such date is specified, the date the program, or part of the program referred to in the scope of work, is completed, or (ii) termination of the master services agreement or the relevant scope of work. Additionally, upon providing written notice, we may cancel certain stages or programs for convenience, and FUJIFILM may terminate for certain unforeseen technical errors. We may also be required to pay FUJIFILM cancellation fees in the event that we decide to terminate the FUJIFILM Agreement pursuant to its terms, calculated as a percentage of the fees payable under the applicable scope of work agreement.

Intellectual Property

We actively seek to protect our proprietary technology, inventions, and other intellectual property that is commercially important to the development of our business by a variety of means, for example seeking, maintaining, and defending patent rights, whether developed internally or licensed from third parties. We also rely on trade secrets and know-how relating to our proprietary technology for our product candidates and on continuing technological innovation, and we may rely on in-licensing opportunities to develop, strengthen and maintain the strength of our position in the field of microglia-based therapeutics and TREM2 agonists that may be important for the development of our business. Our commercial success depends, in part, on our ability to obtain, maintain, enforce and protect our intellectual property and other proprietary rights for the technology, inventions and improvements and to defend any patents we may own or in-license in the future, prevent others from infringing any patents we may own or in-license in the future, preserve the confidentiality of our trade secrets, and operate without infringing, misappropriating or otherwise violating the valid and enforceable patents and proprietary rights of third parties.

Patent Protection

As with other biotechnology and pharmaceutical companies, our ability to maintain and solidify our proprietary and intellectual property position for our product candidates and technologies will depend on our success in obtaining effective patent claims and enforcing those claims if granted. However, our pending patent applications, and any patent applications that we may in the future file or license from third parties, may not result in the issuance of patents and any issued patents we may obtain do not guarantee us the right to practice our technology or commercialize our product candidates. We also cannot predict the breadth of claims that may be allowed or enforced in any patents we may own or in-license in the future. Any issued patents that we may own or in-license in the future may be challenged, invalidated, circumvented or have the scope of their claims

narrowed. In addition, because of the extensive time required for clinical development and regulatory review of a product candidate we may develop, it is possible that, before any of our product candidates can be commercialized, any related patent may expire or remain in force for only a short period following commercialization, thereby limiting the protection such patent would afford the respective product and any competitive advantage such patent may provide.

The term of individual patents depends upon the date of filing of the patent application, the date of patent issuance, and the legal term of patents in the countries in which they are obtained. In most countries, including the United States, the patent term is 20 years from the earliest filing date of a non-provisional patent application. In the United States, a patent's term may be lengthened by patent term adjustment, which compensates a patentee for administrative delays by the USPTO in examining and granting a patent, or may be shortened if a patent is terminally disclaimed over an earlier expiring patent. The term of a U.S. patent claiming a new drug product may also be eligible for a limited patent term extension when FDA approval is granted, provided statutory and regulatory requirements are met. The term extension period granted on a U.S. patent covering a product is typically one-half the time between the effective date of a clinical investigation involving human beings is begun and the submission date of an application, plus the time between the submission date of an application and the ultimate approval date. The term extension period cannot be longer than five years, and the term extension period may not extend the patent term beyond 14 years from the date of FDA approval. The United States Patent and Trademark Office reviews and approves the application for any patent term extension in consultation with the FDA. In the future, if our product candidates receive approval by the FDA, we expect to apply for patent term extensions on any issued patents covering those products, depending upon the length of the clinical studies for each product and other factors. There can be no assurance that our pending patent applications, and any patent applications that we may in the future file or license from third parties, will issue or that we will benefit from any patent term extension or favorable adjustments to the terms of any patents we may own or in-license in the future. In addition, the actual protection afforded by a patent varies on a product-by-product basis, from country-to-country, and depends upon many factors, including the type of patent, the scope of its coverage, the availability of regulatory-related extensions, the availability of legal remedies in a particular country and the validity and enforceability of the patent. Patent term may be inadequate to protect our competitive position on our products for an adequate amount of time.

Our policy is to file patent applications to protect technology, inventions and improvements to inventions that may be commercially important to the development of our business. We seek patent protection in the United States and foreign countries for a variety of technologies, including our TREM2 agonist therapeutic product candidates, VGL101 and small molecule TREM2 agonists, methods for treating neurodegenerative diseases, and methods of selecting patient populations based on biomarkers.

VGL101

We have an exclusive license from Amgen to one patent family directed to VGL101 and other TREM2 antibodies, and this patent family contains a U.S. patent directed to compositions of matter, along with patent applications directed to compositions of matter and certain methods of their use. As of February 28, 2022, this family contains one U.S. patent, one pending U.S. continuation patent application, and patent applications in Europe, Japan, Australia, Canada, China and over 30 additional countries. The U.S. patent is scheduled to expire in 2038, and any foreign patents or additional U.S. patents that issue from these patent applications, if granted, are expected to expire in 2038; in each instance provided that all appropriate maintenance fees are paid and not including any patent term adjustment, patent term extension, or Supplementary Protection Certificate (SPC).

As of February 28, 2022, we also solely own two U.S. provisional patent applications and two patent applications in Greece directed to methods of treatment using a TREM2 antibody, such as VGL101, according to certain protocols. Any U.S. or foreign patents that issue based on these patent applications, if granted and all appropriate maintenance fees paid, are expected to expire in year 2042, not including any patent term adjustment, patent term extension, or SPC.

Small Molecule TREM2 Agonists

We solely own one patent family and jointly own with Amgen two patent families, each of which is directed to a first series of small molecule TREM2 agonist compositions of matter and methods of their use. We exclusively license Amgen's rights in the two jointly owned patent families. As of February 28, 2022, our solely owned patent family to small molecule TREM2 agonists contains two U.S. provisional patent applications, whereby any U.S. or foreign patents that issue based on these patent applications, if granted and all appropriate maintenance fees paid, are expected to expire in year 2042, not including any patent term adjustment, patent term extension, or SPC. As of February 28, 2022, the first jointly owned patent family to small molecule TREM2 agonists contains one international patent application, whereby any U.S. or foreign patents that issue from this patent application, if granted and all appropriate maintenance fees paid, are expected to expire in year 2041, not

including any patent term adjustment, patent term extension, or SPC. Additionally, as of February 28, 2022, the second jointly owned patent family to small molecule TREM2 agonists contains one international patent application, one U.S. patent application, along with patent applications in Argentina and Taiwan, whereby any U.S. or foreign patents that issue from these patent applications, if granted and all appropriate maintenance fees paid, are expected to expire in year 2041, not including any patent term adjustment, patent term extension, or SPC.

In addition, as of February 28, 2022, we solely own three U.S. provisional patent applications directed to additional small molecule TREM2 agonist compositions of matter and methods of their use. Any U.S. or foreign patents that issue based on these patent applications, if granted and all appropriate maintenance fees paid, are expected to expire in year 2042, not including any patent term adjustment, patent term extension, or SPC.

TREM2 Agonists for CSF1R Dysfunction

We solely own one patent family directed to methods of treating diseases associated with CSF1R dysfunction using a TREM2 agonist, such as VGL101 or other TREM2 antibody. As of February 28, 2022, this family contains one international patent application, one U.S. patent application, and one patent application in Taiwan. Any U.S. or foreign patents that issue based on these patent applications, if granted and all appropriate maintenance fees paid, are expected to expire in year 2041, not including any patent term adjustment, patent term extension, or SPC.

Methods of Treatment & Biomarkers for Alzheimer's Disease

As of February 28, 2022, we exclusively license from Amgen one international patent application directed to methods of treating AD using a TREM2 agonist, as well as methods for identifying a patient with AD who will benefit from treatment with a TREM2 agonist. Any U.S. or foreign patents that issue based on this patent application, if granted and all appropriate maintenance fees paid, are expected to expire in year 2041, not including any patent term adjustment, patent term extension, or SPC.

TREM2 Agonists for ABCD1 Dysfunction

We solely own one patent family directed to methods of treating diseases associated with ABCD1 dysfunction using a TREM2 agonist. As of February 28, 2022, this family contains one international patent application, one U.S. patent application, and one patent application in Taiwan. Any U.S. or foreign patents that issue based on these patent applications, if granted and all appropriate maintenance fees paid, are expected to expire in year 2041, not including any patent term adjustment, patent term extension, or SPC.

TREM2 Agonist Biomarkers

As of February 28, 2022, we solely own two U.S. provisional patent applications directed to methods of treating a disorder associated with microglial dysfunction in certain patients using a TREM2 agonist, as well as methods of identifying a patient with a condition associated with microglial dysfunction that will benefit from treatment with a TREM2 agonist. Any U.S. or foreign patents that issue based on this patent application, if granted and all appropriate maintenance fees paid, are expected to expire in year 2042, not including any patent term adjustment, patent term extension, or SPC.

Trade Secrets

We also rely on trade secrets, know-how, continuing technological innovation and confidential information to develop and maintain our proprietary position and protect aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection. We seek to protect our proprietary technology and processes, in part, by confidentiality agreements and invention assignment agreements with our employees, consultants, scientific advisors, contractors and others who may have access to proprietary information, under which they are bound to assign to us inventions made during the term of their employment or term of service. We also seek to preserve the integrity and confidentiality of our data and trade secrets by maintaining physical security of our premises and physical and electronic security of our information technology systems.

Commercialization

We do not currently have any approved drugs, and we do not expect to have any approved drugs in the near term. As a company, we do not have sales, marketing or commercial product distribution capabilities. We will evaluate all available options for commercialization of our potential therapies, if approved for commercialization by FDA and other relevant

regulatory worldwide bodies. We may consider building out our own commercialization infrastructure in the United States, Europe, Asia and other geographies, entering into co-commercialization agreements with other biopharmaceutical companies with strong and proven commercial capabilities, and licensing select or all geographical rights for some or all of our therapies.

Manufacturing

We do not own or operate manufacturing facilities for the production of our drug candidates and currently have no plans to build our own clinical or commercial scale manufacturing capabilities. We rely, and expect to continue to rely, on third-party manufacturers to produce our product candidates for use in human clinical trials in compliance with FDA and other foreign regulatory requirements, and on contract development and manufacturing organizations (CDMOs) to manufacture and supply our preclinical and clinical materials.

VGL101 is a monoclonal antibody produced from a recombinant cell line. We have established non-exclusive relationships with CDMOs for the GMP manufacturing of VGL101 drug substance and drug product, and with other third parties for testing, fill finish, packaging and labeling. We have a license from Amgen Inc. for use of its proprietary cell lines and media, which we rely on for manufacturing VGL101. FUJIFILM is currently, and will be for the foreseeable future, the sole supplier of certain testing and manufacturing services for VGL101.

The small molecule compound we are developing is produced through chemical synthesis technology. Our selection of a development candidate, along with potential back up compounds, will be made not only on the basis of potential clinical activity and tolerability, but also on the relative ease and reproducibility of synthesis, reasonable cost of goods and ready availability of starting materials. We plan to retain a contract manufacturing organization to produce our small molecule agonist for use in our clinical trials.

We do not have long-term supply agreements, and we purchase our required drug product on a development manufacturing services agreement or purchase order basis. We expect to continue to rely on third-party manufacturers for the commercial supply of any of our product candidates for which we obtain marketing approval. We have personnel with significant technical, manufacturing, analytical, quality, regulatory, including cGMP, and project management experience to oversee our third-party manufacturers and to manage manufacturing and quality data and information for regulatory compliance purposes.

Our product candidates for clinical trial use must be manufactured in compliance with cGMP regulations. The cGMP regulations include requirements relating to organization of personnel, buildings and facilities, equipment, control of components and drug product containers and closures, production and process controls, packaging and labeling controls, holding and distribution, laboratory controls, records and reports, and returned or salvaged products.

Government Regulation

Government authorities in the United States, at the federal, state and local level and in other countries and jurisdictions, including the European Union, extensively regulate, among other things, the research, development, testing, manufacture, pricing, reimbursement, sales, quality control, approval, packaging, storage, recordkeeping, labeling, advertising, promotion, distribution, marketing, post-approval monitoring and reporting and import and export of drugs and biological products such as those we are developing. The processes for obtaining marketing approvals in the United States and in foreign countries and jurisdictions, along with subsequent compliance with applicable statutes and regulations and other regulatory authorities, require the expenditure of substantial time and financial resources.

Licensure and Regulation of Drugs and Biologics in the United States

In the United States, where we are initially focusing our product development, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act (FDCA), and biologics under the FDCA and the Public Health Service Act (PHSA), and their implementing regulations. Both drugs and biologics are also subject to other federal, state and local statutes and regulations. We are currently developing product candidates that would be regulated under the FDCA, and/or the PHSA, and their implementing regulations, as drugs or biologics, depending on the modality of each product candidate. Our product candidates are early-stage and have not been approved by the FDA for marketing in the United States.

An applicant seeking approval to market and distribute a new drug or biologic in the United States generally must satisfactorily complete each of the following steps:

- preclinical laboratory tests, animal studies and formulation studies all performed in accordance with the FDA's Good Laboratory Practices (GLP) regulations, as applicable;
- completion of the manufacture, under current Good Manufacturing Practices (cGMP) conditions, of the drug substance and drug product that the sponsor intends to use in human clinical trials along with required analytical and stability testing;
- submission to the FDA of an Investigational New Drug application (IND), for human clinical testing, which must become effective before human clinical trials may begin;
- approval by an independent institutional review board (IRB), representing each clinical trial site before each clinical trial site may be initiated;
- performance of adequate and well-controlled human clinical trials, in accordance with current Good Clinical Practices (GCP) and any additional nonclinical studies required to establish the safety, efficacy, potency and purity of the product candidate for each proposed indication;
- preparation and submission to the FDA of a new drug application (NDA), or a Biologics License Application (BLA), for a biologic product, requesting marketing for one or more proposed indications, including submission of detailed information on the manufacture and composition of the product in clinical development and proposed labeling;
- review of the product by an FDA advisory committee, where appropriate or if applicable;
- satisfactory completion of one or more FDA inspections of the manufacturing facility or facilities, including those of third parties, at which the product, or components thereof, are produced to assess compliance with cGMP and to assure that the facilities, methods and controls are adequate to preserve the product's identity, strength, quality and purity;
- satisfactory completion of any FDA audits of the preclinical studies and clinical trial sites to assure compliance with GLP, as applicable, and GCP, and the integrity of clinical data in support of the NDA or BLA;
- payment of user fees under the Prescription Drug User Fee Act (PDUFA), unless exempted;
- securing FDA approval of the NDA or BLA; and
- compliance with any post-approval requirements, including the potential requirement to implement a Risk Evaluation and Mitigation Strategy (REMS) and any post-approval studies or other post-marketing commitments required by the FDA.

The failure to comply with the applicable U.S. requirements at any time during the product development process, including preclinical testing, clinical testing, the approval process, or post-approval process, may subject an applicant to delays in the conduct of the study, regulatory review and approval and/or administrative or judicial sanctions. These sanctions may include, but are not limited to, the FDA's refusal to allow an applicant to proceed with clinical testing, refusal to approve pending applications, license suspension or revocation, withdrawal of an approval, issuance of warning or untitled letters, adverse publicity, product recalls, marketing restrictions, product seizures, import detentions and refusals, total or partial suspension of production or distribution, injunctions, fines and civil or criminal investigations and penalties brought by the FDA or the Department of Justice (DOJ), and other governmental entities, including state agencies.

Preclinical Studies and Investigational New Drug Application

Before testing any therapeutic product candidate in humans, the product candidate must undergo preclinical testing. Preclinical tests include laboratory evaluations of product chemistry, formulation and stability, as well as studies to evaluate the potential for efficacy and toxicity in animal studies. The conduct of the preclinical tests and formulation of the compounds for testing must comply with federal regulations and requirements. The results of the preclinical tests, together with manufacturing information, analytical data, and plans for the proposed clinical studies, are submitted to the FDA as part of an IND. Some preclinical testing may continue after an IND is submitted.

An IND is an exemption from the FDCA that allows an unapproved product candidate to be shipped in interstate commerce for use in a clinical trial and a request for FDA authorization to administer such investigational product to humans.

The IND automatically becomes effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or questions about the product or conduct of the proposed clinical trial, including concerns that human research subjects will be exposed to unreasonable health risks. In that case, the IND sponsor and the FDA must resolve any outstanding FDA concerns before the clinical trials can begin.

As a result, submission of the IND may result in the FDA not allowing the trials to commence or allowing the trial to commence on the terms originally specified by the sponsor in the IND. If the FDA raises concerns or questions either during this initial 30-day period, or at any time during the IND review process, it may choose to impose a partial or complete clinical hold. Clinical holds may be imposed by the FDA when there is concern for patient safety, and may be a result of new data, findings, or developments in clinical, preclinical and/or chemistry, manufacturing and controls or where there is non-compliance with regulatory requirements. This order issued by the FDA would delay either a proposed clinical trial or cause suspension of an ongoing trial, until all outstanding concerns have been adequately addressed and the FDA has notified the company that investigations may proceed. A separate submission to an existing IND must also be made for each successive clinical trial conducted during drug development, and the FDA must grant permission, either explicitly or implicitly by not objecting, before each clinical trial can begin.

Human Clinical Trials in Support of an NDA or BLA

Clinical trials involve the administration of the investigational product candidate to healthy volunteers or patients with the disease or condition to be treated under the supervision of qualified investigators in accordance with GCP requirements. Clinical trials are conducted under protocols detailing, among other things, the objectives of the trial, dosing procedures, inclusion and exclusion criteria, the parameters to be used in monitoring safety, and the effectiveness criteria to be evaluated. A protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND. Clinical testing also must satisfy extensive GCP rules and the requirements for informed consent.

A sponsor who wishes to conduct a clinical trial outside the United States may, but need not, obtain FDA authorization to conduct the clinical trial under an IND. When a foreign clinical trial is conducted under an IND, all FDA IND requirements must be met unless waived. The FDA will accept a well-designed and well-conducted foreign clinical study not conducted under an IND if the study was conducted in accordance with GCP requirements, and the FDA is able to validate the data through an onsite inspection if deemed necessary. The GCP requirements encompass both ethical and data integrity standards for clinical trials. The FDA's regulations are intended to help ensure the protection of human subjects enrolled in non-IND foreign clinical trials, as well as the quality and integrity of the resulting data. They further help ensure that non-IND foreign trials are conducted in a manner comparable to that required for clinical trials in the United States.

Further, each clinical trial must be reviewed and approved by an IRB either centrally or individually at each institution at which the clinical trial will be conducted. The IRB will consider, among other things, clinical trial design, patient informed consent, ethical factors, the safety of human subjects and the possible liability of the institution. An IRB must operate in compliance with FDA regulations. The FDA, IRB, or the clinical trial sponsor may suspend or discontinue a clinical trial at any time for various reasons, including a finding that the clinical trial is not being conducted in accordance with GCP requirements or that the participants are being exposed to an unacceptable health risk.

Additionally, some clinical trials are overseen by an independent group of qualified experts organized by the clinical trial sponsor, known as a data safety monitoring board (DSMB), or data monitoring committee (DMC). This group may recommend continuation of the trial as planned, changes in trial conduct, or cessation of the trial at designated check points based on certain available data from the trial to which only the DSMB/DMC has access.

Clinical trials typically are conducted in three sequential phases, but the phases may overlap or be combined. Additional studies may be required after approval.

- Phase 1 clinical trials are initially conducted in a limited population of healthy subjects or disease-affected patients to test the product candidate for safety, including adverse effects, dose tolerance, absorption, metabolism, distribution, excretion and pharmacodynamics.
- Phase 2 clinical trials are generally conducted in a limited patient population to identify possible adverse effects and safety risks, evaluate the efficacy of the product candidate for specific targeted indications and determine dose tolerance and optimal dosage. Multiple Phase 2 clinical trials may be conducted by the sponsor to obtain information prior to beginning larger and more costly Phase 3 clinical trials.

- Phase 3 clinical trials typically proceed if the Phase 2 clinical trials demonstrate that a dose range of the product candidate is potentially effective and has an acceptable safety profile. Phase 3 clinical trials are generally undertaken within an expanded patient population to further evaluate dosage, provide substantial evidence of clinical efficacy and further test for safety in an expanded and diverse patient population at multiple, geographically dispersed clinical trial sites. A well-controlled, statistically robust Phase 3 trial may be designed to deliver the data that regulatory authorities will use to decide whether or not to approve, and, if approved, how to appropriately label a therapeutic.

In some cases, the FDA may approve an NDA or BLA for a product but require the sponsor to conduct additional clinical trials to further assess the product's safety and effectiveness after approval. Such post-approval trials are typically referred to as Phase 4 clinical trials. These studies are used to gain additional experience from the treatment of patients in the intended therapeutic indication and to document a clinical benefit for products approved under accelerated approval regulations. The failure to exercise due diligence with regard to conducting Phase 4 clinical trials could result in withdrawal of approval for products.

Information about applicable clinical trials must be submitted within specific timeframes to the NIH for public dissemination on its ClinicalTrials.gov website.

Progress reports detailing the results of the clinical trials, among other information, must be submitted at least annually to the FDA and written IND safety reports must be submitted to the FDA and the investigators for serious and unexpected suspected adverse events, findings from other studies or animal or *in vitro* testing that suggest a significant risk for human subjects and any clinically important increase in the rate of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. The sponsor must submit an IND safety report within 15 calendar days after the sponsor determines that the information qualifies for reporting. The sponsor also must notify the FDA of any unexpected fatal or life-threatening suspected adverse reaction within seven calendar days after the sponsor's initial receipt of the information.

Under the Pediatric Research Equity Act of 2003, an NDA, BLA or supplement thereto must contain data that are adequate to assess the safety and effectiveness of the product for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The FDCA requires that a sponsor who is planning to submit a marketing application for a product that includes a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration submit an initial Pediatric Study Plan (PSP), within sixty days of an end-of-Phase 2 meeting or as may be agreed between the sponsor and FDA. Those plans must contain an outline of the proposed pediatric study or studies the applicant plans to conduct, including study objectives and design, any deferral or waiver requests and other information required by regulation. The sponsor and the FDA must reach agreement on the PSP. The FDA or the applicant may request an amendment to the plan at any time.

The FDA may, on its own initiative or at the request of the applicant, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults, or full or partial waivers from the pediatric data requirements. Additional requirements and procedures relating to deferral requests and requests for extension of deferrals are contained in the Food and Drug Administration Safety and Innovation Act. Unless otherwise required by regulation, the pediatric data requirements do not apply to products with orphan designation.

Compliance with cGMP Requirements

Concurrent with clinical trials, companies must finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the product and, among other things, companies must develop methods for testing the identity, strength, quality and purity of the final product. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the product candidates do not undergo unacceptable deterioration over their shelf life. Before approving an NDA or BLA, the FDA will typically inspect the facility or facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. The PHSA emphasizes the importance of manufacturing controls for products like biologics whose attributes cannot be precisely defined.

Manufacturers and others involved in the manufacture and distribution of products must also register their establishments with the FDA and certain state agencies. Both domestic and foreign manufacturing establishments must register and provide additional information to the FDA upon their initial participation in the manufacturing process. Any product manufactured by or imported from a facility that has not registered, whether foreign or domestic, is deemed misbranded under the FDCA.

Establishments may be subject to periodic unannounced inspections by government authorities to ensure compliance with cGMPs and other laws. Noncompliance with such requirements can lead to adverse findings by the FDA during these inspections; in instances of significant or continued noncompliance, such adverse findings can serve as the basis for additional regulatory action by the FDA, including but not limited to warning and "untitled" letters.

Review and Approval of an NDA or BLA

The results of product candidate development, preclinical testing and clinical trials, including negative or ambiguous results as well as positive findings, are submitted to the FDA as part of an NDA or BLA requesting approval to market the product for one or more specified indications. The NDA or BLA must contain extensive manufacturing information and detailed information on the composition of the product and proposed labeling as well as payment of a user fee. Under federal law, the submission of most NDAs and BLAs are subject to an application user fee. The sponsor of an approved NDA or BLA is also subject to an annual program fee. Certain exceptions and waivers are available for some of these fees, such as an exception from the application fee for products with orphan designation and a waiver for certain small businesses.

The FDA has 60 days after submission of the application to conduct an initial review to determine whether to accept it for filing based on the agency's threshold determination that it is sufficiently complete to permit substantive review. If the submission has been accepted for filing, the FDA begins an in-depth review of the application. Under the goals and policies agreed to by the FDA under PDUFA, the FDA has ten months in which to complete its initial review of a standard application and respond to the applicant, and six months for a priority review of the application. The FDA does not always meet its PDUFA goal dates for standard and priority NDAs and BLAs. The review process may be significantly extended by FDA requests for additional information or clarification. The review process and the PDUFA goal date may be extended by three months if the FDA requests or if the applicant otherwise provides additional information or clarification regarding information already provided in the submission within the last three months before the PDUFA goal date.

The FDA reviews an NDA or BLA to determine, among other things, whether the product is safe and effective and whether the facility in which it is manufactured, processed, packaged or held meets standards designed to assure the product's continued safety, quality and purity. The FDA likely will reanalyze the clinical trial data, which could result in extensive discussions between the FDA and the applicant during the review process. On the basis of the FDA's evaluation of the application and accompanying information, including the results of the inspection of the manufacturing facilities and any FDA audits of preclinical and clinical trial sites to assure compliance with GCPs, the FDA may issue an approval letter or a complete response letter. An approval letter authorizes commercial marketing of the product with specific prescribing information for specific indications. If the application is not approved, the FDA will issue a complete response letter, which will contain the conditions that must be met in order to secure final approval of the application, and when possible, will outline recommended actions the sponsor might take to obtain approval of the application. The complete response letter may require additional clinical data and/or other significant and time-consuming requirements related to clinical trials, preclinical studies or manufacturing. Sponsors that receive a complete response letter have one year to submit to the FDA information that represents a complete response to the deficiencies identified by the FDA. The FDA will then re-review the application, taking into consideration the response, and determine whether the application meets the criteria for approval. Failure to respond to a complete response letter will serve as a withdrawal of an application. The FDA will not approve an application until issues identified in any complete response letters have been addressed.

The FDA may refer applications for novel products or products that present difficult questions of safety or efficacy to an advisory committee.

Typically, an advisory committee is a panel of independent experts, including clinicians and other scientific experts, that reviews, evaluates and provides a recommendation as to whether the application should be approved and under what conditions, if any. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

If the FDA approves a new product, it may limit the approved indication(s) for use of the product. It may also require that contraindications, warnings, or precautions be included in the product labeling. In addition, the FDA may require post-approval studies, including Phase 4 clinical trials, to further assess the product's efficacy and/or safety after approval. The agency may also require testing and surveillance programs to monitor the product after commercialization, or impose other conditions, including distribution restrictions or other risk management mechanisms, including a REMS program, to help ensure that the benefits of the product outweigh the potential risks. A REMS can include medication guides, communication plans for healthcare professionals and elements to assure safe use (ETASU). ETASU can include, but are not limited to, special training or certification for prescribing or dispensing, dispensing only under certain circumstances, special monitoring and the

use of patent registries. The FDA may prevent or limit further marketing of a product based on the results of post-market studies or surveillance programs. After approval, many types of changes to the approved product, such as adding new indications, manufacturing changes and additional labeling claims, are subject to further testing requirements and FDA review and approval.

Fast Track, Breakthrough Therapy and Priority Review Designations

FDA provides programs intended to facilitate and expedite development and review of new products that are intended to address an unmet medical need in the treatment of a serious or life-threatening disease or condition. These programs are referred to as fast track designation, breakthrough therapy designation and priority review designation. These designations are not mutually exclusive, and a product candidate may qualify for one or more of these programs. While these programs are intended to expedite product development and approval, they do not alter the standards for FDA approval.

The FDA may designate a product for fast track designation if it is intended, whether alone or in combination with one or more other products, for the treatment of a serious or life-threatening disease or condition, and it demonstrates the potential to address unmet medical needs for such a disease or condition. For products with fast track designation, sponsors may have more frequent interactions with the FDA, the product is potentially eligible for accelerated approval and priority review, if relevant criteria are met, and the FDA may initiate review of sections of a product with fast track designation's application before the application is complete. This rolling review may be available if the FDA determines, after preliminary evaluation of clinical data submitted by the sponsor, that a product with fast track designation may be effective. The sponsor must also provide, and the FDA must approve, a schedule for the submission of the remaining information and the sponsor must pay applicable user fees. However, the FDA's time period goal for reviewing a fast track application does not begin until the last section of the application is submitted. In addition, the fast track designation may be withdrawn by the FDA if the FDA believes that the designation is no longer supported by data emerging in the clinical trial process.

A product may be designated as a breakthrough therapy if it is intended, either alone or in combination with one or more other products, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the product may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. The FDA may take certain actions with respect to breakthrough therapies, including holding meetings with the sponsor throughout the development process; providing timely advice to the product sponsor regarding development and approval; involving more senior staff managers in the review process; assigning a cross-disciplinary lead for the review team; and taking other steps to design the clinical trials in an efficient manner. Breakthrough designation may be rescinded if a product no longer meets the qualifying criteria.

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 and 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.

Accelerated Approval Pathway

The FDA may grant accelerated approval to a product for a serious or life-threatening condition that provides meaningful therapeutic advantage to patients over existing treatments based upon a determination that the product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit. 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. The FDA may also grant accelerated approval for such a condition when the product has an effect on an intermediate clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality (IMM), and that is reasonably likely to predict an effect on IMM or other clinical benefit, taking into account the severity, rarity or prevalence of the condition and the availability or lack of alternative treatments. The FDA has limited experience with accelerated approvals based on intermediate clinical endpoints but has indicated that such endpoints generally may support accelerated approval where the therapeutic effect measured by the endpoint is not itself a clinical benefit and basis for traditional approval, if there is a basis for concluding that the therapeutic effect is reasonably likely to predict the ultimate clinical benefit of a product. Products granted accelerated approval must meet the same statutory standards for safety and effectiveness as those granted traditional approval.

The accelerated approval pathway is most often used in settings in which the course of a disease is long, and an extended period of time is required to measure the intended clinical benefit of a product, even if the effect on the surrogate or intermediate clinical endpoint occurs rapidly. The accelerated approval pathway is usually contingent on a sponsor's agreement to conduct, in a diligent manner, additional post-approval confirmatory studies to verify and describe the product's clinical benefit. As a result, a product candidate approved on this basis is subject to rigorous post-marketing compliance requirements, including the completion of Phase 4 or post-approval clinical trials to confirm the effect on the clinical endpoint. Failure to conduct required post-approval studies, confirm a clinical benefit during post-marketing studies or dissemination of false or misleading promotional materials would allow the FDA to withdraw the product from the market on an expedited basis. All promotional materials for therapeutic candidates approved under accelerated regulations are subject to prior review by the FDA.

Orphan Drug Designation

Orphan drug designation in the United States is designed to encourage sponsors to develop products intended for treatment of rare diseases or conditions. In the United States, a rare disease or condition is statutorily defined as a condition that affects fewer than 200,000 individuals in the United States or that affects 200,000 or more individuals in the United States and for which there is no reasonable expectation that the cost of developing and making available the drug or biologic for the disease or condition will be recovered from sales of the product in the United States.

Orphan drug designation qualifies a company for tax credits and market exclusivity for seven years following the date of the product's marketing approval if granted by the FDA. An application for designation as an orphan product can be made any time prior to the filing of an application for approval to market the product. After FDA grants orphan designation, the product must then go through the review and approval process like any other product.

A sponsor may request orphan drug designation of a previously unapproved product or new orphan indication for an already marketed product. In addition, a sponsor of a product that is otherwise the same product as an already approved orphan drug may seek and obtain orphan drug designation for the subsequent product for the same rare disease or condition if it can present a plausible hypothesis that its product may be clinically superior to the first drug. More than one sponsor may receive orphan drug designation for the same product for the same rare disease or condition, but each sponsor seeking orphan drug designation must file a complete request for designation.

If a product with orphan designation receives the first FDA approval for the disease or condition for which it has such designation or for a select indication or use within the rare disease or condition for which it was designated, the product generally will receive orphan drug exclusivity. Orphan drug exclusivity means that the FDA may not approve another sponsor's marketing application for the same product for the same indication for seven years, except in certain limited circumstances. If a product designated as an orphan drug ultimately receives marketing approval for an indication broader than what was designated in its orphan drug application, it may not be entitled to exclusivity.

The period of exclusivity begins on the date that the marketing application is approved by the FDA and applies only to the indication for which the product has been designated. The FDA may approve a second application for the same product for a different use or a second application for a clinically superior version of the product for the same use. The FDA cannot, however, approve the same product made by another manufacturer for the same indication during the market exclusivity period unless it has the consent of the sponsor, or the sponsor is unable to provide sufficient quantities.

Pediatric Exclusivity

Pediatric exclusivity is another type of non-patent marketing exclusivity in the United States and, if granted, provides for the attachment of an additional six months of marketing protection to the term of any existing regulatory exclusivity, including orphan exclusivity. This six-month exclusivity may be granted if an NDA or BLA sponsor submits pediatric data that fairly respond to a written request from the FDA for such data. The data do not need to show the product to be effective in the pediatric population studied; rather, if the clinical trial is deemed to fairly respond to the FDA's request, the additional protection is granted. If reports of requested pediatric studies are submitted to and accepted by the FDA within the statutory time limits, whatever statutory or regulatory periods of exclusivity that cover the product are extended by six months.

U.S. Patent Term Restoration and Extension and Marketing Exclusivity

In the United States, a patent claiming a new drug or biologic product, its method of use or its method of manufacture may be eligible for a limited patent term extension under the Hatch-Waxman Act, which permits a patent extension of up to five years for patent term lost during product development and FDA regulatory review. Assuming grant of the patent for which

the extension is sought, the restoration period for a patent covering a product is typically one-half the time between the effective date of the IND and the submission date of the NDA or BLA, plus the time between the submission date of the NDA or BLA and the ultimate approval date, except that the review period is reduced by any time during which the applicant failed to exercise due diligence. Patent term restoration cannot be used to extend the remaining term of a patent past a total of 14 years from the product's approval date in the United States. Only one patent applicable to an approved product is eligible for the extension, and the application for the extension must be submitted prior to the expiration of the patent for which extension is sought. A patent that covers multiple products for which approval is sought can only be extended in connection with one of the approvals. The USPTO reviews and approves the application for any patent term extension in consultation with the FDA.

Marketing exclusivity provisions under the FDCA also can delay the submission or the approval of certain applications. The FDCA provides a five-year period of non-patent marketing exclusivity within the United States to the first applicant to gain approval of an NDA for a new chemical entity. A drug is a new chemical entity if the FDA has not previously approved any other new drug containing the same active moiety, which is the molecule or ion responsible for the action of the drug substance. During the exclusivity period, the FDA may not accept for review an abbreviated new drug application (ANDA), or a 505(b)(2) NDA submitted by another company for another version of such drug where the applicant does not own or have a legal right of reference to all the data required for approval. However, an application may be submitted after four years if it contains a certification of patent invalidity or non-infringement. The FDCA also provides three years of marketing exclusivity for an NDA, 505(b)(2) NDA or supplement to an existing NDA if new clinical investigations, other than bioavailability studies, that were conducted or sponsored by the applicant are deemed by the FDA to be essential to the approval of the application, for example, new indications, dosages or strengths of an existing drug. This three-year exclusivity covers only the conditions of use associated with the new clinical investigations and does not prohibit the FDA from approving ANDAs for drugs containing the original active agent. Five-year and three-year exclusivity will not delay the submission or approval of a full NDA. However, an applicant submitting a full NDA would be required to conduct or obtain a right of reference to all of the preclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness.

Biosimilars and Exclusivity

The Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, or, collectively, the ACA, which was signed into law in March 2010, included a subtitle called the Biologics Price Competition and Innovation Act of 2009 (BPCIA). The BPCIA established a regulatory scheme authorizing the FDA to approve biosimilars and interchangeable biosimilars. A biosimilar is a biological product that is highly similar to an existing FDA-licensed "reference product." The FDA has issued multiple guidance documents outlining an approach to review and approval of biosimilars. Under the BPCIA, a manufacturer may submit an application for licensure of a biologic product that is "biosimilar to" or "interchangeable with" a previously approved biological product or "reference product." In order for the FDA to approve a biosimilar product, it must find that there are no clinically meaningful differences between the reference product and proposed biosimilar product in terms of safety, purity and potency. For the FDA to approve a biosimilar product as interchangeable with a reference product, the agency must find that the biosimilar product can be expected to produce the same clinical results as the reference product, and (for products administered multiple times) that the biologic and the reference biologic may be switched after one has been previously administered without increasing safety risks or risks of diminished efficacy relative to exclusive use of the reference biologic.

Under the BPCIA, an application for a biosimilar product may not be submitted to the FDA until four years following the date of approval of the reference product. The FDA may not approve a biosimilar product until 12 years from the date on which the reference product was approved. Even if a product is considered to be a reference product eligible for exclusivity, another company could market a competing version of that product if the FDA approves a full BLA for such product containing the sponsor's own preclinical data and data from adequate and well-controlled clinical trials to demonstrate the safety, purity and potency of their product. The BPCIA also created certain exclusivity periods for biosimilars approved as interchangeable products. At this juncture, it is unclear whether products deemed "interchangeable" by the FDA will, in fact, be readily substituted by pharmacies, which are governed by state pharmacy law. Since the passage of the BPCIA, many states have passed laws or amendments to laws, including laws governing pharmacy practices, which are state regulated, to regulate the use of biosimilars.

Post-Approval Regulation

If regulatory approval for a product or new indication for an existing product is obtained, the sponsor will be required to comply with all post-approval regulatory requirements as well as any specific post-approval requirements that the FDA has imposed as part of the approval process. The sponsor will be required to report certain adverse reactions and production problems to the FDA, provide updated safety and efficacy information and comply with requirements concerning advertising

and promotional labeling, record-keeping, and product tracking and tracing requirements. Manufacturers and certain of their subcontractors are required to register their establishments with the FDA and certain state agencies and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with ongoing regulatory requirements, including cGMP regulations, which impose certain procedural and documentation requirements upon manufacturers. Accordingly, the sponsor and its third-party manufacturers must continue to expend time, money and effort in the areas of production and quality control to maintain compliance with cGMP regulations and other regulatory requirements.

A biological product may also be subject to official lot release, meaning that the manufacturer is required to perform certain tests on each lot of the product before it is released for distribution. If the product is subject to official lot release, the manufacturer must submit samples of each lot, together with a release protocol showing a summary of the history of manufacture of the lot and the results of all of the manufacturer's tests performed on the lot, to the FDA. The FDA may in addition perform certain confirmatory tests on lots of some products before releasing the lots for distribution. Finally, the FDA will conduct laboratory research related to the safety, purity, potency and effectiveness of pharmaceutical products.

Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical trials to assess new safety risks; or imposition of distribution or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of the product;
- complete withdrawal of the product from the market or product recalls;
- fines, warning letters or holds on post-approval clinical trials;
- refusal of the FDA to approve pending applications or supplements to approved applications, or suspension or revocation of product license approvals;
- product recall, seizure or detention, or refusal to permit the import or export of products; or
- injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates the marketing, labeling, advertising and promotion of prescription drug products placed on the market. This regulation includes, among other things, standards and regulations for direct-to-consumer advertising, communications regarding unapproved uses, industry-sponsored scientific and educational activities and promotional activities involving the internet and social media. Promotional claims about a drug's safety or effectiveness are prohibited before the drug is approved. After approval, a drug product generally may not be promoted for uses or patient populations that are not approved by the FDA, as reflected in the product's prescribing information (known as "off-label" use). In the United States, healthcare professionals are generally permitted to prescribe drugs for such off-label uses because the FDA does not regulate the practice of medicine. However, FDA regulations impose rigorous restrictions on manufacturers' communications, prohibiting the promotion of off-label uses. Prescription drug and biologic promotional materials must be submitted to the FDA in conjunction with their first use.

If a company, including any agent of the company or anyone speaking on behalf of the company, is found to have promoted off-label uses, the company may become subject to adverse public relations and administrative and judicial enforcement by the FDA, the DOJ, or the Office of the Inspector General of the Department of Health and Human Services, as well as state authorities. This could subject a company to a range of penalties that could have a significant commercial impact, including civil and criminal fines and agreements that materially restrict the manner in which a company promotes or distributes drug products. The federal government has levied large civil and criminal fines against companies for alleged improper promotion and has also requested that companies enter into consent decrees or permanent injunctions under which specified promotional conduct is changed or curtailed.

Federal and State Data Privacy and Security Laws

Under the federal Health Insurance Portability and Accountability Act of 1996 (HIPAA), the U.S. Department of Health and Human Services (HHS), has issued regulations to protect the privacy and security of protected health information (PHI), used or disclosed by covered entities including certain healthcare providers, health plans and healthcare clearinghouses. HIPAA also regulates standardization of data content, codes and formats used in healthcare transactions and standardization of identifiers for health plans and providers. HIPAA, as amended by the Health Information Technology for Economic and

Clinical Health Act of 2009 or HITECH, and their regulations, including the final omnibus rule published on January 25, 2013, also imposes certain obligations on the business associates of covered entities that obtain protected health information in providing services to or on behalf of covered entities. In addition to federal privacy regulations, there are a number of state laws governing confidentiality and security of health information that are applicable to our business. In addition to possible federal administrative, civil and criminal penalties for HIPAA violations, state attorneys general are authorized to file civil actions for damages or injunctions in federal courts to enforce HIPAA and seek attorney's fees and costs associated with pursuing federal civil actions. Accordingly, state attorneys general have brought civil actions seeking injunctions and damages resulting from alleged violations of HIPAA's privacy and security rules. New laws and regulations governing privacy and security may be adopted in the future as well.

Additionally, states, such as California, Virginia and Colorado have recently enacted the consumer privacy laws that grant rights to data subjects and place increased privacy and security obligations on entities handling personal data of consumers or households. While we are not currently subject to laws such as the California Consumer Privacy Act (CCPA), some observers note that the CCPA and similar legislation could mark the beginning of a trend toward more stringent privacy legislation in the U.S., which could increase our potential liability and adversely affect our business.

Because of the breadth of these laws and the narrowness of the statutory exceptions under such laws, it is possible that some of our current or future business activities, including certain clinical research, sales and marketing practices and the provision of certain items and services to our customers, could be subject to challenge under one or more of such privacy and data security laws. The heightening compliance environment and the need to build and maintain robust and secure systems to comply with different privacy compliance and/or reporting requirements in multiple jurisdictions could increase the possibility that we may fail to comply fully with one or more of these requirements. If our operations are found to be in violation of any applicable privacy or data security laws or regulations, we may be subject to penalties, including potentially significant criminal, civil and administrative penalties, damages, fines, imprisonment, contractual damages, reputational harm, diminished profits and future earnings, additional reporting requirements and/or oversight if we become subject to a consent decree or similar agreement to resolve allegations of non-compliance with these laws, and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations. To the extent that we collect or otherwise process personal information, we may be subject to privacy or data protection laws that are in effect in such third countries foreign laws.

Regulation and Procedures Governing Approval of Medicinal Products Outside the United States

In order to market any product outside of the United States, a company must also comply with numerous and varying regulatory requirements of other countries and jurisdictions regarding quality, safety and efficacy and governing, among other things, clinical trials, marketing authorization, commercial sales and distribution of products. Whether or not it obtains FDA approval for a product, an applicant will need to obtain the necessary approvals by the comparable foreign regulatory authorities before it can commence clinical trials or marketing of the product in those countries or jurisdictions. For example, the process governing approval of medicinal products in the European Union generally follows the same lines as in the United States. It entails satisfactory completion of preclinical studies and adequate and well-controlled clinical trials to establish the safety and efficacy of the product for each proposed indication. It also requires the submission to the relevant competent authorities of a marketing authorization application (MAA) and granting of a marketing authorization by these authorities before the product can be marketed and sold in the European Union.

Clinical Trial Approval

In April 2014, the European Union adopted the new Clinical Trials Regulation (EU) No 536/2014 (CTR), which replaced the Clinical Trials Directive. The CTR entered into application on January 31, 2022. The transitory provisions of the CTR offer sponsors the possibility to choose between the requirements of the previous Clinical Trials Directive and the CTR if the request for authorization of a clinical trial is submitted in the year after the CTR became applicable. If the sponsor chooses to submit under the Clinical Trials Directive, the clinical trial continues to be governed by the Clinical Trial Directive until three years after the CTR became applicable. If a clinical trial continues for more than three years after the CTR became applicable, the CTR will at that time begin to apply to the clinical trial. The CTR overhauls the current system of approvals for clinical trials in the EU. Specifically, the new legislation, which is directly applicable in all European Union Member States (meaning no national implementing legislation in each Member State is required), aims at simplifying and streamlining the approval of clinical trials in the European Union, simplifying adverse-event reporting procedures, improving the supervision of clinical trials and increasing their transparency. For instance, the CTR provides for a streamlined application procedure via a single-entry point and strictly defined deadlines for the assessment of clinical trial applications. The application procedure is divided into two parts; Part I contains scientific and medicinal product documentation and Part II contains the national and patient-level

documentation. Part I is assessed by a coordinated review by the competent authorities of all EU Member States in which an application for authorization of a clinical trial has been submitted (Member States concerned) of a draft report prepared by a Reference Member State. Part II is assessed separately by each Member State concerned. Strict deadlines have been established for the assessment of clinical trial applications. Parties conducting certain clinical trials must, as in the United States, post clinical trial information in the European Union at the EudraCT website: https://eudract.ema.europa.eu.

PRIME Designation in the European Union

In March 2016, the European Medicines Agency (EMA) launched an initiative to facilitate development of therapeutic candidates in indications, often rare, for which few or no therapies currently exist. The PRIority MEdicines (PRIME), scheme is intended to encourage drug development in areas of unmet medical need and provides accelerated assessment of products representing substantial innovation reviewed under the centralized procedure. Eligible products must target conditions for which there is an unmet medical need (there is no satisfactory method of diagnosis, prevention or treatment in the EU or, if there is, the new medicine will bring a major therapeutic advantage) and they must demonstrate the potential to address the unmet medical need by introducing new methods of therapy or improving existing ones. Products from small- and medium-sized enterprises may qualify for earlier entry into the PRIME scheme than larger companies. Many benefits accrue to sponsors of therapeutic candidates with PRIME designation, including but not limited to, early and proactive regulatory dialogue with the EMA, frequent discussions on clinical trial designs and other development program elements, and accelerated marketing authorization application assessment once a dossier has been submitted. Importantly, a dedicated EMA contact and rapporteur from the Committee for Human Medicinal Products (CHMP), or Committee for Advanced Therapies are appointed early in the PRIME scheme facilitating increased understanding of the product at the EMA's Committee level. A kick-off meeting initiates these relationships and includes a team of multidisciplinary experts at the EMA to provide guidance on the overall development and regulatory strategies. Where, during the course of development, a medicine no longer meets the eligibility criteria, support under the PRIME scheme may be withdrawn.

Marketing Authorization

To obtain a marketing authorization for a product under the European Union regulatory system, an applicant must submit an MAA, either under a centralized procedure administered by the EMA or one of the procedures administered by competent authorities in European Union Member States (decentralized procedure, national procedure, or mutual recognition procedure). A marketing authorization may be granted only to an applicant established in the European Union. Regulation (EC) No 1901/2006 provides that prior to obtaining a marketing authorization in the European Union, an applicant must demonstrate compliance with all measures included in an EMA-approved pediatric investigation plan (PIP), covering all subsets of the pediatric population, unless the EMA has granted a product-specific waiver, class waiver or a deferral for one or more of the measures included in the PIP. The Pediatric Committee of the EMA (PDCO), may grant deferrals for some medicines, allowing a company to delay development of the medicine for children until there is enough information to demonstrate its effectiveness and safety in adults. The PDCO may also grant waivers when development of a medicine for children is not needed or is not appropriate, such as for diseases that only affect the elderly population. The respective requirements for all marketing authorization procedures are laid down in Regulation (EC) No 1901/2006, the so-called Pediatric Regulation. This requirement also applies when a company wants to add a new indication, pharmaceutical form or route of administration for a medicine that is already authorized. Products that are granted a marketing authorization with the results of the pediatric clinical trials conducted in accordance with the PIP (even where such results are negative) are eligible for six months' supplementary protection certificate extension. In the case of orphan medicinal products, a two-year extension of the orphan market exclusivity may be available. This pediatric reward is subject to specific conditions and is not automatically available when data in compliance with the PIP are developed and submitted.

The centralized procedure provides for the grant of a single marketing authorization by the European Commission that is valid for all European Union Member States, as well as the additional Member States of the European Economic Area (Norway, Iceland and Liechtenstein) (EEA). Pursuant to Regulation (EC) No. 726/2004, the centralized procedure is compulsory for specific products, including for medicines produced by certain biotechnological processes, products designated as orphan medicinal products, advanced therapy medicinal products (gene-therapy, somatic cell-therapy or tissue-engineered medicines) and products with a new active substance indicated for the treatment of certain diseases, including products for the treatment of cancer, HIV, AIDS, neurodegenerative disorders, diabetes, auto-immune and other immune dysfunctions and viral diseases. The centralized procedure is optional for products containing a new active substance not yet authorized in the European Union, or for products that constitute a significant therapeutic, scientific or technical innovation or which are in the interest of public health in the European Union.

Under the centralized procedure, the CHMP established at the EMA is responsible for conducting an initial assessment of a product. The maximum timeframe for the evaluation of an MAA is 210 days, excluding clock stops when additional information or written or oral explanation 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 MAA considerably beyond 210 days. Where the CHMP gives a positive opinion, the EMA 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 may be granted by the CHMP in exceptional cases, when a medicinal product is of major public health interest particularly from the viewpoint of therapeutic innovation. If the CHMP accepts such a request, the time limit of 210 days will be reduced to 150 days (excluding clock stops), but it is possible that the CHMP may revert to the standard time limit for the centralized procedure if it determines that it is no longer appropriate to conduct an accelerated assessment.

National marketing authorizations, which are issued by the competent authorities of the Member States of the European Union and only cover their respective territory, are available for products not falling within the mandatory scope of the centralized procedure. Where a product has already been authorized for marketing in a Member State of the European Union, this national authorization can be recognized in other Member States through the mutual recognition procedure. If the product has not received a national authorization in any Member State at the time of application, it can be approved simultaneously in various Member States through the decentralized procedure.

Under the above described procedures, before granting the MA, the EMA or the competent authorities of the Member States of the European Union make an assessment of the risk-benefit balance of the product on the basis of scientific criteria concerning its quality, safety and efficacy.

Now that the UK (which comprises Great Britain and Northern Ireland) has left the European Union, Great Britain will no longer be covered by centralized marketing authorizations (under the Northern Ireland Protocol, centralized marketing authorizations will continue to be recognized in Northern Ireland). All medicinal products with a current centralized marketing authorization were automatically converted to Great Britain marketing authorizations on January 1, 2021. For a period of two years from January 1, 2021, the Medicines and Healthcare Products Regulatory Agency (MHRA), the UK medicines regulator, may rely on a decision taken by the European Commission on the approval of a new marketing authorization in the centralized procedure, in order to more quickly grant a new Great Britain marketing authorization. A separate application will, however, still be required. The MHRA also has the power to have regard to marketing authorizations approved in EU Member States through decentralized or mutual recognition procedures with a view to more quickly granting a marketing authorization in the United Kingdom or Great Britain.

Data and market exclusivity in the European Union

In the European Union, new chemical entities (including both small molecules and biological medicinal products) approved on the basis of a complete independent data package qualify for eight years of data exclusivity upon marketing authorization and an additional two years of market exclusivity pursuant to Regulation (EC) No 726/2004, as amended, and Directive 2001/83/EC, as amended. Data exclusivity, if granted, prevents generic or biosimilar applicants from referencing the innovator's pre-clinical and clinical trial data contained in the dossier of the reference product when applying for a generic or biosimilar marketing authorization, for a period of eight years from the date on which the reference product was first authorized in the European Union. During the additional two-year period of market exclusivity, a generic or biosimilar marketing authorization application can be submitted, and the innovator's data may be referenced, but no medicinal product can be marketed until the expiration of the market exclusivity. The overall ten-year period will be extended to a maximum of eleven years if, during the first eight years of those ten years, the marketing authorization holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to authorization, is held to bring a significant clinical benefit in comparison with currently approved therapies. There is no guarantee that a product will be considered by the EMA to be a new chemical entity, and products may not qualify for data exclusivity. Even if a product is considered to be a new chemical entity so that the innovator gains the prescribed period of data exclusivity, another company could nevertheless also market another version of the product if such company obtained marketing authorization based on an MAA with a complete independent data package of pharmaceutical tests, preclinical tests and clinical trials.

Patent Term Extensions in the European Union and Other Jurisdictions

The European Union also provides for patent term extension through SPCs. The rules and requirements for obtaining a SPC are similar to those in the United States. An SPC may extend the term of a patent for up to five years after its originally scheduled expiration date and can provide up to a maximum of fifteen years of marketing exclusivity for a drug. In certain

circumstances, these periods may be extended for six additional months if pediatric exclusivity is obtained; and in the case of orphan medicinal products, a two-year extension of the orphan market exclusivity may be available. Although SPCs are available throughout the European Union, sponsors must apply on a country-by-country basis. Similar patent term extension rights exist in certain other foreign jurisdictions outside the European Union.

Periods of Authorization and Renewals

A marketing authorization is valid for five years, in principle, and it may be renewed indefinitely after five years on the basis of a re-evaluation of the risk-benefit balance by the EMA (for a centrally authorized product), or by the competent authority of the authorizing Member State (for a nationally authorized product). Once renewed, the marketing authorization is valid for an unlimited period, unless the European Commission or the competent authority decides, on justified grounds relating to pharmacovigilance, to proceed with one additional five-year renewal period. Any authorization that is not followed by the placement of the drug on the European Union market (in the case of the centralized procedure) or on the market of the authorizing Member State (in the case of a national procedure) within three years after authorization, or which is not placed on the market for a consecutive period of three years at any time during its authorization, ceases to be valid (the so-called sunset clause).

Regulatory Requirements After Marketing Authorization

Following approval, the holder of the marketing authorization is required to comply with a range of requirements applicable to the manufacturing, marketing, promotion and sale of the medicinal product, and must adhere in strict compliance with the applicable European Union laws, regulations and guidance, including Directive 2001/83/EC, Directive 2003/94/EC, Regulation (EC) No 726/2004 and the European Commission Guidelines for Good Manufacturing Practice. These include compliance with the European Union's stringent pharmacovigilance or safety reporting rules, pursuant to which post-authorization studies and additional monitoring obligations can be imposed. In addition, the manufacturing of authorized products, for which a separate manufacturer's license is mandatory, must also be conducted in strict compliance with the EMA's GMP requirements and comparable requirements of other regulatory bodies in the European Union, which mandate the methods, facilities and controls used in manufacturing, processing and packing of drugs to assure their safety and identity.

Much like the Anti-Kickback Statue prohibition in the United States, the provision of benefits or advantages to physicians to induce or encourage the prescription, recommendation, endorsement, purchase, supply, order or use of medicinal products is also prohibited in the European Union. The provision of benefits or advantages to induce or reward improper performance generally is sometimes governed by the national anti-bribery laws of European Union member states and the Bribery Act 2010 in the UK. Infringement of these laws could result in substantial fines and imprisonment. EU Directive 2001/83/EC, which is the EU Directive governing medicinal products for human use, further provides that, where medicinal products are being promoted to persons qualified to prescribe or supply them, no gifts, pecuniary advantages or benefits in kind may be supplied, offered or promised to such persons unless they are inexpensive and relevant to the practice of medicine or pharmacy. This provision has been transposed into the Human Medicines Regulations 2012 and so remains applicable in the UK despite its departure from the European Union.

Payments made to physicians in certain European Union member states must be publicly disclosed. Moreover, agreements with physicians often must be the subject of prior notification and approval by the physician's employer, his or her competent professional organization and/or the regulatory authorities of the individual EU Member States. These requirements are provided in the national laws, industry codes or professional codes of conduct, applicable in the EU Member States. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines or imprisonment.

The advertising and promotion of medicinal products is also subject to laws concerning promotion of medicinal products, interactions with physicians, misleading and comparative advertising and unfair commercial practices. All advertising and promotional activities for the product must be consistent with the approved summary of product characteristics, and therefore all off-label promotion is prohibited. Direct-to-consumer advertising of prescription medicines is also prohibited in the European Union. Although general requirements for advertising and promotion of medicinal products are established under European Union directives, the details are governed by regulations in each Member State and can differ from one country to another.

Orphan Designation and Exclusivity

Regulation (EC) No 141/2000 and Regulation (EC) No. 847/2000 provide that a product can be designated as an orphan medicinal product by the European Commission if its sponsor can establish that: (1) the product is intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition, (2) either (i) such condition affects no more than five in ten thousand persons in the European Union when the application is made, or (ii) without the benefits derived from orphan status, it is unlikely that the marketing of the drug in the European Union would generate sufficient return to justify the necessary investment in its development; (3) there exists no satisfactory method of diagnosis, prevention or treatment of the condition in question that has been authorized in the European Union or, if such method exists, the product would be of significant benefit to those affected by that condition.

An orphan designation provides a number of benefits, including fee reductions, regulatory assistance and the possibility to apply for a centralized European Union marketing authorization. Marketing authorization for an orphan medicinal product leads to a ten-year period of market exclusivity being granted following marketing approval of the orphan product. During this market exclusivity period, the EMA, the European Commission or the Member States may only grant marketing authorization to a "similar medicinal product" for the same therapeutic indication if: (i) a second applicant can establish that its product, although similar to the authorized product, is safer, more effective or otherwise clinically superior; (ii) the marketing authorization holder for the authorized product consents to a second orphan medicinal product application; or (iii) the marketing authorization holder for the authorized product cannot supply enough orphan medicinal product. A "similar medicinal product" is defined as a medicinal product containing a similar active substance or substances as contained in an authorized orphan medicinal product, and which is intended for the same therapeutic indication. The market exclusivity period for the authorized therapeutic indication may, however, be reduced to six years if, at the end of the fifth year, it is established that the product no longer meets the criteria for orphan designation because, for example, the product is sufficiently profitable not to justify market exclusivity. Orphan designation must be requested before submitting an application for marketing approval. Orphan designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process.

The aforementioned EU rules are generally applicable in the EEA.

Brexit and the Regulatory Framework in the United Kingdom

On June 23, 2016, the electorate in the UK voted in favor of leaving the European Union (commonly referred to as "Brexit"), and the UK formally left the European Union on January 31, 2020. There was a transition period during which European Union pharmaceutical law remained applicable to the UK, which ended on December 31, 2020. However, the European Union and the UK have concluded a trade and cooperation agreement, or TCA, which was provisionally applicable since January 1, 2021 and has been formally applicable since May 1, 2021. The TCA includes specific provisions concerning pharmaceuticals, which include the mutual recognition of GMP, inspections of manufacturing facilities for medicinal products and GMP documents issued, but does not foresee wholesale mutual recognition of UK and European Union pharmaceutical regulations. At present, Great Britain has implemented European Union legislation on the marketing, promotion and sale of medicinal products through the Human Medicines Regulations 2012 (as amended) (under the Northern Ireland Protocol, the European Union regulatory framework will continue to apply in Northern Ireland). The regulatory regime in Great Britain therefore currently broadly aligns with European Union regulations, however it is possible that these regimes will diverge in future now that Great Britain's regulatory system is independent from the European Union and the TCA does not provide for mutual recognition of UK and European Union pharmaceutical legislation.

In addition, once we begin to conduct business in the United Kingdom, we will be subject to stringent data protection laws that are in effect in the United Kingdom. As of January 1, 2021, the United Kingdom's European Union (Withdrawal) Act 2018 incorporated the GDPR (as it existed on December 31, 2020 but subject to certain UK specific amendments) into UK law, referred to as the UK GDPR. The UK GDPR and the UK Data Protection Act 2018 set out the United Kingdom's data protection regime, which is independent from but aligned to the European Union's data protection regime. Non-compliance with the UK GDPR may result in monetary penalties of up to £17.5 million or 4% of worldwide revenue, whichever is higher. Although the UK is regarded as a third country under the European Union's GDPR, the European Commission has now issued a decision recognizing the UK as providing adequate protection under the EU GDPR and, therefore, transfers of personal data originating in the EU to the UK remain unrestricted. Like the EU GDPR, the UK GDPR restricts personal data transfers outside the UK to countries not regarded by the UK as providing adequate protection. The UK government has confirmed that personal data transfers from the UK to the EEA remain free flowing.

General Data Protection Regulation

Once we begin processing of personal data regarding individuals in the EEA, including personal health data, our activities will be subject to the GDPR, which became effective on May 25, 2018. The GDPR is wide-ranging in scope and imposes numerous requirements on companies that process personal data, including requirements relating to processing health and other sensitive data, obtaining consent of the individuals to whom the personal data relates, providing information to individuals regarding data processing activities, implementing safeguards to protect the security and confidentiality of personal data, providing notification of data breaches and taking certain measures when engaging third-party processors. The GDPR also imposes strict rules on the transfer of personal data to countries outside the EEA, including the United States, and permits data protection authorities to impose large penalties for violations of the GDPR, including potential fines of up to €20 million or 4% of annual global revenues, whichever is greater. The GDPR also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies and obtain compensation for damages resulting from violations of the GDPR. Compliance with the GDPR will be a rigorous and time-intensive process that may increase the cost of doing business or require us to change our business practices to ensure full compliance.

Coverage and Reimbursement

In the United States 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 product candidates will depend in part on the extent to which coverage and adequate reimbursement for these products and related treatments will be available from government health administration authorities, private health insurers and other organizations. 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 United States, the principal decisions about reimbursement for new medicines are typically made by the Centers for Medicare & Medicaid Services, or CMS, an agency within the U.S. Department of Health and Human Services. 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.

Further, net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. 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 product 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 product 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 product 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.

Healthcare Reform

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 United States 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.

Other legislative changes have been proposed and adopted in the United States since the Affordable Care Act was enacted. For example, on March 11, 2021, President Biden signed the American Rescue Plan Act of 2021 into law, which eliminates the statutory Medicaid drug rebate cap, currently set at 100% of a drug's average manufacturer price, for single source and innovator multiple source drugs, beginning January 1, 2024. Further, in August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs, including aggregate reductions of Medicare payments to providers of 2% per fiscal year. These reductions went into effect in April 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 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.

Further, 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.

Other Healthcare Laws

Pharmaceutical companies are subject to additional healthcare regulation and enforcement by the federal government and by authorities in the states and foreign jurisdictions in which they conduct their business that may constrain the financial arrangements and relationships through which we research, as well as sell, market and distribute any products for which we obtain marketing authorization. Such laws include, without limitation, state and federal anti-kickback, fraud and abuse, false claims and transparency laws and regulations related to drug pricing and payments and other transfers of value made to physicians and other healthcare providers. If our operations are found to be in violation of any of such laws or any other governmental regulations that apply, we may be subject to penalties, including, without limitation, administrative, civil and criminal penalties, damages, fines, disgorgement, the curtailment or restructuring of operations, integrity oversight and reporting obligations, exclusion from participation in federal and state healthcare programs and responsible individuals may be subject to imprisonment.

Human Capital Resources

As of February 28, 2022, we had 41 full-time employees and 11 consultants; 16 of our employees have M.D. or Ph.D. degrees. Within our workforce, 28 employees are engaged in research and development and 13 are engaged in business development, finance, legal, and general management and administration. Our human capital resources objectives include identifying, recruiting, retaining, incentivizing and integrating our existing and new employees, advisors and consultants. None of our employees are represented by a labor union or covered by a collective bargaining agreement. We consider our relationship with our employees to be good.

Corporate Information

We were incorporated under the laws of the State of Delaware on June 22, 2020 under the name "Vigil Neuroscience, Inc." Our principal corporate office is located at 1 Broadway, 7th Floor, Suite 07-300, Cambridge, MA 02142, and our telephone number is (857) 254-4445. Our website address is www.vigilneuro.com. We do not incorporate the information on or accessible through our website into this Annual Report on Form 10-K, and you should not consider any information on, or that can be accessed through, our website as part of this Annual Report on Form 10-K.

Available Information

Our website address is www.vigilneuro.com. Our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K, including exhibits, proxy and information statements and amendments to those reports filed or furnished pursuant to Sections 13(a), 14, and 15(d) of the Securities Exchange Act of 1934, as amended, or the Exchange Act, are available through the "Media & Investors" portion of our website free of charge as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC. Information on our website is not part of this Annual Report on Form 10-K or any of our other securities filings unless specifically incorporated herein by reference. In addition, our filings with the SEC may be accessed through the SEC's Interactive Data Electronic Applications system at www.sec.gov. All statements made in any of our securities filings, including all forward-looking statements or information, are made as of the date of the document in which the statement is included, and we do not assume or undertake any obligation to update any of those statements or documents unless we are required to do so by law.

Our code of conduct, corporate governance guidelines and the charters of our Audit Committee, Research and Development Committee, Compensation Committee and Nominating and Corporate Governance Committee are available through the "Media & Investors" portion of our website.

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 Annual Report on Form 10-K, 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 $43.3 million for the year ended December 31, 2021. As of December 31, 2021, we had an accumulated deficit of $71.8 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 December 31, 2021.

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 intend to begin 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, enroll 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. The FDA has cleared our IND to evaluate VGL101 in a Phase 1 trial in healthy volunteers at doses up to 20 mg/kg with a partial clinical hold on doses higher than 20 mg/kg. We do not believe the partial clinical hold will have a material impact on our current clinical development plans and timelines for our clinical trial in ALSP. 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 initiated the 20 mg/kg MAD cohort. Pending safety results of the Phase 1 trial and discussions with the FDA, we plan to later evaluate VGL101 in a Phase 2/3 trial at doses up to 20 mg/kg based on our current dosing rationale for VGL101. In addition, we have a small molecule program that is in an earlier stage of development, for which we have not yet initiated or 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. We 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 in the first half of 2023. 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. The FDA has cleared our IND to evaluate VGL101 in a Phase 1 trial in healthy volunteers at doses up to 20 mg/kg with a partial clinical hold on doses higher than 20 mg/kg. The partial clinical hold was placed based on the FDA's review of non-clinical data and in the absence of adverse drug-related effects up to the highest dose tested of 200 mg/kg, which was identified as the No Observed Adverse Effect Level (NOAEL) in our non-human primate toxicology study. Following our response to the FDA's initial request for information, as communicated in the agency's partial clinical hold letter, we received an updated letter from the FDA requesting additional non-clinical data. We intend to resubmit a response to the FDA in Q2 2022 with new data from our 6-month GLP toxicology study in nonhuman primates and Phase 1 clinical data.. We do not believe the partial clinical hold will have a material impact on our current clinical development plans and timelines for our clinical trial in ALSP. 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 initiated the 20 mg/kg MAD cohort. Pending safety results of the Phase 1 trial and discussions with the FDA, we plan to evaluate VGL101 in a Phase 2/3 trial at doses up to 20 mg/kg based on our current dosing rationale for VGL101. However, if changes in our understanding of the therapeutic concentrations of VGL101 necessitate exploration of doses higher than 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 for 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 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 clinical trials, or to enroll a sufficient number of patients in our clinical trials, specifically our natural history study, 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 “Business—Exclusive License Agreement with Amgen Inc.”

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 Annual Report on Form 10-K 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. For more information on the terms of the license agreement with Amgen, see “Business—Exclusive License Agreement with Amgen Inc.”

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. For example, the Tax Cuts and Jobs Act (the TCJA) was enacted in 2017 and made significant changes to corporate taxation, including the reduction of the corporate tax rate from a top marginal rate of 35% to a flat rate of 21%, the limitation of the tax deduction for net interest expense to 30% of adjusted taxable income (except for certain small businesses), the limitation of the deduction for net operating losses from taxable years beginning after December 31, 2017 to 80% of current year taxable income and the elimination of net operating loss carrybacks (though any such net operating losses may be carried forward indefinitely) and the modification or repeal of many business deductions and credits, in each case, as modified by the CARES Act (as defined below). In addition, on March 27, 2020, former President Trump signed into law the Coronavirus Aid, Relief, and Economic Security Act (the CARES Act), which included certain changes in tax law intended to stimulate the U.S. economy in light of the COVID-19 coronavirus outbreak, including temporary beneficial changes to the treatment of net operating losses, interest deductibility limitations and payroll tax matters. Under the CARES Act, the limitation of the tax deduction for net operating losses to 80% of taxable income applies only to taxable years beginning after December 31, 2020 and net operating losses generated in 2018, 2019 and 2020 by a calendar-year taxpayer may be carried back five taxable years. Further, under the CARES Act, the limitation of the tax deduction for net interest expense to 30% of adjusted taxable income is increased to 50% of adjusted taxable income for taxable years beginning in 2019 and 2020.

Additional changes to U.S. federal income tax law are currently being contemplated. 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. As of December 31, 2021, we had U.S. federal and state net operating loss carryforwards of approximately $45.6 million and $45.0 million, respectively, and our ability to utilize those 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 February 28, 2022, we had 41 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 77% of our outstanding voting stock as of February 28, 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 this 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 this 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 this 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 Annual Report on Form 10-K, 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 1B. Unresolved Staff Comments.

None.

Item 2. Properties.

Our corporate headquarters is located in Cambridge, Massachusetts, where we lease and occupy 6,940 square feet of office space. The current term of our Cambridge lease expires on December 31, 2022 with an option to continue thereafter on a month to month basis for up to six months.

In September 2021, we also entered into a lease agreement for 19,734 square feet of laboratory and office space in Watertown, Massachusetts. The current term of our Watertown lease expires ten years after the lease commencement date, which is anticipated to be in the second quarter of 2022, and includes an option to extend the term with at least 15 months' notice and rent set at an agreed upon market rate.

We believe our existing facilities in Cambridge and Watertown are sufficient for our needs for the foreseeable future. To meet the future needs of our business, we may lease additional or alternate space, and we believe suitable additional or alternative space will be available in the future on commercially reasonable terms.

Item 3. 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 4. Mine Safety Disclosures.

Not Applicable.

PART II

Item 5. Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities.

Market Information for Common Stock

Our common stock has been publicly traded on the Nasdaq Global Select Market under the symbol "VIGL" since the initial public offering of our common stock on January 7, 2022. Prior to that time, there was no public market for our common stock. As of February 28, 2022, there were 32 holders of record of our common stock.

Dividend Policy

We have never declared or paid any cash dividends on our common shares. We currently anticipate that we will retain all available funds and future earnings for the development, operation and expansion of our business and do not anticipate declaring or paying any cash dividends for the foreseeable future.

Securities Authorized for Issuance Under Equity Compensation Plans

Information about our equity compensation plans will be included in our definitive proxy statement to be filed with the SEC with respect to our 2022 Annual Meeting of Stockholders and is incorporated herein by reference.

Recent Sales of Unregistered Securities

Set forth below is information regarding stock options granted by us and exercised, and the securities we have issued during the period covered by this Annual Report on Form 10-K that were not registered under the Securities Act of 1933, as amended, or the Securities Act. These stock options and securities were granted and issued, respectively, prior to the consummation of our initial public offering in January 2022. Included is the consideration, if any, we received for such shares and options and information relating to the section of the Securities Act under which exemption from registration was claimed.

In May 2021, we issued and sold an aggregate of 7,852,373 shares of Series A Preferred Stock at a purchase price of $2.547 per share for an aggregate purchase price of approximately $20 million. Additionally, we issued 1,963,093 shares of Series A Preferred Stock pursuant to certain agreements with Amgen Inc. In August 2021, we issued and sold an aggregate of 25,657,096 shares of Series B Preferred Stock at a purchase price of $3.5078 per share for an aggregate purchase price of approximately $90 million.

No underwriters were involved in the foregoing sales of securities. Unless otherwise stated, the sales of securities described above were deemed to be exempt from registration pursuant to Section 4(a)(2) of the Securities Act, including Regulation D and Rule 506 promulgated thereunder, as transactions by an issuer not involving a public offering. All of the purchasers in these transactions represented to us in connection with their purchase that they were acquiring the securities for investment and not distribution, that they could bear the risks of the investment and could hold the securities for an indefinite period of time. Such purchasers received written disclosures that the securities had not been registered under the Securities Act and that any resale must be made pursuant to a registration or an available exemption from such registration. All of the foregoing securities are deemed restricted securities for the purposes of the Securities Act.

From January 1, 2021 to December 31, 2021, we granted options to purchase an aggregate of 2,095,899 shares of common stock, with exercise prices ranging from $1.89 to $11.79 per share, to directors, employees and consultants pursuant to our 2020 Equity Incentive Plan, as amended, or the 2020 Plan. During such period, 20,394 shares of common stock were issued for gross proceeds of $38 thousand upon the exercise of stock options pursuant to the 2020 Plan.

No underwriters were involved in the foregoing issuances of securities. The issuances of the securities described above were deemed to be exempt from registration pursuant to Section 4(a)(2) of the Securities Act as transactions by an issuer not involving a public offering or Rule 701 promulgated under the Securities Act as transactions pursuant to compensatory benefit plans. All recipients either received adequate information about us or had access, through employment or other relationships, to such information. On January 10, 2022, we filed a registration statement on Form S-8 under the Securities Act to register

all of the shares of our common stock subject to outstanding options and all shares of our common stock otherwise issuable pursuant to our equity compensation plans.

Use of Proceeds

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.

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.

Issuer Purchases of Equity Securities

We did not purchase any of our registered equity securities during the period covered by this Annual Report on Form 10-K.

Item 6. Reserved

Not Applicable.

Item 7. 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 Annual Report on Form 10-K and our consolidated financial statements and related notes included elsewhere in this Annual Report on Form 10-K. Some of the information contained in this discussion and analysis or set forth elsewhere in this Annual Report on Form 10-K, 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 Annual Report on Form 10-K, 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, or 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 for genetically defined patient subpopulations, that we believe will activate and restore microglial function.

Our lead candidate, VGL101, is a fully human monoclonal antibody, or mAb, that is designed to activate Triggering Receptor Expressed on Myeloid Cells 2, or TREM2. In November 2021, the FDA cleared our Investigational New Drug application, or IND, for VGL101 in ALSP at doses up to 20 mg/kg. We initiated our first-in-human Phase 1 clinical trial with VGL101 in healthy volunteers in December 2021 and as of today, we have completed dosing of the 20 mg/kg SAD cohort without any safety signals and initiated the 20 mg/kg MAD cohort. We expect to announce topline data in the second half of 2022.

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 December 31, 2021, we had $91.4 million of cash and cash equivalents. As of December 31, 2021, we raised aggregate gross proceeds of $140.0 million from the sale of equity securities as follows:

- During the period from June 22, 2020 (inception) to December 31, 2020, 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 and $25.0 million gross proceeds from the issuance of 9,815,467 shares of Series A convertible preferred stock at a purchase price of $2.547 per share. Costs associated with these issuances were approximately $0.2 million.
- During the twelve months ended December 31, 2021, we raised $20.0 million gross proceeds from the issuance of 7,852,373 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 $0.4 million.

Subsequently, 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. 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 $28.5 million at December 31, 2020 and $71.8 million at December 31, 2021, 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 “Business Section—Exclusive License Agreement with Amgen Inc.” and Note 12 to the consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K 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.

Related Party Acquired In-process Research and Development

Related party acquired in-process research and development, or IPR&D, expenses consist primarily of the upfront costs to acquire the IPR&D assets at inception of the Amgen Agreement and the initial recognition of the fair value of the Related Party Antidilution Obligation. Upfront and milestone payments are accrued for and expensed as IPR&D expense when the achievement of the milestone is probable up to the point of regulatory approval. Milestone payments made upon regulatory approval will be capitalized and amortized over the remaining useful life of the related product. We did not incur related party IPR&D expenses during the year ended December 31, 2021.

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 and preclinical 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 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;
- payments made under our licensing agreement with a related party; 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:

	December 31, 2021	Period from June 22, 2020 (Inception) to December 31, 2020
	($ in thousands)	
Direct, external research and development expenses by program:		
VGL101	$ 15,407	$ 974
Small molecule TREM2	5,545	1,087
Unallocated research and development expenses:		
External costs and other	3,787	946
Facilities, personnel-related, and other	7,591	1,507
Total research and development expenses	$ 32,330	$ 4,514

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.

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, discussed below. Concurrently with this issuance, the SAFE converted to 1,963,093 shares of Series A convertible preferred stock. 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 consolidated statement of operations and comprehensive loss.

Interest Income

Interest income consists of interest earned from our cash and cash equivalents. 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 year ended December 31, 2021, and the period from June 22, 2020 (inception) to December 31, 2020.

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 year ended December 31, 2021, and the period from June 22, 2020 (inception) to December 31, 2020.

Income Taxes

Since our inception, we have not recorded any income tax benefits for the net losses we have incurred in each year or for our research and development tax credits, as we believe, based upon the weight of available evidence, that it is more likely than not that all of our net operating loss, or NOL, carryforwards and tax credits will be realized. As of December 31, 2021, we had federal NOL carryforwards of approximately $45.6 million and state NOL carryforwards of approximately $45.0 million which may be available to offset future taxable income and begin to expire in 2035. The total federal NOL of $45.6 million are not subject to expiration. As of December 31, 2021, we also had federal and state tax research and development credit carryforwards of approximately $1.2 million and $0.5 million, respectively, to offset future tax liabilities, which begin to expire in 2035. We have recorded a full valuation allowance against our net deferred tax assets at December 31, 2021. As of December 31, 2021, we had no unrecognized tax benefits.

Results of Operations

Year Ended December 31, 2021 Compared with Period from June 22, 2020 (inception) to December 31, 2020

The following table summarizes our results of operations for the year ended December 31, 2021 compared with period from June 22, 2020 (inception) to December 31, 2020:

	December 31, 2021	Period from June 22, 2020 (Inception) to December 31, 2020
	($ in thousands)	
Operating expenses:		
Related party acquired in-process research and development	$ —	$ 20,923
Research and development	32,330	4,514
General and administrative	10,079	1,777
Total operating expenses	42,409	27,214
Loss from operations	(42,409)	(27,214)
Other income (expense):		
Change in fair value of the related party antidilution obligation	(836)	(1,307)
Change in fair value of Series A preferred stock tranche obligation	(28)	(24)
Interest income	3	—
Other expense, net	(13)	(1)
Total other expense, net	(874)	(1,332)
Net loss and comprehensive loss	$ (43,283)	$ (28,546)

Related Party Acquired In-process Research and Development Expenses

We did not incur any related party acquired IPR&D expense for the year ended December 31, 2021. Related party acquired IPR&D expenses was $20.9 million for the year ended December 31, 2020 and consisted of the costs to acquire the IPR&D assets at inception of the Amgen Agreement, including (i) $20.4 million initial recognition of a Related Party Antidilution Obligation that obligates us to issue shares of the Series A convertible preferred stock equal to 25% of our capital stock until we have raised $45.0 million in net cash proceeds from equity financings and (ii) the upfront cash consideration for the license arrangement of $0.5 million.

Research and Development Expenses

Research and development expenses were $32.3 million for the year ended December 31, 2021, as compared to $4.5 million for the period June 22, 2020 (inception) through December 31, 2020. The increase of $27.8 million consisted primarily of the following:

- $7.6 million of external manufacturing expenses related to the development and manufacturing of VGL101, which was primarily incurred during the year ended December 31, 2021. These manufacturing expenses are primarily related to the drug substance manufacturing of VGL101, which we expect to use in conducting our clinical trials;
- $6.8 million of other VGL101 program expenses, including $3.5 million associated with IND-enabling studies;
- $4.5 million of small molecule TREM2 agonist program expenses;
- $2.8 million of external costs and other expenses; and
- $6.1 million of facilities, personnel-related and other expenses, of which $5.4 million related to personnel-related costs, including salaries, bonuses, and other compensation-related costs, including stock-based compensation of $0.7 million

General and Administrative Expenses

General and administrative expenses were $10.1 million for the year ended December 31, 2021, as compared to $1.8 million for the period June 22, 2020 (inception) through December 31, 2020. The increase of $8.3 million consisted primarily of the following:

- $3.5 million of personnel-related costs, including salaries, bonuses, and other compensation-related costs, including stock-based compensation of $1.1 million;
- $3.4 million of professional fees, including legal, accounting and other expenses; and
- $1.4 million of other general and administrative expenses

Change in Fair Value of Related Party Antidilution Obligation

The change in fair value of Related Party Antidilution Obligation was $0.8 million for the year ended December 31, 2021, as compared to $1.3 million for the period June 22, 2020 (inception) through December 31, 2020. This decrease of $0.5 million was related to the re-measurement to fair value of the Related Party Antidilution Obligation associated with the Amgen Agreement as well as the partial settlement of the Related Party Antidilution Obligation which was fully settled in May 2021. 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 $24 thousand for the period from June 22, 2020 (inception) to December 31, 2020 as compared to $28 thousand for the year ended December 31, 2021. This increase of $4 thousand related to the remeasurement to fair value 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 December 31, 2021, we have funded our operations with net proceeds from sales of our convertible preferred stock and SAFE of $139.5 million. As of December 31, 2021, we had cash and cash equivalents of $91.4 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

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:

	December 31, 2021	Period from June 22, 2020 (Inception) to December 31, 2020
	($ in thousands)	
Net cash used in operating activities	$ (39,347)	$ (5,180)
Net cash used by investing activities	(204)	(500)
Net cash provided by financing activities	107,747	29,831
Net increase in cash, cash equivalents and restricted cash	$ 68,196	$ 24,151

Operating Activities

During the year ended December 31, 2021, operating activities consisted primarily of our net loss of $43.3 million, partially offset by (i) $0.6 million of changes in operating assets and liabilities, (ii) $0.8 million change in Related Party Antidilution Obligation, (iii) $2.1 million stock-based compensation expense, and (iv) $0.3 million change in operating lease expenses. The net loss primarily consisted of $32.3 million of research and development expenses, $10.1 million of general and administrative expenses and a $0.8 million unfavorable change in fair value of Related Party Antidilution Obligation.

During the period from June 22, 2020 (inception) to December 31, 2020, operating activities consisted primarily of our net loss of $28.5 million, partially offset by (i) $20.9 million acquired IPR&D fee associated with the Amgen Agreement, (ii) $1.3 million change in Related Party Antidilution Obligation, (iii) $0.8 million of changes in operating assets and liabilities and (iv) $0.3 million stock-based compensation expense. The net loss consisted of $20.9 million of related party acquired IPR&D, $4.5 million of research and development expenses, $1.8 million of general and administrative expenses and a $1.3 million unfavorable change in fair value of Related Party Antidilution.

Investing Activities

During the year ended December 31, 2021, net cash used by investing activities consisted of $0.2 million of capital expenditures.

During the period from June 22, 2020 (inception) to December 31, 2020, net cash used by investing activities consisted of $0.5 million paid as part of the Amgen Agreement.

Financing Activities

During the year ended December 31, 2021, net cash provided by financing activities consisted primarily of $20.0 million gross proceeds from the issuance of 7,852,373 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, offset by approximately $0.4 million of issuance costs.

During the period from June 22, 2020 (inception) to December 31, 2020, net cash provided by financing activities consisted primarily of $5.0 million in gross proceeds from the SAFE and $25.0 million gross proceeds from the issuance of 9,815,467 shares of Series A convertible preferred stock at a purchase price of $2.547 per share. The gross proceeds are partially offset by approximately $0.2 million of issuance costs during the period from June 22, 2020 (inception) to December 31, 2020.

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. See “Contractual Obligations and Commitments”.

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

The following table summarizes our operating and finance lease commitments as of December 31, 2021:

	Payments Due by Period				
Description	**Total**	**Less than 1 year**	**1 – 3 years**	**3 – 5 years**	**More than 5 years**
			($ in thousands)		
Operating and finance leases	$ 937	$ 873	$ 64	$ —	$ —
Total	$ 937	$ 873	$ 64	$ —	$ —

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 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 December 31, 2021, 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 Judgements 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.

While our significant accounting policies are described in more detail in Note 2 to our consolidated financial statements included elsewhere in this Annual Report on Form 10-K, we believe that the following accounting policies are those most critical to the judgments and estimates used in the preparation of our audited financial statements.

Research and Development

As part of the process of preparing our consolidated financial statements, we are required to estimate our accrued research and development expenses. This process involves estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of actual costs. The majority of our service providers invoice us in arrears for services performed, on a pre-determined schedule or when contractual milestones are met; however, some require advance payments. We make estimates of our accrued expenses as of each balance sheet date in the consolidated financial statements based on facts and circumstances known to us at that time. At each period end, we corroborate the accuracy of these estimates with the service providers and make adjustments, if necessary. Examples of estimated accrued research and development expenses include those related to fees paid to:

- vendors in connection with discovery and preclinical development activities;
- CROs in connection with preclinical and clinical studies and testing; and
- CMOs in connection with the process development and scale up activities and the production of materials.

We record the expense and accrual related to contract research and manufacturing based on our estimates of the services received and efforts expended considering a number of factors, including our knowledge of the progress towards completion of the research, development, and manufacturing activities; invoicing to date under contracts; communication from the CROs, CMOs, and other companies of any actual costs incurred during the period that have not yet been invoiced; and the costs included in the contracts and purchase orders. The financial terms of these agreements are subject to negotiation, vary from contract to contract, and may result in uneven payment flows. There may be instances in which payments made to our vendors will exceed the level of services provided and result in a prepayment of the expense. In accruing service fees, we estimate the time period over which services will be performed and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from the estimate, we adjust the accrual or the amount of prepaid expense accordingly. Although we do not expect our estimates to be materially different from amounts actually incurred, our understanding of the status and timing of services performed relative to the actual status and timing of services performed may vary and may result in reporting amounts that are too high or too low in any particular period. To date, there have not been any material adjustments to our prior estimates of accrued research and development expenses, however, there is no guarantee there will not be any such adjustments in the future.

Stock Compensation

We have limited public market historical information for our common stock as we completed our IPO in January 2020. Historically, the estimated fair value of our common stock has been determined by our board of directors as of the date of each option grant, with input from management, considering our most recently available third-party valuations of common stock and our board of directors' assessment of additional objective and subjective factors that it believed were relevant and which may have changed from the date of the most recent valuation through the date of the grant. These third-party valuations were performed in accordance with the guidance outlined in the American Institute of Certified Public Accountants' Accounting and Valuation Guide, Valuation of Privately-Held-Company Equity Securities Issued as Compensation.

Our common stock valuations were prepared using either an option pricing method, or OPM, or a hybrid method of OPM and probability-weighted expected return method, or PWERM. Both the OPM and hybrid method used market approaches to estimate our enterprise value. The OPM treats common stock and preferred stock as call options on the total equity value of a company, with exercise prices based on the value thresholds at which the allocation among the various holders of a company's securities changes. Under this method, the common stock has value only if the funds available for distribution to stockholders exceeded the value of the preferred stock liquidation preferences at the time of the liquidity event, such as a strategic sale or a merger.

The PWERM is a scenario-based methodology that estimates the fair value of common stock based upon an analysis of future values for the company, assuming various outcomes. The common stock value is based on the probability-weighted present value of expected future investment returns considering each of the possible outcomes available as well as the rights of each class of stock. The future value of the common stock under each outcome is discounted back to the valuation date at an appropriate risk-adjusted discount rate and probability weighted to arrive at an indication of value for the common stock. A discount for lack of marketability of the common stock is then applied to arrive at an indication of value for the common stock.

The hybrid method is a hybrid between the PWERM and OPM, estimating the probability-weighted value across multiple scenarios but using the OPM to estimate the allocation of value within one or more of those scenarios. When using the hybrid method, we assumed two scenarios: an IPO scenario and a sale scenario. The IPO scenario estimated an equity value based on the guideline public company method under a market approach. The guideline public companies considered for this scenario consist of biopharmaceutical companies with recently completed initial public offerings. We converted our estimated future value in an IPO to present value using a risk-adjusted discount rate. The equity value for the sale scenario was estimated using the price of a recently issued preferred security, as well as a milestone-based tranche closing. We utilized an option pricing model to quantify or attribute value to these economic rights of convertible preferred stock as compared to the common stock, such as liquidation preferences, dividend provisions, and participation rights after liquidation preferences.

These third-party valuations were performed at various dates, which resulted in valuations of our common stock of $1.89 as of September 18, 2020, $3.78 as of May 1, 2021, $6.02 as of July 21, 2021, $9.57 as of October 14, 2021 and $11.79 as of November 19, 2021. In addition to considering the results of these third-party valuations, our board of directors considered various objective and subjective factors to determine the fair value of our common stock as of each grant date, including:

- the prices at which we sold shares of preferred stock and the superior rights and preferences of the preferred stock relative to our common stock at the time of each grant;
- the progress of our research and development programs, including the status and results of preclinical studies for our therapeutic candidates;
- our stage of development and our business strategy;
- external market conditions affecting the biopharmaceutical industry and trends within the biopharmaceutical industry;
- our financial position, including cash on hand, and our historical and forecasted performance and operating results;
- the lack of an active public market for our common stock and our preferred stock;
- significant changes to the key assumptions underlying the factors used could have resulted in different fair values of common stock at each valuation date;
- the likelihood of achieving a liquidity event, such as an initial public offering, or IPO, or sale of our company in light of prevailing market conditions; and
- the analysis of IPOs and the market performance of similar companies in the therapeutics industry.

The assumptions underlying these valuations represented management's best estimate, which involved inherent uncertainties and the application of management's judgment. As a result, if we had used significantly different assumptions or estimates, the fair value of our common stock and our stock-based compensation expense could have been materially different.

In the course of preparing for our IPO, in June 2021, we performed a retrospective fair value assessment and concluded that (i) the fair value of our common stock underlying restricted shares that we granted on July 8, 2020 was $2.42 per share for accounting purposes and (ii) the fair value of our common stock underlying stock options that we granted on November 19, 2020, November 23, 2020 and February 23, 2021 was $3.53 per share for accounting purposes. These reassessed values were based, in part, upon third-party valuations of our common stock prepared on a retrospective basis as of July 8, 2020 and September 18, 2020, respectively. The third-party retrospective valuations were prepared using the OPM or the PWERM, both which used a market approach to determine our enterprise value.

In the course of preparing for our IPO, in September 2021, we performed a retrospective fair value assessment and concluded that the fair value of our common stock underlying stock options that we granted on September 1, 2021 was $6.55 per share for accounting purposes. The reassessed value was based, in part, upon a third-party valuation of our common stock prepared on a retrospective basis as of September 1, 2021. The third-party retrospective valuation was prepared using the hybrid method, which used a market approach to determine our enterprise value.

In the course of preparing for our IPO, in November 2021, we performed a retrospective fair value assessment and concluded that the fair value of our common stock underlying stock options that we granted on November 4 and 16, 2021 was $11.79 per share for accounting purposes. The reassessed value was based, in part, upon a third-party valuation of our common stock prepared on a retrospective basis as of November 19, 2021. The third-party retrospective valuation was prepared using the hybrid method, which used a market approach to determine our enterprise value.

We applied the fair values of our common stock from our retrospective fair value assessments performed in June 2021 and September 2021 to determine the fair value of the July 2020, November 2020, February 2021 and September 2021 awards as of each respective grant date and to calculate stock-based compensation expense for accounting purposes for all applicable periods, from the date such awards were granted.

As a public trading market for our common stock has been established it will no longer be necessary for our board of directors to estimate the fair value of our common stock in connection with our accounting for granted stock options and other such awards we may grant, as the fair value of our common stock will be determined based on the quoted market price of our common stock. Following the close of our IPO in January 2022, the fair value of our common stock is determined based on the closing price of our common stock as reported by Nasdaq Global Select Market on the date of grant.

Valuation of Series A Preferred Stock Tranche Obligation and Related Party Antidilution 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 Series A Preferred Stock Tranche Obligation was settled during the year ended December 31, 2021.

The Related Party Antidilution Obligation was valued using a probability-weighted expected return method, which 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 fair value of the Related Party Antidilution Obligation when it was settled in May 2021 was $5.1 million which was based on 1,963,093 shares of preferred stock issued at a price of $2.589 per share.

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

A description of recently issued accounting pronouncements that may potentially impact our financial position, results of operations and cash flows is disclosed in Note 2 to our consolidated financial statements included elsewhere in this Annual Report on Form 10-K.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk.

Interest Rate Risk

As of December 31, 2021, we had cash and cash equivalents of $91.4 million. As of December 31, 2020, we had cash and cash equivalents of $24.2 million. Interest income is sensitive to changes in the general level of interest rates. Our surplus cash has been invested in money market fund accounts and interest-bearing savings accounts. We have not entered into investments for trading or speculative purposes. Due to the conservative nature of our investment portfolio, which is predicated on capital preservation of investments with short-term maturities, we do not believe an immediate one percentage point change in interest rates would have a material effect on the fair market value of our portfolio, and therefore we do not expect our operating results or cash flows to be significantly affected by changes in market interest rates. As of December 31, 2021, and December 31, 2020, we had no debt outstanding. Therefore, we are not exposed to interest rate risk with respect to debt.

All of our employees and our operations are currently located in the United States. We have, from time to time, engaged in contracts with contractors or other vendors in a currency other than the U.S. dollar.

To date, we are not currently exposed to significant market risk related to changes in foreign currency exchange rates. Our operations may be subject to fluctuations in foreign currency exchange rates in the future.

We do not believe that inflation has had a material effect on our business, financial condition or results of operations. Our operations may be subject to inflation in the future.

Item 8. Financial Statements and Supplementary Data.

Our consolidated financial statements, together with the reports of our independent registered public accounting firm, appear beginning on page F-1 of this Annual Report for the year ended December 31, 2021.

Item 9. Changes in and Disagreements With Accountants on Accounting and Financial Disclosure.

None.

Item 9A. 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 December 31, 2021. 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 December 31, 2021, 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 December 31, 2021.

Notwithstanding the material weakness described in Management's Report on Internal Control Over Financial Reporting, our management has concluded that our 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.

Management's Annual Report on Internal Controls Over Financial Reporting

This Annual Report on Form 10-K does not include a report of management's assessment regarding our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) or an attestation report of our independent registered accounting firm due to a transition period established by rules of the SEC for newly public companies. Additionally, our independent registered accounting firm will not be required to opine on the effectiveness of our internal control over financial reporting pursuant to Section 404 until we are no longer an "emerging growth company" as defined in the JOBS Act, and our unaffiliated market capitalization exceeds $700 million.

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 December 31, 2021 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information.

As of the date of this Annual Report on Form 10-K, we intend to hold our 2022 Annual meeting of Stockholders (the "2022 Annual Meeting") on or about June 9, 2022 at 8:30 a.m. local time virtually. We are providing the following disclosure in accordance with our Amended and Restated Bylaws (the "Bylaws") and Rule 14a-8 under the Securities Exchange Act of 1934, as amended (the "Exchange Act").

Bylaws Advance Notice Deadline for Submission of Stockholder Proposals and Director Nominations

Pursuant to our Bylaws, since the 2022 Annual Meeting is the first Annual Meeting following our initial public offering, for notice of stockholder proposals submitted outside of Rule 14a-8 of the Exchange Act and director nominations to be timely, they must be so received not later than the later of (A) the close of business on the 90th day before the 2022 Annual Meeting; or (B) the close of business on the 10th day following the day on which public announcement of the date of the 2022 Annual Meeting is first made by us. As this is our first public disclosure of the date of the 2022 Annual Meeting, to be considered timely, stockholder proposals submitted outside of Rule 14a-8 of the Exchange Act and director nominations, in each case intended to be brought before the 2022 Annual Meeting, must be received no later than the close of business on Monday, April 4, 2022. Any such stockholder proposals and director nominations must be directed to our Corporate Secretary at our corporate offices at Vigil Neuroscience, Inc., One Broadway, Suite 07-300, Cambridge, MA 02142. Such stockholder proposals and director nominations must also comply with the advance notice provisions contained in Sections 2 of our Bylaws.

Rule 14a-8 Deadline for the Submission of Stockholder Proposals

As we did not hold an annual meeting in 2021, pursuant to Rule 14a-8(e)(2) under the Exchange Act, the deadline for the receipt of any stockholder proposals submitted pursuant to Rule 14a-8 of the Exchange Act for inclusion in the Company's proxy materials for the 2022 Annual Meeting would be a reasonable time before the company begins to print and send its proxy materials. We have determined that Monday, April 4, 2022 is a reasonable time before we expect to begin to print and distribute its proxy materials for the 2022 Annual Meeting, and that any stockholder proposals must be received on or before the close of business on that day. Such proposals must be directed to our Corporate Secretary at our corporate offices at Vigil Neuroscience, Inc., One Broadway, Suite 07-300, Cambridge, MA 02142. Such proposals must also comply with Rule 14a-8 of the Exchange Act.

Item 9C. Disclosure Regarding Foreign Jurisdictions that Prevent Inspections.

Not applicable.

PART III

Item 10. Directors, Executive Officers and Corporate Governance.

The information required under this item is incorporated herein by reference to the Company's definitive proxy statement pursuant to Regulation 14A, which proxy statement will be filed with the Securities and Exchange Commission not later than 120 days after the close of the Company's fiscal year ended December 31, 2021.

Item 11. Executive Compensation.

The information required under this item is incorporated herein by reference to the Company's definitive proxy statement pursuant to Regulation 14A, which proxy statement will be filed with the Securities and Exchange Commission not later than 120 days after the close of the Company's fiscal year ended December 31, 2021.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters.

The information required under this item is incorporated herein by reference to the Company's definitive proxy statement pursuant to Regulation 14A, which proxy statement will be filed with the Securities and Exchange Commission not later than 120 days after the close of the Company's fiscal year ended December 31, 2021.

Item 13. Certain Relationships and Related Transactions, and Director Independence.

The information required under this item is incorporated herein by reference to the Company's definitive proxy statement pursuant to Regulation 14A, which proxy statement will be filed with the Securities and Exchange Commission not later than 120 days after the close of the Company's fiscal year ended December 31, 2021.

Item 14. Principal Accounting Fees and Services.

Our independent public accounting firm is PricewaterhouseCoppers LLP, Boston, Massachusetts, PCAOB Auditor ID 238.

The information required under this item is incorporated herein by reference to the Company's definitive proxy statement pursuant to Regulation 14A, which proxy statement will be filed with the Securities and Exchange Commission not later than 120 days after the close of the Company's fiscal year ended December 31, 2021.

PART IV

Item 15. Exhibits, Financial Statement Schedules.

(1) For a list of the financial statements included herein, see Index to the Consolidated Financial Statements on page F-1 of this Annual Report on Form 10-K, incorporated into this Item by reference.

(2) Financial statement schedules have been omitted because they are either not required or not applicable or the information is included in the consolidated financial statements or the notes thereto.

The exhibits filed as part of this Annual Report on Form 10-K are set forth on the Exhibit Index immediately preceding the signature page of this Annual Report on Form 10-K. The Exhibit Index is incorporated herein by reference.

Item 16. Form 10-K Summary

None.

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Board of Directors and Stockholders of Vigil Neuroscience, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Vigil Neuroscience, Inc. and its subsidiary (the "Company") as of December 31, 2021 and December 31, 2020, and the related consolidated statements of operations and comprehensive loss, of convertible preferred stock and stockholders' deficit and of cash flows for the year ended December 31, 2021 and for the period from June 22, 2020 (Inception) to December 31, 2020, including the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2021 and December 31, 2020, and the results of its operations and its cash flows for the year ended December 31, 2021 and for the period from June 22, 2020 (Inception) to December 31, 2020 in conformity with accounting principles generally accepted in the United States of America.

Basis for Opinion

These consolidated financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's consolidated financial statements based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits of these consolidated financial statements in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audits to obtain reasonable assurance about whether the consolidated financial statements are free of material misstatement, whether due to error or fraud.

Our audits included performing procedures to assess the risks of material misstatement of the consolidated financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the consolidated financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the consolidated financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ PricewaterhouseCoopers LLP

Boston, Massachusetts
March 25, 2022

We have served as the Company's auditor since 2021.

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

	December 31, 2021	December 31, 2020
Assets		
Current assets:		
Cash and cash equivalents	$ 91,420	$ 24,151
Prepaid expenses and other current assets [1]	6,063	1,145
Total current assets	97,483	25,296
Property and equipment, net	301	—
Operating lease right-of-use assets	882	—
Financing lease right-of-use assets	91	—
Restricted cash	927	—
Other assets	2,757	—
Total assets	$ 102,441	$ 25,296
Liabilities, Convertible Preferred Stock and Stockholders' Deficit		
Current liabilities:		
Accounts payable	$ 3,977	$ 1,107
Accrued expenses and other current liabilities [2]	5,031	888
Operating lease liabilities	830	—
Financing lease liabilities	43	—
Total current liabilities	9,881	1,995
Related party antidilution obligation	—	4,247
Operating lease liabilities, net of current portion	41	—
Finance lease liabilities, net of current portion	23	—
Series A preferred stock tranche obligation	—	303
Total liabilities	9,945	6,545
Commitments and contingencies (Note 14)		
Series A convertible preferred stock, net of issuance costs, $0.0001 par value; 28,522,592 shares authorized as of December 31, 2021 and December 31, 2020; 28,522,592 and 18,707,126 shares issued and outstanding as of December 31, 2021 and December 31, 2020, respectively; liquidation preference of $72,647 and $47,647 as of December 31, 2021 and December 31, 2020, respectively	72,327	47,034
Series B convertible preferred stock, net of issuance costs, $0.0001 par value; 25,657,096 and 0 shares authorized as of December 31, 2021 and December 31, 2020, respectively; 25,657,096 and 0 shares issued and outstanding as of December 31, 2021 and December 31, 2020, respectively; liquidation preference of $90,000 and $0 as of December 31, 2021 and December 31, 2020, respectively	89,612	—
Stockholders' deficit:		
Common stock, $0.0001 par value; 72,000,000 shares authorized at December 31, 2021 and 40,000,000 shares authorized at December 31, 2020; 1,748,879 shares issued as of December 31, 2021 and December 31, 2020, respectively; and 1,727,093 and 1,748,879 shares outstanding as of December 31, 2021 and December 31, 2020, respectively	—	—
Additional paid-in capital	2,386	263
Accumulated deficit	(71,829)	(28,546)
Total stockholders' deficit	(69,443)	(28,283)
Total liabilities, convertible preferred stock and stockholders' deficit	$ 102,441	$ 25,296

(1) Includes related party amounts of $0 and $354 at December 31, 2021 and December 31, 2020, respectively (see Note 13).

(2) Includes related party amounts of $221 (accrued expenses and other current liabilities) at December 31, 2021; $424 (accounts payable) at December 31, 2020 (see Note 13).

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

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

	Year Ended December 31, 2021	Period from June 22, 2020 (Inception) to December 31, 2020
Operating expenses:		
Related party acquired in-process research and development	$ —	$ 20,923
Research and development [3]	32,330	4,514
General and administrative	10,079	1,777
Total operating expenses	42,409	27,214
Loss from operations	(42,409)	(27,214)
Other income (expense):		
Change in fair value of the related party antidilution obligation	(836)	(1,307)
Change in fair value of Series A preferred stock tranche obligation	(28)	(24)
Interest income, net	3	—
Other expense, net	(13)	(1)
Total other expense, net	(874)	(1,332)
Net loss and comprehensive loss	$ (43,283)	$ (28,546)
Net loss per share attributable to common stockholders, basic and diluted	$ (28.26)	$ (21.15)
Weighted—average common shares outstanding, basic and diluted	1,531,686	1,349,702

(3) Includes related party amounts of $2,672 for the year ended December 31, 2021, and $811 for the period from June 22, 2020 (inception) to December 31, 2020 (see Note 13).

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

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

	Convertible Preferred Stock		Common Stock		Additional Paid-in Capital	Accumulated Deficit	Total Stockholders' Deficit
	Shares	Amount	Shares	Amount			
Balances at June 22, 2020 (Inception)	—	$ —	—	$ —	$ —	$ —	$ —
Issuance of common stock	—	—	1,442,376	—	1	—	1
Issuance of Series A convertible preferred stock in exchange for license and partial settlement of the related party antidilution obligation	6,928,566	17,483	—	—	—	—	—
Issuance of Series A convertible preferred stock, net of Series A preferred stock tranche obligation of $233 and issuance costs of $170	9,815,467	24,597	—	—	—	—	—
Conversion of SAFE to preferred stock, net of Series A preferred stock tranche obligation of $46	1,963,093	4,954	—	—	—	—	—
Grant of restricted stock	—	—	306,503	—	—	—	—
Stock-based compensation expense	—	—	—	—	262	—	262
Net loss	—	—	—	—	—	(28,546)	(28,546)
Balances at December 31, 2020	18,707,126	$ 47,034	1,748,879	$ —	$ 263	$ (28,546)	$ (28,283)
Issuance of Series A convertible preferred stock, net of issuance costs of $121	7,852,373	19,879	—	—	—	—	—
Reclassification of Series A preferred stock tranche obligation upon settlement	—	331	—	—	—	—	—
Reclassification of the related party antidilution obligation upon settlement	1,963,093	5,083	—	—	—	—	—
Issuance of Series B convertible preferred stock, net of issuance costs of $388	25,657,096	89,612	—	—	—	—	—
Forfeiture of restricted stock			(44,323)	—	—	—	—
Exercise of stock options			20,394	—	38	—	38
Stock-based compensation expense	—	—	—	—	2,085	—	2,085
Net loss	—	—	—	—	—	(43,283)	(43,283)
Balances at December 31, 2021	54,179,688	$ 161,939	1,724,950	$ —	$ 2,386	$ (71,829)	$ (69,443)

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

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

	Year Ended December 31, 2021	Period from June 22, 2020 (Inception) to December 31, 2020
Cash flows from operating activities:		
Net loss	$ (43,283)	$ (28,546)
Adjustments to reconcile net loss to net cash used by operating activities:		
Acquired in-process research and development	—	20,923
Stock-based compensation expense	2,085	262
Non-cash operating lease expense	317	—
Change in fair value of the related party antidilution obligation	836	1,307
Change in fair value of Series A preferred stock tranche obligation	28	24
Depreciation and amortization	28	—
Changes in operating assets and liabilities:		
Prepaid expenses and other current assets	(4,918)	(1,145)
Accounts payable	2,350	1,107
Accrued expenses and other current liabilities	3,597	888
Operating lease liabilities	(328)	—
Other assets	(59)	—
Net cash used in operating activities	(39,347)	(5,180)
Cash flows from investing activities:		
Purchases of property and equipment	(204)	—
Payment made for Amgen license	—	(500)
Net cash used in investing activities	(204)	(500)
Cash flows from financing activities:		
Proceeds from issuance of Series A convertible preferred stock, net of issuance costs paid	19,879	24,830
Proceeds from issuance of Series B convertible preferred stock, net of issuance costs paid	89,755	—
Payments of finance lease obligations	(38)	—
Payments of offering costs	(1,887)	—
Proceeds from stock option exercised	38	
Net proceeds from SAFE	—	5,000
Net proceeds from issuance of common stock	—	1
Net cash provided by financing activities	107,747	29,831
Net increase in cash and cash equivalents	68,196	24,151
Cash, cash equivalents and restricted cash at beginning of period	24,151	—
Cash, cash equivalents and restricted cash at end of period	$ 92,347	$ 24,151
Supplemental disclosure of non-cash investing and financing activities:		
Issuance of Series A convertible preferred stock in exchange for license and partial settlement of the related party antidilution obligation	$ —	$ 17,483
Conversion of SAFE to Series A convertible preferred stock	$ —	$ 4,954
Recognition of the related party antidilution obligation	$ —	$ 3,992
Recognition of Series A preferred stock tranche obligation	$ —	$ 279
Settlement of related party antidilution obligation	$ 5,083	$ —
Settlement of Series A preferred stock tranche obligation	$ 331	$ —
Right-of-use assets obtained in exchange for operating lease liabilities	$ 1,199	$ —
Right-of-use assets obtained in exchange for financing lease liabilities	$ 104	$ —
Issuance costs included in accrued expenses	$ 143	$ —
Deferred offering costs included in accounts payable and accrued expenses	$ 811	$ —
Purchases of property and equipment included in accounts payable and accrued expenses	$ 112	

The accompanying notes are an integral part of these 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 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 consolidated financial statements are issued. As of December 31, 2021, the Company had cash and cash equivalents of $91.4 million and an accumulated deficit of $71.8 million. In January 2022, the Company completed their 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 the 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 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 consolidated financial statements reflect the operations of the Company and its wholly-owned subsidiary. Intercompany balances and transactions have been eliminated in consolidation. The accompanying consolidated financial statements have been prepared in conformity with generally accepted accounting principles in the United States of America ("GAAP"). Any reference in these notes to applicable guidance is meant to refer to the authoritative GAAP as found in the Accounting Standards Codification ("ASC") and Accounting Standards Updates ("ASU") of the Financial Accounting Standards Board ("FASB").

2. Summary of Significant Accounting Policies

Use of Estimates

The preparation of financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities, the disclosure of contingent assets and liabilities at the date of the consolidated financial statements, and the reported amounts of expenses during the reporting periods. Significant estimates and assumptions reflected in these 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 12) and Series A Preferred Stock Tranche Obligation (as defined within this Note 2). 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 December 31, 2021 and December 31, 2020, the Company's cash equivalents are 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 14), the Company is required to maintain a certificate of deposit ("CD") of $0.9 million for the benefit of the landlord.

Cash, cash equivalents and restricted cash were comprised of the following (in thousands):

	December 31, 2021	Period from June 22, 2020 (Inception) to December 31, 2020
Cash and cash equivalents	$ 91,420	$ 24,151
Restricted cash, non-current	927	—
Total cash, cash equivalents and restricted cash	$ 92,347	$ 24,151

Deferred Offering Costs

The Company capitalizes certain legal, accounting and other third-party fees that are directly associated with in-process equity financings as deferred offering costs until such financings are consummated. After consummation of the equity financing, these costs are recorded as a reduction of the proceeds from the offering, either as a reduction of the carrying value of preferred stock or in stockholders' deficit as a reduction of additional paid-in capital generated as a result of the offering. Should the in-process equity financing be abandoned, the deferred offering costs would be expensed immediately as a charge to operating expenses in the consolidated statement of operations and comprehensive loss. The Company had no deferred offering costs recorded as of December 31, 2020. As of December 31, 2021, the Company had deferred offering costs totaling $2.7 million in other assets in the consolidated balance sheet.

Concentrations of Credit Risk and Off-Balance Sheet Risk

Financial instruments that potentially subject the Company to concentrations of credit risk consist primarily of cash and cash equivalents. The Company maintains its cash and cash equivalents with high quality, accredited financial institutions and, accordingly, such funds are subject to minimal credit risk. The Company has no significant off-balance sheet concentrations of credit risk, such as foreign currency exchange contracts, option contracts or other hedging arrangements.

The Company is dependent on third-party organizations to manufacture and process its therapeutic candidates for its development programs. In particular, the Company relies on a single third-party contract manufacturer, Fujifilm Diosynth Biotechnologies U.S.A., Inc. and Fujifilm Diosynth Biotechnologies Texas, LLC (collectively "FUJIFILM"), to produce clinical supply and process its current product candidate, VGL101 pursuant to the FUJIFILM agreement (see Note 12). The Company expects to continue to be dependent on a small number of manufacturers to supply it with its requirements for all products. The Company's research and development programs, including any associated potential commercialization efforts, could be adversely affected by a significant interruption in the supply of the necessary materials.

The Company is dependent on a limited number of third parties that provide license rights used by the Company in the development and potential commercialization of its therapeutic candidates and programs. Through December 31, 2021 and December 31, 2020, the Company's research and development programs primarily relate to rights conveyed by Amgen, Inc. ("Amgen") (see Note 12). The Company could experience delays in the development and potential commercialization of its therapeutic candidates and programs if the Amgen license arrangement or any other license agreement utilized in the Company's research and development activities is terminated, if the Company fails to meet the obligations required under its arrangements, or if the Company is unable to successfully secure new strategic alliances or licensing agreements.

Fair Value Measurements

Certain assets and liabilities of the Company are carried at fair value under GAAP. Fair value is defined as the exchange price that would be received for an asset or paid to transfer a liability (an exit price) in the principal or most advantageous market for the asset or liability in an orderly transaction between market participants on the measurement date. Valuation techniques used to measure fair value must maximize the use of observable inputs and minimize the use of unobservable inputs. Financial assets and liabilities carried at fair value are to be classified and disclosed in one of the following three levels of the fair value hierarchy, of which the first two are considered observable and the last is considered unobservable:

- Level 1 – Quoted prices in active markets for identical assets or liabilities.
- Level 2 – Observable inputs (other than Level 1 quoted prices), such as quoted prices in active markets for similar assets or liabilities, quoted prices for identical or similar assets or liabilities, or other inputs that are observable or can be corroborated by observable market data.

- Level 3 – Unobservable inputs that are supported by little or no market activity and that are significant to determining the fair value of the assets or liabilities, including pricing models, discounted cash flow methodologies and similar techniques.

The Company's cash equivalents, Related Party Antidilution Obligation and Series A Preferred Stock Tranche Obligation are carried at fair value, determined according to the fair value hierarchy described above (see Note 3). The carrying values of the Company's accounts payable and accrued expenses approximate their fair values, due to the short-term nature of these liabilities.

Research and Development Expenses

Research and development expenses are expensed as incurred. Research and development expenses consist of costs incurred in performing research and development activities, including amounts incurred under agreements with external vendors and consultants engaged to perform preclinical studies and to manufacture research and development materials for use in such studies, salaries and related personnel costs, stock-based compensation, consultant fees, and third-party license fees.

Upfront payments under license agreements are expensed upon receipt of the license, and annual maintenance fees under license agreements are expensed over the maintenance period. Milestone payments under license agreements are accrued, with a corresponding expense being recognized, in the period in which the milestone is determined to be probable of achievement and the related amount is reasonably estimable.

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

Patent Costs

Costs to secure, defend and maintain patents, including those incurred in connection with filing and prosecuting patent applications, are expensed as incurred due to the uncertainty about the recovery of the expenditure. Amounts incurred for patent-related expenditures are classified as general and administrative expenses in the consolidated statements of operations and comprehensive loss.

Accrued Research and Development Expenses

The Company has entered into various research, development and manufacturing contracts with third-party service providers, including contract research organizations and contract manufacturing organizations. These agreements are generally cancelable. The Company recognizes research and development expense associated with such arrangements as the costs are incurred and records accruals for estimated ongoing research, development and manufacturing costs, where necessary. When billing terms under these contracts do not coincide with the timing of when the work is performed, the Company is required to make estimates of outstanding obligations to those third parties as of period end. Any accrual estimates are based on a number of factors, including the Company's knowledge of the progress towards completion of the specific tasks to be performed, invoicing to date under the contracts, communication from the vendors of any actual costs incurred during the period that have not yet been invoiced and the costs included in the contracts. Significant judgments and estimates may be made in determining the accrued balances at the end of any reporting period. Actual results could differ from the estimates made by the Company. The historical accrual estimates made by the Company have not been materially different from the actual costs.

Acquired In-Process Research and Development Expenses

The Company measures and recognizes asset acquisitions or licenses to intellectual property that are not deemed to be business combinations based on the cost to acquire or license the asset or group of assets, which includes transaction costs. Goodwill is not recognized in asset acquisitions or transaction to license intellectual property. In an asset acquisition or license to intellectual property, the cost allocated to acquire in-process research and development ("IPR&D") with no alternative future use is recognized as expense on the acquisition date.

Upfront and milestone payments made are accrued for and expensed when the achievement of the milestone is probable up to the point of regulatory approval. Milestone payments made upon regulatory approval are capitalized and amortized over the remaining useful life of the related product.

Acquired IPR&D expense recognized for the period from June 22, 2020 (inception) to December 31, 2020 consisted of (i) $20.4 million initial recognition of a Related Party Antidilution Obligation that obligates the Company to issue shares of the Series A convertible preferred stock equal to 25% of the Company's capital stock until the Company has raised $45.0 million in net cash proceeds from equity financings and (ii) the upfront cash consideration for the license arrangement of $0.5 million (see Note 12). There were no acquired IPR&D expenses recognized for the year ended December 31, 2021.

Comprehensive Loss

Comprehensive loss includes net loss as well as other changes in stockholders' deficit that result from transactions and economic events other than those with stockholders. There was no difference between net loss and comprehensive loss for each of the periods presented in the consolidated financial statements.

Stock-Based Compensation

The Company grants stock-based awards to employees, directors and non-employee consultants in the form of stock options to purchase shares of its common stock. The Company measures stock options with service-based vesting granted to employees, non-employees and directors based on the fair value of the award on the date of the grant using the Black-Scholes option-pricing model. The Company measures restricted common stock awards using the difference, if any, between the purchase price per share of the award and the fair value of the Company's common stock at the date of the grant. Compensation expense for employee awards is recognized over the requisite service period, which is generally the vesting period of the award. Compensation expense for non-employee awards is recognized in the same manner as if the Company had paid cash in exchange for the goods or services, which is generally the vesting period of the award. The Company uses the straight-line method to record the expense of awards with service-based vesting conditions. For stock awards that have a performance condition, the Company recognizes compensation expense based on its assessment of the probability that the performance condition will be achieved, using an accelerated attribution model, over the explicit or implicit service period. The Company accounts for forfeitures as they occur.

The Company classifies stock-based compensation expense in its statements of operations and comprehensive loss in the same manner in which the award recipient's salary and related costs are classified or in which the award recipient's service payments are classified.

The Black-Scholes option-pricing model requires inputs based on certain subjective assumptions, which determine the fair value of stock-based awards, including the price, volatility of the underlying stock, the option's expected term, the risk-free interest rate and expected dividends. The Company calculates the fair value of options granted by using the Black-Scholes option-pricing model with the following assumptions:

Expected Volatility – Due to a lack of company-specific historical and implied volatility data, the Company has based its estimate of expected volatility on the historical volatility of a group of similar companies that are publicly traded. The historical volatility is calculated based on a period commensurate with the expected term assumption.

Expected Term – The expected term of the Company's options represents the period that the stock-based awards are expected to be outstanding. The Company uses the simplified method to calculate the expected term, as it does not have sufficient historical exercise data to develop reasonable expectations about future exercise patterns and post-vesting employment termination behavior.

Risk-Free Interest Rate – The risk-free interest rate is based on yield from the United States Treasury zero-coupon bonds whose term is consistent with the expected term of the stock options.

Dividend Yield – The expected dividend yield is assumed to be zero as the Company has never paid dividends and has no current plans to pay any dividends.

Classification and Accretion of Convertible Preferred Stock

The Company's Series A convertible preferred stock and Series B convertible preferred stock (collectively, "Convertible Preferred Stock") are classified outside of stockholders' deficit in the consolidated balance sheets because the holders of such shares have liquidation rights in the event of a deemed liquidation that, in certain circumstances, is not solely within the control of the Company and would require the redemption of the then-outstanding Convertible Preferred Stock. The Company's Convertible Preferred Stock are not redeemable, except in the event of a deemed liquidation (see Note 7). Because the occurrence of a deemed liquidation event is not currently probable, the carrying values of the Convertible Preferred Stock are

not being accreted to their redemption values. Subsequent adjustments to the carrying values of the Convertible Preferred Stock would be made only when a deemed liquidation event becomes probable.

The Company recorded the Series A convertible preferred stock at fair value upon issuance, net of the Series A Preferred Stock Tranche Obligation (see to Note 7 for details of the Series A Preferred Stock Tranche Obligation) and associated issuance costs. The Company recorded the Series B convertible preferred stock at fair value upon issuance, net of associated issuance costs. The Company's Convertible Preferred Stock is subject to a non-cumulative dividend when, as and if declared by the Company's board of directors (the "Board"). Since the issuance of the Company's outstanding Convertible Preferred Stock, no dividends have been declared on any shares of convertible preferred stock.

Segment Information

The Company manages its operations as a single segment for the purposes of assessing performance and allocating resources. The Company is focused on microglia biology to improve the lives of patients, caregivers, and families affected by rare and common neurodegenerative diseases through development of disease-modifying treatments that aim to restore the vigilance of microglia, the sentinel immune cells of the brain. The Company's chief operating decision maker reviews the Company's financial information on an aggregated basis for purposes of assessing performance and allocating resources. All assets are in the United States. The Company has not earned any revenue through December 31, 2021.

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 Company did not have any property and equipment during the period from June 22, 2020 (inception) to December 31, 2020. The following is the summary of property and equipment and related accumulated depreciation as of December 31, 2021 (in thousands):

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

Depreciation expense was $15 thousand during the year ended December 31, 2021.

Series A Preferred Stock Tranche Obligation

The Company's Series A Convertible Preferred Stock Purchase Agreement obligated the Series A investors to participate in a subsequent offering of Series A convertible preferred stock upon the achievement of specified development milestones by the Company.

The Company classified this Series A Preferred Stock Tranche Obligation as a liability in its consolidated balance sheets (the "Series A Preferred Stock Tranche Obligation'') as the preferred stock tranche right was a freestanding financial instrument that would require the Company to transfer assets upon exercise of the right. The Series A Preferred Stock Tranche Obligation was initially recorded at fair value upon the issuance date of the preferred stock tranche right and was subsequently remeasured to fair value at each reporting date until settled (see Note 3). Changes in fair value of the Series A Preferred Stock Tranche

Obligation were recognized within change in fair value of the Series A Preferred Stock Tranche Obligation in the consolidated statements of operations and comprehensive loss.

Impairment of Long-Lived Assets

Long-lived assets consist of property and equipment, operating lease and financing lease right-to-use assets. Long-lived assets to be held and used are tested for recoverability whenever events or changes in business circumstances indicate that the carrying amount of the assets may not be fully recoverable. Factors that the Company considers in deciding when to perform an impairment review include significant underperformance of the business in relation to expectations, significant negative industry or economic trends, and significant changes or planned changes in the use of the assets. If an impairment review is performed to evaluate a long-lived asset group for recoverability, the Company compares forecasts of undiscounted cash flows expected to result from the use and eventual disposition of the long-lived asset group to its carrying value. An impairment loss would be recognized in loss from operations when estimated undiscounted future cash flows expected to result from the use of an asset group are less than its carrying amount. Impairment is measured based on the excess of the carrying value of the related assets over the fair value of such assets. The Company did not record any impairment losses on long-lived assets during the year ended December 31, 2021 and the period from June 22, 2020 (inception) to December 31, 2020.

Income Taxes

The Company accounts for income taxes using the asset and liability method, which requires the recognition of deferred tax assets and liabilities for the expected future tax consequences of events that have been recognized in the consolidated financial statements or in the Company's tax returns. Deferred tax assets and liabilities are determined on the basis of the differences between financial statement and tax basis of assets and liabilities using enacted tax rates in effect for the year in which the differences are expected to reverse. Changes in deferred tax assets and liabilities are recorded in the provision for income taxes. The Company assesses the likelihood that its deferred tax assets will be recovered from future taxable income, and to the extent it believes, based upon the weight of available evidence, that it is more likely than not that all or a portion of the deferred tax assets will not be realized, a valuation allowance is established through a charge to income tax expense. Potential for recovery of deferred tax assets is evaluated by estimating the future profits expected and considering prudent and feasible tax planning strategies.

The Company accounts for uncertainty in income taxes recognized in the consolidated financial statements by applying a two-step process to determine the amount of tax benefit to be recognized. First, the tax position must be evaluated to determine the likelihood that it will be sustained upon external examination by the taxing authorities. If the tax position is deemed more likely than not to be sustained, the tax position is then assessed to determine the amount of benefit to recognize in the consolidated financial statements. The amount of the benefit that may be recognized is the largest amount that has a greater than 50% likelihood of being realized upon ultimate settlement. The provision for income taxes includes the effects of any resulting tax reserves, or unrecognized tax benefits, that are considered appropriate as well as the related net interest and penalties. The Company's policy is to record estimated interest and penalties related to uncertain tax positions as a component of income tax expense. The Company had no amounts accrued for interest and penalties in its consolidated balance sheets as of December 31, 2020 and December 31, 2021.

Leases

In accordance with ASC 842, *Leases*, which the Company adopted at inception, the Company determines if an arrangement is or contains a lease at inception. A contract is or contains a lease if the contract conveys the right to control the use of an identified asset for a period of time in exchange for consideration. The Company classifies leases at the lease commencement date as operating or finance leases and records a right-of-use asset and a lease liability on the consolidated balance sheet for all leases with an initial lease term of greater than 12 months. Leases with an initial term of 12 months or less are not recorded in the balance sheet, but payments are recognized as expense on a straight-line basis over the lease term. The Company has elected not to recognize leases with terms of 12 months or less.

A lease qualifies as a finance lease if any of the following criteria are met at the inception of the lease: (i) there is a transfer of ownership of the leased asset to the Company by the end of the lease term, (ii) the Company holds an option to purchase the leased asset that it is reasonably certain to exercise, (iii) the lease term is for a major part of the remaining economic life of the leased asset, (iv) the present value of the sum of lease payments equals or exceeds substantially all of the fair value of the leased asset, or (v) the nature of the leased asset is specialized to the point that it is expected to provide the lessor no alternative use at the end of the lease term. All other leases are recorded as operating leases.

The Company enters into contracts that contain both lease and non-lease components. Non-lease components may include maintenance, utilities, and other operating costs. The Company combines the lease and non-lease components of fixed costs in its lease arrangements as a single lease component. Variable costs, such as utilities or maintenance costs, are not included in the measurement of right-of-use assets and lease liabilities, but rather are expensed when the event determining the amount of variable consideration to be paid occurs.

Finance and operating lease assets and liabilities are recognized at the lease commencement date based on the present value of the lease payments over the lease term using the discount rate implicit in the lease. If the rate implicit is not readily determinable, the Company utilizes an estimate of its incremental borrowing rate based upon the available information at the lease commencement date. Operating lease assets are further adjusted for prepaid or accrued lease payments. Operating lease payments are expensed using the straight-line method as an operating expense over the lease term. The Company's lease terms may include options to extend or terminate the lease when it is reasonably certain that the Company will exercise that option. Finance lease assets are amortized to depreciation expense using the straight-line method over the shorter of the useful life of the related asset or the lease term. Finance lease payments are bifurcated into (i) a portion that is recorded as imputed interest expense and (ii) a portion that reduces the finance liability associated with the lease.

Certain of the Company's leases include options to extend or terminate the lease. The amounts determined for the Company's right-of-use assets and lease liabilities generally do not assume that renewal options or early-termination provisions, if any, are exercised, unless it is reasonably certain that the Company will exercise such options.

Net Income (Loss) Per Share

The Company follows the two-class method when computing net income (loss) per common share as the Company has issued shares that meet the definition of participating securities. The two-class method determines net income (loss) per common share for each class of common and participating securities according to dividends declared or accumulated and participation rights in undistributed earnings. The two-class method requires income (loss) available to common stockholders for the period to be allocated between common and participating securities based upon their respective rights to receive dividends as if all income for the period had been distributed. The Company considers its (i) convertible preferred stock, (ii) restricted stock, and (iii) SAFE (as defined in Note 12) during the periods they were outstanding (See Note 7) to be participating securities as, in the event a dividend is paid on common stock, the holders of these securities would be entitled to receive dividends on a basis consistent with the common stockholders. The Company also considers the shares issued upon the early exercise of stock options that are subject to repurchase to be participating securities because holders of such shares have non-forfeitable dividend rights in the event a dividend is paid on common stock. There is no allocation required under the two-class method during periods of loss since the participating securities do not have a contractual obligation to share in the losses of the Company.

Basic net income (loss) per common share is computed by dividing the net income (loss) per common share by the weighted-average number of common shares outstanding for the period. Diluted net income (loss) per common share is computed by adjusting net income (loss) to reallocate undistributed earnings based on the potential impact of dilutive securities. Diluted net loss per common share is computed by dividing the diluted net loss by the weighted-average number of common shares outstanding for the period, including potential dilutive common shares. For purpose of this calculation, outstanding stock options, SAFE, convertible preferred stock and unvested restricted common stock are considered potential dilutive common shares.

In periods in which the Company reported a net loss, diluted net loss per common share was the same as basic net loss per common share, since dilutive common shares were not assumed to have been issued if their effect was anti-dilutive. The Company reported a net loss for the year ended December 31, 2021, and the period from June 22, 2020 (inception) to December 31, 2020..

Recently Adopted Accounting Pronouncements

In December 2019, the FASB issued ASU No. 2019-12, *Income Taxes (ASC 740): Simplifying the Accounting for Income Taxes* ("ASU 2019-12"). ASU 2019-12 simplifies the accounting for income taxes by removing certain exceptions to the general principles in ASC 740 and clarifies and amends existing guidance to improve consistent application. The amendment that removed the incremental approach for intra-period tax allocations when there is a loss from continuing operations and income or a gain from other items, including, but not limited to discontinued operations or other comprehensive income should be applied on a prospective basis. The Company early adopted ASU 2019-12 effective January 1, 2021. The adoption of this new standard did not have a material impact on the Company's financial statements.

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 December 31, 2021 and December 31, 2020,, by level within the fair value hierarchy (in thousands):

	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

	Fair Value Measurement at December 31, 2020 Using:			
	Level 1	Level 2	Level 3	Total
Assets:				
Cash equivalents (money market)	$ 20,938	$ —	$ —	$ 20,938
	$ 20,938	$ —	$ —	$ 20,938
Liabilities:				
Related party antidilution obligation	$ —	$ —	$ 4,247	$ 4,247
Series A preferred stock tranche obligation			303	303
	$ —	$ —	$ 4,550	$ 4,550

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 year ended December 31, 2021, and the period from June 22, 2020 (inception) to December 31, 2020.

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 12). 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 December 31, 2020 are as follows:

Expected term (years)	0.83
Risk-free rate	0.15%
Probability of finance event occurring	85%

Upon entering into the license agreement with Amgen in July 2020, the Company recorded a $20.4 million liability related to the Related Party Antidilution Obligation. On September 18, 2020, the Company completed the first closing pursuant to the Series A Convertible Preferred Stock Purchase Agreement which triggered the partial settlement of a 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. As such, on September 18, 2020, the Related Party Antidilution Obligation was partially settled through this issuance of $17.5 million of Series A preferred stock.

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 May 1, 2021 (valuation) and December 31, 2020 are as follows:

	May 1, 2021	December 31, 2020
Probability of meeting Series A milestones	95%	85%
Time until Series A milestones (years)	0.50	0.83
Risk-free rate	0.03%	0.08%
Expected value adjustment to Series A if second tranche milestones are not met	10%	10%

The Related Party Antidilution Obligation and Series A Preferred Stock Tranche Obligation were settled during the year ended December 31, 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
Beginning balance at June 22, 2020 (inception)	$ —	$ —	$ —
Issuance of related party antidilution obligation and Series A preferred stock tranche obligation	20,423	279	20,702
Change in fair value	1,307	24	1,331
Issuance of Series A preferred shares in partial settlement of related party antidilution obligation	(17,483)		(17,483)
Ending balance at December 31, 2020	$ 4,247	$ 303	$ 4,550
Change in fair value through the settlement date	836	28	864
Reclassification of Series A preferred stock tranche obligation and related party antidilution obligation upon settlement	(5,083)	(331)	(5,414)
Ending balance at December 31, 2021	$ —	$ —	$ —

4. Prepaid Expenses and Other Current Assets

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

	December 31, 2021	Period from June 22, 2020 (Inception) to December 31, 2020
Research and development	$ 5,597	$ 1,075
Other	466	70
Total	$ 6,063	$ 1,145

5. Accrued Expenses and Other Current Liabilities

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

	December 31, 2021	Period from June 22, 2020 (Inception) to December 31, 2020
Research and development	$ 1,422	$ 292
Payroll and employee related	2,017	512
Professional fees	933	68
Deferred IPO	543	—
Other	116	16
Total	$ 5,031	$ 888

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.

Under the 2020 Plan, the Company authorized 1,499,040 shares of its common stock for issuance upon exercise of options granted under the 2020 Plan as of December 31, 2020. On June 4, 2021, the Company amended the 2020 Plan to increase the aggregate number of shares of the Company's common stock reserved for issuance pursuant to the 2020 Plan by 624,600 shares, from 1,499,040 shares to a new total of 2,123,640 shares, and increased the aggregate number of shares of the

Company's common stock that may be issued pursuant to the exercise of incentive stock options by 1,873,800 shares, from 4,497,122 shares to a new total of 6,370,922 shares. On August 12, 2021, the Company amended the 2020 Plan to increase the aggregate number of shares of the Company's common stock reserve for issuance pursuant to the 2020 Plan by 1,262,080 shares to a new total of 3,385,720 shares.

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.

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.

As of December 31, 2021, no 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 year ended December 31, 2021 related to the 2021 ESPP.

Service-Based Stock Options

The Company issues stock options to directors, employees, and consultants under the 2020 Plan. Options granted by the Company vest over periods of 36-48 months, subject in each case to the individual's continued service through the applicable vesting date. Options vest either (i) 25% at the one-year anniversary followed by 36 equal monthly installments beginning one month after the one-year anniversary of the vesting start date, (ii) 48 monthly installments beginning one month after the vesting start date, or (iii) 36 equal monthly installments beginning one month after the vesting start date. Options generally expire 10 years after the date of the grant.

The following table summarizes the activity of the Company's options to purchase common stock for the year ended December 31, 2021:

	Number of Shares	Weighted-Average Grant Date Fair Value	Weighted-Average Exercise Price Per Share	Weighted-Average Remaining Contractual Term (in years)	Aggregate Intrinsic Value (in thousands)
Outstanding as of December 31, 2020	951,848	$ 2.72	$ 1.89	9.88	$ 1,557
Granted	2,095,899	4.23	5.91		
Exercised	(2,004)	2.73	1.89		
Forfeited	(167,307)	3.07	3.70		
Expired	—	—	—		
Outstanding as of December 31, 2021	2,878,436	$ 3.80	$ 4.71	9.38	$ 20,380
Vested and exercisable as of December 31, 2020	2,503	$ 2.72	$ 1.89	9.88	$ 4
Vested and exercisable as of December 31, 2021	397,032	$ 3.02	$ 2.77	9.04	$ 3,580
Vested and expected to vest as of December 31, 2020	951,848	$ 2.72	$ 1.89	9.88	$ 1,557
Vested and expected to vest as of December 31, 2021	2,878,436	$ 3.80	$ 4.71	9.38	$ 20,380

No options were exercised for the period June 22, 2020 (inception) to December 31, 2020. The aggregate intrinsic value of options exercised was $20 thousand for the year ended December 31, 2021.

The total fair value of options vested was approximately $1.2 million and $7 thousand during the year ended December 31, 2021, and the period from June 22, 2020 (inception) to December 31, 2020, respectively.

Stock Option Valuation

The following assumptions on a weighted-average basis were used to determine the fair value of stock options for the following periods:

	December 31, 2021	December 31, 2020
Weighted-average risk-free interest rate	1.0%	0.5%
Weighted-average expected term (in years)	6.0	5.9
Expected volatility	72.7% - 80.2%	80.4% - 81.0%
Expected dividend yield	0.0%	0.0%
Fair value of common stock	$ 3.53 - $11.79	$ 3.53
Weighted-average fair value	$ 4.23	$ 2.72

Performance-Based Stock Options

During the period from June 22, 2020 (inception) to December 31, 2020, the Company granted performance-based stock options to purchase 229,019 shares of common stock. The performance-based options commence vesting upon the Company completing the second tranche of its Series A convertible preferred stock financing and then vest over 48 equal monthly installments. The Company completed the second tranche of its Series A convertible preferred stock financing in May 2021.

The following table summarizes the activity of the Company's performance-based options to purchase common stock for the year ended December 31, 2021:

	Number of Shares	Weighted-Average Grant Date Fair Value	Weighted-Average Exercise Price Per Share	Weighted-Average Remaining Contractual Term (in years)	Aggregate Intrinsic Value (in thousands)
Outstanding as of December 31, 2020	229,019	$ 2.76	$ 1.89	9.88	$ 375
Granted	—	—	—		
Exercised	(18,390)	2.76	1.89		
Forfeited	—	—	—		
Expired	—	—	—		
Outstanding as of December 31, 2021	210,629	$ 2.76	$ 1.89	8.88	$ 2,085
Vested and exercisable as of December 31, 2020	—	$ 2.76	$ —		
Vested and exercisable as of December 31, 2021	19,780	$ 2.76	$ 1.89	8.88	$ 196
Vested and expected to vest as of December 31, 2020	229,019	$ 2.76	$ 1.89	9.88	$ 375
Vested and expected to vest as of December 31, 2021	210,629	$ 2.76	$ 1.89	8.88	$ 2,085

No options were exercised for the period June 22, 2020 (inception) to December 31, 2020. The aggregate intrinsic value of options exercised was $0.2 million for the year ended December 31, 2021.

No options vested during the period from June 22, 2020 (inception) to December 31, 2020. The total fair value of options vested during the year ended December 31, 2021 was approximately $105 thousand.

The fair value for performance options granted under the stock option plan are determined at the date of grant using the Black-Scholes option-pricing model, and the following assumptions were used for grants:

	December 31, 2020
Weighted-average risk-free interest rate	0.5%
Expected term (in years)	5.9
Expected volatility	81.0%
Expected dividend yield	0.0%
Fair value of common stock	$ 3.53
Weighted-average fair value	$ 2.76

Restricted Stock

The following table summarizes the activity of the Company's restricted stock:

	December 31, 2021
Outstanding as of beginning of period	306,503
Granted	—
Forfeited/cancelled	(44,323)
Outstanding as of end of period	262,180
Vested during period	75,871
Outstanding unvested shares, expected to vest	141,610
Remaining weighted-average vesting period for unvested shares	2.33 years

In July 2020, the Company granted 306,503 restricted shares that vest in 48 equal monthly installments commencing on the one-month anniversary of the vesting commencement date. Shares of restricted common stock granted to employees and directors are not deemed, for accounting purposes, to be outstanding until those shares have vested. For a period of up to 120 days from a grantee ceasing to provide services to the Company, the Company has an irrevocable option to repurchase unvested restricted shares at the lower of (i) the purchase price per share ($0.0003) or (ii) the fair market value per share as of the date of repurchase. In July 2021 and November 2021, the Company exercised its option to repurchase 21,786 and 22,537 unvested restricted shares, respectively, at their original purchase price after the grantee ceased providing services. The compensation

expense relating to the remaining 14,273 and 13,522 restricted shares of the grantee, respectively, that were not purchased by the Company was not material.

The fair value of the restricted shares granted was equal to the fair value of the Company's common stock on the date of grant. The fair value of the Company's common stock was determined using an option pricing method which utilized a market approach.

Stock-Based Compensation Expense

The Company recorded stock-based compensation of $2.1 million, and $262 thousand in the year ended December 31, 2021, and the period from June 22, 2020 (inception) to December 31, 2020, respectively. Stock-based compensation expense was classified as follows in the consolidated statements of operations and comprehensive loss (in thousands):

	December 31, 2021	Period from June 22, 2020 (Inception) to December 31, 2020
Research and development	$ 797	$ 93
General and administrative	1,288	169
Total stock-based compensation	$ 2,085	$ 262

As of December 31, 2021 and December 31, 2020, respectively, there is approximately $9.2 million and $2.5 million of unrecognized stock-based compensation expense related to service-based options to purchase common stock under the 2020 Plan, which is expected to vest over a weighted-average period of 3.35 years and 3.62 years.

As of December 31, 2021 and December 31, 2020, respectively, there is approximately $0.3 million and $0.6 million of unrecognized stock-based compensation expense related to performance-based options to purchase common stock under the 2020 Plan, which is expected to vest over a weighted-average period of 3.32 years and 4.32 years.

As of December 31, 2021 and December 31, 2020, respectively, there is approximately $0.3 million and $0.6 million of unrecognized stock-based compensation expense related to restricted stock under the 2020 Plan, which is expected to vest over a weighted-average period of 2.33 years and 3.33 years.

7. Preferred Stock

Simple Agreement for Future Equity

In July 2020, the Company entered into a Simple Agreement for Future Equity ("SAFE") with Atlas Venture Fund XII, L.P., a related party (see Note 13), receiving $5.0 million of aggregate gross proceeds in exchange for the investor's right to participate in a future equity financing. The SAFE contained a number of conversion and redemption provisions, including settlement upon liquidity or dissolution events. On September 18, 2020, Atlas Venture Fund XII, L.P. exercised its right to convert the SAFE in connection with the Company's Series A equity financing and exchanged the SAFE for an aggregate of 1,963,093 shares of Series A convertible preferred stock, with a fair value of $5.0 million at issuance. The fair value of the Series A convertible preferred stock issued in exchange for the SAFE was offset by $46 thousand related to the Series A Preferred Stock Tranche Obligation, as discussed below.

Convertible Preferred Stock

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 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 December 31, 2021 and December 31, 2020.

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

Dividends

Holders of the Convertible Preferred Stock are entitled to receive non-cumulative dividends when, as and if declared by the Board at a rate of 8% of the Original Issue Price (as defined below) per share (the “Dividend Rate”), subject to adjustment. Holders of Convertible Preferred Stock shall participate in any dividends payable to common stockholders on an as-converted basis. The Company has not, and has no plans to, declare dividends on any class of preferred or common stock.

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 and December 31, 2020, each share of each series of Convertible Preferred Stock was convertible into shares of common stock on a one-for-one basis.

The Series A preferred stock is convertible into 10,285,077 and 6,745,679 and shares of common stock as of December 31, 2021 and December 31, 2020, respectively. The Series B preferred stock is convertible into 9,251,793 shares of common stock as of December 31, 2021.

Liquidation

In the event of any liquidation, dissolution, or winding-up of the Company, which would include the sale of the Company, the holders of the then-outstanding Convertible Preferred Stock would be entitled to receive, in preferential payment to any distributions to the common stockholders, an amount equal to the greater of (i) the respective Original Issue Price of each series of the Convertible Preferred Stock, plus dividends declared but unpaid or (ii) the amount payable with respect to such share if it was converted to common stock immediately prior to settlement. In the event that there are additional assets to be distributed, the holders of the Convertible Preferred Stock will share in the distribution along with common stockholders as if the shares of Convertible Preferred Stock had converted to common stock immediately prior to the distribution.

Voting

The holders of Convertible Preferred Stock are entitled to vote, together with the holders of common stock, on matters submitted to stockholders for a vote. The holders of Convertible Preferred Stock are entitled to the number of votes equal to the number of shares of common stock into which each share of Convertible Preferred Stock could convert on the record date for determination of stockholders entitled to vote.

8. Common Stock

The voting, dividend, and liquidation rights of the holders of the Company's common stock are subject to and qualified by the rights, powers, and preferences of the holders of the Convertible Preferred 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, if any, subject to the respective preferential dividend rights of the Convertible Preferred Stock. Through December 31, 2021 and December 31, 2020, no dividends have been declared or paid.

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.

	Year Ended December 31, 2021	Period from June 22, 2020 (Inception) to December 31, 2020
Common stock options	3,089,065	1,180,867
Shares available for issuance under the 2020 Plan	276,261	318,173
Shares available for issuance under the 2021 Plan	3,145,281	—
Shares available for issuance under the 2021 ESPP	286,127	—
Series A convertible preferred stock outstanding	10,285,087	6,745,679
Series B convertible preferred stock outstanding	9,251,793	—
Total common stock reserved for future issuance	26,333,614	8,244,719

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):

	Year Ended December 31, 2021	Period from June 22, 2020 (Inception) to December 31, 2020
Numerator:		
Net loss attributable to common stockholders	$ (43,283)	$ (28,546)
Denominator:		
Weighted-average common shares outstanding, basic and diluted	1,531,686	1,349,702
Net loss per share attributable to common stockholders, basic and diluted	$ (28.26)	$ (21.15)

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:

	Year Ended December 31, 2021	Period from June 22, 2020 (Inception) to December 31, 2020
Series A convertible preferred stock	10,285,077	6,745,679
Series B convertible preferred stock	9,251,793	—
Related party antidilution obligation	—	707,880
Options to purchase common stock – service based	2,878,436	951,848
Options to purchase common stock – performance based	210,629	229,019
Unvested restricted common stock	141,610	261,807
Total	22,767,545	8,896,233

10. Income Taxes

The Company's income tax provision was computed based on the federal statutory rate and the average state statutory rates, net of the related federal benefit. The Company did not record a federal or state income tax provision or benefit during the year ended December 31, 2021 and the period from June 22, 2020 (inception) to December 31, 2020, respectively due to the pre-tax net losses incurred. In addition, the Company has recorded a full valuation allowance against its net deferred tax assets at December 31, 2021, and December 31, 2020.

The Company's effective income tax rate differs from the statutory federal income tax rate as follows for the year ended December 31, 2021 and the period from June 22, 2020 (inception) to December 31, 2020:

	December 31, 2021	Period from June 22, 2020 (Inception) to December 31, 2020
Statutory U.S. federal rate	21.00%	21.00%
State income taxes (NoFB)	6.06%	6.24%
Other permanent differences	(0.59)%	(0.21)%
Research and development credits	3.54%	0.22%
Valuation allowance	(30.01)%	(27.25)%
Effective Tax Rate	—%	—%

Deferred income taxes reflect the net tax effects of loss and credit carryforwards and temporary differences between the carrying amounts of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes. The Company's deferred income tax assets and liabilities as of December 31, 2021 and 2020 are comprised of the following (in thousands):

	December 31, 2021	December 31, 2020
Deferred tax assets:		
Net operating loss carryforwards	$ 12,420	$ 1,432
Research and development credits	1,592	62
Intangible assets	5,845	6,032
Start-up costs	92	99
Accruals and other	1,099	155
Total deferred tax assets	21,048	7,780
Less valuation allowance	(20,775)	(7,780)
Total deferred tax assets, net of valuation allowance	273	—
Deferred tax liabilities:		
Depreciation	(7)	—
Right-of-use asset	(266)	—
Net deferred tax assets (liabilities)	$ —	$ —

In assessing the realization of deferred tax assets, management considers whether it is more likely than not that some portion or all of the deferred tax assets will not be realized. The ultimate realization of deferred tax assets is dependent upon the generation of future taxable income during the periods in which those temporary differences become deductible. Management considers the scheduled reversal of deferred tax liabilities, projected future taxable income and tax planning strategies in making this assessment. Based on the level of historical operating results and the uncertainty of the economic conditions, the Company has recorded a valuation allowance of $20.8 million and $7.8 million at December 31, 2021 and December 31, 2020, respectively.

At December 31, 2021, the Company had federal net operating losses ("NOLs") of approximately $45.6 million and state NOLs of $45.0 million. At December 31, 2020, the Company had federal net operating losses ("NOLs") of approximately $5.3 million and state NOLs of $5.2 million. As a result of the Tax Act, for U.S. income tax purposes, NOLs generated for tax years beginning after December 31, 2017 carry forward indefinitely and can be used to offset taxable income. The total federal NOLs of $45.6 million as of December 31, 2021 will not expire. The state NOL carryover of $45.0 million will begin to expire in 2035.

Pursuant of Internal Revenue Code ("IRC") Sections 382 and 383, annual use of the Company's net operating loss and research and development credit carryforwards may be limited in the event a cumulative change in ownership of more than 50% occurs within a three-year period. The Company has not completed an ownership change analysis pursuant to IRC Section 382. If ownership changes within the meaning of IRC Section 382 are identified as having occurred, the amount of remaining tax attribute carryforwards available to offset future taxable income and income tax expense in future years may be significantly restricted or eliminated. Further, the Company's deferred tax assets associated with such tax attributes could be significantly reduced upon realization of an ownership change within the meaning of IRC Section 382 that has occurred or may occur in the future. Any adjustment to the Company's tax attributes as a result of an ownership change will result in a corresponding decrease to the valuation allowance recorded against the Company's deferred tax assets. As of December 31, 2021, the Company also has federal and state tax research and development credit carryforwards of approximately $1.2 million and $0.5 million, respectively, to offset future income taxes, which will begin to expire in 2035. As of December 31, 2020, the Company had no federal tax research and development credit carryforwards, and had state tax research and development credit carryforwards of approximately $78 thousand to offset future income taxes.

The Company's valuation allowance increased by $13.0 million and $7.8 million during the year ended December 31, 2021 and the period from June 22, 2020 (inception) to December 31, 2020, respectively. This increase is due primarily to NOL carryforwards and the generation of an intangible asset.

The Company has not incurred any material interest or penalties as of the current reporting date with respect to income tax matters. The Company does not expect that there will be unrecognized tax benefits of a significant nature that will increase or decrease within 12 months of the reporting date. The Company is subject to U.S. Federal income tax as well as income tax in Massachusetts and Maryland. Carryforward attributes that were generated in years where the statute of limitations is closed may still be adjusted upon examination by the Internal Revenue Service or other respective tax authority.

The unrecognized tax benefit amounts are not reflected in the determination of the Company's deferred tax assets. If recognized, none of these amounts would affect the Company's effective tax rate, since it would be offset by an equal corresponding adjustment in the deferred tax asset valuation allowance. The Company assesses the uncertainty in its income tax positions to determine whether a tax position of the Company is more likely than not to be sustained upon examination, including resolution of any related appeals of litigation processes, based on the technical merits of the position. For tax positions meeting the more-likely-than-not threshold, the tax amount recognized in the financial statements is reduced by the largest benefit that has a greater than 50% likelihood of being realized upon the ultimate settlement with the relevant taxing authority. As of December 31, 2021, the Company had not recorded any reserves for uncertain tax positions or related interest and penalties.

The Company files income tax returns as prescribed by the tax laws of the jurisdictions in which it operates. In the normal course of business, the Company is subject to examination by federal and state jurisdictions, where applicable. As of December 31, 2021, there were no pending tax examinations. No federal or state tax audits are currently in process.

11. 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 13). 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 determination of the lease term.

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.

The components of lease expense are as follows:

	Year Ended December 31, 2021	Period from June 22, 2020 (Inception) to December 31, 2020
Operating lease cost	$ 339	$ —
Short term lease cost	123	23
Variable lease cost	19	—
Finance lease cost:		
Amortization of right-to-use assets	13	—
Interest on lease liabilities	3	—
Total finance lease cost	16	$ —

Supplemental cash flow information related to leases are as follows:

	Year Ended December 31, 2021	Period from June 22, 2020 (Inception) to December 31, 2020
Cash paid for amounts included in the measurement of lease liabilities		
Operating cash flows from operating leases	$ (310)	$ —
Operating cash flows from finance leases	$ (3)	$ —
Financing cash flows from finance leases	$ (19)	$ —

At December 31, 2021, the weighted-average remaining lease terms related to the finance and operating leases are 1.5 years and 1.0 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 5.21% for the finance leases and 6.34% for the operating leases.

Future minimum lease payments due under the Company's operating and finance lease liabilities as of December 31, 2021 are as follows:

Years ended December 31, 2021	Operating Leases	Financing Leases
2022	855	45
2023	41	24
Total lease payments	896	69
Less: imputed interest	(25)	(3)
Total future minimum lease payments	$ 871	$ 66

12. 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 is required to reimburse Amgen for amounts it paid to its contract manufacturers on the Company's behalf of $3.2 million through December 31, 2021. 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 December 31, 2021, Amgen owned approximately 15.08% of the Company's outstanding shares of capital stock.

The Company determined that the Amgen Agreement represented an asset acquisition of IPR&D assets with no alternative future use and recognized the aggregate acquisition cost as related party acquired in-process research and development expense in the consolidated statement of operations and comprehensive loss. The acquisition did not qualify as a business combination as the acquisition did not include both an input and substantive processes, including an assembled workforce, that together contribute to the ability to create outputs. For the period from June 22, 2020 (inception) to December 31, 2020, the Company recognized $20.9 million of related party acquired in-process research and development expense in connection with the consideration due under the Amgen Agreement. The $20.9 million consisted of (i) $20.4 million initial recognition of the Related Party Antidilution Obligation that obligates the Company to issue shares of the Series A convertible preferred stock equal to 25% until the Company has raised $45.0 million in net cash proceeds from equity financings and (ii) the upfront cash consideration for the license arrangement of $0.5 million. The Company did not incur IPR&D expense in connection with the Amgen Agreement during the year ended December 31, 2021.

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 year ended December 31, 2021, and the period from June 22, 2020 (inception) to December 31, 2020, the Company recognized $2.4 million and $0.8 million, respectively, of expense in connection with goods provided by Amgen.

13. 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 $0.3 million for the year ended December 31, 2021, and $0.1 million for the period from June 22, 2020 (inception) to December 31, 2020. The lease payments are included in general and administrative expenses for office space and research and development expenses for lab space in the 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 December 31, 2021. 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 consolidated balance sheet as of December 31, 2021. In addition, as of December 31, 2020, the Company recognized $9 thousand in accounts payable and as of December 31, 2021, the Company recognized $84 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. In June 2020, the Company also issued SAFE to Atlas Venture Fund XII, L.P which was exchanged in September 2020 for an aggregate of 1,963,093 shares of Series A convertible preferred stock, with a fair value of $5.0 million at issuance. (see Note 7)

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, 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 12).

Expenses to reimburse Amgen's contract manufacturers incurred by the Company were $2.4 million and $0.8 million during the year ended December 31, 2021, and in the period from June 22, 2020 (inception) to December 31, 2020, respectively. These costs are included in research and development expenses in the consolidated statements of operations and comprehensive loss.

As of December 31, 2021, $0.2 million was due to Amgen by the Company, which was included in accrued expenses and other current liabilities in the Company's consolidated balance sheet as of December 31, 2021. As of December 31, 2020, $0.4 million was due to Amgen by the Company and was included in accounts payable in the consolidated balance sheet.

The Company did not have any amounts in connection with prepaid reservation fees as of December 31, 2021. As of December 31, 2020, $0.4 million was associated with a prepaid reservation fee related to services due to the Company by Amgen. The amounts was included in prepaid expenses and other current assets in the Company's consolidated balance sheet as of December 31, 2020.

14. Commitments and Contingencies

License Agreement

The Company entered into a license agreement with Amgen (see Note 12).

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 consolidated balance sheet.

Purchase Commitment

In November 2021, the Company entered into a statement of work with FUJIFILM for $3.8 million under our existing master services agreement for the manufacturing of VGL101. If the Company terminates the statement of work 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 statement of work. As of December 31, 2021, no significant work had begun. The statement of work 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. During the year ended December 31, 2021, and the period from June 22, 2020 (inception) to December 31, 2020, the Company was not a party to any pending material litigation or other material legal proceedings.

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.

15. Subsequent Events

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 amended and restated 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.

EXHIBIT INDEX

Exhibit Number	Description
3.1	Third Amended and Restated Certificate of Incorporation of the Registrant (incorporated by reference to Exhibit 3.2 of the Registrant's Registration Statement on Form S-1/A (File No. 333-261230) filed on January 3, 2022).
3.2	Amended and Restated Bylaws of the Registrant (incorporated by reference to Exhibit 3.3 of the Registrant's Registration Statement on Form S-1/A (File No. 333-261230) filed on January 3, 2022).
4.1	Amended and Restated Investors' Rights Agreement among the Registrant and certain of its stockholders, effective as of August 13, 2021 (incorporated by reference to Exhibit 4.2 of the Registrant's Registration Statement on Form S-1 (File No. 333-261230) filed on November 19, 2021).
4.2	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).
4.3*	Description of Securities
10.1#	2020 Equity Incentive Plan and form of award agreement thereunder (incorporated by reference to Exhibit 10.1 of the Registrant's Registration Statement on Form S-1 (File No. 333-261230) filed on November 19, 2021).
10.2#	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).
10.3#	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).
10.4#	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).
10.5#	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).
10.6#	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).
10.7#	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).
10.8#	Transition Agreement, by and between the Registrant and Richard A. Fisher, dated November 17, 2021 (incorporated by reference to Exhibit 10.8 of the Registrant's Registration Statement on Form S-1 (File No. 333-261230) filed on November 19, 2021).
10.9†	Exclusive License Agreement, by and between the Registrant and Amgen Inc., dated July 9, 2020 (incorporated by reference to Exhibit 10.9 of the Registrant's Registration Statement on Form S-1 (File No. 333-261230) filed on November 19, 2021).
10.10†	Master Services Agreement, by and between the Registrant and Fujifilm Diosynth Biotechnologies UK Limited, Fujifilm Diosynth Biotechnologies Texas, LLC, Fujifilm Diosynth Biotechnologies U.S.A., Inc, and Fujifilm Diosynth Biotechnologies Denmark APS, dated February 24, 2021 (incorporated by reference to Exhibit 10.10 of the Registrant's Registration Statement on Form S-1 (File No. 333-261230) filed on November 19, 2021).
10.11	Lease, by and between 100 Forge Holding LLC and the Registrant, dated as of September 20, 2021 (incorporated by reference to Exhibit 10.11 of the Registrant's Registration Statement on Form S-1 (File No. 333-261230) filed on November 19, 2021).
10.12	Service Agreement and Space-Specific Amendment, by and between CIC Innovation Communities, LLC and the Registrant, dated as of October 13, 2021 (incorporated by reference to Exhibit 10.12 of the Registrant's Registration Statement on Form S-1 (File No. 333-261230) filed on November 19, 2021).

21.1	Subsidiaries of the Registrant (incorporated by reference to Exhibit 21.1 of the Registrant's Registration Statement on Form S-1 (File No. 333-261230) filed on November 19, 2021).
23.1*	Consent of PricewaterhouseCoopers LLP, independent registered public accounting firm.
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.

* Filed herewith.

** The certifications furnished in Exhibit 32.1 and Exhibit 32.2 hereto are deemed to accompany this Annual Report on Form 10-K 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.

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

# Indicates management contract or compensatory plan, contract or arrangement.

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: March 25, 2022

By: /s/ Ivana Magovčević-Liebisch
Ivana Magovčević-Liebisch, PhD, JD
President and Chief Executive Officer
(Principal Executive Officer)

POWER OF ATTORNEY AND SIGNATURES

Each person whose individual signature appears below hereby authorizes and appoints Ivana Magovčević-Liebisch, PhD, JD and Jennifer Ziolkowski, and each of them, with full power of substitution and resubstitution and full power to act without the other, as his or her true and lawful attorney-in-fact and agent to act in his or her name, place and stead and to execute in the name and on behalf of each person, individually and in each capacity stated below, and to file any and all amendments to this Annual Report on Form 10-K and to file the same, with all exhibits thereto, and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing, ratifying and confirming all that said attorneys-in-fact and agents or any of them or their or his or her substitute or substitutes may lawfully do or cause to be done by virtue thereof.

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, this Report has been signed below by the following persons on behalf of the Registrant in the capacities and on the dates indicated.

Name	Title	Date
/s/ Ivana Magovčević-Liebisch Ivana Magočević-Liebisch, PhD, JD	President and Chief Executive Officer *(Principal Executive Officer)*	March 25, 2022
/s/ Jennifer Ziolkowski Jennifer Ziolkowski, CPA	Chief Financial Officer *(Principal Financial Officer and Principal Accounting Officer)*	March 25, 2022
/s/ Bruce Booth Bruce Booth, D.Phil	Director, Chairperson	March 25, 2022
/s/ Cheryl Renee Blanchard Cheryl Renee Blanchard, PhD	Director	March 25, 2022
/s/ Shaan Gandhi Shaan Gandhi, MD, PhD, MBA	Director	March 25, 2022
/s/ Gerhard Koenig Gerhard Koenig, PhD	Director	March 25, 2022
/s/ Clay Bernardin Thorp Clay Bernardin Thorp	Director	March 25, 2022
/s/ Stefan Vitorovic Stefan Vitorovic, MS, MBA	Director	March 25, 2022

Exhibit 4.3

DESCRIPTION OF THE REGISTRANT'S SECURITIES REGISTERED PURSUANT TO SECTION 12 OF THE SECURITIES EXCHANGE ACT OF 1934

The summary of the general terms and provisions of the registered securities of Vigil Neuroscience, Inc. (the "Company," "we," "us," and "our") set forth below does not purport to be complete. It is subject to and qualified in its entirety by reference to our Third Amended and Restated Certificate of Incorporation ("certificate of incorporation") and our Amended and Restated Bylaws ("bylaws"), each of which are incorporated by reference as an exhibit to the Annual Report on Form 10-K of which this Exhibit 4.3 is a part, and by applicable law. We encourage you to read our certificate of incorporation, our bylaws and the applicable provisions of the Delaware General Corporation Law for additional information.

General

Our authorized capital stock consists of 150,000,000 shares of common stock, par value $0.0001 per share, and 10,000,000 shares of preferred stock, par value $0.0001 per share, all of which shares of preferred stock are undesignated.

Common Stock

Only our common stock is registered under Section 12 of the Securities Exchange Act of 1934, as amended (the "Exchange Act").

The holders of our common stock are entitled to one vote for each share held on all matters submitted to a vote of the stockholders. The holders of our common stock do not have any cumulative voting rights. Holders of our common stock are entitled to receive ratably any dividends declared by our board of directors out of funds legally available for that purpose, subject to any preferential dividend rights of any outstanding preferred stock. Our common stock has no preemptive rights, conversion rights or other subscription rights or redemption or sinking fund provisions.

In the event of our liquidation, dissolution or winding up, holders of our common stock will be entitled to share ratably in all assets remaining after payment of all debts and other liabilities and any liquidation preference of any outstanding preferred stock. All outstanding shares are validly issued, fully paid and non-assessable.

Undesignated Preferred Stock

Our board of directors has the authority, without further action by our stockholders, to issue up to 10,000,000 shares of preferred stock in one or more series and to fix the rights, preferences, privileges and restrictions thereof. These rights, preferences and privileges could include dividend rights, conversion rights, voting rights, terms of redemption, liquidation preferences, sinking fund terms and the number of shares constituting, or the designation of, such series, any or all of which may be greater than the rights of common stock. The issuance of our preferred stock could adversely affect the voting power of holders of common stock and the likelihood that such holders will receive dividend payments and payments upon our liquidation. In addition, the issuance of preferred stock could have the effect of delaying, deferring or preventing a change in control of our company or other corporate action. The purpose of authorizing our board of directors to issue preferred stock in one or more series and determine the number of shares in the series and its rights and preferences is to eliminate delays associated with a stockholder vote on specific issuances. In addition, the issuance of preferred stock could have the effect of delaying, deferring or preventing a change in control of our company or other corporate action.

The existence of authorized but unissued shares of preferred stock may enable our board of directors to discourage an attempt to obtain control of us by means of a merger, tender offer, proxy contest or otherwise. For example, if in the due exercise of its fiduciary obligations, our board of directors were to determine that a takeover proposal is not in the best interests of our stockholders, our board of directors could cause shares of preferred stock to be issued without stockholder approval in one or more private offerings or other transactions that might dilute the voting or other rights of the proposed acquirer or insurgent stockholder or stockholder group. In this regard, our Certificate of Incorporation grants our board of directors broad power to establish the rights and preferences of authorized and unissued shares of preferred stock. The issuance of shares of preferred stock could decrease the amount of earnings and assets available for distribution to holders of shares of common stock. The issuance may also adversely affect the rights and powers, including voting rights, of these holders and may have the effect of delaying, deterring or preventing a change in control of us.

No shares of preferred stock are outstanding as of the date of our Annual Report on Form 10-K with which this Exhibit 4.3 is filed as an exhibit.

Registration Rights

Certain of our stockholders are entitled to rights with respect to the registration of these securities under the Securities Act. These rights are provided under the terms of the Amended and Restated Investors' Rights Agreement between us and the holders of our preferred stock dated as of August 13, 2021 (the "investors' rights agreement"). The investors' rights agreement includes demand registration rights, short-form registration rights and piggyback registration rights. All fees, costs and expenses of underwritten registrations under this agreement will be borne by us and all selling expenses, including underwriting discounts and selling commissions, will be borne by the holders of the shares being registered.

Demand Registration Rights

Beginning six months after our initial public offering, certain of our stockholders are entitled to demand registration rights. Under the terms of the investors' rights agreement, we will be required, upon the written request of a majority of holders of the registerable securities then outstanding that would result in an aggregate offering price of at least $10 million, to file a registration statement on Form S-1 with respect to at least 40% of the registrable securities then outstanding and to use commercially reasonable efforts to effect the registration of all or a portion of these shares for public resale.

Short-Form Registration Rights

Pursuant to the investors' rights agreement, if we are eligible to file a registration statement on Form S-3, upon the written request of at least 20% in interest of these holders to sell registrable securities at an aggregate price of at least $3 million, we will be required to use commercially reasonable efforts to effect a registration of such shares. We are required to effect only two registrations in any twelve month period pursuant to this provision of the investor rights agreement.

Piggyback Registration Rights

Pursuant to our investors' rights agreement, if we register any of our securities either for our own account or for the account of other security holders, the holders of these shares are entitled to include their shares in the registration. Subject to certain exceptions contained in the investors' rights agreement, we and the underwriters may limit the number of shares included in the underwritten offering to the number of shares which we and the underwriters determine in our sole discretion will not jeopardize the success of the offering.

Indemnification

Our investors' rights agreement contains customary cross-indemnification provisions, under which we are obligated to indemnify holders of registrable securities in the event of material misstatements or omissions in the registration statement attributable to us, and they are obligated to indemnify us for material misstatements or omissions attributable to them.

Expiration of Registration Rights

The demand registration rights and short-form registration rights granted under the investor rights agreement will terminate on the fifth anniversary of the completion of our initial public offering.

Anti-Takeover Effects of our Certificate of Incorporation and Bylaws and Delaware Law

Our certificate of incorporation and bylaws include a number of provisions that may have the effect of delaying, deferring or preventing another party from acquiring control of us and encouraging persons considering unsolicited tender offers or other unilateral takeover proposals to negotiate with our board of directors rather than pursue non-negotiated takeover attempts. These provisions include the items described below.

Board Composition and Filling Vacancies

Our certificate of incorporation will provide for the division of our board of directors into three classes serving staggered three-year terms, with one class being elected each year. Our certificate of incorporation also will provide that directors may be removed only for cause and then only by the affirmative vote of the holders of two-thirds or more of the shares then entitled to vote at an election of directors. Furthermore, any vacancy on our board of directors, however occurring, including a vacancy resulting from an increase in the size of our board, may only be filled by the affirmative vote of a majority of our directors then in office even if less than a quorum. The classification of directors, together with the limitations on removal of directors and treatment of vacancies, has the effect of making it more difficult for stockholders to change the composition of our board of directors.

No Written Consent of Stockholders

Our certificate of incorporation provides that all stockholder actions are required to be taken by a vote of the stockholders at an annual or special meeting, and that stockholders may not take any action by written consent in lieu of a meeting. This limit may lengthen the amount of time required to take stockholder actions and would prevent the amendment of our bylaws or removal of directors by our stockholders without holding a meeting of stockholders.

Meetings of Stockholders

Our certificate of incorporation and bylaws provide that only a majority of the members of our board of directors then in office may call special meetings of stockholders and only those matters set forth in the notice of the special meeting may be considered or acted upon at a special meeting of stockholders. Our bylaws limit the business that may be conducted at an annual meeting of stockholders to those matters properly brought before the meeting.

Advance Notice Requirements

Our bylaws establish advance notice procedures with regard to stockholder proposals relating to the nomination of candidates for election as directors or new business to be brought before meetings of our stockholders. These procedures provide that notice of stockholder proposals must be timely given in writing to our corporate secretary prior to the meeting at which the action is to be taken. Generally, to be timely, notice must be received at our principal executive offices not less than 90 days nor more than 120 days prior to the first anniversary date of the annual meeting for the preceding year. Our bylaws specify the requirements as to form and content of all stockholders' notices. These requirements may preclude stockholders from bringing matters before the stockholders at an annual or special meeting.

Amendment to Certificate of Incorporation and Bylaws

Any amendment of our certificate of incorporation must first be approved by a majority of our board of directors, and if required by law or our certificate of incorporation, must thereafter be approved by a majority of the outstanding shares entitled to vote on the amendment and a majority of the outstanding shares of each class entitled to vote thereon as a class, except that the amendment of the provisions relating to stockholder action, board composition, and limitation of liability must be approved by not less than two-thirds of the outstanding shares entitled to vote on the amendment, and not less than two-thirds of the outstanding shares of each class entitled to vote thereon as a class. Our bylaws may be amended by the affirmative vote of a majority of the directors then in office, subject to any limitations set forth in the bylaws; and may also be amended by the affirmative vote of a majority of the outstanding shares entitled to vote on the amendment, voting together as a single class, except that the amendment of the provisions relating to notice of stockholder business and nominations and special meetings must be approved by not less than two-thirds of the outstanding shares entitled to vote on the amendment, and not less than two-thirds of the outstanding shares of each class entitled to vote thereon as a class, or, if our board of directors recommends that the stockholders approve the amendment, by the affirmative vote of the majority of the outstanding shares entitled to vote on the amendment, in each case voting together as a single class.

Undesignated Preferred Stock

Our certificate of incorporation provides for 10,000,000 authorized shares of preferred stock. The existence of authorized but unissued shares of preferred stock may enable our board of directors to discourage an attempt to obtain control of us by means of a merger, tender offer, proxy contest or otherwise. For example, if in the due exercise of its fiduciary obligations, our board of directors were to determine that a takeover proposal is not in the best interests of our stockholders, our board of directors could cause shares of preferred stock to be issued without stockholder approval in one or more private offerings or other transactions that might dilute the voting or other rights of the proposed acquirer or insurgent stockholder or stockholder group. In this regard, our certificate of incorporation grants our board of directors broad power to establish the rights and preferences of authorized and unissued shares of preferred stock. The issuance of shares of preferred stock could decrease the amount of earnings and assets available for distribution to holders of shares of common stock. The issuance may also adversely affect the rights and powers, including voting rights, of these holders and may have the effect of delaying, deterring or preventing a change in control of us.

Choice of Forum

Our bylaws provide that, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware shall be the sole and exclusive forum for any state law claims for (1) any derivative action or proceeding brought on our behalf, (2) any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers, and employees to us or our stockholders, (3) any action asserting a claim arising pursuant to the Delaware General Corporation Law, our certificate of incorporation or our bylaws (including the interpretation, validity or enforceability thereof), or (4) any action asserting a claim that is governed by the

internal affairs doctrine; provided, however, that the this provision shall not apply to any causes of action arising under the Securities Act or Exchange Act. In addition, our bylaws 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, including all causes of action asserted against any defendants to such complaint. For the avoidance of doubt, this provision is intended to benefit and may be enforced by us, our officers and directors, the underwriters to any offering giving rise to such complaint, and any other professional entity whose profession gives authority to a statement made by that person or entity and who has prepared or certified any part of the documents underlying the offering. While the Delaware courts have determined that such choice of forum provisions are facially valid, a stockholder may nevertheless seek to bring a claim in a venue other than those designated in the exclusive forum provisions, and there can be no assurance that such provisions will be enforced by a court in those other jurisdictions. Any person or entity purchasing or otherwise acquiring any interest in our securities shall be deemed to have notice of and consented to these forum provisions. These forum provisions may impose additional costs on stockholders, may limit our stockholders' ability to bring a claim in a forum they find favorable, and the designated courts may reach different judgments or results than other courts.

Section 203 of the Delaware General Corporation Law

We are subject to the provisions of Section 203 of the Delaware General Corporation Law. In general, Section 203 prohibits a publicly held Delaware corporation from engaging in a "business combination" with an "interested stockholder" for a three-year period following the time that this stockholder becomes an interested stockholder, unless the business combination is approved in a prescribed manner. Under Section 203, a business combination between a corporation and an interested stockholder is prohibited unless it satisfies one of the following conditions:

- before the stockholder became interested, our board of directors approved either the business combination or the transaction which resulted in the stockholder becoming an interested stockholder;
- before the stockholder became interested, our board of directors approved either the business combination or the transaction which resulted in the stockholder becoming an interested stockholder;
- upon consummation of the transaction which resulted in the stockholder becoming an interested stockholder, the interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced, excluding for purposes of determining the voting stock outstanding, shares owned by persons who are directors and also officers, and employee stock plans, in some instances, but not the outstanding voting stock owned by the interested stockholder; or
- at or after the time the stockholder became interested, the business combination was approved by our board of directors and authorized at an annual or special meeting of the stockholders by the affirmative vote of at least two-thirds of the outstanding voting stock which is not owned by the interested stockholder.

Section 203 defines a business combination to include:

- any merger or consolidation involving the corporation and the interested stockholder;
- any sale, transfer, lease, pledge or other disposition involving the interested stockholder of 10% or more of the assets of the corporation;
- subject to exceptions, any transaction that results in the issuance or transfer by the corporation of any stock of the corporation to the interested stockholder;
- subject to exceptions, any transaction involving the corporation that has the effect of increasing the proportionate share of the stock of any class or series of the corporation beneficially owned by the interested stockholder; and
- the receipt by the interested stockholder of the benefit of any loans, advances, guarantees, pledges, or other financial benefits provided by or through the corporation.

In general, Section 203 defines an interested stockholder as any entity or person beneficially owning 15% or more of the outstanding voting stock of the corporation and any entity or person affiliated with or controlling or controlled by the entity or person.

Nasdaq Global Select Market Listing

Our common stock is listed on The Nasdaq Global Select Market under the symbol “VIGL”.

Transfer Agent and Registrar

The transfer agent and registrar for our common stock will be Computershare Trust Company, N.A. The transfer agent and registrar’s address is 250 Royall Street, Canton, Massachusetts 02021, and its telephone number is (800) 962-4284.

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Exhibit 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We hereby consent to the incorporation by reference in the Registration Statements on Form S-8 (No. 333-262083) of Vigil Neuroscience, Inc. of our report dated March 25, 2022 relating to the financial statements, which appears in this Form 10-K.

/s/ PricewaterhouseCoopers LLP
Boston, Massachusetts
March 25, 2022

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 annual report on Form 10-K 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: March 25, 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 annual report on Form 10-K 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 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: March 25, 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 Annual Report on Form 10-K of Vigil Neuroscience, Inc. (the "Company") for the year ended December 31, 2021 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: March 25, 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 Annual Report on Form 10-K of Vigil Neuroscience, Inc. (the "Company") for the year ended December 31, 2021 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: March 25, 2022

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

(Principal Financial Officer)