Vigil Neuroscience, Inc.

2024 Annual Report

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, 2024

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.)**
100 Forge Road, Suite 700 Watertown, MA	**02472**
(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. ☐

If securities are registered pursuant to Section 12(b) of the Act, indicate by check mark whether the financial statements of the registrant included in the filing reflect the correction of an error to previously issued financial statements. ☐

Indicate by check mark whether any of those error corrections are restatements that required a recovery analysis of incentive-based compensation received by any of the registrant's executive officers during the relevant recovery period pursuant to §240.10D-1(b). ☐

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

The aggregate market value of the voting and non-voting common equity held by non-affiliates of the Registrant was $106.1 million based on the closing price of the shares of common stock on The Nasdaq Global Select Market on June 28, 2024, the last business day of the registrant's most recently completed second quarter. In determining the market value of non-affiliate common stock, shares of the Registrant's common stock beneficially owned by officers, directors and affiliates have been excluded. This determination of affiliate status is not necessarily a conclusive determination for other purposes.

The number of shares of Registrant's Common Stock outstanding as of February 28, 2025 was 46,671,534.

DOCUMENTS INCORPORATED BY REFERENCE

The Registrant intends to file a definitive proxy statement pursuant to Regulation 14A relating to the 2025 Annual Meeting of Stockholders within 120 days of the end of the registrant's fiscal year ended December 31, 2024. Portions of such definitive proxy statement are incorporated by reference into Part III of this Annual Report on Form 10-K to the extent stated herein.

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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 and on acceptable terms, or at all, could force us to delay, limit, reduce or terminate our development programs, commercialization efforts or other operations.
- We are early in our development efforts and have never successfully completed any late-stage 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 early 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 and ongoing 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 iluzanebart for ALSP and VG-3927 for Alzheimer's disease (AD), 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 clinical candidate, iluzanebart.
- 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 on-going and 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 timing, progress, results and cost of developing iluzanebart and VG-3927, as well as our other 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 Triggering Receptor Expressed on Myeloid Cells 2, or TREM2, and subsequent plans to expand into larger and more common neurodegenerative indications;
- 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, including at the pace that we project;
- the ability to efficiently discover, identify, research and develop product candidates;
- the timing, scope and likelihood of regulatory filings and approvals, including timing of any Investigational New Drug applications, or INDs, and final U.S. Food and Drug Administration, or 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 and cash runway;

- 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 a public health crisis on any of the foregoing or other aspects of our business operations, including any 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 clinical-stage biotechnology company dedicated to improving the lives of patients, caregivers, and families affected by rare and common neurodegenerative diseases by pursuing the development of disease-modifying therapeutics to restore the vigilance of microglia. Microglia are the sentinel immune cells of the brain and play a critical role in maintaining central nervous system (CNS) health and responding to damage caused by disease. Leveraging recent research implicating microglial dysfunction in neurodegenerative diseases, we utilize a precision medicine approach to develop a pipeline of therapeutic candidates, initially addressing genetically defined patient subpopulations, that we believe will activate and restore microglial function. Our first therapeutic candidates are designed to activate Triggering Receptor Expressed on Myeloid Cells 2 (TREM2), a key microglial receptor protein that mediates responses to environmental signals in order to maintain brain health and whose dysfunction is linked to neurodegeneration. We have two clinical programs that are designed to target TREM2. Our lead clinical candidate, iluzanebart, is a fully human monoclonal antibody (mAb) TREM2 agonist that is currently being studied in a Phase 2 clinical trial in patients with adult-onset leukoencephalopathy with axonal spheroids and pigmented glia (ALSP), a rare and fatal neurodegenerative disease. We plan to report data from the Phase 2 trial in ALSP in the second quarter of 2025. Our second clinical candidate, VG-3927, is an orally bioavailable small molecule TREM2 agonist that is being developed for the potential treatment of Alzheimer's disease (AD). We reported Phase 1 data from our VG-3927 program in January 2025 and plan to initiate a Phase 2 trial in AD patients in the third quarter of 2025.

We believe that each therapeutic candidate in our pipeline has the potential to be developed for multiple neurodegenerative diseases. Our precision medicine approach focuses on indications where there are strong, genetic mechanistic or biochemical associations to microglial dysfunction and then utilizes findings from these efforts to inform expansion into broader populations and additional indications of neurodegenerative diseases. We believe our strategy has the potential to mitigate downstream translational risk as we seek to advance our programs through early development and into the clinic. We believe this iterative, sequential approach is a key differentiator, potentially allowing us to generate clinical proof-of-concept (PoC) efficiently and leverage our initial development programs as well as research by others, in pursuing additional neurodegenerative disease opportunities.

Our lead clinical candidate, iluzanebart, is currently being studied in IGNITE, a Phase 2 clinical trial and the first-ever interventional trial in ALSP patients. ALSP is a rare, inherited, autosomal dominant neurological disease with high penetrance. ALSP is caused by a loss-of-function mutation in the Colony Stimulating Factor 1 Receptor (CSF1R), a receptor that shares a common downstream signaling pathway with TREM2. Based on analysis from the UK Biobank genome sequencing data published in *Neurology Genetics* by Wade et al. (2024), we estimate the U.S. prevalence of ALSP to be approximately 19,000 with an estimated combined EU and UK prevalence of approximately 29,000. There are currently no approved therapies for ALSP, underscoring the unmet need for people living with this serious, rapidly progressing disease. The Food and Drug Administration (FDA) has granted Fast Track designation and orphan drug designation for iluzanebart for the treatment of ALSP. The European Commission has also granted orphan drug designation for iluzanebart.

In November 2023, we reported interim data from the ongoing Phase 2 IGNITE trial from the first 6 patients following 6 months of treatment with 20 mg/kg of iluzanebart. These data further supported the favorable safety, tolerability, pharmacokinetics (PK) and pharmacodynamics (PD) profile of iluzanebart previously demonstrated in the Phase 1 single ascending dose/multiple ascending dose (SAD/MAD) trial of iluzanebart in healthy volunteers. Importantly, iluzanebart demonstrated clear target engagement as measured by changes in soluble TREM2 (sTREM2), soluble CSF1R (sCSF1R), and osteopontin/secreted phosphoprotein 1 (SPP1) in cerebral spinal fluid (CSF). Individual ALSP patients treated with iluzanebart also demonstrated directionally supportive changes in magnetic resonance imaging (MRI) and neurofilament light chain (NfL) biomarkers. Enrollment for the Phase 2 IGNITE trial was completed in March 2024 with 20 patients enrolled in the trial. The final analysis from the Phase 2 IGNITE trial is planned for the second quarter of 2025 and will include data from all patients at 12 months dosed with either 20 mg/kg or 40 mg/kg of iluzanebart.

In addition to IGNITE, we are also conducting ILLUMINATE, a natural history study of symptomatic and prodromal carriers of CSF1R mutations that are pathogenic for ALSP. We define individuals as being symptomatic if they have MRI evidence and three or more characteristic clinical symptoms of ALSP or as being prodromal if they have early MRI evidence of ALSP and less than three clinical symptoms. The purpose of this study is to better characterize disease progression, inform our clinical trial design, and facilitate recruitment into our clinical trials. The ILLUMINATE study is focused on understanding MRI findings and certain fluid biomarker levels in symptomatic ALSP participants and the potential for those biomarkers to act as measurable descriptors of ALSP disease pathophysiology and progression. In November 2023, we reported findings from

the ongoing ILLUMINATE study. These results provided critical insights on MRI and fluid biomarkers and how they present in ALSP. Specifically, sCSF1R levels were altered in both prodromal and symptomatic ALSP patients, positioning this measure as an emerging biomarker of ALSP disease pathology. Similarly, NfL levels were highly elevated in symptomatic ALSP patients, suggesting this biomarker may be useful in characterizing active neurodegeneration in ALSP. These data also showed that MRI measurements on ventricular volume and gray matter volume are also emerging as measurable indicators of disease progression. Based on 12-month data from ILLUMINATE we have also observed a statistically significant correlation between MRI biomarkers and cognitive changes.

Engagement with our stakeholders, including patients and scientific and provider communities, is central to our approach in rare neurodegenerative diseases. We have established the world's first patient-facing ALSP informational website to build disease awareness and actively support patient advocacy organizations. Through this work, we 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. In May 2023, we launched *ALSPAware*, a program providing no-cost genetic testing to aid in the diagnosis of ALSP as well as supportive counseling services. Developed with both patients and healthcare providers in mind, the program includes a no-cost single gene confirmatory test for individuals with a family history of ALSP and a custom gene panel available for physicians to use in diagnosing late onset neurodegenerative diseases. Trained genetic counselors are available to facilitate testing and discuss results, and participants will have access to a range of specialized information and services created to support participants and their families.

In addition to iluzanebart, we are developing VG-3927, our orally bioavailable small molecule TREM2 agonist for the treatment of common neurodegenerative diseases associated with microglial dysfunction, with initial development for the treatment of AD. In January 2025, we reported complete data from the Phase 1 clinical trial evaluating VG-3927 for the potential treatment of AD. The Phase 1 SAD/MAD trial assessed the safety, tolerability, PK, and PD of VG-3927 across 14 cohorts, including 8 SAD cohorts of healthy volunteers up to a 140 mg dose and 4 MAD cohorts of healthy volunteers up to a 50 mg dose. The trial also included a multiple dose elderly cohort and a single dose cohort of AD patients, including some participants who carry TREM2 or other genetic risk factors for AD. The trial enrolled a total of 115 participants with 89 participants receiving VG-3927, including 34 participants that were 55 years of age and older. These data demonstrated a favorable safety and tolerability profile across all cohorts, including the elderly cohort. All related adverse events were mild or moderate in severity and self-resolving without drug discontinuations. No serious AEs were reported. In addition, VG-3927 was observed to be highly CNS penetrant with a favorable and predictable PK profile that supports once-daily dosing. Importantly, VG-3927 achieved a robust and dose-dependent reduction of sTREM2 of up to approximately 50% in the CSF demonstrating a strong PK/PD relationship, sustained target engagement and TREM2 agonist activity.

Genome wide association studies (GWAS) have shown that a specific mutation in a TREM2 variant (R47H) is one of the strongest genetic risk factors for AD, second in magnitude only to that associated with the apolipoprotein E4 (ApoE4) genotype. We included genetic variants of TREM2 in our Phase 1 trial, the data from which indicated that the PK profile and sTREM2 reduction of VG-3927 observed in AD patients were consistent with results from healthy volunteers and similar across evaluated TREM2 and ApoE genetic variants supporting development in AD across genotypes. The PK profile and sTREM2 reduction observed in the elderly cohort were also consistent with results from healthy volunteers. Based on the Phase 1 results and preclinical profile of VG-3927, we plan to advance a once-daily oral dose of 25 mg that fully engages the desired pharmacology and expect to initiate the Phase 2 trial in the third quarter of 2025.

VG-3927 has a novel mode of action that acts as both an agonist and a positive allosteric modulator (PAM), which may amplify functional responses around sites of pathology leading to strong modulation of microglia and potentially greater neuroprotection. VG-3927 is designed to enhance protective microglial responses to aggregated amyloid and tau without increasing inflammation. In contrast to antibody TREM2 agonists, VG-3927 maximizes receptor activation and microglial function because it does not bind to sTREM2, which may increase its access to the site of therapeutic action in AD. Additionally, VG-3927 does not have an Fc (fragmented crystallizable region) domain, which engages elements of the immune system that have been associated with increased risk of amyloid-related imaging abnormalities (ARIA). Collectively across preclinical and clinical data, these key differentiators create a compelling profile for VG-3927 as an investigational next-generation therapy for the treatment of AD.

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. Over time, we plan to expand our pipeline through internal discovery and development and/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 neurodegenerative diseases that have strong genetic, mechanistic, and biochemical associations to microglial dysfunction and then utilize findings from these efforts to inform expansion into broader populations and additional indications of neurodegenerative diseases. We believe 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 PoC efficiently and leverage our initial development programs as well as research by others, in pursuing additional neurodegenerative disease opportunities.
- **Advance our lead clinical candidate, iluzanebart, a mAb TREM2 agonist, for the treatment of ALSP and other rare leukoencephalopathies and leukodystrophies.** We are currently developing iluzanebart, our fully human mAb that is highly selective for TREM2, for the treatment of ALSP, a rare and fatal neurodegenerative disease. 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. 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 our trials are successful. We plan to leverage our work in ALSP to target other rare leukoencephalopathies and leukodystrophies. To that end, iluzanebart is currently being studied in the Phase 2 clinical trial, IGNITE, in patients with ALSP. The final analysis from the Phase 2 IGNITE trial is planned for the second quarter of 2025 and will include data from all patients at 12 months dosed with either 20 mg/kg or 40 mg/kg of iluzanebart. We also continue to enroll people living with ALSP in ILLUMINATE, a natural history study of ALSP patients designed to better characterize disease progression, inform our clinical trial design, and facilitate recruitment into our clinical trials.
- **Advance our second clinical candidate VG-3927, an orally bioavailable, small molecule TREM2 agonist for the treatment of more common neurodegenerative diseases** associated with microglial dysfunction, with the initial development for the treatment of AD. An oral and highly active, TREM2-selective and CNS penetrant small molecule with a novel mechanism of action has many potential clinical and commercial advantages in large chronic indications, like AD, including ease of administration and use in outpatient settings. Peer reviewed literature suggest a strong genetic association between certain TREM2 variants and the development and progression of AD. Our initial strategy for VG-3927 in AD included evaluating a single dose cohort of AD patients in our Phase 1 clinical trial, including patients with TREM2 and ApoE genetic variants, to evaluate the biomarker response of VG-3927 in individuals with these AD genotypes. These data were reported in January 2025 and indicated that the PK profile and sTREM2 reduction of VG-3927 observed in AD patients were consistent with results from healthy volunteers and similar across the evaluated genetic variants supporting development in AD across genotypes. Based on the Phase 1 results and preclinical profile of VG-3927, we plan to advance a once-daily oral dose of 25 mg that fully engages the desired pharmacology and expect to initiate the Phase 2 trial in the third quarter of 2025.
- **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 dedicated 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. In May 2023, we launched *ALSPAware*, a program providing no-cost genetic testing to aid in the diagnosis of ALSP as well as supportive counseling services. Developed with both patients and healthcare providers in mind, the program includes a single gene confirmatory test for individuals with a family history of ALSP, as well as a custom gene panel available for physicians to use in diagnosing late onset neurodegenerative diseases.

- **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 through internal discovery and development and/or through strategic collaborations or alliances with academic organizations or pharmaceutical or biotechnology companies.

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, by sensing and responding to pathogens and to damage caused by disease or injury. They also play a central role in ongoing maintenance and "housekeeping" in the brain environment. 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 cellular components. Upon sensing damage, homeostatic microglia can transition to a disease-associated microglia (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), and removal of unneeded neural connections (axonal pruning) to maintain synaptic health. In doing this, they display a protective phenotype that maintains the CNS environment. In the context of neurodegenerative disease, microglia in the DAM state are believed to protect healthy cells by responding to and either removing or isolating protein clumps and cellular debris that accumulate in the brains of patients with neurodegenerative diseases and, to a lesser extent, during normal aging. These clumps and debris can be toxic to nearby cells and therefore, the response and protective functions of microglia are believed to be important for preventing or slowing neuroinflammation and neuropathology that contribute to disease progression. Our initial focus on microglia and microglia-targeted therapeutics is based on research linking impaired microglia function to both rare and common neurodegenerative diseases via genetic mutations that interfere with microglia's normal sentinel and response functions, thereby predisposing individuals to conditions that cause neurodegeneration. These conditions include leukoencephalopathies and leukodystrophies, a set of rare, mainly genetic disorders affecting neurons and white matter, such as ALSP, as well as the most common cause of dementia. Due to their multiple functions, microglia are also implicated in other CNS diseases, including, Frontotemporal dementia (FTD), Multiple sclerosis (MS), Parkinson's disease (PD), amyotrophic lateral sclerosis (ALS), and certain rare epilepsies.

TREM2: Our Initial Therapeutic Target

Our most advanced therapeutic programs are aimed at developing agonists 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 microglia encounter damage associated materials, 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. In preclinical studies across multiple models of neurodegenerative conditions, it has been shown that the transition from homeostatic microglia to fully activated DAM requires activation of the TREM2 receptor.

TREM2's protective role in neurodegenerative disease was discovered through GWAS. Follow up studies in cells and animals have demonstrated the important role of this receptor for initiating neuroprotective response of microglia in models of neurodegenerative disease. TREM2 signals through an association with its adapter protein DAP12, 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.

Multiple preclinical studies have shown that TREM2 deficiency is a likely contributor to 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 of brain debris to TREM2 and/or through reduced TREM2 levels at the cell surface. The following findings further support the link between TREM2 loss-of-function and disease:

- Evidence for importance of TREM2 in the CNS and its involvement in microglial dysfunction comes 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 TREM2 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 increased risk for FTD, ALS, PD and AD. For example, GWAS have shown that a specific mutation in a *TREM2* variant (R47H) is one of the strongest genetic risk factors for AD, second in magnitude only to that associated with the *ApoE4* genotype.
- *TREM2* mutations lead to increased disease pathology in multiple animal studies, such as studies for AD, stroke, MS, and other white matter diseases. For example, in an AD mouse model study, microglial inactivation via *TREM2* deletion enhanced the spreading of both pathological ß-amyloid and tau proteins.

In our preclinical and clinical studies to date, we have not observed any significant adverse effects resulting from TREM2 agonism. To our knowledge, no association has been established between gain-of-function mutations for *TREM2* and any disease. 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.

Our Precision Medicine Approach to Development

We are pursuing a 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 neurodegenerative diseases that have strong genetic, mechanistic, and biochemical associations to microglial dysfunction and then utilize findings from these efforts to inform expansion into broader populations and additional indications of neurodegenerative diseases. We believe 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 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 two current product candidates, iluzanebart and VG-3927. Iluzanebart 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, support our efforts to rapidly achieve clinical PoC for iluzanebart 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 regulatory approval, if these trials are successful. We plan to leverage our work in ALSP to target other rare leukoencephalopathies and leukodystrophies.

We are also following our precision medicine approach with VG-3927, which is initially being developed for the treatment of AD. Loss-of-function mutations in TREM2 have been shown to increase the risk of developing AD. Mutations in other genes that are involved in the microglial response to neuropathology have also been shown to increase AD risk. These data suggest a genetically-defined subset of AD where impaired function of microglia may be an important contributor to disease pathology. Our initial strategy for VG-3927 in AD included evaluating a single dose cohort of AD patients in our Phase 1 clinical trial, including patients with TREM2 and ApoE genetic variants, to evaluate the biomarker response of VG-3927 in individuals with these AD genotypes. These data were reported in January 2025 and indicated that the PK profile and sTREM2 reduction of VG-3927 observed in AD patients were consistent with results from healthy volunteers and similar across the evaluated genetic variants supporting development in AD across genotypes.

Our Clinical Development Programs

Our precision medicine strategy is focused on advancing a pipeline aimed at developing microglia-targeted TREM2 agonists for the treatment of neurodegenerative diseases. We believe we are differentiated by developing both large molecule (i.e., injectable) antibodies as well as small molecule (i.e., orally bioavailable) drugs. Our current clinical candidates include iluzanebart, our fully human mAb TREM2 agonist and VG-3927, an orally bioavailable small molecule TREM2 agonist.

Iluzanebart, Monoclonal Antibody TREM2 Agonist Candidate

Our lead clinical candidate, iluzanebart, is a highly-selective fully human monoclonal antibody directed against TREM2 for the treatment of rare genetically defined microgliopathies. Iluzanebart is currently being studied in IGNITE, a Phase 2 proof-of-concept trial in patients with ALSP. The final analysis from the Phase 2 IGNITE trial is planned for the second quarter of 2025 and will include data from all patients at 12 months dosed with either 20 mg/kg or 40 mg/kg of iluzanebart.

Our Clinical Candidate Iluzanebart for the Treatment of 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. Based on analysis from the UK Biobank genome sequencing data published in *Neurology Genetics* by Wade et al. (2024), we estimate the U.S. prevalence of approximately 19,000 and an estimated combined EU and UK prevalence of approximately 29,000. The FDA has granted Fast Track designation and orphan drug designation for iluzanebart for the treatment of ALSP. The European Commission has also granted orphan drug designation for iluzanebart.

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.

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 6 to 7 years following symptom onset.

To our knowledge, there are no approved products for ALSP, and beyond iluzanebart, there are none in clinical development, underlining the high unmet need in this rare indication. Current medical practice is limited to the management of motor and psychiatric symptoms. This provides limited supportive care and modest improvements to quality of life and does not address the most debilitating symptoms, such as cognitive decline. In addition, these approaches have no effect on the underlying disease process and do not slow the progression of the disorder. 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.

Treatment Rationale for Iluzanebart in ALSP

Mutations in the CSF1R gene that result in the development of ALSP cause the loss of proper receptor signaling, reducing microglia cell numbers and their activity. 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. CSF1R and TREM2 are both expressed on the surface of microglia and they share common elements in their downstream signaling after activation such as phosphorylation of SYK. Iluzanebart is designed to bind to TREM2 as an agonist and initiate a cascade of cellular responses including phosphorylation of SYK. The therapeutic hypothesis is that activation of TREM2 with iluzanebart will initiate signaling in microglia that can compensate for deficiencies caused by dysfunctional sCSF1R and act as a treatment for ALSP.

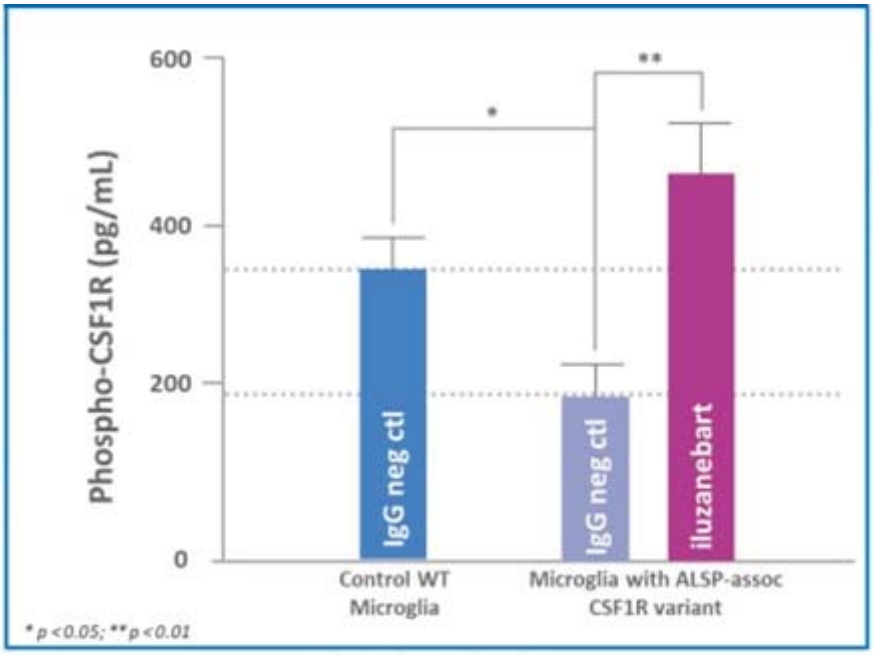
Human genetic data suggest functional similarities between TREM2 and CSF1R. Loss-of-function mutations in TREM2 lead to the rare, fatal genetic disease, NHD. The disease presentation, adult onset, imaging findings, and brain pathology of ALSP and NHD are similar, highlighting that converging, dysfunctional biochemical pathways produce similar pathobiology.

In *in vitro* systems that model CSF1R loss-of-function in ALSP, we have demonstrated that iluzanebart activation of TREM2 can compensate for deficiency of CSF1R signaling. For these studies, we used human microglia derived from induced pluripotent stem cells (iPSCs) and are dependent on the growth factor CSF1 for survival and differentiation. In one such experiment, we induced CSF1R signaling deficiency by treating microglia with PLX5622, a selective CSF1R inhibitor. Microglia treated with PLX5622 alone displayed significantly reduced viability compared to untreated cells. Exposure of PLX5622-treated cultures to iluzanebart rescued the cells from effects of CSF1R inhibition and restored viability.

As illustrated in Figure 1, heterozygous expression of an I794T mutation in CSF1R that is known to be pathogenic for ALSP results in a decrease in the phosphorylation of CSF1R. This deficit can be rescued by treatment of these microglia with iluzanebart, demonstrating that increased TREM2 activation translates to increased CSF1R activation.

Figure 1: Iluzanebart Proof-of-Mechanism in ALSP – Rescue of Microglia Viability and Activity under CSF1R Deficiency

Iluzanebart Compensation of CSF1R Signaling Defect



Human iPSC derived microglia, expressing either wild-type or a known ALSP associated variant of CSF1R (I794T), were stimulated with VGL101 or IgG Control for 7 days. Levels of the activated form of CSF1R were measured using a quantitative assay of phosphorylated CSF1R. Data were reported as the average across multiple experiments +/- the standard error of the mean.

We believe that there are quantifiable, disease-associated biomarkers which correlate with disease severity or with disease progression and could have the measurement properties to detect treatment effects in ALSP clinical trials. Published data indicate that MRI of brain lesions could correlate with disease progression. In our ongoing natural history study in ALSP, ILLUMINATE, we have observed that NfL and CSF1R levels are highly altered in ALSP compared to age-corrected expectations at baseline and may be useful in measuring disease severity. Data from this study also support the potential of volumetric MRI measurements to assess disease progression and treatment effect. We believe these data from ILLUMINATE on MRI and fluid biomarkers support their utility as potential early indicators of iluzanebart's therapeutic response and could be used to support the declaration of PoC in our Phase 2 trial, IGNITE, in ALSP. Along with the high unmet need in the disease, we believe the availability of these quantifiable biomarkers make ALSP an attractive initial indication for iluzanebart.

Iluzanebart Clinical Development in ALSP

- ***ILLUMINATE, ALSP Natural History Study:*** In September 2021, we began ILLUMINATE, a non-interventional natural history study of symptomatic and prodromal carriers of CSF1R mutations that are pathogenic for ALSP. We define individuals as being symptomatic if they have three or more characteristic clinical symptoms of the ALSP or as being prodromal if they have early MRI evidence of ALSP and less than three clinical symptoms. The objectives of the study are to further understand the phenotype and natural course of ALSP, disease progression, and the treatment paradigm. The ILLUMINATE study is focused on understanding MRI findings and certain fluid biomarker levels in symptomatic ALSP participants and the potential for those biomarkers to act as measurable descriptors of ALSP disease pathophysiology and progression. ILLUMINATE is also intended to potentially serve as a contemporaneous external comparator arm for efficacy studies. ILLUMINATE is designed to evaluate ALSP patients with a CSF1R gene mutation for a period of 36 months. Some participants in our natural history study may

also participate in our interventional clinical trials. In November 2023, we reported findings from the ongoing ILLUMINATE study. These results provided critical insights on MRI and fluid biomarkers and how they present in ALSP. Specifically, sCSF1R levels were altered in both prodromal and in symptomatic ALSP patients positioning measure as an emerging biomarker of ALSP disease pathology. Similarly, NfL levels were highly elevated in symptomatic ALSP patients, suggesting this biomarker may be useful in characterizing active neurodegeneration in ALSP. These data also showed that MRI measurements on ventricular volume and gray matter volume are also emerging as measurable indicators of disease progression. Additionally, based on 12-month data from ILLUMINATE, we have observed a statistically significant correlation between MRI biomarkers and cognitive changes in ALSP patients using the Montreal Cognitive Assessment (MoCA) scale, which is widely used to assess cognition. Analysis of these data showed a statistically significant correlation between increased ventricular volume and lower MoCA scores in symptomatic ALSP patients, both indicating disease worsening. In addition, a statistically significant relationship between loss of gray matter volume and reduction in MoCA scores were observed, which are also indicative of disease worsening. These relationships may support the use of changes in ventricular volume and gray matter volume as biomarkers of disease progression.

- ***Phase 1 Healthy Volunteer Trial:*** This clinical trial was designed as a SAD/MAD trial of iluzanebart in healthy volunteers, including subjects of various ethnic backgrounds, to evaluate safety and tolerability, PK and to measure changes in CSF microglial activity biomarkers sCSF1R, osteopontin, and sTREM2. We conducted our Phase 1 trial in the U.S. and Australia. In September 2023, we reported complete topline data from the Phase 1 trial. The trial enrolled 136 healthy volunteers who received either iluzanebart (n=113) at fixed single doses ranging from 1 to 60 mg/kg or three ascending doses ranging from 20 to 60 mg/kg, or placebo (n=23). Based on these data, iluzanebart demonstrated a favorable safety and tolerability profile in SAD and MAD cohorts at doses up to 60 mg/kg. In addition, iluzanebart showed:
    - Linear and predictable PK characteristics and an observed half-life that supports monthly IV dosing;
    - Proof-of-target engagement based on dose-dependent, robust and durable reductions in sTREM2 in CSF following repeat dosing;
    - Increased sCSF1R and osteopontin levels in CSF that were durable following repeat dosing suggesting that iluzanebart impacted microglial activity downstream of TREM2 target engagement; and,
    - Target engagement and downstream PD responses following 20 mg/kg and 40 mg/kg of iluzanebart, which support evaluating these doses in the ongoing IGNITE Phase 2 trial in ALSP patients.
- ***IGNITE, Phase 2 Clinical Trial in ALSP:*** In December 2022, we initiated IGNITE, the first-ever interventional trial conducted in ALSP patients. The IGNITE trial is a global Phase 2, open-label trial, designed to evaluate the safety and tolerability of iluzanebart in 20 patients with symptomatic ALSP and a CSF1R gene mutation confirmed by genetic testing. Secondary outcome assessments include the effects of iluzanebart on MRI measures and on the fluid biomarkers NfL, sTREM2, sCSF1R, and osteopontin. Exploratory outcome assessments include the evaluation of clinical efficacy measures using standard cognitive, motor and functional assessments as well as assessment of the PK of iluzanebart in patients with ALSP. Patients enrolled in the trial receive an intravenous, (IV) infusion of 20 mg/kg or 40 mg/kg of iluzanebart approximately every four weeks, for a treatment duration of one year. In November 2023, we reported interim data from the ongoing Phase 2 IGNITE trial from the first 6 patients following 6 months of treatment with 20 mg/kg of iluzanebart. These data further supported the favorable safety, tolerability, PK and PD profile of iluzanebart previously demonstrated in the Phase 1 SAD/MAD trial of iluzanebart in healthy volunteers. Importantly, iluzanebart demonstrated clear target engagement as measured by changes in sTREM2, sCSF1R, and osteopontin in CSF. Individual ALSP patients treated with iluzanebart also demonstrated directionally supportive changes in MRI and NfL biomarkers. Enrollment for the Phase 2 IGNITE clinical trial was completed in March 2024 with 20 patients enrolled in the trial. The final analysis from the Phase 2 IGNITE trial is planned for the second quarter of 2025 and will include data from all patients at 12 months dosed with either 20 mg/kg or 40 mg/kg of iluzanebart.
- ***ALSP Disease Progression Model:*** We are exploring a disease progression model (DPM) to support the development of iluzanebart through the evaluation of all available data from patients with ALSP. The DPM can be used to synthesize and quantitatively summarize knowledge about disease progression, including but not limited to the correlation of biomarkers to clinical outcomes and the influence of drug treatment on disease trajectory.

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, Asia and Latin America).

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 more about ALSP on a continuous basis and deepen our relationship with the community. We have also partnered with genetic testing companies to increase disease awareness and access to genetic testing. In May 2023, we launched *ALSPAware*, a program providing no-cost genetic testing to aid in the diagnosis of ALSP as well as supportive counseling services. Developed with both patients and healthcare providers in mind, the program includes a single gene confirmatory test for individuals with a family history of ALSP, as well as a custom gene panel available for physicians to use in diagnosing late onset neurodegenerative diseases.

We are also partnering with larger leukodystrophy umbrella organizations, including the United Leukodystrophy Foundation (ULF), Hunter's Hope and ALEX The Leukodystrophy Charity, as well as rare disease umbrella organizations such as the National Organization for Rare Diseases (NORD), Global Genes and the EveryLife Foundation to provide disease education and raise awareness of ALSP.

We are engaging with ALSP families and health care providers who offer a well-rounded patient and caregiver perspective. This includes guidance on elements of the patient experience to help us embed the patient voice and insights into all aspects of our clinical program.

We are playing 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.

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 trials.

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 prioritize target indications which TREM2 agonists can potentially address.

We have identified several white matter diseases as potential therapeutic opportunities that share characteristics with ALSP and appear to be driven by either peroxisomal or lysosomal deficits. Our hypothesis is that we can restore microglial function resulting from loss-of-function mutations with TREM2 agonists in these diseases.

Small Molecule TREM2 Agonists for the Treatment of Neurodegenerative Diseases

We are advancing our orally bioavailable, small molecule TREM2 agonist program for the treatment of more common neurodegenerative diseases associated with microglial dysfunction. An orally bioavailable, once-daily, highly active, TREM2-selective and CNS penetrant small molecule therapy with a novel mechanism of action has many potential clinical and commercial advantages in large chronic indications, including ease of administration and use in outpatient settings.

Our Clinical Candidate VG-3927 for the Treatment of AD

We are developing VG-3927, an orally bioavailable, once-daily, small molecule TREM2 agonist for the treatment of common neurodegenerative diseases associated with microglial dysfunction with initial development for the treatment of AD. In 2023, we initiated a Phase 1 trial for VG-3927 in healthy volunteers. The trial included a single dose cohort of AD patients, including patients with TREM2 and ApoE genetic variants, to evaluate the biomarker response of VG-3927 in individuals with these AD genotypes. These data were reported in January 2025 and indicated that the PK profile and sTREM2 reduction of VG-3927 observed in AD patients were consistent with results from healthy volunteers and similar across the evaluated genetic variants supporting development in AD across genotypes. Based on the Phase 1 results and preclinical profile of VG-3927, we plan to advance a once-daily oral dose of 25mg that fully engages the desired pharmacology and expect to initiate the Phase 2 trial in the third quarter of 2025.

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 4 to 8 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 6.9 million people in the U.S. age 65 and older are living with AD in 2024. 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 $360 billion in 2024, and this number could increase to nearly $1 trillion by 2050.

Treatment Rationale for VG-3927 in AD

Loss-of-function TREM2 variants occur in 7 to 8 percent of the AD population and are linked to both more rapid disease progression and worsened patient outcomes. Several genetic variants in *TREM2* have emerged from GWAS including the R47H variant, which is one of the strongest genetic risk factors for developing AD, second in magnitude only to that associated with the *ApoE4* genotype. The R47H variant, which represents 2 to 3 percent of the AD population, has been reported to triple AD risk in GWAS and is associated with a 23 percent 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, H157Y and T96K, all of which are loss-of-function variants.

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. R47H *TREM2* AD patients also experienced more rapid disease progression and a greater number of co-morbidities, such as a neuropathological protein accumulation, called α-synucleinopathy.

We believe the robust body of experimental and genetic evidence points to TREM2 as a key modulator of microglial response to the pathology and processes associated with neurodegeneration in AD, and that activating TREM2 has potential to provide disease modifying benefit to those living with this disease.

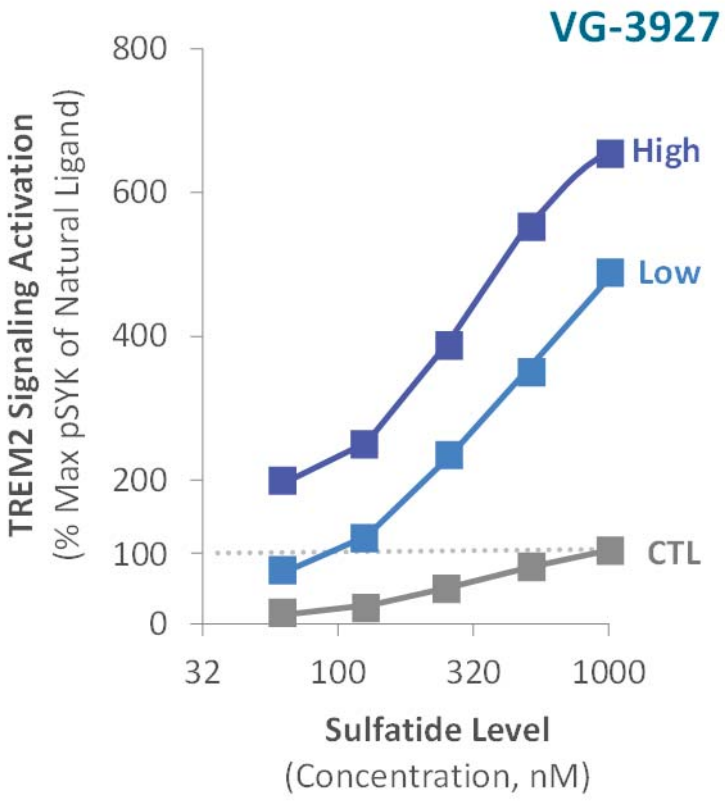
VG-3927 exhibits low single-digit nanomolar potency in *in vitro* assays measuring TREM2 activation in microglia derived from human iPSCs. Additionally, it retains similar levels of activity across key genetic variants of TREM2 believed to be associated with increased AD risks. VG-3927 is highly selective for primate TREM2 and it does not bind to or activate human TREM1.

VG-3927 has a novel mode of action that acts as both an agonist and a PAM, which may amplify functional responses around sites of pathology leading to strong modulation of microglia and potentially greater neuroprotection. VG-3927 is designed to enhance protective microglial responses to aggregated amyloid and tau without increasing inflammation. In contrast to antibody TREM2 agonists, VG-3927 maximizes receptor activation and microglial function because it does not bind to sTREM2, which may increase its access to the site of therapeutic action in AD. Additionally, VG-3927 does not have an Fc domain, which engages elements of the immune system that have been associated with increased risk of ARIA. Collectively

across preclinical and clinical data, these key differentiators create a compelling profile for VG-3927 as an investigational next-generation therapy for the treatment of AD.

Figure 2 shows amplification of TREM2 signaling by VG-3927 in the presence of sulfatide, which is a lipid component of myelin sheath and also a natural TREM2 ligand, at various concentrations. This synergistic interaction between VG-3927 and damage-associated ligands may enable greater specificity in disease states, which may contribute to a favorable tolerability profile.

Figure 2: VG-3927 potentiates TREM2 response to damage-associated ligands

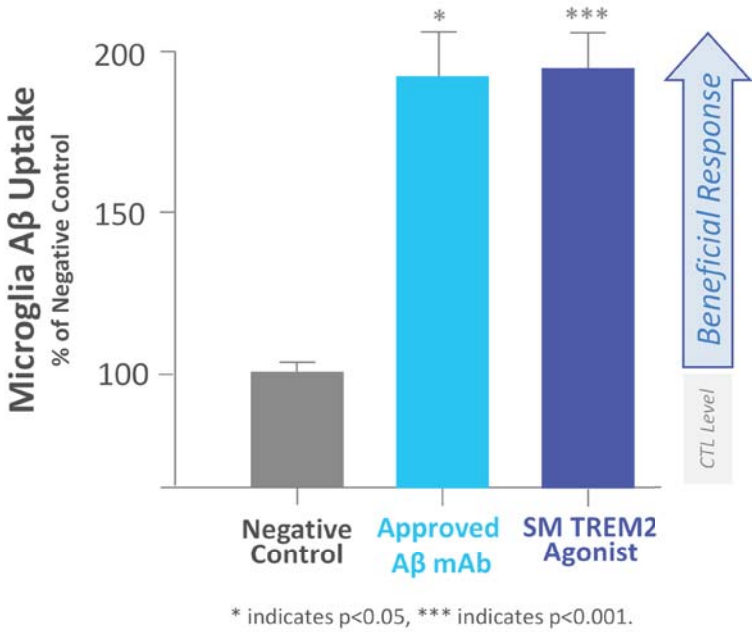


Cultured human iPSC-derived microglia were co-stimulated with varying nanomolar concentrations (nM, x-axis) of a brain-extracted sulfoglycolipid TREM2 ligand, Sulfatide, in the absence (gray) or presence of varying levels of VG-3927 (light blue and dark blue). To quantify small molecule potentiation of TREM2 signaling, data were normalized to and expressed as the % of maximal pSYK level induced by Sulfatide stimulation in the absence of VG-3927 (0 nM set as 100%).

Further *in vivo* pharmacological characterization of VG-3927 shows it recapitulated the agonist effects observed with an antibody TREM2 agonist in a mouse model for AD. We have demonstrated good correlation across an unbiased panel of several hundred brain markers between VG-3927 and iluzanebart. These data indicate that VG-3927 elicits *in vivo* TREM2 responses within the CNS at a magnitude and specificity similar to iluzanebart.

We have optimized a sophisticated preclinical platform, FEAST (Flow-cytometry Engulfment Assay of Specific Targets), inspired by Dr. Beth Stevens' laboratory at Harvard Medical School, to assess microglial clearance of neurotoxic aggregates such as amyloid beta (Aß) in a mouse model of AD (5xFAD:hTREM2). This approach enables rapid functional evaluation of microglial neuroprotection in response to pharmacological stimulation. Following 8 days of oral dosing, we observed that a small molecule TREM2 agonist significantly enhances microglial uptake of Aß. This preclinical finding, along with additional preclinical data, demonstrate the functional benefits of small-molecule TREM2 activation and underscores the potential of VG-3927 to neutralize drivers of neurotoxicity and support its neuroprotective potential as it advances in clinical development.

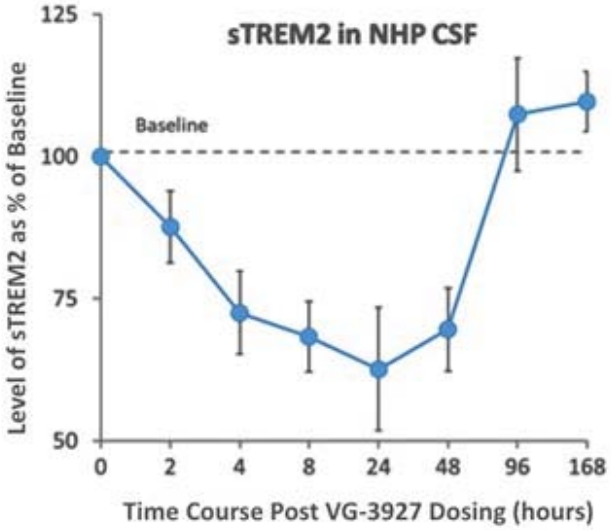
Figure 3: Small molecule TREM2 agonism promotes microglia neuroprotection via increasing engulfment of amyloid beta (Aß) in plaque burdened mice



Humanized TREM2 Alzheimer's disease mice (6-7 months old) engineered to develop progressive amyloid plaque burden (5xFAD: hTREM2) were given a daily dose of a small molecule TREM2 agonist (30 mg/kg, po), approved Aß mAb for treatment of AD (150 mg/kg, i.v.), or a vehicle negative control (Neg Ctrl). Following 8 days on study, the proportion of isolated microglia co-stained with amyloid-beta (Aß) was measured by flow cytometry, normalized to Neg Ctrl (set as 100%), and subsequently subject to statistical analyses using a t-test (p<0.001).

We have also conducted translational studies with non-human primates, focusing on CSF target engagement biomarkers for clinical assessment such as sTREM2. Figure 4 demonstrates CSF target engagement in non-human primates seen from the significant reduction in sTREM2, following a single oral administration of VG-3927. These data support the use of changes in CSF sTREM2, a target engagement biomarker for clinical development.

Figure 4: Oral dosing of VG-3927 in non-human demonstrates CNS activity via reduction of sTREM2 in CSF



Non-human primates were administered with a single oral dose of our small molecule TREM2 agonist and the level of sTREM2 in the CSF was measured as a percentage change over baseline (y-axis) over time (x-axis).

VG-3927 Clinical Development in AD

- **Phase 1 Healthy Volunteer Trial:** In January 2025, we reported complete data from the Phase 1 clinical trial evaluating VG-3927 for the potential treatment of AD. The Phase 1 SAD/MAD trial assessed the safety, tolerability, PK, and PD of VG-3927 across 14 cohorts, including 8 SAD cohorts of healthy volunteers up to a 140 mg dose and 4 MAD cohorts of healthy volunteers up to a 50 mg dose. The trial also included a multiple dose elderly cohort and a single dose cohort of AD patients, including some participants who carry TREM2 or other genetic risk factors for AD. The trial enrolled a total of 115 participants with 89 participants receiving VG-3927, including 34 participants that were 55 years of age and older. These data demonstrated a favorable safety and tolerability profile across all cohorts, including the elderly cohort. All related adverse events were mild or moderate in severity and self-resolving without drug discontinuations. No serious AEs were reported. In addition, VG-3927 was observed to be highly CNS penetrant with a favorable and predictable PK profile that supports once-daily dosing. Importantly, VG-3927 achieved a robust and dose-dependent reduction of sTREM2 of up to approximately 50% in the CSF demonstrating a strong PK/PD relationship, sustained functional target engagement and TREM2 agonist activity. Furthermore, the PK profile and sTREM2 reduction of VG-3927 observed in AD patients were consistent with results from healthy volunteers and similar across evaluated TREM2 and ApoE genetic variants supporting development in AD across genotypes. The PK profile and sTREM2 reduction observed in the elderly cohort were also consistent with results from healthy volunteers.
- Based on the Phase 1 results and preclinical profile of VG-3927, we plan to advance a once-daily oral dose of 25 mg that fully engages the desired pharmacology and expect to initiate the Phase 2 trial in the third quarter of 2025.

Material Agreements

To enhance and further exploit our product candidates, we have and may continue to enter into research, development, or commercialization agreements with universities, hospitals, independent research centers, non-profit organizations, pharmaceutical and biotechnology companies and other entities for complementary or new technologies.

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 8,891,659 shares of our Series A preferred stock to Amgen; all of our then outstanding preferred stock converted into common stock at our initial public offering in January 2022. 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 (10th) 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.

Patent Protection

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 actively seek patent protection in the United States and foreign countries, as appropriate, for a variety of technologies, including active ingredients, such as iluzanebart and VG-3927, pharmaceutical compositions, and methods of use, such as for treating neurodegenerative diseases, and methods of selecting patient populations based on biomarkers. Our decision to seek patent protection in specific foreign markets outside of the US is based on many factors, such as our available resources, the size of the commercial market, the availability of patent protection under the local patent laws and the ability to effectively enforce patents upon grant under the local patent laws.

Our product candidates are primarily protected by composition of matter and method of use patents and patent applications. Our patent estate protecting iluzanebart and our small molecule TREM2 agonists, including VG-3927, is summarized as follows.

Iluzanebart Patent Estate

Patent protection for iluzanebart is based upon several patent families, that we own or exclusively license from Amgen, and that are directed to composition of matter (antibody TREM2 agonists) and methods of use. These patent families have been filed in all major markets including the U.S. and Europe. Patents issuing in these families have a standard 20-year term that expire between 2038 and 2043; 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) that may be available on a country-by-country basis.

VG-3927 and Small Molecule TREM2 Agonist Patent Estate

Patent protection for our small molecule TREM2 agonists, including VG-3927 and other discovery stage programs, is based upon several patent families, that we either solely own, jointly own with, or exclusively license from, Amgen. These patent families are directed to small molecule TREM2 agonists, and corresponding compositions and methods of use. These patent families were filed in all major markets including the U.S. and Europe. Patents issuing in these families have a standard 20-year term that expire between 2041 and 2044; 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) that may be available on a country-by-country basis.

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.

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 IND application, 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 6 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 10 months to 6 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. Under the Food and Drug Omnibus Reform Act of 2022 (FDORA), the FDA is permitted to require, as appropriate, that a post-approval confirmatory study or studies be underway prior to approval or within a specified time period after the date of approval for a product granted accelerated approval. Sponsors are also required to send updates to the FDA every 180 days on the status of such studies, including progress toward enrollment targets, and the FDA must promptly post this information publicly. Under FDORA, the FDA is empowered to take action, such as issuing fines, against companies that fail to conduct with due diligence any post-approval confirmatory study or submit timely reports to the agency on their progress. 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. In addition, the FDA generally

requires, unless otherwise informed by the agency, pre-approval of promotional materials for product candidates approved under accelerated approval, which could adversely impact the timing of the commercial launch of the product.

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 6 months of marketing exclusivity to the term of any existing regulatory exclusivity, including orphan exclusivity, for all formulations, dosage forms, and indications of the active moiety and, for drugs, patent terms. This 6-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, provided that at the time pediatric exclusivity is granted there is not less than nine months of term remaining. 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 6 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.

From time to time, legislation is drafted, introduced, passed in Congress and signed into law that could significantly change the statutory provisions governing the approval, manufacturing, and marketing of products regulated by the FDA. In addition to new legislation, FDA regulations, guidances, and policies are often revised or reinterpreted by the agency in ways that may significantly affect the manner in which pharmaceutical products are regulated and marketed.

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, 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 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 have been proposed and may be adopted in the future as well.

In addition to federal privacy regulations, there are a number of state laws governing confidentiality and security of personal information, including health information, that are applicable to our business. For example, numerous states have enacted comprehensive 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. Similar laws have been passed in numerous other states and other states have proposed similar new privacy laws. Although many of the existing state privacy laws exempt clinical trial information and health information governed by HIPAA, future privacy and data protection laws may be broader in scope, thus complicating compliance efforts. In addition, to the extent that we collect or otherwise process personal information, we may also be subject to privacy or data protection laws that are in effect in such third countries.

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 the laws. The increasingly stringent compliance environment and the need 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 significant penalties, damages, fines, imprisonment, contractual damages, reputational harm, diminished profits and future earnings, additional reporting requirements and/or additional oversight, 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.

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 CTR overhauls the previous system of approvals for clinical trials in the European Union. Specifically, the CTR, 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 (the Clinical Trials Information System) 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.

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 European Union 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 Medicinal Products for Human Use (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 or the additional Member States of the European Economic Area (Norway, Iceland and Liechtenstein) (EEA). 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 6 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 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 marketing authorization, 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.

Data and market exclusivity in the European Union

In the European Union, new active substances (i.e. reference products, 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 active substance, and products may not qualify for data exclusivity. Even if 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 6 additional months for products which are granted a marketing authorization with the results of the pediatric clinical trials conducted in accordance with the PIP. 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 (EU) 2017/1572, 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 European Union Member States. These requirements are provided in the national laws, industry codes or professional codes of conduct, applicable in the European Union 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 European Union 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.

We have obtained orphan medicinal product designation in the European Union for iluzanebart. 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 as the authorized orphan product if: (i) a second applicant can establish that its product, although similar to the authorized orphan product, is safer, more effective or otherwise clinically superior; (ii) the marketing authorization holder for the authorized orphan product consents to a second 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, including if the product is sufficiently profitable not to justify market exclusivity. Orphan designation must be requested before submitting an application for marketing authorization. Orphan designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process.

All of the aforementioned European Union rules are generally applicable in the EEA.

Reform of the Regulatory Framework in the European Union

The European Commission introduced legislative proposals in April 2023 that, if implemented, will replace the current regulatory framework in the European Union for all medicines (including those for rare diseases and for children). The European Commission has provided the legislative proposals to the European Parliament and the European Council for their review and approval, and, in April 2024, the European Parliament proposed amendments to the legislative proposals. Once the European Commission's legislative proposals are approved (with or without amendment), they will be adopted into EU law.

Brexit and the Regulatory Framework in the United Kingdom

The UK formally left the EU on January 31, 2020. As a result of the Northern Ireland Protocol, following Brexit, the EMA remained responsible for approving novel medicines for supply in Northern Ireland under the EU centralized procedure, and a separate authorization was required to supply the same medicine in Great Britain (England, Wales and Scotland). A new framework named the Windsor Framework was approved by the EU-UK Joint Committee on March 24, 2023, and the medicines aspects of the Windsor Framework have applied since January 1, 2025. This new framework fundamentally changes the previous system under the Northern Ireland Protocol, including with respect to the regulation of medicinal products in the UK. The MHRA is now responsible for approving all medicinal products destined for the UK market (i.e., Great Britain and Northern Ireland), and the EMA no longer has any role in approving medicinal products destined for Northern Ireland under the EU centralized procedure. A single UK-wide marketing authorization will be granted by the MHRA for all novel medicinal products to be sold in the UK, enabling products to be sold in a single pack and under a single authorization throughout the UK. However, although a separate authorization is now required to market medicinal products in the UK, under an international recognition procedure which was put in place by the MHRA on January 1, 2024, the MHRA may take into account decisions on the approval of a marketing authorization from the EMA (and certain other regulators) when considering an application for a UK marketing authorization.

European Data Protection Regulation

Where we are processing personal data regarding individuals in the EEA or UK, including personal health data, our activities are subject to the EU General Data Protection Regulation, or GDPR with respect to the EEA and the UK General Data Protection Regulation and UK Data Protection Act 2018 with respect to the UK, or UK GDPR, and collectively with the EU GDPR referred to as the "GDPR" in this document unless specified otherwise. The GDPR applies to companies established in the EEA/UK, as well as to any company established outside the EEA/UK, if they collect and use personal data in connection with the offering of goods or services to individuals in the EEA/UK or the monitoring of their behavior in the EEA/UK. 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/UK, 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 (£17.5 million for the UK GDPR) 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.

There is significant uncertainty related to the insurance coverage and reimbursement of newly-approved products. Increasing efforts by governmental and other third-party payors in the United States and abroad to cap or reduce healthcare costs may cause such organizations to limit both coverage and the level of reimbursement for newly approved products and, as a result, they may not cover or provide adequate payment for our product candidates. There has been increasing legislative and enforcement interest in the United States with respect to specialty drug pricing practices. Specifically, there have been several recent 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, review the relationship between pricing and manufacturer patient programs and reform government program reimbursement methodologies for drugs.

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, 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; 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 Medicare Part D coverage gap discount program, in which manufacturers were obligated to offer 70% point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period (later revised under the Inflation Reduction Act); and provided incentives to programs that increase the federal government's comparative effectiveness research.

Other legislative and regulatory changes have also been proposed and adopted in the U.S. since the ACA was enacted. This includes provisions that reduce the amount of Medicare payments made to providers and that eliminate the statutory Medicaid drug rebate cap, previously set at 100% of a drug's average manufacturer price, for single source and innovator multiple source drugs, effective January 1, 2024.

The Inflation Reduction Act of 2022 (the "IRA") included several provisions that will impact our business to varying degrees, including provisions that create a $2,000 out-of-pocket cap for Medicare Part D beneficiaries, impose new manufacturer financial liability on all drugs in Medicare Part D, allow the U.S. government to negotiate Medicare Part B and Part D pricing for certain high-cost drugs and biologics without generic or biosimilar competition, require companies to pay rebates to Medicare for drug prices that increase faster than inflation, and delay the rebate rule that would require pass through of pharmacy benefit manager rebates to beneficiaries. Further, under the IRA, orphan drugs are exempted from the Medicare drug price negotiation program, but only if they have one orphan designation and for which the only approved indication is for that disease or condition. If a product receives multiple orphan designations or has multiple approved indications, it may not qualify for the orphan drug exemption. The implementation of the IRA is currently subject to ongoing litigation challenging the constitutionality of the IRA's Medicare drug price negotiation program. The effect of IRA on our business and the healthcare industry in general is not yet known.

There has also 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 these and 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.

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. 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. federal transparency requirements under the ACA, including the provision commonly referred to as the Physician Payments Sunshine Act, and its implementing regulations, which requires applicable manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program to report annually to CMS, information related to payments or other transfers of value made to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), certain other licensed healthcare practitioners, and teaching hospitals, as well as ownership and investment interests held by the physicians described above 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. 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 laws 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 stringent foreign laws governing the privacy and security of health information, many of which differ from each other in significant ways, thus complicating compliance efforts.

Competition

The biotechnology and pharmaceutical industries are 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, particularly 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 and obtain patent protection, and establish collaborative arrangements, sometimes exclusive, for research, development, manufacturing and commercialization.

Competition can arise from third parties which are pursuing therapeutics that target the same molecular targets as our product candidates, therapeutics that are being developed for the same diseases or disorders as our product candidates, or both, therapeutics that target the same molecular targets and are being developed for the same diseases or disorders as our product candidates. In general, we consider our closest competitors as third parties that are conducting clinical trials to evaluate such therapeutics.

We further define and evaluate competition based on the nature of the disease or disorder that is potentially addressed by our product candidates. For instance, we consider competition more broadly in the context of rare diseases and more narrowly for diseases or disorders that are common. That is, we are more apt to consider a third party a competitor if it is clinically developing a therapeutic for the same rare disease in which we are developing our product candidates, irrespective of the molecular target of the third-party therapeutic. On the other hand, we are less inclined to consider a third party a competitor in the case of a common disease, unless the third party is clinically developing a therapeutic that targets the same molecular target as our product candidates. Nevertheless, the competitive landscape, particularly for common diseases, is highly complex and can be influenced by the success or failure of third-party therapeutics that are being developed for the same disease or disorder as our product candidates. As a result, our share price may be positively or negatively influenced by the activities of such third parties irrespective of whether we consider them to be a competitor or not.

We are aware of third parties which are pursuing therapeutics that target the same molecular targets as our product candidates. Third parties developing therapeutics targeting TREM2 include Novartis AG which is developing VHB937, a TREM2 targeting antibody, for amyotrophic lateral sclerosis and Alzheimer's disease.

Regarding therapeutics that are being developed for the same diseases or disorders as our product candidates, we consider the main competitors as follows:

- *Iluzanebart for ALSP:* we are not aware of any third parties that are clinically developing therapeutics for ALSP. Further, no products have been approved to treat ALSP. Academics have investigated the use of hematopoietic stem cell transplantation in a small number of ALSP patients, however, we believe this procedure has limited benefits and several key limitations.
- *VG-3927 for AD:* we are not aware of any third parties clinically developing small molecules that target TREM2 for AD. There are, however, many third parties pursuing clinical development of therapeutics for AD. As

mentioned, Novartis is clinically developing a TREM2 targeting antibody therapeutics. The University of Oxford in collaboration with Janssen Pharmaceutica NV has reported a Phase I trial of JNJ-40346527 (edicotinib), a small molecule CSF-1R antagonist. Elixiron Immunotherapeutics, Inc. has reported a Phase I trial of EI-1071, a small molecule that inhibits the tyrosine kinase activity of CSF-1R. In addition, there are others developing therapeutics for AD that do not target TREM2. Notable examples include those that are based on reduction of ß-amyloid plaques, such as LEQEMBI™ (lecanemab-irmb), which is from Biogen, Inc. and was FDA approved in 2023. Also, in July 2024, the FDA approved Kisunla™ (donanemab) which is marketed by Eli Lilly for the treatment of people living with early symptomatic AD. Other ß-amyloid therapeutics and additional approaches for AD are being pursued by Roche (Genentech) and others.

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.

Human Capital Resources

As of February 28, 2025, we had 69 full-time employees and 20 of our employees have M.D. or Ph.D. degrees. Within our workforce, 47 employees are engaged in research and development and 22 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 100 Forge Road, Suite 700, Watertown, MA 02472, 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.

Internet Posting of Information

Our website address is www.vigilneuro.com. We routinely post information that may be important to investors in the "Investors" section of our website, and we encourage investors and potential investors to consult our website regularly for important information about us. 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.

Available Information

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 "Investors" portion of our website, www.vigilneuro.com, 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 "Investors" portion of our website at https://investors.vigilneuro.com/corporate-governance/documents-charters. We will also post to our website any amendments to the code of conduct and any waivers that are required to be disclosed by SEC or Nasdaq Rules. Additionally, we routinely post information that may be important to inventors to the "Investors" section of our website. We encourage investors and potential investors to consult our website regularly for important information about our Company.

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 preclinical research and clinical studies. As a clinical-stage organization, we have not yet completed any late-stage 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 $84.3 million for the year ended December 31, 2024. As of December 31, 2024, we had an accumulated deficit of $307.0 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 potentially 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 relative to cost of sales. This will require us to be successful in a range of challenging activities, including developing our clinical candidates, discovering additional therapeutic candidates, conducting preclinical studies prior to submitting investigational new drug applications (INDs), obtaining clearance for such INDs, 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 many 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 novel therapeutic approach makes assessments of our future success or viability subject to significant uncertainty. We will encounter risks and difficulties frequently experienced by clinical-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 a clinical organization, we will encounter unforeseen expenses, difficulties, complications, delays and other known and unknown circumstances. As we advance our therapeutic candidates into and through the clinic and towards potential commercialization, we will need to transition from a company with a research and clinical development focus, to a company also capable of supporting commercial activities. We may fail in this transition.

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

We believe that our existing cash, cash equivalents and marketable securities will enable us to fund our operations into 2026. 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. Based on our available cash resources, we believe we do not have sufficient cash and cash equivalents on hand to support current operations for at least one year from the date of issuance of the financial statements appearing within this Annual Report on Form 10-K. As a result, we have substantial doubt about our ability to continue as a going concern. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. If we are unable to raise additional funding, we will be forced to delay, reduce or discontinue our product development programs efforts.

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, conduct our current, and initiate new, clinical trials for and in support of 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.

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 in support 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 and related non-interventional natural history studies;
- 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, enforcing, and defending our patents and other intellectual property rights;
- the costs associated with our efforts to maintain the necessary operational systems and retain the necessary personnel to satisfy our obligations as a public company, including enhanced internal control over financial reporting, corporate compliance and corporate governance;
- 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 existing license and any potential collaboration agreements;
- 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;
- 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; and
- costs associated with continuing to operate as a public company.

In the future, 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. 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.

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 (mAb product), and first small molecule TREM2 agonist product (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, subject to post-grant modification of an award, 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 iluzanebart and VG-3927 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 iluzanebart, VG-3927 or therapeutic candidates from any of our discovery programs;
- our ability to enroll patients in clinical trials and non-interventional natural history studies 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 or desire to conduct preclinical studies or clinical trials, in countries outside of the United States, or studies or trials that are otherwise larger, lengthier or more complex than anticipated, any of which may be unanticipated;
- competition from existing and potential future products that compete with iluzanebart, VG-3927 or any of our other 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 iluzanebart, VG-3927 or any of our discovery programs;
- our ability to commercialize iluzanebart, VG-3927 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;
- the changing and volatile global economic and political environment, including inflation or political instability in particular foreign economies and markets; and
- the impact of the current and future armed conflicts, including Russia and Ukraine and the armed conflict in the Middle East, 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 and social effects.

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.

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. Pursuant to the rules and regulations of the SEC regarding compliance with Section 404 of the Sarbanes-Oxley Act of 2002, we are required to furnish a report by our management on our internal control over financial reporting. However, while we remain an emerging growth company or a smaller reporting company with less than $100 million in revenue, we will not be required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. Failure to comply with the rules and regulations of the SEC could potentially subject us to sanctions or investigations by the SEC, the applicable stock exchange or other regulatory authorities, which would require additional financial and management resources. We have begun the process of compiling the system and processing documentation necessary to perform the evaluation needed to comply with the rules and regulations of the SEC in the future, but we may not be able to complete our evaluation, testing and any required remediation in a timely fashion. An independent assessment of the effectiveness of our internal control over financial reporting could detect deficiencies in our internal control over financial reporting that our management's assessment might not. Undetected material weaknesses in our internal control over financial reporting could lead to financial statement restatements and require us to incur the expense of remediation.

We can give no assurance that a material weakness in our internal controls over financial reporting will not be identified in the future. Maintaining adequate internal control over financial reporting and ensuring that we can produce accurate financial statements on a timely basis may distract our officers and employees and entail substantial costs. 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 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 compromises or incidents of, loss or leakage of data from, or other disruptions in, our internal information technology systems and infrastructure, 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 or protected 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 and maintain our confidential or protected information, systems, and/or infrastructure.

Despite the implementation of security measures, given their size and complexity and the increasing amounts of confidential or protected information that they maintain, our internal information technology systems and infrastructure 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 compromises or 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, digital extortion, business email compromise, and denial-of-service attacks, social engineering and other means to affect service reliability and threaten the confidentiality, integrity and availability of information, systems, or infrastructure), which may compromise our systems infrastructure, data, or that of our third-party CROs, vendors and other contractors and consultants, or lead to data compromise, misuse, misappropriation, or leakage. The risk of a security compromise, incident, or disruption, particularly through cyber-attacks or cyber intrusion, including by computer hackers, foreign governments, insider threats, and cyber terrorists, has generally increased as the number, intensity and sophistication of attempted attacks and intrusions from around the world have increased. Further, bad actors around the world use increasingly sophisticated methods, including the use of artificial intelligence (AI) systems, to engage in illegal activities, including security incidents, that can result in the theft and misuse of personal information, confidential information, and intellectual property. Also, we have 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, decreased physical oversight of employees, as well as increased disbursement of physical machines. While we implement information technology controls to reduce the risk of a cyber security or data security compromise or incident, there is no guarantee that these measures will be adequate to safeguard all systems, data, or infrastructure, especially with an increased number of employees working remotely. The techniques used by cyber criminals change and evolve frequently, may not be recognized until launched and can originate from a wide variety of sources, including outside groups such as external service providers, insider threats, organized crime affiliates, terrorist organizations or hostile foreign governments or agencies. Disruptions or security compromises or incidents resulting in a loss of, or damage to, our data, systems, infrastructure, or applications, or those of our third-party CROs, vendors and other contractors and consultants, or inappropriate use, access, or disclosure of confidential, protected, or proprietary information, could generate liability and reputational damage and the further development and commercialization, if approved, of iluzanebart, VG-3927 or any future therapeutic candidates could be delayed. The costs related to significant security compromises, incidents, or disruptions could be material and not be covered by or exceed the limits of the cybersecurity insurance we maintain against such risks. We may have limited recourse for disruptions, compromises, or breaches of the information technology systems or infrastructure of our third-party CROs, vendors and other contractors and consultants, and we may have to expend significant resources to respond to, mitigate, and remediate 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, incidents, compromises, or vulnerabilities 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 iluzanebart, VG-3927 or any other future clinical candidates could result in delays in our marketing approval efforts and significantly increase our costs to recover or reproduce the data.

Furthermore, security incidents, compromises, or significant disruptions of our internal information technology systems, data, or infrastructure, or those of our third-party CROs, vendors and other contractors and consultants, could result in the loss, misappropriation and/or unauthorized access, use, acquisition, or disclosure of, or the prevention of access to, confidential or protected 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, acquisition, or disclosure of confidential, protected, or 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 protected information, including personal information, including through litigation or regulatory investigations or enforcement actions, which could result in significant legal and financial exposure and reputational damages that could potentially have an adverse effect on our business.

We have in the past, and may in the future, rely on sales of our common shares through our at-the-market (ATM) offering program. Increased volatility and decreases in market prices of equity securities generally and of our common shares in particular may have an adverse impact on our willingness and/or ability to sell our common shares through our ATM program. Decreases in these sales could affect the cost or availability of equity capital, which could in turn have an adverse effect on our business, including current operations, future growth, revenues, net income and the market prices of our common shares.

On March 21, 2023, we filed a Registration Statement on Form S-3, as amended (the 2023 Shelf) with the SEC, which was declared effective on March 30, 2023 (File No. 333-270710) in relation to the registration of common stock, preferred stock, debt securities, warrants and units of any combination thereof. We also simultaneously entered into an Open Market Sale Agreement (the Sale Agreement) with Jefferies LLC (the Sales Agent) to provide for the offering, issuance and sale of up to an aggregate amount of $100.0 million of our common stock from time to time in "at-the-market" offerings under the 2023 Shelf and subject to the limitations thereof. Under the terms of the Sale Agreement, we agreed to pay the Sales Agent cash commissions of up to 3.0% of the gross proceeds of sales of common stock under the Sale Agreement. As of March 11, 2025, we have sold 8,671,793 shares of common stock under the ATM program and received aggregate net proceeds of $22.8 million. As of March 11, 2025, approximately $76.5 million of our common stock remained available for issuance under our ATM program.

Given the volatility in the capital markets, we may not be willing or able to raise additional equity capital through our ATM program. We may, therefore, need to turn to other sources of funding that may have terms that are not favorable to us, or reduce our business operations given capital constraints. In addition, sales of a substantial number of shares of our outstanding common stock in the public market could occur at any time. These sales, or the perception in the market that the holders of a large number of shares of common stock intend to sell shares, could reduce the market price of our common stock. We cannot predict the effect that future sales of common stock or other equity-related securities would have on the market price of our common stock. Investors who purchase shares in this offering at different times will likely pay different prices, and so may experience different outcomes in their investment results. We will have discretion, subject to market demand, to vary the timing, prices and numbers of shares sold, and there is no minimum or maximum sales price. Investors may experience a decline in the value of their shares as a result of share sales made at prices lower than the prices they paid.

Subject to certain limitations in the Sale Agreement and compliance with applicable law, we have the discretion to deliver a placement notice to the Sales Agent at any time throughout the term of the Sale Agreement. The number of shares that are sold by the Sales Agent after delivering a placement notice will fluctuate based on the market price of our common stock during the sales period and limits we set with the Sales Agent in any instruction to sell shares, and the demand for our common stock during the sales period. Because the price per share of each share sold will fluctuate based on the market price of our common stock during the sales period, it is not possible at this stage to predict the number of shares or the gross proceeds to be raised in connection with those sales, if any, that will be ultimately issued.

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

We are early in our development efforts. We have not successfully completed any late-stage clinical trials, and if we are unable to complete our current clinical trials or identify and advance additional 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.

We are early in our development efforts, and we have not yet demonstrated our ability to successfully complete any late-stage 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 and clinical studies. As an early-clinical organization, our experience in conducting clinical trials is limited. Our lead clinical candidate, iluzanebart, a TREM2 agonist, has been evaluated in a Phase 1 healthy volunteer study and is currently being studied in a Phase 2 clinical trial in patients with adult-onset leukoencephalopathy with axonal spheroids and pigmented glia (ALSP). In addition, we are conducting a non-interventional natural history study of patients with ALSP.

In addition, we are developing VG-3927, a novel small molecule TREM2 agonist, for the treatment of common neurodegenerative diseases associated with microglial dysfunction, with initial development for the treatment of AD. In January 2025, we reported completed data from the Phase 1 clinical trial evaluating VG-3927 for the potential treatment of AD.

We may never advance these programs beyond their current clinical trials, advance any other current or future therapeutic candidates to an IND filing or receive clearance from the FDA to commence additional clinical trials for our current or future 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 future clinical trials to be delayed or prevent us from conducting clinical trials. Even after we receive and incorporate guidance from 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 the United Kingdom and 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, patient recruitment, enrollment and retention 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 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;
- 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 particular therapeutic candidates or indications, such as our initial focus on developing iluzanebart for ALSP and VG-3927 for AD, 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 clinical candidates.

One of our strategies is to identify and pursue clinical development of therapeutic candidates beyond iluzanebart and VG-3927. 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 indications other than ALSP and AD that later prove to have greater commercial potential. We are highly dependent on the success of the ongoing and future clinical trials of iluzanebart, our lead clinical candidate, and an ongoing related natural history study, 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. If either of our clinical candidates 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 preclinical 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, and multiple investigational AD therapies have not succeeded in clinical trials such as solanezumab, gantenerumab, and idalopirdine. More recently, a former competitor ceased development of a TREM2 agonist product candidate for AD after it failed to reach the primary endpoint in a Phase 2 clinical trial. No effective therapeutic options are available for patients with ALSP, and limited options exist for AD 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 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 neurodegenerative diseases that have strong genetic, mechanistic, and biochemical associations to microglial dysfunction and then utilize findings from these efforts to inform expansion into broader populations and additional indications of neurodegenerative diseases. We believe our strategy has the potential to mitigate downstream translational risk as we seek to advance our programs through early development and into the clinic. 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 currently conduct, and in the future, may conduct clinical trials that utilize an "open-label" trial design, 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 currently conduct, and in the future, 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 with different dosing regimens. 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, on one hand, patients perceive their symptoms to have improved merely due to their awareness of receiving an experimental treatment. 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. 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. In any event, results from an open-label trial may not be predictive of future clinical trial results, including blinded and/or controlled trials, that test any of our therapeutic candidates.

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 the therapeutic candidate in humans. 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. 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 or other regulatory authorities will accept any additional 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 or foreign equivalents for our preclinical programs on the timelines we expect, if at all, and we cannot be sure that submission of INDs or foreign equivalents will result in the FDA or other regulatory authorities 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. Through our interactions with the FDA to date we cannot be certain how many clinical trials of iluzanebart, VG-3927 or any other therapeutic candidates will be required or how such future 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 indication for iluzanebart, our lead clinical candidate, is a rare disease, 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 or completion 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 study 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 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, including clinical holds, 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 ongoing or 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 if 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.

Additionally, if the results of any 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 may offer to certain volunteers of our natural history study enrollment in potential future interventional clinical trials for ALSP and therefore any potential delays in enrollment in the natural history study could have adverse consequences for our clinical development program for iluzanebart.

In addition, we may experience delays or disruptions in the initiation of or enrollment in our clinical trials due to external factors such as changes in local site or IRB policies, availabilities or changes of site staff, or a public health crisis. 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 AD and rare leukoencephalopathies and leukodystrophies, and may in the future initiate trials in our lead clinical 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 or trial completion 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 iluzanebart or VG-3927, in relation to available or investigational drugs;
- clinicians' misdiagnosis of patients with existing neurodegenerative diseases in our targeted indications and our inability to recruit these patients successfully;
- design of the trial protocol;
- efforts to facilitate timely enrollment in clinical trials;
- eligibility and exclusion criteria;
- availability of competing therapies and clinical trials;

- severity of the disease or disorder under investigation;
- proximity and availability of clinical trial sites for prospective patients;
- ability to obtain and maintain patient consent;
- size of the patient population required for analysis of the trial's primary endpoints;
- ability to recruit clinical trial investigators with the appropriate competencies and experience;
- risk that enrolled patients will drop out before completion of the trial;
- performance of third-party vendors, including CROs;
- patient referral practices of physicians; and
- ability to monitor patients adequately during and after treatment.

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

Even if we are able to enroll a sufficient number of patients for our clinical trials, we may have difficulty retaining patients in our clinical trials. In our ongoing and 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 late-stage clinical trials of any of our therapeutic candidates, and our understanding of the clinical safety profile of these candidates is still limited to our in-progress Phase 2 clinical trial, Phase 1 clinical trial and pre-clinical studies. There may be serious adverse events or undesirable side effects related to our therapeutic candidates. To our knowledge, no approved products target TREM2. 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 any of our therapeutic candidates reach the market, safety problems may thereafter occur or be identified and 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, or, if applicable, pause or terminate any ongoing studies.

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 requirements, 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. In addition, the U.S. Supreme Court's July 2024 decision to overturn prior established case law giving deference to regulatory agencies' interpretations of ambiguous statutory language has introduced uncertainty regarding the extent to which FDA's regulations, policies and decisions may become subject to increasing legal challenges, delays, and/or changes. 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 early preclinical studies and prior clinical trials are not necessarily predictive of the results of later preclinical studies and any subsequent clinical trials of our therapeutic candidates, and interim, topline and preliminary data from our 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 early 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 iluzanebart, and although iluzanebart has been studied in a Phase 1 clinical trial in healthy volunteers and is being studied in a Phase 2 clinical trial in ALSP patients, we have not

completed any trials in ALSP patients, and we do not know whether its performance in its prior clinical trial and preclinical studies will be indicative of the performance of iluzanebart in ALSP patients. Similarly, although VG-3927 has been studied in preclinical studies and a recently completed Phase 1 clinical trial, we do not know whether its performance in preclinical studies or its prior clinical trial will be indicative of the performance of VG-3927 in future clinical trials or in AD patients, nor do we know whether performance of our other potential therapeutic candidates in preclinical studies will be indicative of their performance in clinical trials. 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 considering or 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 iluzanebart, VG-3927 or our other development programs.

From time to time, we may publicly disclose interim, preliminary or topline data from our 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 candidates, 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 and other lawsuits against us or our contract development and manufacturing partners (CDMOs) could divert our resources, could cause us to incur substantial liabilities and could limit commercialization of any therapeutic candidates we may develop.

We face an inherent risk of clinical trial and product liability and other exposure related to the testing of any therapeutic candidates we develop in clinical trials, and we will face an even greater risk if we commercially sell any products that we may develop. We additionally rely on the services of CDMOs who manufacture our therapeutic candidates or conduct clinical trials on our behalf. Our agreements with CDMOs may require us to indemnify the CDMOs in the event of a third-party claim arising from the use or manufacture of our therapeutic candidates, which could divert our resources and incur substantial liabilities, possibly prior to the potential commercialization of our therapeutic candidates. The use of therapeutic candidates by us or our CDMOs in clinical trials, and the sale of any approved products in the future, may expose us to liability claims. These claims against us or our CDMOs might be made by patients who use the product, purchasers of our products, healthcare providers, pharmaceutical companies or others selling such products. If we cannot successfully defend ourselves or our CDMOs 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.

If we expand our clinical trial activities or if we commence commercialization of any therapeutic candidates, we will need to increase our insurance coverage beyond what is currently maintained. 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 pursue 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 currently plan to pursue accelerated approval for iluzanebart from the FDA for the treatment of ALSP, and we may also seek an accelerated approval pathway for one or more of our therapeutic candidates from the 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. Under the Food and Drug Omnibus Reform Act of 2022 (FDORA), the FDA is permitted to require, as appropriate, that a post-approval confirmatory study or studies be underway prior to approval or within a specified time period after the date of approval for a product granted accelerated approval. FDORA also gives the FDA increased authority to withdraw approval of a drug or biologic granted accelerated approval on an expedited basis if the sponsor fails to conduct such studies in a timely manner, send status updates on such studies to the FDA every 180 days to be publicly posted by the agency, or if such post-approval studies fail to verify the drug's predicted clinical benefit. The FDA is empowered to take action, such as issuing fines, against companies that fail to conduct with due diligence any post-approval confirmatory study or submit timely reports to the agency on their progress.

Prior to seeking accelerated approval, we plan to seek feedback from the FDA, EMA or comparable foreign regulatory authorities and evaluate our ability to seek and receive such accelerated approval. Regulatory authorities may not agree with our proposed clinical development plans, and 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. For example, following our Type C meetings with the FDA, the agency stated it was open to considering the accelerated approval pathway for iluzanebart in ALSP and we continue to engage with the agency regarding this possibility. However, as we continue to engage with FDA and receive feedback from the Agency, there can be no assurance that we will continue to pursue or apply for accelerated approval or any other form of expedited development, review or

approval, including from EMA or comparable foreign regulatory authorities, 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 preclinical or clinical 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 have received fast track designation and orphan drug designation for iluzanebart. We may in the future seek these and other designations, such as breakthrough therapy designation and/or priority review 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 hold or in the future 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. Although we have received fast track designation for iluzanebart, if iluzanebart or any of our therapeutic candidates that may in the future receive fast track designation 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, 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, and (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. 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 European Union. Regulatory authorities may not grant our requests for orphan designation, or may require submission of additional data before making such determination. For example, even though we obtained orphan drug designation from the FDA in the U.S. and an orphan medicinal product designation in the European Union for iluzanebart, we may not be able to obtain orphan drug designation from other health authorities or for other product candidates in the future. Further, even after obtaining orphan drug designation for a therapeutic candidate, including iluzanebart, we may not be able to obtain or maintain orphan drug exclusivity for that therapeutic candidate. Legislation has been proposed by the European Commission that, if approved and implemented, has the potential in some cases to shorten the ten-year period of orphan marketing exclusivity.

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, and even when received, 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, as initial consideration for the license, we paid an upfront payment of $500,000 and also issued 8,891,659 shares of our Series A preferred stock to Amgen; all of our then outstanding preferred stock converted into common stock at our initial public offering in January 2022. 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 ongoing and planned clinical trials. For instance, iluzanebart 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 iluzanebart 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 iluzanebart drug substance or drug product would delay our ability to conduct and complete clinical trials. In addition, these third-party manufacturers may not be able to comply with cGMP regulations or similar regulatory requirements outside the United States. Our failure, or the failure of third-party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of product candidates or medicines, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our medicines and harm our business and results of operations.

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 clinical trials in a satisfactory manner, if the quality or accuracy of the data they obtain is compromised due to the failure to adhere to our 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 data they obtain is compromised due to the failure to adhere to our 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 a pandemic or government policy, 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. 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 iluzanebart (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 any of our 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 have in the past, and may in the future, 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 have in the past, and may in the future, seek third-party collaborators for the research, development and commercialization of certain of the therapeutic candidates we may develop. For example, in June 2024, in connection with an equity investment, we provided Genzyme Corporation, a wholly-owned subsidiary of Sanofi, with a right of first negotiation for an exclusive license, grant or transfer of rights to research, develop, manufacture and commercialize our small molecule TREM2 agonist program, including our clinical candidate, VG-3927. We cannot predict whether Genzyme Corporation will exercise such rights, or, if it does, whether we will reach an agreement with Genzyme Corporation, or if any such agreement will be beneficial to us. 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;
- 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;

- collaboration agreements may not lead to development or commercialization of therapeutic candidates in the most efficient manner or at all; and
- our collaborators' business or operations could be disrupted due to a 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.

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 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. 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. Our issued patents in the U.S. or other major markets may not cover all of our technologies 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 patents 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, 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 iluzanebart and related molecules, intellectual property and manufacturing know-how, and our small molecule agonist program, including VG-3927, which includes a portfolio of approximately 1,000 compounds. The Amgen Agreement imposes, and we expect that any future license agreement will impose, specified diligence, milestone payments, royalty, commercialization, development and other obligations on us and require us to meet development timelines, or to exercise diligent or commercially reasonable efforts to develop and commercialize licensed products, in order to maintain the licenses.

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

and our technology. Any of the foregoing could have a material adverse effect on our competitive position, business, financial condition, results of operations and prospects.

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

- the scope of rights granted and obligations imposed under the license agreement and other interpretation-related issues;
- our or our licensors' ability to obtain, maintain and defend intellectual property and to enforce intellectual property rights against third parties;
- the extent to which our technology, therapeutic candidates and processes infringe, misappropriate or otherwise violate the intellectual property of the licensor that is not subject to the license agreement;
- the sublicensing of patent and other intellectual property rights under our license agreements;
- our diligence, development, regulatory, commercialization, financial or other obligations under the license agreement and what activities satisfy those diligence obligations;
- the inventorship and ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our current or future licensors and us and our partners; and
- the priority of invention of patented technology.

In addition, any current or future license agreements to which we are a party, including our license agreement with Amgen, are likely to be complex, and certain provisions in such agreements may be susceptible to multiple interpretations. The resolution of any contract interpretation disagreement that may arise could narrow what we believe to be the scope of our rights to the relevant intellectual property or technology, or increase what we believe to be our diligence, development, regulatory, commercialization, financial or other obligations under the relevant agreement. In addition, if disputes over intellectual property that we have licensed or any other dispute related to our license agreements prevent or impair our ability to maintain our current license agreements on commercially acceptable terms, we may be unable to successfully develop and commercialize the affected therapeutic candidates and technology. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations and prospects.

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

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

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

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

Filing, prosecuting, maintaining, enforcing and defending patents and other intellectual property rights on our technology and any therapeutic candidates we are developing or 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 are developing or 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 are developing or 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 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, U.S. patents that we own or 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, 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. Such third-party registered trademark owners may seek and obtain a court order that could prevent us from continuing to use

our trademarks or trade names or order a payment of monetary damages. Our efforts to enforce, protect or defend 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 and clinical 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. Through executive and legislative action, the federal government has also taken steps to restrict data transactions involving certain sensitive data categories – including health data, genetic data, and biospecimens – with persons affiliated with China, Russia, and other countries of concern.

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, the California Consumer Privacy Act ("CCPA") is a comprehensive privacy law that creates individual privacy rights and places stringent privacy and security obligations on businesses covered by the law, including obligations to provide detailed disclosures to California consumers about their data collection, use and sharing practices and provide such consumers with ways to opt out of certain uses of sensitive personal information. It also provides for civil penalties for violations and allows for a private right of action for data breaches that is expected to increase data breach litigation. The law also created a new state regulatory agency that was vested with authority to implement and enforce the CCPA. Additionally, comprehensive privacy laws akin to the CCPA have been passed in numerous other states, and, with bills being proposed in several other states, it is quite possible that other U.S. states will follow suit. Like the CCPA, these laws grant consumers rights in relation to their personal information and impose new obligations on regulated businesses,

including, in some instances, broader data security requirements but unlike the CCPA, which also applies to personal information collected in the business-to-business and human resources contexts, to date, the other state privacy laws are generally limited to personal information collected from consumers. In addition to these comprehensive consumer privacy laws and proposals, a number of other states have passed or proposed more limited privacy laws that focus on specific privacy issues such as biometric data and the privacy of health and medical information, such as Washington state's My Health My Data Act. The existence of privacy laws in different states in the country will make our compliance obligations more complex and costly.

Regulators and legislators in the U.S. are increasingly scrutinizing and restricting certain personal data transfers and transactions involving foreign countries. For example, Executive Order 14117 of February 28, 2024, Preventing Access to Americans' Bulk Sensitive Personal Data and United States Government-Related Data by Countries of Concern as implemented by Department of Justice regulations issued in December 2024, prohibits data brokerage transactions involving certain sensitive personal data categories, including health data, genetic data, and biospecimens, to countries of concern, including China. The regulations also restrict certain investment agreements, employment agreements and vendor agreements involving such data and countries of concern, absent specified cybersecurity controls. Actual or alleged violations of these regulations may be punishable by criminal and/or civil sanctions, and may result in exclusion from participation in federal and state programs.

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, we conduct studies in the European Economic Area, the EEA and are subject to the EU General Data Protection Regulation, the EU GDPR. The EU GDPR governs the collection, use, disclosure, transfer or other processing of personal data of individuals in the EEA. Among other things, the EU GDPR imposes strict requirements regarding the security of personal data and notification of data breaches to the competent national data protection authorities, imposes limitations on retention of personal data, imposes stringent requirements relating to the consent of data subjects or ensuring another appropriate legal basis applies to the processing of personal data, requires us to maintain records of our processing activities and to document data protection impact assessments where there is high risk processing, ensuring certain measures are in place with third-party processors, provides a broad definition of personal data and requires detailed notices for clinical trial subjects and investigators. In addition, the EU 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 (EC) does not recognize as having "adequate" data protection laws. These transfers are prohibited unless a valid transfer mechanism is implemented, such as the Standard Contractual Clauses (SCCs) published by the EC, binding corporate rules or certification to the EU-U.S. Data Privacy Framework that the EC adopted on July 10, 2023. Any inability to transfer personal data from the EEA to the United States in compliance with data protection laws may impede our ability to conduct trials and may adversely affect our business and financial position. The EU GDPR imposes substantial fines for breaches and violations (up to the greater of €20 million or 4% of our consolidated annual worldwide gross revenue). The EU GDPR also confers a private right of action on data subjects and consumer associations to lodge complaints with competent national data protection authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of the EU GDPR. Non-compliance could also result in the imposition of orders to stop data processing activities.

In particular, national laws of Member States of the EU have implemented national laws which may partially deviate from the EU GDPR and impose different and more restrictive obligations from country to country, so that we do not expect to operate in a uniform legal landscape in the EU. Also, as it relates to processing and transfer of sensitive data (such as health data), the EU GDPR specifically allows EU Member State nations to enact laws that impose additional and more specific requirements or restrictions, and European laws have historically differed quite substantially in this field, leading to additional uncertainty.

The U.K. GDPR and the U.K. Data Protection Act 2018 set out the U.K.'s data protection regime, which is independent from but largely aligned to the EU's data protection regime with the same requirements as set out above for the EU GDPR. Like the EU GDPR, the U.K. GDPR restricts personal data transfers outside the U.K. to countries not regarded by the U.K. as providing adequate protection. It is not subject to the new form of SCCs but has issued its own transfer mechanism – the U.K. international data transfer agreement and addendum. Moreover, on September 21, 2023, the U.K. Government adopted the Data Protection (Adequacy) Regulations 2023, also referred to as the "UK-U.S. Data Bridge", which will allow companies to transfer personal data from the U.K. to the U.S. on the basis of the EU-U.S. Data Privacy Framework. The U.K.'s government has confirmed that personal data transfers from the U.K. to the EEA remain free flowing. The European Commission has adopted an adequacy decision in favor of the U.K., enabling data transfers from EU member states to the U.K. without additional safeguards. However, the U.K. adequacy decision will automatically expire in June 2025 unless the European Commission renews or extends that decision. There may be further divergence in the future, including with regard to administrative burdens. The U.K. Government has announced plans to reform the country's data protection legal framework in its Data Reform Bill introduced into the U.K. legislative process, which if passed, may have the effect of further altering the similarities between the U.K. and EEA data protection regimes and threaten the U.K.'s adequacy decision from the European

Commission. The potential for the provisions and enforcement of the EU GDPR and UK GDPR further diverging in the future and the lack of clarity on future UK laws and regulations and their interaction with EU laws may lead to additional compliance costs and could increase our overall risk exposure as we may no longer be able to take a unified approach across the EEA and the U.K. 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.

These and other future developments regarding data protection laws and the flow of data across borders could increase the cost and complexity of delivering our services in some markets and may lead to governmental and/or data protection authority enforcement actions, litigation, fines, and penalties or adverse publicity, which could adversely affect our business and financial position.

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, implementing certain security controls and related technologies, 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 our systems, infrastructure, and confidential or protected information, including personal information could result in governmental and/or data protection authority enforcement actions, litigation, or negative publicity, any of which could inhibit our ability to grow our business. Potential claims that we have violated individuals' privacy rights, failed to comply with data protection laws, or breached our contractual obligations, even if we are not found liable, could be expensive and time consuming to defend and could result in adverse publicity that could harm our business.

Organizations are also increasingly subject to a wide variety of sophisticated attacks on their networks, systems, infrastructure, and endpoints, including the theft and subsequent misuse of employee credentials, denial-of-service attacks, ransomware attacks, digital extortion, business email compromises, malware, viruses, and social engineering (including phishing). The techniques used to obtain unauthorized access or to sabotage systems, networks, infrastructure, or physical facilities in which data is stored or through which data is transmitted, or on which our services and operations rely, evolve and 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 or on which our services and operations rely, failure to prevent or mitigate the loss of confidential or protected information, including personal or business information, and delays in detecting, remediating, or providing prompt notice of any such compromise or loss could disrupt our operations, harm our reputation, result in loss of business or customers, 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 incident or compromise, including 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 incidents or to address and alleviate problems caused by such disruptions, compromises, incidents, or breaches, including costs to deploy additional personnel and protection technologies, train employees, and engage third-party experts and consultants, including legal counsel, 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. Additionally, under FDORA, sponsors of approved drugs and biologics must provide six months' notice to the FDA of any changes in marketing status, such as the withdrawal of a drug, and failure to do so could result in the FDA placing the product on a list of discontinued products, which would revoke the product's ability to be marketed.

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 and vice-versa. Failure to obtain marketing approval in the U.S. or 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). For more information, please see *"Business – Government Regulation – Marketing Authorization"*.

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 iluzanebart, VG-3927 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 iluzanebart, VG-3927 and future therapeutic candidates for which we obtain marketing approval. For more information regarding the risks related to these laws and regulations please see "*Business – Government Regulation – Other Healthcare Laws*."

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. Any action against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management's attention from the operation of our

business. The shifting compliance environment and the need to build and maintain robust and expandable systems to comply with multiple jurisdictions with different compliance or reporting requirements increases the possibility that a healthcare company may run afoul of one or more of the requirements.

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.

The U.S. and many foreign jurisdictions have enacted or proposed legislative and regulatory changes affecting the healthcare system. The U.S. government, state legislatures and foreign governments also have shown significant interest in implementing cost-containment programs to limit the growth of government- paid healthcare costs, including price controls, restrictions on reimbursement and requirements for substitution of generic products for branded prescription drugs. Additional changes that may affect our business include those governing enrollment in federal healthcare programs, reimbursement changes, rules regarding prescription drug benefits under the health insurance exchanges and fraud and abuse and enforcement. Continued implementation of the ACA and the passage of additional laws and regulations may result in the expansion of new programs such as Medicare payment for performance initiatives, and may impact existing government healthcare programs, such as by improving the physician quality reporting system and feedback program. For more information regarding the risks related to recently enacted and future legislation please see *"Business – Government Regulation – Healthcare Reform."*

We cannot predict the initiatives that may be adopted in the future. The continuing efforts of the government, insurance companies, managed care organizations and other payors of healthcare services to contain or reduce costs of healthcare and/or impose price controls may adversely affect:

- the demand for our product candidates, if we obtain regulatory approval;
- our ability to set a price that we believe is fair for our approved products;
- our ability to generate revenue and achieve or maintain profitability;
- the level of taxes that we are required to pay; and
- the availability of capital.

We expect that additional U.S. federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that the U.S. federal government will pay for healthcare drugs and services, which could result in reduced demand for our drug candidates or additional pricing pressures. Individual states in the United States have also become increasingly active in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain drug access and marketing cost disclosure and transparency measures, and designed to encourage importation from other countries and bulk purchasing.

Legally mandated price controls on payment amounts by third-party payors or other restrictions could harm our business, financial condition, results of operations and prospects. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other healthcare programs. This could reduce the ultimate demand for our drugs or put pressure on our drug pricing, which could negatively affect our business, financial condition, results of operations and prospects.

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 or treatment methods or other standards of care;
- the indications for which our therapeutic candidates are approved;
- the identification of patients eligible to receive our therapeutics for which our therapeutics 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.

There are examples of therapies for neurodegenerative diseases that have obtained regulatory approval, but ultimately were unsuccessful in achieving an adequate level of acceptance by physicians, hospitals, healthcare payors or patients. For instance, in January 2024, Biogen, Inc. announced it would discontinue development and commercialization of ADUHELM® (aducanumab-avwa) which received approval for the treatment of AD in 2021.

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. For more information, please see "*Business – Government Regulation – Coverage and Reimbursement.*"

Third-party payors increasingly are challenging prices charged for biopharmaceutical products and services, and many third-party payors may refuse to provide coverage and reimbursement for particular drugs or biologics when an equivalent generic drug, biosimilar or a less expensive therapy is available. It is possible that a third-party payor may consider our product candidates as substitutable and only offer to reimburse patients for the cost of the less expensive product. Even if we show improved efficacy or improved convenience of administration with our product candidates, pricing of existing third-party therapeutics may limit the amounts we will be able to charge for our product candidates. These payors may deny or revoke the reimbursement status of a given product or establish prices for new or existing marketed products at levels that are too low to enable us to realize an appropriate return on our investment in our product candidates.

We cannot be sure that coverage and reimbursement in the U.S., the European Union or elsewhere will be available for our product candidates or any product that we may develop, and any reimbursement that may become available may be decreased or eliminated in the future. In the U.S., third-party payors, and governmental healthcare plans, such as the Medicare and Medicaid programs, play an important role in determining the extent to which new drugs and biologics will be covered. The Medicare and Medicaid programs increasingly are used as models in the U.S. for how private payors and other governmental payors develop their coverage and reimbursement policies for drugs and biologics. Some third-party payors may require pre-approval of coverage for new or innovative drug therapies before they will reimburse healthcare providers who use such therapies. If reimbursement is not available or is available only at limited levels, we may not be able to successfully commercialize our product candidates and may not be able to obtain a satisfactory financial return on our investment in the development of product candidates. Outside the U.S., international operations are generally subject to extensive governmental price controls and other market regulations, and we believe the increasing emphasis on cost-containment initiatives in Europe and other foreign jurisdictions have and will continue to put pressure on the pricing and usage of our product candidates. We cannot predict at this time what third-party payors will decide with respect to the coverage and reimbursement for our product candidates.

We expect that healthcare reform measures that may be adopted in the future may result in more rigorous coverage criteria and in additional downward pressure on the price that we receive for any approved product. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our products. Legislative and regulatory proposals have been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical products. We cannot be sure whether additional legislative changes will be enacted, or whether the FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals or clearances of our product candidates, if any, may be.

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, radioactive, 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 and claims associated with upgrades, maintenance and construction at our facilities or changes to our operating procedures, or injunctions limiting or altering our operations. Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with our storage or disposal of biological, hazardous or radioactive materials.

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

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

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

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

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

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

Under current law, 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. The completion of private placements and other transactions that have occurred since inception, may trigger such ownership change pursuant to Section 382 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. Any such limitation, whether as the result of the mergers, prior private placements, sales of our common stock by our existing stockholders, or additional sales of our common stock by us after the mergers, could have a material adverse effect on our results of operations in future years. Our net operating losses and tax credits may also be impaired or restricted under state law. As of December 31, 2024, we had approximately $133.6 million of U.S. federal and $137.2 million of state net operating loss carryforwards due to prior period losses. Our federal NOLs can be carried forward indefinitely and our State NOLs expire at various dates beginning in 2040.

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 greater Boston 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. To provide added incentives to retain and motivate key contributors, in May 2024, our board of directors approved a stock option repricing. In addition, at our 2024 Annual Meeting of Stockholders, our stockholders approved a Certificate of Amendment to our Third Amended and Restated Certificate of Incorporation to provide for the exculpation of our executive officers, as permitted under Delaware law, which amendment became effective on June 5, 2024. Despite this, we may have difficulty retaining key personnel, which could adversely affect our business and further development of our product candidates.

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, 2025, we had 69 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 receive 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 iluzanebart or VG-3927, 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 and employment 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 industries are 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, particularly 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 and obtain patent protection, and establish collaborative arrangements, sometimes exclusive, for research, development, manufacturing and commercialization.

Competition can arise from third parties which are pursuing therapeutics that target the same molecular targets as our product candidates, therapeutics that are being developed for the same diseases or disorders as our product candidates, or both, therapeutics that target the same molecular targets and are being developed for the same diseases or disorders as our product candidates. In general, we consider our closest competitors as third parties that are conducting clinical trials to evaluate such therapeutics.

We further define and evaluate competition based on the nature of the disease or disorder that is potentially addressed by our product candidates. For instance, we consider competition more broadly in the context of rare diseases and more narrowly for diseases or disorders that are common. That is, we are more apt to consider a third party a competitor if it is clinically developing a therapeutic for the same rare disease in which we are developing our product candidates, irrespective of the molecular target of the third-party therapeutic. On the other hand, we are less inclined to consider a third party a competitor in the case of a common disease, unless the third party is clinically developing a therapeutic that targets the same molecular target as our product candidates. Nevertheless, the competitive landscape, particularly for common diseases, is highly complex and can be influenced by the success or failure of third-party therapeutics that are being developed for the same disease or disorder as our product candidates. As a result, our share price may be positively or negatively influenced by the activities of such third parties irrespective of whether we consider them to be a competitor or not.

We are aware of third parties which are pursuing therapeutics that target the same molecular targets as our product candidates.

Regarding therapeutics that are being developed for the same diseases or disorders as our product candidates, we consider the main competitors as follows:

- *Iluzanebart for ALSP*: we are not aware of any third parties that are clinically developing therapeutics for ALSP. Further, no products have been approved to treat ALSP. Academics have investigated the use of hematopoietic stem cell transplantation in a small number of ALSP patients, however, we believe this procedure has limited benefits and several key limitations.
- *VG-3927 for AD*: third parties developing therapeutics targeting TREM2 include Novartis AG which is developing VHB937, a TREM2 targeting antibody, for amyotrophic lateral sclerosis and Alzheimer's Disease. In addition, there are many third parties pursuing clinical development of therapeutics for AD. The University of Oxford in collaboration with Janssen Pharmaceutica NV has reported a Phase I trial of JNJ-40346527 (edicotinib), a small molecule CSF-1R antagonist. Elixiron Immunotherapeutics, Inc. has reported a Phase I trial of EI-1071, a small molecule that inhibits the tyrosine kinase activity of CSF-1R. In addition, there are others developing therapeutics for AD that do not target TREM2. Notable examples include those that are based on reduction of ß-amyloid plaques, such as LEQEMBI™ (lecanemab-irmb), which is from Biogen, Inc. and was FDA approved in 2023. Also, in July 2024, the FDA approved Kisunla™(donanemab) which is marketed by Eli Lilly for the treatment of people living with early symptomatic AD. Other ß-amyloid therapeutics and additional approaches for AD are being pursued by Roche (Genentech) and others.

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 may be influenced by the research and reports that securities or industry analysts publish about us, our business or our market. 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, directly or indirectly, to the COVID-19 pandemic, record inflation, the Russia/Ukraine conflict and the conflict in the Middle East, 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 these or other events, 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, more dilutive, or not possible at all.

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 37% of our outstanding voting stock as of February 28, 2025 based on the amounts reported in the most recent filings made by such significant stockholders under Section 13(d) and 13(g) of the Exchange Act.

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 ATM Facility or 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. As of December 31, 2024, we have sold 2,887,021 shares of common stock under our ATM program. Subsequent to December 31, 2024 through March 11, 2025, we sold 5,784,772 shares of common stock under our ATM program. Additionally, pursuant to our 2021 Stock Option and Incentive Plan (2021 Plan), our management is authorized to grant stock options to our employees, directors and consultants. Unless the administrator of the 2021 Plan elects otherwise, the number of shares reserved under our 2021 Plan increases annually by up to five percent of the number of shares of stock issued and outstanding on the immediately preceding December 31 and our stockholders will 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, and has exercised such discretion, to affect the repricing of stock options and stock appreciation rights and there may be adverse consequences to our business due to the exercise of discretion by the administrator of the 2021 Plan.

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. To provide added incentives to retain and motivate key contributors, our board of directors approved a stock option repricing in May 2024. As a result of such repricing or any potential future repricing, 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, as a result of the May 2024 stock option repricing or any potential future repricing, even absent negative reactions from proxy advisory firms and institutional investors, we could incur significant costs, including accounting and administrative costs and attorneys' fees. We may also be required to recognize incremental compensation expense as a result of such repricing. These actions could cause our stock price to decrease and experience periods of increased volatility, which could result in material adverse consequences to our business.

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

We do not have any committed external source of funds or other support for our development and commercialization efforts, and we cannot be certain that additional funding will be available on acceptable terms, or at all. Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through equity offerings, debt financings, or other capital sources, including potential collaborations, licenses and other similar arrangements. To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect your rights as a common stockholder. Any future debt financing and preferred equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, selling or licensing our assets, making capital expenditures, declaring dividends or encumbering our assets to secure future indebtedness. Such restrictions could adversely impact our ability to conduct our operations and execute our business plan.

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

development or future commercialization efforts or grant rights to develop and market therapeutic candidates that we would otherwise prefer to develop and market ourselves. Any of the above events could significantly harm our business, prospects, financial condition and results of operations and cause the price of our common stock to decline.

We are an "emerging growth company" and a smaller reporting company, and we cannot be certain if the reduced reporting requirements applicable to emerging growth companies and smaller reporting companies will make our common stock less attractive to investors.

We are an "emerging growth company," as defined in the Jumpstart Our Business Startups Act of 2012 (JOBS Act). For as long as we continue to be an emerging growth company, we intend to take advantage of exemptions from various reporting requirements that are applicable to other public companies that are not emerging growth companies, including:

- being permitted to provide only two years of audited financial statements, in addition to any required unaudited interim financial statements, with correspondingly reduced "Management's Discussion and Analysis of Financial Condition and Results of Operations" disclosure in our Annual Report on Form 10-K;
- not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002, as amended (Sarbanes-Oxley Act);
- not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements;
- reduced disclosure obligations regarding executive compensation in our Annual Report on Form 10-K and our periodic reports and proxy statements; and
- exemptions from the requirements of holding nonbinding advisory stockholder votes on executive compensation and stockholder approval of any golden parachute payments not previously approved.

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

We will remain an emerging growth company until the earliest to occur of: (i) the last day of the fiscal year in which we have more than $1.235 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 in January 2022.

Even after we no longer qualify as an emerging growth company, we may still qualify as a "smaller reporting company," which would allow us to continue to take advantage of many of the same exemptions from disclosure requirements, including not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act and reduced disclosure obligations regarding executive compensation in our Annual Report on Form 10-K and our periodic reports and proxy statements. We cannot predict if investors will find our common stock less attractive because we may rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile.

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

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

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

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

- a board of directors divided into three classes serving staggered three-year terms, such that not all members of the board will be elected at one time;
- a prohibition on stockholder actions through written consent, which requires that all stockholder actions be taken at a meeting of our stockholders;
- a requirement that special meetings of stockholders be called only by the board of directors acting pursuant to a resolution approved by the affirmative vote of a majority of the directors then in office;
- advance notice requirements for stockholder proposals and nominations for election to our board of directors;
- a requirement that no member of our board of directors may be removed from office by our stockholders except for cause and, in addition to any other vote required by law, upon the approval of not less than two-thirds of all outstanding shares of our voting stock then entitled to vote in the election of directors;
- a requirement of approval of not less than two-thirds of all outstanding shares of our voting stock to amend any bylaws by stockholder action or to amend specific provisions of our certificate of incorporation; and
- the authority of the board of directors to issue preferred stock on terms determined by the board of directors without stockholder approval and which preferred stock may include rights superior to the rights of the holders of common stock.

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

Any provision of our third 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 continue to 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 continue to require that we incur substantial legal and financial compliance costs and to make some activities more time-consuming and costly, which will increase our operating expenses. 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, we are 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 maintain compliance with Section 404, we have engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to continue to dedicate internal resources, potentially engage outside consultants and adopt a detailed work plan to assess and document the adequacy of 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.

The global economy, including credit and financial markets, has experienced extreme volatility and disruptions, including severely diminished liquidity and credit availability, declines in consumer confidence, declines in economic growth, increases in unemployment rates, increases in inflation rates and uncertainty about economic stability. For example, the current Russia-Ukraine conflict, Middle East conflict and recent armed attacks in global shipping lanes have created extreme volatility in the global capital markets and is expected to have further global economic consequences, including disruptions of the global supply chain and energy markets. Continuing concerns over United States health care reform legislation have also contributed to increased volatility. Any such volatility and disruptions may have adverse consequences on us or the third parties on whom we rely.

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, 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;
- 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.

Our board of directors has the authority, without stockholder approval, to issue preferred stock which may include rights superior to the rights of the holders of common stock. The conversion of such preferred stock to common stock and any potential resales could adversely affect the market price of our common stock and result in dilution to existing shareholders.

In June 2024, we created and established the rights of the Series A Non-Voting Convertible Preferred Stock (the "Series A Preferred Stock") and issued 537,634 shares of Series A Preferred Stock to Aventis Inc., a wholly-owned subsidiary of Sanofi (Sanofi), all of which are outstanding as of the date of this filing. Each share of Series A Preferred Stock is convertible into ten shares of common stock. We cannot predict the time at which Sanofi may elect to exercise its conversion rights or the effect that future sales of the as-converted common stock would have on the market price of our common stock or the percentage of ownership of our existing shareholders.

Our certificate of incorporation allows us to issue shares of preferred stock without any vote or further action by our stockholders. In the future, our board of directors may authorize the issuance of a series of preferred stock that would grant to holders of preferred stock the rights to our assets upon liquidation, the right to receive dividend payments before dividends to the holders of common stock and the right to the redemption of the shares, together with a premium, prior to the redemption of our common stock.

Inadequate funding for the FDA, the SEC and other government agencies, including from government shutdowns, or other disruptions to these agencies' operations, could hinder their ability to hire and retain key leadership and other personnel, prevent new products and services from being developed or commercialized in a timely manner or otherwise prevent those agencies from performing normal business functions on which the operation of our business may rely, which could negatively impact our business.

Recently, federal agencies in the U.S. have been operating under a continuing resolution that is set to expire on March 14, 2025. Without appropriation of additional funding to federal agencies, our business operations related to our product development activities for the U.S. market could be impacted. The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, the ability to hire and retain key personnel and accept the payment of user fees, and statutory, regulatory and policy changes. Average review times at the agency have fluctuated in recent years as a result. In addition, government funding of the SEC and other government agencies on which our operations may rely is subject to the political process, which is inherently fluid and unpredictable.

Disruptions at the FDA and other agencies may also slow the time necessary for new product candidates to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. If a prolonged government shutdown occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Further, future government shutdowns could impact our ability to access the public markets and obtain necessary capital in order to properly capitalize and continue our operations.

Unfavorable global economic or political conditions could adversely affect our business, financial condition or results of operations or our vendors. Our business, financial condition and results of operations could be materially adversely affected by any negative impact on the global economy and capital markets.

Our results of operations could be adversely affected by general conditions in the global economy and in the global financial markets. A global financial crisis or a global or regional political disruption could cause extreme volatility in the capital markets and lead to diminished liquidity and credit availability, higher interest rates, declines in consumer confidence and economic growth, increases in unemployment rates and uncertainty about economic stability.

In addition, the impact of geopolitical tension, such as a deterioration in the bilateral relationship between the United States and China or the ongoing war in Ukraine and the conflict in the Middle East, including any resulting sanctions, export controls or other restrictive actions, also could lead to disruption, instability, and volatility in the global markets and our ability

to work with vendors in such geographic regions. Legislation was proposed in 2024 in the U.S. Congress that, if enacted, would have negatively impacted U.S. funding for certain Chinese biotechnology providers, including some of our vendors, who have relationships with certain foreign governments or which pose a threat to national security. While Congress did not pass this legislation, similar future legislation may be proposed. The potential downstream adverse impacts of any such restrictions on entities having only commercial relationships with any impacted Chinese biotechnology providers is unknown but could include supply chain disruptions or delays. The potential downstream adverse impacts on entities having only commercial relationships with any impacted biotechnology providers is unknown but may include supply chain disruptions or delays.

A severe or prolonged economic downturn or political disruption could result in a variety of risks to our business, and our ability to raise additional capital when needed on acceptable terms, if at all. A weak or declining economy or political disruption could also strain our manufacturers or suppliers, possibly resulting in supply disruption, or resulting in the inability of any future customers to demand and pay for iluzanebart or VG-3927, if either are approved. Any of the foregoing could harm our business and we cannot anticipate all of the ways in which the political or economic climate and financial market conditions could adversely impact our business.

Item 1B. Unresolved Staff Comments.

None.

Item 1C. Cybersecurity.

Cybersecurity Risk Management and Strategy

The Company, under the oversight of the audit committee of the board of directors, has implemented and maintains an enterprise risk management program that includes a cybersecurity risk management program designed to identify, assess, and mitigate critical risks from cybersecurity threats.

Our cybersecurity risk management program is informed by industry standards and includes, but is not limited to, ongoing monitoring for potential critical risks from cybersecurity threats using automated tools. We have a process designed to monitor and address identified cybersecurity risks. To support our cybersecurity risk management program, we leverage a managed security service provider (MSSP) and also engage with other third-party providers and cybersecurity consultants as appropriate, including engagement of third parties to assist with managed detection and response and vulnerability management and to perform periodic penetration testing, and other vulnerability analyses.

As part of our cybersecurity risk management program, we have a process to assess and review the cybersecurity practices of certain third-party vendors and service providers that may be critical to the operations of our business and who have access to our information systems or store our confidential data, including, as appropriate, through review of vendor questionnaires and the inclusion of cybersecurity requirements in contracts.

We also have an employee education and training program, offered during onboarding and on a periodic basis thereafter, that is designed to raise awareness of cybersecurity threats across functions as well as to encourage consideration of cybersecurity risks across our Company. As part of this employee training program, we periodically conduct phishing simulations designed to raise employee awareness of such risks.

We have not identified any cybersecurity incidents or threats that have materially affected us or are reasonably likely to materially affect us, including our business strategy, results of operations or financial condition; however, like other companies in our industry, we and our third-party vendors have, from time to time, experienced threats and security incidents relating to our and our third-party vendors' information systems. See Item 1A "Risk Factors" in this Annual Report on Form 10K for more information.

Cybersecurity Program Oversight and Governance

Our Head of Information Technology serves as our Information Security Officer (ISO) and has primary responsibility for managing our information technology team and external service providers and for generally assessing and managing our cybersecurity risk management program. Currently, the ISO role is held by an individual who has more than 20 years of experience in leading information security teams and who has implemented and managed cybersecurity programs for other publicly-traded biotechnology companies. Our ISO's experience includes developing and maintaining tools and processes designed to protect internal computer and telecommunications networks used to store, process, and transmit personal and confidential data.

Our ISO reports directly to, and meets periodically with, our Chief Financial Officer (CFO) to discuss and review our cybersecurity risk management processes, including our cybersecurity metrics, with input from the Company's MSSP and other third-party providers and cybersecurity consultants, as appropriate. Our ISO also works closely with our Chief Compliance Officer (CCO) in the establishment and management of controls and processes that underpin our cybersecurity risk management program and meets periodically with our entire executive management team, including our Chief Executive Officer, regarding cybersecurity threats and our cybersecurity risk management program. We have implemented a process for the ISO to report relevant findings from penetration testing and cybersecurity assessments conducted by third-party consultants to members of our management team, including our CFO and CCO, as appropriate.

Our board of directors has delegated oversight of the Company's cybersecurity program to the audit committee of the board of directors. As provided in the audit committee charter, the audit committee is responsible for reviewing and discussing the Company's information security and risk management programs, controls, and procedures, including high-level review of the threat landscape facing the Company and the Company's strategy to mitigate cybersecurity risks and potential breaches. Under the audit committee charter, the audit committee is also responsible for reviewing the recovery and communication plans for any unplanned outage or security breach, where applicable.

In connection with its oversight of our broader enterprise risk management program, our ISO, on a periodic basis, provides reports to the audit committee on the status of our cybersecurity program, including measures implemented to monitor and address risks from cybersecurity threats, as appropriate. The chair of the audit committee and the ISO provide periodic reports on cybersecurity risk management to the full board of directors.

Item 2. Properties.

Our corporate headquarters are located in Watertown, Massachusetts, where we lease and occupy 19,734 square feet of laboratory and office space.

The current term of our Watertown lease expires ten years after the rent commencement date of December 2022, and includes a five-year renewal option. The lease commenced for accounting purposes in January 2023 when the leased space was made available for the Company's use.

We believe our existing facilities 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, 2025, there were 6 holders of record of our common stock. Certain shares are held in "street" name and accordingly, the number of beneficial owners of such shares is not known or included in the foregoing number. This number of holders of record also does not include stockholders whose shares may be held in trust by other entities.

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. In addition, future debt instruments may materially restrict our ability to pay dividends on our common stock. Payment of future cash dividends, if any, will be at the discretion of the board of directors after taking into account various factors, including our financial condition, operating results, current and anticipated cash needs, the requirements of then-existing debt instruments and other factors the board of directors deems relevant.

Securities Authorized for Issuance Under Equity Compensation Plans

The information required by Item 5 of Form 10-K regarding equity compensation plans is incorporated herein by reference to Item 12 of Part III of this Annual Report.

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 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 clinical-stage biotechnology company dedicated to improving the lives of patients, caregivers, and families affected by rare and common neurodegenerative diseases by pursuing the development of disease-modifying therapeutics to restore the vigilance of microglia. Microglia are the sentinel immune cells of the brain and play a critical role in maintaining central nervous system (CNS) health and responding to damage caused by disease. Leveraging recent research implicating microglial dysfunction in neurodegenerative diseases, we utilize a precision medicine approach to develop a pipeline of therapeutic candidates, initially addressing genetically defined patient subpopulations, that we believe will activate and restore microglial function. Our first therapeutic candidates are designed to activate Triggering Receptor Expressed on Myeloid Cells 2 (TREM2), a key microglial receptor protein that mediates responses to environmental signals in order to maintain brain health and whose dysfunction is linked to neurodegeneration. We have two clinical programs that are designed to target TREM2. Our lead clinical candidate, iluzanebart, is a fully human monoclonal antibody (mAb) TREM2 agonist that is currently being studied in a Phase 2 clinical trial in patients with adult-onset leukoencephalopathy with axonal spheroids and pigmented glia (ALSP), a rare and fatal neurodegenerative disease. We plan to report data from the Phase 2 trial in ALSP in the second quarter of 2025. Our second clinical candidate, VG-3927, is an orally bioavailable small molecule TREM2 agonist that is being developed for the potential treatment of Alzheimer's disease (AD). We reported Phase 1 data from our VG-3927 program in January 2025 and plan to initiate a Phase 2 trial in AD patients in the third quarter of 2025.

We believe that each therapeutic candidate in our pipeline has the potential to be developed for multiple neurodegenerative diseases. Our precision medicine approach focuses on indications where there are strong, genetic mechanistic or biochemical associations to microglial dysfunction and then utilizes findings from these efforts to inform expansion into broader populations and additional indications of neurodegenerative diseases. We believe our strategy has the potential to mitigate downstream translational risk as we seek to advance our programs through early development and into the clinic. We believe this iterative, sequential approach is a key differentiator, potentially allowing us to generate clinical proof-of-concept (PoC) efficiently and leverage our initial development programs as well as research by others, in pursuing additional neurodegenerative disease opportunities.

Our lead clinical candidate, iluzanebart, is currently being studied in IGNITE, a Phase 2 clinical trial and the first-ever interventional trial in ALSP patients. ALSP is a rare, inherited, autosomal dominant neurological disease with high penetrance. ALSP is caused by a loss-of-function mutation in the Colony Stimulating Factor 1 Receptor (CSF1R), a receptor that shares a common downstream signaling pathway with TREM2. Based on analysis from the UK Biobank genome sequencing data published in *Neurology Genetics* by Wade et al. (2024), we estimate the U.S. prevalence of ALSP to be approximately 19,000 with an estimated combined EU and UK prevalence of approximately 29,000. There are currently no approved therapies for ALSP, underscoring the unmet need for people living with this serious, rapidly progressing disease. The Food and Drug Administration (FDA) has granted Fast Track designation and orphan drug designation for iluzanebart for the treatment of ALSP. The European Commission has also granted orphan drug designation for iluzanebart.

In November 2023, we reported interim data from the ongoing Phase 2 IGNITE trial from the first 6 patients following 6 months of treatment with 20 mg/kg of iluzanebart. These data further supported the favorable safety, tolerability, pharmacokinetics (PK) and pharmacodynamics (PD) profile of iluzanebart previously demonstrated in the Phase 1 single ascending dose/multiple ascending dose (SAD/MAD) trial of iluzanebart in healthy volunteers. Importantly, iluzanebart demonstrated clear target engagement as measured by changes in soluble TREM2 (sTREM2), soluble CSF1R (sCSF1R), and osteopontin/secreted phosphoprotein 1 (SPP1) in cerebral spinal fluid (CSF). Individual ALSP patients treated with iluzanebart also demonstrated directionally supportive changes in magnetic resonance imaging (MRI) and neurofilament light chain (NfL) biomarkers. Enrollment for the Phase 2 IGNITE trial was completed in March 2024 with 20 patients enrolled in the trial. The final analysis from the Phase 2 IGNITE trial is planned for the second quarter of 2025 and will include data from all patients at 12 months dosed with either 20 mg/kg or 40 mg/kg of iluzanebart.

In addition to IGNITE, we are also conducting ILLUMINATE, a natural history study of symptomatic and prodromal carriers of CSF1R mutations that are pathogenic for ALSP. We define individuals as being symptomatic if they have MRI evidence and three or more characteristic clinical symptoms of ALSP or as being prodromal if they have early MRI evidence of ALSP and less than three clinical symptoms. The purpose of this study is to better characterize disease progression, inform our clinical trial design, and facilitate recruitment into our clinical trials. The ILLUMINATE study is focused on understanding MRI findings and certain fluid biomarker levels in symptomatic ALSP participants and the potential for those biomarkers to act as measurable descriptors of ALSP disease pathophysiology and progression. In November 2023, we reported findings from the ongoing ILLUMINATE study. These results provided critical insights on MRI and fluid biomarkers and how they present in ALSP. Specifically, sCSF1R levels were altered in both prodromal and symptomatic ALSP patients, positioning this measure as an emerging biomarker of ALSP disease pathology. Similarly, NfL levels were highly elevated in symptomatic ALSP patients, suggesting this biomarker may be useful in characterizing active neurodegeneration in ALSP. These data also showed that MRI measurements on ventricular volume and gray matter volume are also emerging as measurable indicators of disease progression. Based on 12-month data from ILLUMINATE we have also observed a statistically significant correlation between MRI biomarkers and cognitive changes.

Engagement with our stakeholders, including patients and scientific and provider communities, is central to our approach in rare neurodegenerative diseases. We have established the world's first patient-facing ALSP informational website to build disease awareness and actively support patient advocacy organizations. Through this work, we 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. In May 2023, we launched *ALSPAware*, a program providing no-cost genetic testing to aid in the diagnosis of ALSP as well as supportive counseling services. Developed with both patients and healthcare providers in mind, the program includes a no-cost single gene confirmatory test for individuals with a family history of ALSP and a custom gene panel available for physicians to use in diagnosing late onset neurodegenerative diseases. Trained genetic counselors are available to facilitate testing and discuss results, and participants will have access to a range of specialized information and services created to support participants and their families.

In addition to iluzanebart, we are developing VG-3927, our orally bioavailable small molecule TREM2 agonist for the treatment of common neurodegenerative diseases associated with microglial dysfunction, with initial development for the treatment of AD. In January 2025, we reported complete data from the Phase 1 clinical trial evaluating VG-3927 for the potential treatment of AD. The Phase 1 SAD/MAD trial assessed the safety, tolerability, PK, and PD of VG-3927 across 14 cohorts, including 8 SAD cohorts of healthy volunteers up to a 140mg dose and 4 MAD cohorts of healthy volunteers up to a 50mg dose. The trial also included a multiple dose elderly cohort and a single dose cohort of AD patients, including some participants who carry TREM2 or other genetic risk factors for AD. The trial enrolled a total of 115 participants with 89 participants receiving VG-3927, including 34 participants that were 55 years of age and older. These data demonstrated a favorable safety and tolerability profile across all cohorts, including the elderly cohort. All related adverse events were mild or moderate in severity and self-resolving without drug discontinuations. No serious AEs were reported. In addition, VG-3927 was observed to be highly CNS penetrant with a favorable and predictable PK profile that supports once-daily dosing. Importantly, VG-3927 achieved a robust and dose-dependent reduction of sTREM2 of up to approximately 50% in the CSF demonstrating a strong PK/PD relationship, sustained functional target engagement and TREM2 agonist activity.

Genome wide association studies (GWAS) have shown that a specific mutation in a TREM2 variant (R47H) is one of the strongest genetic risk factors for AD, second in magnitude only to that associated with the apolipoprotein E4 (ApoE4) genotype. We included genetic variants of TREM2 in our Phase 1 trial, the data from which indicated that the PK profile and sTREM2 reduction of VG-3927 observed in AD patients were consistent with results from healthy volunteers and similar across evaluated TREM2 and ApoE genetic variants supporting development in AD across genotypes. The PK profile and sTREM2 reduction observed in the elderly cohort were also consistent with results from healthy volunteers. Based on the Phase 1 results and preclinical profile of VG-3927, we plan to advance a once-daily oral dose of 25mg that fully engages the desired pharmacology and expect to initiate the Phase 2 trial in the third quarter of 2025.

VG-3927 has a novel mode of action that acts as both an agonist and a positive allosteric modulator (PAM), which may amplify functional responses around sites of pathology leading to strong modulation of microglia and potentially greater neuroprotection. VG-3927 is designed to enhance protective microglial responses to aggregated amyloid and tau without increasing inflammation. In contrast to antibody TREM2 agonists, VG-3927 maximizes receptor activation and microglial function because it does not bind to sTREM2, which may increase its access to the site of therapeutic action in AD. Additionally, VG-3927 does not have an Fc (fragmented crystallizable region) domain, which engages elements of the immune system that have been associated with increased risk of amyloid-related imaging abnormalities (ARIA). Collectively across preclinical and clinical data, these key differentiators create a compelling profile for VG-3927 as an investigational next-generation therapy for the treatment of AD.

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

Recent Developments

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. Through March 11, 2025, we have raised approximately $376.5 million in gross proceeds primarily from equity offerings, including $180.0 million from convertible preferred stock, $98.0 million from our initial public offering (IPO) of our common stock, $53.2 million in private placement sales of our common stock, $21.8 million from the sale of pre-funded warrants, and $23.5 million from at-the-market, or ATM, offerings. As of December 31, 2024, we had $97.8 million of cash, cash equivalents, and marketable securities.

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 $222.8 million at December 31, 2023 and $307.0 million at December 31, 2024, 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 iluzanebart and VG-3927;
- 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;
- expand clinical candidate manufacturing to support our clinical trials for iluzanebart and VG-3927, and, subject to marketing approval, future commercialization of such clinical candidates;
- 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 Russia/Ukraine military conflict, conflicts in the Middle East, 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. 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 continue to incur additional costs associated with operating as a public company.

Components of Our Results of Operations

Operating Expenses

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

Research and Development

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

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

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

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

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

	December 31, 2024	December 31, 2023
	($ in thousands)	
Direct, external research and development expenses by program:		
Iluzanebart	$ 13,057	$ 19,728
Small molecule TREM2	21,477	17,741
Unallocated research and development expenses:		
External costs and other	4,348	2,617
Facilities, personnel-related, and other	23,424	20,848
Total research and development expenses	$ 62,306	$ 60,934

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 over the next several years as we expect to (i) continue development of our iluzanebart and small molecule TREM2 programs, (ii) develop iluzanebart 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; and
- launching commercial sales of our therapeutic candidates, if approved, whether alone or in collaboration with others.

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 other 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 continuing to incur 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)

Interest Income, net

Interest income, net primarily consists of interest earned from our cash, cash equivalents, and marketable securities.

Other Expense, net

Other expense, net primarily consists of gains and losses from the remeasurement of foreign currency transactions into our functional currency.

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, 2024, we had federal NOL carryforwards of approximately $133.6 million and state NOL carryforwards of approximately $137.2 million which may be available to offset future taxable income and begin to expire in 2040. The total federal NOL of $133.6 million are not subject to expiration. As of December 31, 2024, we also had federal and state tax research and development credit carryforwards of approximately $12.2 million and $3.6 million, respectively, to offset future tax liabilities, which begin to expire in 2040. We have recorded a full valuation allowance against our net deferred tax assets at December 31, 2024. As of December 31, 2024, we had no unrecognized tax benefits.

Results of Operations

Year Ended December 31, 2024 Compared with Year Ended December 31, 2023

The following table summarizes our results of operations for the year ended December 31, 2024 compared with year ended December 31, 2023:

	December 31, 2024	December 31, 2023	Change
		($ in thousands)	
Operating expenses:			
Research and development	$ 62,306	$ 60,934	$ 1,372
General and administrative	27,377	27,932	(555)
Total operating expenses	89,683	88,866	817
Loss from operations	(89,683)	(88,866)	(817)
Other income (expense):			
Interest income, net	5,418	6,241	(823)
Other income (expense), net	9	(13)	22
Total other income, net	5,427	6,228	(801)
Net loss	$ (84,256)	$ (82,638)	$ (1,618)

Research and Development Expenses

Research and development expenses were $62.3 million for the year ended December 31, 2024, as compared to $60.9 million for the year ended December 31, 2023. The increase of $1.4 million consisted primarily of the following:

- $3.7 million of small molecule TREM2 agonist program expenses, primarily driven by an increase of $5.5 million in clinical expenses for VG-3927, partially offset by a decrease of $1.9 million in preclinical expenses;
- $2.6 million of personnel-related, facilities, and other expenses, of which $2.0 million related to personnel-related costs, including salaries, bonuses, and other headcount-related costs, including stock-based compensation of $0.1 million, and $0.5 million of lease, depreciation, and facilities expenses; and
- $1.7 million of other external expenses, which is primarily driven by general research activities.

The increases in research and development expenses were partially offset by a decrease of $6.7 million in iluzanebart-related activities, primarily driven by a decrease in manufacturing-related expenses, clinical related expenses, and pre-clinical expenses.

General and Administrative Expenses

General and administrative expenses were $27.4 million for the year ended December 31, 2024, as compared to $27.9 million for the year ended December 31, 2023. The decrease of $0.5 million consisted primarily of the following:

- $2.2 million of professional fees, including legal, accounting and other expenses; and
- $0.4 million of business insurance expenses.

The decrease in general and administrative expenses were offset by a net increase of $2.1 million related to personnel-related costs, including salaries, bonuses, and other headcount-related costs, including stock-based compensation of $1.1 million.

Interest Income, net

Interest income, net was $5.4 million for the year ended December 31, 2024, as compared to $6.2 million for the year ended December 31, 2023. The decrease of $0.8 million was due to a decrease in our cash equivalents and marketable securities from prior period which resulted in lower interest income being generated.

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, 2024, we have funded our operations primarily with net proceeds from sales of our convertible preferred stock and common stock totaling gross proceeds of approximately $362.8 million. Subsequent to December 31, 2024 through March 11, 2025, we also raised gross proceeds from our sales of our common stock of approximately $13.7 million. As of December 31, 2024, we had cash, cash equivalents, and marketable securities of $97.8 million.

During 2024, we sold 2,887,021 shares of common stock under our Open Market Sales Agreement, or the Sales Agreement, at an average price of $3.41 per share, for net proceeds after deducting commissions and other offering expenses of $9.5 million. Subsequent to December 31, 2024 through March 11, 2025, the Company sold 5,784,772 shares of common stock under the Sales Agreement at an average price of $2.36 per share, for net proceeds of $13.3 million.

In June 2024, we entered into the Securities Purchase Agreement with Aventis Inc., a wholly-owned subsidiary of Sanofi, a global healthcare and pharmaceutical company, pursuant to which we agreed to issue an aggregate of 537,634 shares of Series A non-voting convertible preferred stock at an as-converted price of $7.44 per common share for gross proceeds of $40.0 million. The Securities Purchase Agreement transaction closed, on July 1, 2024. Issuance costs were $0.4 million.

Based on our current operating plan, we expect our current cash, cash equivalents, and marketable securities will be sufficient to fund our planned operating expenses and capital expenditures into 2026.

Cash Flows

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

	December 31, 2024	December 31, 2023
	($ in thousands)	
Net cash used in operating activities	$ (51,223)	$ (70,363)
Net cash provided (used) by investing activities	8,760	(65,138)
Net cash provided by financing activities	29,490	888
Net increase in cash, cash equivalents and restricted cash	$ (12,973)	$ (134,613)

Operating Activities

During the year ended December 31, 2024, operating activities consisted primarily of our net loss of $84.3 million and $1.5 million amortization of premium/discount on marketable securities. This was partially offset by cash proceeds of $20.0

million from the contract liability related to the Securities Purchase Agreement with Sanofi, $2.6 million of changes in operating assets and liabilities, excluding the contract liability, $10.1 million of stock-based compensation expense, $0.5 million of depreciation and amortization, and $1.4 million in non-cash operating lease expenses. The net loss primarily consisted of $62.3 million of research and development expenses, $27.4 million of general and administrative expenses partially offset by $5.4 million in interest income, net.

During the year ended December 31, 2023, operating activities consisted primarily of our net loss of $82.6 million and $1.5 million amortization/discount on marketable securities. This was partially offset by $3.1 million of changes in operating assets and liabilities, $8.9 million of stock-based compensation expense, $0.4 million of depreciation and amortization, and $1.4 million in non-cash operating lease expenses. The net loss primarily consisted of $60.9 million of research and development expenses, $27.9 million of general and administrative expenses partially offset by $6.2 million in interest income, net.

Investing Activities

During the year ended December 31, 2024, net cash provided from investing activities consisted of $89.6 million of proceeds from the sales and maturities of marketable securities, partially offset by $80.8 million of purchases of marketable securities.

During the year ended December 31, 2023, net cash used for investing activities consisted of $147.5 million of purchases of marketable securities and $0.7 million of capital expenditures, partially offset by $83.0 million of proceeds from the sales and maturities of marketable securities.

Financing Activities

During the year ended December 31, 2024, net cash provided from financing activities consisted of $19.8 million in proceeds from issuance of Series A preferred stock from the Securities Purchase Agreement with Sanofi, net of offering costs, $9.6 million in proceeds from issuance of common stock from the ATM, net of offering costs, and $0.1 million from the exercise of options.

During the year ended December 31, 2023, net cash provided from financing activities consisted of $0.9 million from the exercise of options, partially offset by $23 thousand related to finance lease obligations.

Our primary uses of cash are to fund our research and development activities related to our iluzanebart and small molecule TREM2 agonist programs, personnel costs, 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, iluzanebart or VG-3927**,** 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 and seek marketing approval for our iluzanebart and VG-3927 programs. 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 Russia/Ukraine military conflict 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, cash equivalents, and marketable securities will enable us to fund our operating expenses and capital expenditure requirements into 2026 at which point we would need to obtain substantial additional funding in connection with our continuing operations.

Contractual Obligations and Commitments

In September 2021, we entered into a lease for laboratory and office space in Watertown, Massachusetts with an initial term of ten years, and a five-year renewal option at the end of the initial lease term. The monthly lease payment is approximately $0.2 million with annual escalation of approximately 3%. The lease includes a $3.7 million construction allowance. The Watertown lease commenced in the first quarter of 2023 when the lease space was made available for use. The minimum base rent payment ranges from $1.9 million annually and increasing to $2.1 million annually over the next 5 years. From year 6 through the term end date of the lease the rent payments are approximately $9.1 million.

On June 27, 2024, we entered into a Securities Purchase Agreement with Aventis Inc., a wholly-owned subsidiary of Sanofi, a global healthcare and pharmaceutical company, (together with Aventis, Inc., "Sanofi"), pursuant to which we agreed to issue an aggregate of 537,634 shares of Series A non-voting preferred stock, each convertible into 10 shares of common stock, at an as-converted price of $7.44 per common share for gross proceeds of $40.0 million. The closing date of this issuance was July 1, 2024 and we incurred issuance costs of $0.4 million. In connection with the Securities Purchase Agreement, we granted Genzyme Corporation, a wholly-owned subsidiary of Sanofi, the exclusive right of first negotiation (ROFN) for an exclusive license, grant or transfer of rights to research, develop, manufacture and commercialize our small molecule TREM2 agonist program, including VG-3927.

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

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

Critical Accounting Policies and Significant Judgments and Estimates

Our management's discussion and analysis of our financial condition and results of operations are based on our financial statements, which have been prepared in accordance with United States generally accepted accounting principles, or GAAP. The preparation of our financial statements and related disclosures requires us to make estimates and judgments that affect the reported amounts of assets, liabilities, expenses, and the disclosure of our contingent liabilities in our financial statements. We base our estimates on historical experience, known trends and events and various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. We evaluate our estimates and assumptions on an ongoing basis. Our actual results may differ from these estimates under different assumptions or conditions.

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.

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 $1.235 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, 2024, we had cash, cash equivalents, and marketable securities of $97.8 million. Interest income is sensitive to changes in the general level of interest rates. Our surplus cash has been invested in securities issued by the U.S. government and its agencies, investment-grade corporate bonds, and money market funds. 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- and intermediate-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, 2024, and December 31, 2023, 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, 2024.

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

None.

Item 9A. Controls and Procedures.

Evaluation of Disclosure Controls and Procedures

We maintain 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 designing and evaluating our disclosure controls and procedures, management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives, and management necessarily applies judgement in evaluating the benefits of possible controls and procedures relative to their costs.

Our management, with the participation of our Chief Executive Officer and Chief Financial Officer, has evaluated the effectiveness of our disclosure controls and procedures as of December 31, 2024. Based on such evaluation, our Chief Executive Officer and Chief Financial Officer have concluded that our disclosure controls and procedures were effective at the reasonable assurance level as of December 31, 2024.

Management's Annual Report on Internal Controls Over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting for. Internal control over financial reporting is defined in Rule 13a-15(f) or 15d-15(f) promulgated under the Exchange Act as a process designed by, or under the supervision of, the company's principal executive and principal financial officers and effected by the company's board of directors, management and other personnel, 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 and includes those policies and procedures that:

- pertain to the maintenance of records, that in reasonable detail, accurately and fairly reflect the transactions and dispositions of our assets;
- provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures are being made only in accordance with authorizations of management and our directors; and
- provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use or disposition of our assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate. We continue to review our internal control over financial reporting and may from time to time make changes aimed at enhancing their effectiveness and to ensure that our internal control over financial reporting evolves with our business.

Management conducted an assessment of our internal control over financial reporting based on the framework established by the Committee of Sponsoring Organizations of the Treadway Commission in "Internal Control-Integrated Framework" (2013). Based on the assessment, management concluded that, as of December 31, 2024, our internal control over financial reporting was effective. This Annual Report does not include an attestation report of our registered public accounting firm regarding internal control over financial reporting due to an exemption established by the JOBS Act for "emerging growth companies".

Changes in Internal Control Over Financial Reporting

There were no changes in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) that occurred during the quarter ended December 31, 2024 that have materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information.

Trading Arrangements

None of our directors or "officers," as defined in Rule 16a-1(f) under the Securities Exchange Act of 1934, adopted or terminated a Rule 10b5-1 trading plan or arrangement or a non-Rule 10b5-1 trading plan or arrangement, as defined in Item 408(c) of Regulation S-K, during the fiscal quarter ended December 31, 2024.

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

Not applicable.

PART III

Item 10. Directors, Executive Officers and Corporate Governance.

The information required by this Item 10 will be included in our Definitive Proxy Statement to be filed with the Securities and Exchange Commission, or SEC, with respect to our 2025 Annual Meeting of Stockholders and is incorporated herein by reference.

Item 11. Executive Compensation.

The information required by this Item 11 will be included in our Definitive Proxy Statement to be filed with the SEC with respect to our 2025 Annual Meeting of Stockholders and, other than the information required by Item 402(v) of Regulation S-K, is incorporated herein by reference.

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

The information required by this Item 12 will be included in our Definitive Proxy Statement to be filed with the SEC with respect to our 2025 Annual Meeting of Stockholders and is incorporated herein by reference.

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

The information required by this Item 13 will be included in our Definitive Proxy Statement to be filed with the SEC with respect to our 2025 Annual Meeting of Stockholders and is incorporated herein by reference.

Item 14. Principal Accounting Fees and Services.

Our independent public accounting firm is PricewaterhouseCoopers LLP, Boston, Massachusetts, United States, PCAOB Auditor ID 238.

The information required by this Item 14 will be included in our Definitive Proxy Statement to be filed with the SEC with respect to our 2025 Annual Meeting of Stockholders and is incorporated herein by reference.

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

Not applicable.

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, 2024 and 2023, and the related consolidated statements of operations and comprehensive loss, of convertible preferred stock and stockholders' equity (deficit) and of cash flows for the years then ended, 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, 2024 and 2023, and the results of its operations and its cash flows for the years then ended in conformity with accounting principles generally accepted in the United States of America.

Substantial Doubt About the Company's Ability to Continue as a Going Concern

The accompanying consolidated financial statements have been prepared assuming that the Company will continue as a going concern. As discussed in Note 1 to the consolidated financial statements, the Company has incurred recurring losses from operations since inception, has an accumulated deficit, has an expectation of continuing operating losses for the foreseeable future, and the need to raise additional capital to finance its future operations, which raises substantial doubt about its ability to continue as a going concern. Management's plans in regard to these matters are also described in Note 1. The consolidated financial statements do not include any adjustments that might result from the outcome of this uncertainty.

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. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

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 13, 2025

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, 2024	December 31, 2023
Assets		
Current assets:		
Cash and cash equivalents	$ 39,019	$ 51,992
Marketable securities	58,776	65,948
Prepaid expenses and other current assets	2,789	3,967
Total current assets	100,584	121,907
Property and equipment, net	1,319	1,745
Operating lease right-of-use assets	14,740	16,147
Financing lease right-of-use assets	28	49
Restricted cash	927	927
Other assets	93	83
Total assets	$ 117,691	$ 140,858
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$ 1,967	$ 1,946
Contract liability	20,009	—
Accrued expenses and other current liabilities	11,135	8,810
Operating lease liabilities	1,036	905
Total current liabilities	34,147	11,661
Operating lease liabilities, net of current portion	11,909	12,945
Total liabilities	46,056	24,606
Commitments and contingencies (Note 14)		
Stockholders' equity:		
Undesignated preferred stock, $0.0001 par value, 10,000,000 shares authorized as of December 31, 2024 and December 31, 2023; 537,634 shares issued and outstanding at December 31, 2024 and 0 share issued and outstanding at December 31, 2023	—	—
Common stock, $0.0001 par value; 150,000,000 shares authorized at December 31, 2024 and December 31, 2023; 40,931,085 shares issued as of December 31, 2024 and 35,929,035 shares issued as of December 31, 2023; and 40,886,762 shares outstanding as of December 31, 2024 and 35,884,712 shares outstanding as of December 31, 2023	4	4
Additional paid-in capital	378,632	339,025
Accumulated other comprehensive income (loss)	27	(5)
Accumulated deficit	(307,028)	(222,772)
Total stockholders' equity	71,635	116,252
Total liabilities and stockholders' equity	$ 117,691	$ 140,858

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, 2024	Year Ended December 31, 2023
Operating expenses:		
Research and development [1]	$ 62,306	$ 60,934
General and administrative	27,377	27,932
Total operating expenses	89,683	88,866
Loss from operations	(89,683)	(88,866)
Other income (expense):		
Interest income, net	5,418	6,241
Other income (expense), net	9	(13)
Total other income (expense), net	5,427	6,228
Net loss	$ (84,256)	$ (82,638)
Net loss per share attributable to common stockholders, basic and diluted	$ (2.07)	$ (2.13)
Weighted-average common shares outstanding, basic and diluted	40,668,444	38,712,207
Comprehensive loss:		
Net loss	$ (84,256)	$ (82,638)
Unrealized gain (loss) on available for sale securities	32	(5)
Total comprehensive loss	$ (84,224)	$ (82,643)

(1) Includes related party amounts of $0 for the year ended December 31, 2024, and $50 for the year ended December 31, 2023 (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' EQUITY (DEFICIT)
(In thousands, except share amounts)

	Convertible Preferred Stock		Common Stock		Additional Paid-in	Accumulated Other Comprehensive	Accumulated	Total Stockholders' Equity
	Shares	Amount	Shares	Amount	Capital	Income (Loss)	Deficit	(Deficit)
Balances at December 31, 2021	54,179,688	$ 161,939	1,724,950	$ —	$ 2,386	$ —	$ (71,829)	$ (69,443)
Conversion of convertible preferred stock to common stock upon closing of initial public offering	(54,179,688)	(161,939)	19,536,870	2	161,937	—	—	161,939
Issuance of common stock from initial public offering, net of issuance costs of $10.0 million	—	—	7,000,000	1	87,985	—	—	87,986
Issuance of common stock from PIPE, net of issuance costs of $2.6 million	—	—	7,293,084	1	50,594	—	—	50,595
Issuance of prefunded warrants for the purchase of common stock, net of issuance costs of $1.1 million	—	—	—	—	20,678	—	—	20,678
Exercise of stock options	—	—	65,431	—	154	—	—	154
Stock-based compensation expense	—	—	—	—	5,477	—	—	5,477
Net loss	—	—	—	—	—	—	(68,305)	(68,305)
Balances at December 31, 2022	—	$ —	35,620,335	$ 4	$ 329,211	$ —	$ (140,134)	$ 189,081
Exercise of stock options	—	—	264,377	—	911	—	—	911
Stock-based compensation expense	—	—	—	—	8,903	—	—	8,903
Unrealized gain (loss) on available for sale securities	—	—	—	—	—	(5)	—	(5)
Net loss	—	—	—	—	—	—	(82,638)	(82,638)
Balances at December 31, 2023	—	$ —	35,884,712	$ 4	$ 339,025	$ (5)	$ (222,772)	$ 116,252
Issuance of common stock, net of issuance costs	—	—	2,887,021	—	9,542	—	—	9,542
Issuance of Series A Non-voting Convertible Preferred Stock, net of issuance costs of $0.2 million	537,634	—	—	—	19,810	—	—	19,810
Exercise of pre-funded warrants	—	—	2,054,795	—	—	—	—	—
Exercise of stock options	—	—	60,234	—	138	—	—	138
Stock-based compensation expense	—	—	—	—	10,117	—	—	10,117
Unrealized gain (loss) on available for sale securities	—	—	—	—	—	32	—	32
Net loss	—	—	—	—	—	—	(84,256)	(84,256)
Balances at December 31, 2024	537,634	$ —	40,886,762	$ 4	$ 378,632	$ 27	$ (307,028)	$ 71,635

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, 2024	Year Ended December 31, 2023
Cash flows from operating activities:		
Net loss	$ (84,256)	$ (82,638)
Adjustments to reconcile net loss to net cash used by operating activities:		
Stock-based compensation expense	10,117	8,903
Non-cash operating lease expense	1,407	1,364
Depreciation and amortization	453	399
Amortization of premium/discount on marketable securities	(1,546)	(1,481)
Realized gain on investments	(16)	(8)
Changes in operating assets and liabilities:		
Prepaid expenses and other current assets	1,177	4,183
Other non-current assets	(10)	(83)
Accounts payable	21	5
Contract liability	20,009	—
Accrued expenses and other current liabilities	2,326	(384)
Operating lease liabilities	(905)	(623)
Net cash used in operating activities	(51,223)	(70,363)
Cash flows from investing activities:		
Purchases of marketable securities	(80,852)	(147,468)
Proceeds from sales and maturities of marketable securities	89,617	83,004
Purchases of property and equipment	(5)	(674)
Net cash used in investing activities	8,760	(65,138)
Cash flows from financing activities:		
Proceeds from issuance of Series A preferred stock, net of offering costs	19,810	—
Proceeds from issuance of common stock, net of offering costs	9,542	—
Payments of finance lease obligations	—	(23)
Proceeds from stock options exercised	138	911
Net cash provided by financing activities	29,490	888
Net increase in cash and cash equivalents	(12,973)	(134,613)
Cash, cash equivalents and restricted cash at beginning of period	52,919	187,532
Cash, cash equivalents and restricted cash at end of period	$ 39,946	$ 52,919
Supplemental disclosure of non-cash investing and financing activities:		
Right-of-use assets obtained in exchange for operating lease liabilities	$ —	$ 14,319
Prepaid rent reclassified to right-of-use-assets	$ —	$ 2,887

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 Security Corporation ("Vigil" or the "Company"), is a clinical-stage biotechnology 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, the Company utilizes a precision medicine approach to develop a pipeline of therapeutic candidates, initially addressing genetically defined patient subpopulations, that it believes will activate and restore microglial function. The Company was incorporated in the State of Delaware in June 2020 and is located in Watertown, 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, 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.

Going Concern

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, 2024, the Company had cash, cash equivalents and marketable securities of $97.8 million. The Company has incurred recurring losses since its inception, and as of December 31, 2024, the Company had an accumulated deficit of $307.0 million.

On March 21, 2023, the Company entered into an Open Market Sales Agreement, or the ATM facility, with Jefferies LLC, or the Agent, pursuant to which the Company can sell, from time to time, at its option, up to an aggregate of $100.0 million of shares of its common stock, through the Agent, as its sales agent. As of December 31, 2024, the Company sold 2,887,021 shares of common stock under the ATM facility at an average price of $3.41 per share, for net proceeds after deducting commissions and other offering expenses of $9.5 million. Subsequent to December 31, 2024 through March 11, 2025, the Company sold 5,784,772 shares of common stock under the ATM facility at an average price of $2.36 per share, for net proceeds of $13.3 million.

On June 27, 2024, the Company entered into a Securities Purchase Agreement (SPA) with Aventis Inc., a wholly-owned subsidiary of Sanofi, a global healthcare and pharmaceutical company, (together with Aventis Inc., "Sanofi"). Pursuant to the SPA, on July 1, 2024 the Company issued an aggregate of 537,634 shares of Series A non-voting convertible preferred stock (Series A Preferred Stock) for net proceeds of $39.6 million.

Based on its recurring losses from operations incurred since inception, accumulated deficit, expectation of continuing operating losses for the foreseeable future, and the need to raise additional capital to finance its future operations, as of March 13, 2025, the issuance date of the consolidated financial statements for the year ended December 31, 2024, the Company has concluded that there is substantial doubt about its ability to continue as a going concern for a period of one year from the date that these consolidated financial statements are issued.

The Company will 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 accompanying consolidated financial statements do not include any adjustments relating to the recoverability and classification of recorded asset amounts or the amounts and classification of liabilities that might result from the outcome of this uncertainty. Accordingly, 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.

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 stock-based compensation. 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 original maturities when purchased of three months or less that are readily convertible to known amounts of cash to be cash equivalents. The carrying values of these instruments approximate their respective fair value due to the short-term maturity of these investments. At December 31, 2024 and December 31, 2023, the Company's cash equivalents were in money market funds and government securities. 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 11), the Company is required to maintain a certificate of deposit ("CD") of $0.9 million for the benefit of the landlord.

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

	December 31, 2024	December 31, 2023
Cash and cash equivalents	$ 39,019	$ 51,992
Restricted cash, non-current	927	927
Total cash, cash equivalents and restricted cash	$ 39,946	$ 52,919

Marketable securities

Investments in marketable securities are classified as available-for-sale. Available-for-sale securities are measured and reported at fair value using quoted prices in active markets for similar securities. Unrealized gains and losses on available-for-sale securities are reported as a separate component of stockholders' equity in other comprehensive loss. Premiums or discounts from par value are amortized to investment income over the life of the underlying investment. All of the Company's available-for-sale securities are available to the Company for use in current operations. As a result, the Company classified all of its securities as current assets even if the stated maturity of some individual securities may be one year or more beyond the balance sheet date.

The cost of securities sold is determined on a specific identification basis, and realized gains and losses are included in other income (expense) within the consolidated statements of operations and comprehensive loss. If any adjustment is required to reflect a decline in the value of the investment that the Company considers to be "other than temporary", the Company recognizes a charge to the consolidated statement of operations and comprehensive loss. No such adjustments were necessary during the periods presented.

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' equity (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, 2024 or December 31, 2023.

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 ("iluzanebart"). 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. From inception through December 31, 2024, 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 and marketable securities are carried at fair value (see Note 3), determined according to the fair value hierarchy described above. 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 and clinical 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.

Comprehensive Loss

Comprehensive loss includes net loss as well as other changes in stockholders' equity (deficit) that result from transactions and economic events other than those with stockholders. The Company's only element of other comprehensive loss is unrealized gains and losses on marketable securities.

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 of Preferred Stock

The Company's Series A non-voting convertible preferred stock is classified in stockholders' deficit in the consolidated balance sheet because the holder participates in dividends in the same form as dividends paid on shares of common stock, the shares are only redeemable upon a liquidation event, and each share of Series A non-voting convertible preferred stock is convertible into a predetermined amount of ten shares of common stock. The Company recorded the Series A non-voting convertible preferred stock at fair value upon issuance, net of issuance costs. See Note 7 for additional information.

Segment Information

The Company operates as a single operating segment 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 ("CODM") is its Chief Executive Officer ("CEO"), and reviews the Company's financial information on an aggregated basis for purposes of assessing segment performance and allocating resources. See Note 15 for additional information.

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 are removed from

the accounts and any resulting gain or loss is included in loss from operations. Expenditures for repairs and maintenance that do no improve or extend the life of the respective assets are charged to expense in the period incurred.

The following is the summary of property and equipment and related accumulated depreciation as of December 31, 2024 and 2023 (in thousands):

	Useful Life	December 31, 2024	December 31, 2023
Computer software and equipment	3 years	$ 76	$ 71
Furniture and fixtures	5 years	138	138
Lab equipment	5 years	1,753	1,753
Leasehold improvements	Lesser of (i) useful life or (ii) lease term	233	233
Total property and equipment		2,200	2,195
Less: accumulated depreciation		(881)	(450)
Total property and equipment, net		$ 1,319	$ 1,745

Depreciation expense was $432 thousand and $378 thousand during the years ended December 31, 2024 and 2023, respectively.

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 years ended December 31, 2024 and December 31, 2023.

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, 2024 and December 31, 2023.

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. The Company has elected not to recognize leases with terms of 12 months or less under ASC 842. As such, 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.

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 and (ii) restricted stock 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, 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 years ended December 31, 2024 and December 31, 2023.

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 November 2024, the FASB issued ASU No. 2024-03, *Disaggregation of Income Statement Expenses (Topic 220)*, requiring that public business entities disclose additional information about specific expense categories in the notes to financial statements at interim and annual reporting periods. The amendments in this ASU are effective for annual reporting periods beginning after December 15, 2026, and interim reporting periods beginning after December 15, 2027. The requirements in this ASU may be applied either prospectively to financial statements issued for reporting periods after the effective date or retrospectively to any or all prior periods presented in the financial statements. The Company is currently evaluating the impact of adopting this ASU on its consolidated financial statements and disclosures.

Recently Adopted Accounting Guidance

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 is permitted. The Company has adopted this ASU in fiscal year 2024. The Company has determined this ASU does not materially impact its financial position and results of operations.

In November 2023, the FASB issued ASU No. 2023-07, *Segment Reporting (Topic 280): Improvements to Reportable Segment Disclosure*. Among other disclosure enhancements, this ASU requires all public entities, including public entities with a single reportable segment, to disclose the title and position of the entity’s CODM, and one or more measures of profit or loss reviewed by the CODM to allocate resources and assess performance. This ASU is effective for fiscal years beginning after December 15, 2023, and interim periods within fiscal years beginning after December 15, 2024, with retrospective application

required and early adoption permitted. The Company adopted this ASU in December 2024 on a retrospective basis for all periods presented and does not believe that the adoption of this ASU has a material impact on its consolidated financial statements. See Segment Information above within this Note 2 and Note 15, for additional disclosures related to this new standard.

3. Fair Value Measurements and Financial Instruments

The following table presents the Company's fair value hierarchy for its asset items that are measured at fair value on a recurring basis as of December 31, 2024 and December 31, 2023, by level within the fair value hierarchy (in thousands):

	Fair Value Measurement at December 31, 2024 Using:			
	Level 1	Level 2	Level 3	Total
Cash equivalents				
Money market funds	$ 35,183	$ —	$ —	$ 35,183
Total cash equivalents	$ 35,183	$ —	$ —	$ 35,183
Marketable securities				
U.S. government securities	$ —	$ 14,382	$ —	$ 14,382
Corporate bonds	—	44,394	—	44,394
Total marketable securities	$ —	$ 58,776	$ —	$ 58,776
Restricted cash (non-current)	927	—	—	927
Total	$ 36,110	$ 58,776	$ —	$ 94,886

	Fair Value Measurement at December 31, 2023 Using:			
	Level 1	Level 2	Level 3	Total
Cash equivalents				
Money market funds	$ 41,649	$ —	$ —	$ 41,649
U.S. government securities	—	1,997	—	1,997
Corporate bonds	—	2,577	—	2,577
Total cash equivalents	$ 41,649	$ 4,574	$ —	$ 46,223
Marketable securities				
U.S. government securities	$ —	$ 21,149	$ —	$ 21,149
Corporate bonds	—	44,799	—	44,799
Total marketable securities	$ —	$ 65,948	$ —	$ 65,948
Restricted cash (non-current)	927	—	—	927
Total	$ 42,576	$ 70,522	$ —	$ 113,098

Marketable securities

The following table summarizes the Company's marketable securities as of December 31, 2024 and December 31, 2023 (in thousands):

	At December 31, 2024			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
U.S. government securities	$ 14,371	$ 11	$ —	$ 14,382
Corporate bonds	44,378	32	(16)	44,394
Total	$ 58,749	$ 43	$ (16)	$ 58,776

	At December 31, 2023			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
U.S. government securities	$ 21,146	$ 5	$ (2)	$ 21,149
Corporate bonds	44,807	31	(39)	44,799
Total	$ 65,953	$ 36	$ (41)	$ 65,948

The contractual maturity dates of the Company's marketable securities are less than one year.

As of December 31, 2024, the Company held 27 securities, 7 of which were in an unrealized loss position. All investments in an unrealized loss position were in this position for less than 12 months. The Company evaluated its securities for potential other-than-temporary impairment and considered the decline in market value to be primarily attributable to current economic and market conditions. Additionally, the Company does not intend to sell the securities in an unrealized loss position and does not expect it will be required to sell the securities before recovery of the unamortized cost basis. Given the Company's intent and ability to hold such securities until recovery, and the lack of a significant change in credit risk for these investments, the Company does not consider these investments to be impaired as of December 31, 2024. The Company did not recognize any credit losses during the years ended December 31, 2024 and 2023. Additionally, there were $16 thousand and $8 thousand of realized gains on marketable securities for the years ended December 31, 2024 and 2023, respectively.

4. Prepaid Expenses and Other Current Assets

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

	December 31, 2024	December 31, 2023
Research and development	$ 1,231	$ 1,563
Interest receivable	371	348
Other receivables	228	1,137
Business insurance	113	122
Other	846	797
Total	$ 2,789	$ 3,967

5. Accrued Expenses and Other Current Liabilities

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

	December 31, 2024	December 31, 2023
Research and development	$ 5,734	$ 3,278
Payroll and employee related	4,402	4,208
Professional fees	710	1,000
Other	289	324
Total	$ 11,135	$ 8,810

6. Stock-Based Compensation

2020 Equity Incentive Plan

On September 18, 2020, the Company's board of directors adopted and its stockholders approved the Company's 2020 Equity Incentive Plan (the "2020 Plan"). The 2020 Plan was terminated and replaced by the 2021 Stock Option and Incentive Plan (the "2021 Plan") 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; however, options or other awards granted under the 2020 Plan prior to the adoption of the 2021 Plan that have not been settled or forfeited remain outstanding and effective. The options granted under the 2020 Plan are either service-based options or performance-based options. We no longer make grants under the 2020 Plan, and any equity awards that are forfeited, cancelled, or are otherwise terminated, other than by exercise, are added to the shares of common stock available for issuance under the 2021 Plan. As of December 31, 2024, 2,213,935 options were outstanding under the 2020 Plan.

2021 Stock Option and Incentive Plan

On November 16, 2021, the Company's board of directors adopted, and on December 3, 2021 its stockholders approved, the 2021 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 was 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 "2021 Plan Evergreen Provision"). On January 1, 2024 and January 1, 2025, respectively, the shares reserved for future grants under the 2021 Plan increased by 1,794,235 and 2,044,338 pursuant to the 2021 Plan Evergreen Provision.

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

In March of 2024, as part of the Company's annual grant of equity, the Company granted 1,786,100 stock options to employees. As of December 31, 2024, there were 4,956,656 options outstanding under the 2021 Plan.

In March of 2025, as part of the Company's annual grant of equity, the Company granted 1,913,000 stock options to employees.

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 (the "2021 ESPP Evergreen Provision"). On January 1, 2023, the shares reserved for future grants under the 2021 ESPP increased by 286,127 pursuant to the 2021 Plan Evergreen Provision. There was no increase of shares reserved for future grants under the 2021 ESPP plan on either January 1, 2024 or January 1, 2025. As of December 31, 2024, a total of 572,254 shares of common stock were reserved for issuance under this plan. No stock-based compensation expense was recognized during the year ended December 31, 2024 related to the 2021 ESPP.

Inducement Awards

The Company also maintains an inducement award program that is separate from the Company's equity plans under which inducement awards may be granted consistent with Nasdaq Listing Rule 5635(c)(4). During the twelve months ended December 31, 2024, the Company granted 330,000 options to purchase shares of the Company's common stock to new hires as inducements material to such employees entering into employment with the Company, of which 330,000 options remained outstanding as of December 31, 2024.

Stock Option Repricing

On May 3, 2024 (the "Effective Date"), the Company's Board of Directors approved a one-time stock option repricing (the "Option Repricing") for certain previously granted and still outstanding options held by the Company's employees and certain independent contractors. Pursuant to the Option Repricing, stock options granted under the Company's 2021 Stock Option and Incentive Plan prior to January 1, 2024, with an exercise price greater than $3.03 per share, were repriced to $3.03 per share, which was the closing trading price of the Company's common stock on the Nasdaq Global Market on the Effective Date.

Under the terms of the Option Repricing, a repriced option will revert to its original exercise price if, prior to the one-year anniversary of the Effective Date, (a) the option holder's employment is terminated by the Company with cause or by the

option holder, or (b) the option is exercised. The repriced options otherwise retained their existing terms and conditions as set forth in the 2021 Stock Option and Incentive Plan. The Option Repricing resulted in $2.7 million of incremental stock compensation expense, which was calculated using the Black-Scholes option-pricing model.

During the year ended December 31, 2024, the Company recognized incremental compensation cost of $0.9 million. At December 31, 2024, there was approximately $1.5 million of unrecognized stock-based compensation expense which is expected to be recognized on a straight-line basis over the remaining vesting period of the repriced options. The incremental cost is included in general and administrative expense and research and development expense on the condensed consolidated statements of operations and comprehensive loss.

Service-Based Stock Options

The Company issues stock options to directors, employees, and consultants under the 2021 Plan and 2020 Plan. Options granted by the Company vest over periods of 12-48 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, (iii) 36 equal monthly installments beginning one month after the vesting start date, (iv) 4 equal quarterly installments, (v) 100% vesting at the one-year anniversary of the vesting start date, or (vi) 50% at the end of calendar year one after the grant date and 50% at the end of calendar year two after the grant 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, 2024:

	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, 2023	5,998,245	$ 6.03	$ 8.79	8.37	$ 1,082
Granted	2,633,772	2.28	3.38		
Exercised	(60,234)	2.72	2.28		
Forfeited	(974,583)	4.71	5.97		
Expired	(307,238)	6.22	6.90		
Outstanding as of December 31, 2024	7,289,962	$ 4.90	$ 7.16	7.82	$ —
Vested and exercisable as of December 31, 2024	3,824,522	$ 5.30	$ 7.59	7.10	$ —
Vested and expected to vest as of December 31, 2024	7,289,962	$ 4.90	$ 7.16	7.82	$ —

The weighted average exercise prices and aggregate intrinsic values of the options subject to the Option Repricing in the table above are based on the original exercise prices due to the one-year retention period.

There were 264,377 options exercised for the year ended December 31, 2023. The aggregate intrinsic value of options exercised was $1.7 million for the year ended December 31, 2023. The aggregate intrinsic value of options exercised was $81 thousand for the year ended December 31, 2024.

The total fair value of options vested was approximately $10.7 million and $8.4 million during the years ended December 31, 2024 and December 31, 2023, 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, 2024	December 31, 2023
Weighted-average risk-free interest rate	4.2%	4.2%
Weighted-average expected term (in years)	6.0	6.0
Expected volatility	72.8% - 73.9%	71.7% - 73.8%
Expected dividend yield	0.0%	0.0%
Fair value of common stock	$2.65 - $4.01	$3.20 - $12.40
Weighted-average fair value	$ 2.28	$ 7.06

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 commenced vesting in May 2021 when the Company completed the second tranche of its Series A convertible preferred stock financing and then vest over 48 equal monthly installments.

The following table summarizes the activity of the Company's performance-based options to purchase common stock for the year ended December 31, 2024:

	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, 2023	210,629	$ 2.76	$ 1.89	6.88	$ 314
Granted	—	—	—		
Exercised	—	—	—		
Forfeited	—	—	—		
Expired	—	—	—		
Outstanding as of December 31, 2024	210,629	$ 2.76	$ 1.89	5.88	$ —
Vested and exercisable as of December 31, 2024	191,544	$ 2.76	$ 1.89	5.88	$ —
Vested and expected to vest as of December 31, 2024	210,629	$ 2.76	$ 1.89	5.88	$ —

No options were exercised during the years ended December 31, 2024 and December 31, 2023.

The total fair value of options vested during the year ended December 31, 2023 was approximately $158 thousand. The total fair value of options vested during the year ended December 31, 2024 was approximately $158 thousand.

The fair value of performance options granted under the stock option plan is determined at the date of grant using the Black-Scholes option-pricing model. There were no performance options granted during the years ended December 31, 2024 and December 31, 2023.

Restricted Stock

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

	December 31, 2024
Outstanding as of beginning of period	262,180
Granted	—
Forfeited/cancelled	—
Outstanding as of end of period	262,180
Vested during period	24,417
Outstanding unvested shares, expected to vest	—
Remaining weighted-average vesting period for unvested shares	0.00 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 expense of $10.1 million and $8.9 million during the years ended December 31, 2024 and December 31, 2023, respectively. Stock-based compensation expense was classified as follows in the consolidated statements of operations and comprehensive loss (in thousands):

	December 31, 2024	December 31, 2023
Research and development	$ 3,630	$ 3,494
General and administrative	6,487	5,409
Total stock-based compensation	$ 10,117	$ 8,903

As of December 31, 2024 and December 31, 2023, respectively, there was approximately $16.2 million and $22.2 million of unrecognized stock-based compensation expense related to service-based options to purchase common stock under the 2020 and 2021 Plans, which is expected to vest over a weighted-average period of 2.35 years and 2.53 years.

As of December 31, 2024 and December 31, 2023, respectively, there was approximately $2 thousand and $37 thousand 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 0.20 years and 0.70 years.

As of December 31, 2024 restricted stock issued under the 2020 Plan were fully vested. As of December 31, 2023 there was approximately $47 thousand of unrecognized stock-based compensation expense related to restricted stock under the 2020 Plan, which was expected to vest over a weighted-average period of 0.33 years.

7. Preferred Stock

Issuance of Series A Non-Voting Convertible Preferred Stock

On June 27, 2024, the Company entered into a $40.0 million Securities Purchase Agreement (SPA) with Sanofi. On the closing date of July 1, 2024, pursuant to the terms of the SPA, the Company issued an aggregate of 537,634 shares of Series A non-voting convertible preferred stock at an as-converted price of $7.44 per share (the "Private Placement"). Each preferred share is convertible into ten shares of the Company's common stock. The SPA restricts Sanofi's ability to sell the Series A non-voting convertible preferred stock for ten months following the closing date, subject to customary exceptions for permitted transfers. In connection with the SPA , the Company also granted Genzyme Corporation, a wholly-owned subsidiary of Sanofi, an exclusive right of first negotiation (ROFN) for an exclusive license, grant or transfer of rights to research, develop, manufacture and commercialize the Company's small molecule TREM2 agonist program, including its clinical candidate, VG-3927.

The Company assessed the accounting for the SPA and concluded there were two units of accounting (i) Series A Convertible Preferred Stock and (ii) the ROFN. The Series A convertible preferred stock qualified as permanent equity and was recorded at its fair value of $20.0 million. There were no imbedded features that required bifurcation. The remaining $20.0 million in proceeds was recognized as the contract liability for the ROFN (see Note 14).

The Company also incurred $0.4 million of issuance costs which were allocated to Series A non-voting convertible preferred stock and contract liability proportionately and recognized $0.2 million as deferred offering costs in other assets in the condensed consolidated balance sheet and $0.2 million in general and administrative expenses in the condensed consolidated statement of operations in June 2024, respectively. Upon issuance of Series A non-voting convertible preferred stock on July 1, 2024, the deferred offering costs were recorded as a reduction of proceeds of the Private Placement in additional paid in capital in the condensed consolidated balance sheet.

The holders of Series A non-voting convertible preferred stock have the followings rights and privileges:

Voting

Holders of Series A non-voting convertible preferred stock do not have voting rights.

Dividends

Holders of Series A non-voting convertible preferred stock are entitled to receive dividends on shares of Series A non-voting convertible preferred stock equal (on an as-if-converted to common stock basis) to and in the same form as dividends actually paid on shares of the Company's common stock. The Company has not, and has no plans to, declare dividends on any class of preferred or common stock.

Conversion

At the option of the holder, each share of Series A non-voting convertible preferred stock is convertible into a number of shares of Common Stock equal to the product of the number of shares of Series A non-voting convertible preferred stock held by such holder multiplied by the conversion ratio.

Initially, each share of Series A non-voting convertible preferred stock converts into ten shares of Common Stock, subject to adjustments for stock dividends, stock splits, combinations, or other similar recapitalizations.

Liquidation

In the event of any voluntary or involuntary liquidation, dissolution or winding up of the Company, including a change of control transaction, or deemed liquidation event (any such event, a "Liquidation"), the assets of the Company available for distribution to its stockholders shall be distributed among the holders of the shares of Series A non-voting convertible preferred stock and common stock pro rata based on the number of shares held by each such holder, treating for this purpose all shares of Series A non-voting convertible preferred stock as if they had been converted to common stock pursuant to the terms of this Certificate of Designation immediately prior to such liquidation, without regard to any limitations on conversion set forth herein or otherwise and without regard as to whether sufficient shares of common stock are available out of the Company's authorized but unissued stock for the purpose of effecting the conversion of the Series A non-voting convertible preferred stock.

8. Common Stock

Each share of common stock entitles the holder to one vote for each share of common stock held. Common stockholders are entitled to receive dividends, as may be declared by the Company's Board. During each year ending December 31, 2024 and December 31, 2023, no dividends have been declared or paid.

At-the-Market Facility

In March 2023, the Company established an at-the-market, or ATM, equity offering program pursuant to which it was able to offer and sell up to $100.0 million of its common stock at the then current market price from time to time. Through December 31, 2024, the Company sold 2,887,021 shares of common stock under this program with net proceeds, after deducting commissions and other offering expenses, of $9.5 million. Subsequent to December 31, 2024 and through March 11, 2025, the Company sold 5,784,772 shares of common stock under this program with net proceeds, after deducting commissions and other offering expenses, of $13.3 million.

Pre-funded Warrants

In August 2022, the Company issued pre-funded warrants to purchase up to an aggregate of 2,980,889 shares of common stock at a purchase price of $7.2999 per pre-funded warrant. Each pre-funded warrant is exercisable for one share of common stock at an exercise price of $0.0001 per share of common stock, is immediately exercisable and will remain exercisable until exercised in full. The pre-funded warrants have no expiration date and the price of the pre-funded warrants does not include any discounts. The Company evaluated the pre-funded warrants for liability or equity classification in accordance with the provisions of ASC Topic 480, Distinguishing Liabilities from Equity, and determined that equity treatment was appropriate because the pre-funded warrants did not meet the definition of liability instruments and met the criteria for permanent equity. As of December 31, 2024, 2,054,795 of the pre-funded warrants were exercised.

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, 2024	Year Ended December 31, 2023
Common stock options	7,500,591	6,208,874
Series A convertible preferred stock	5,376,340	—
Pre-funded warrants	926,094	2,980,889
Shares available for issuance under the 2021 Plan	2,248,964	1,160,388
Shares available for issuance under the 2021 ESPP	572,254	572,254
Total common stock reserved for future issuance	16,624,243	10,922,405

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, 2024	Year Ended December 31, 2023
Numerator:		
Net loss attributable to common stockholders	$ (84,256)	$ (82,638)
Denominator:		
Weighted-average common shares outstanding, basic and diluted	40,668,444	38,712,207
Net loss per share attributable to common stockholders, basic and diluted	$ (2.07)	$ (2.13)

Basic and diluted weighted average shares of common stock outstanding for the years ended December 31, 2024 and December 31, 2023 include the weighted average effect of outstanding pre-funded warrants for the purchase of shares of common stock for which the remaining unfunded exercise price is $0.0001 or less per share.

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, 2024	Year Ended December 31, 2023
Options to purchase common stock – service based	7,289,962	5,998,245
Options to purchase common stock – performance based	210,629	210,629
Unvested restricted common stock	—	24,417
Total	7,500,591	6,233,291

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 years ended December 31, 2024 and December 31, 2023, 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, 2024, and December 31, 2023.

The Company's effective income tax rate differs from the statutory federal income tax rate as follows for the years ended December 31, 2024 and December 31, 2023:

	December 31, 2024	December 31, 2023
Statutory U.S. federal rate	21.0%	21.0%
State income taxes	5.9%	6.2%
Other permanent differences	(1.2)%	(0.6)%
Research and development credits	6.6%	5.8%
Valuation allowance	(31.6)%	(32.4)%
Change in Income Tax Rates	(0.4)%	—%
Other Rate Items	(0.3)%	—%
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, 2024 and 2023 are comprised of the following (in thousands):

	December 31, 2024	December 31, 2023
Deferred tax assets:		
Net operating loss carryforwards	$ 36,726	$ 26,310
Research and development credits	15,108	9,582
Intangible assets	4,501	4,977
Start-up costs	71	79
Accruals and other	8,544	7,622
Capitalized R&D Expenses	34,181	24,283
Depreciation	540	657
Total deferred tax assets	99,671	73,510
Less valuation allowance	(95,677)	(69,087)
Total deferred tax assets, net of valuation allowance	3,994	4,423
Deferred tax liabilities:		
Depreciation	—	—
Right-of-use asset	(3,994)	(4,423)
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 $95.7 million and $69.1 million at December 31, 2024 and December 31, 2023, respectively.

The Company has incurred net operating losses ("NOLs") since inception. At December 31, 2024, the Company had federal NOLs of approximately $133.6 million and state NOLs of $137.2 million. At December 31, 2023, the Company had federal NOLs of approximately $95.7 million and state NOLs of $98.3 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 $133.6 million as of December 31, 2024 will not expire. The state NOL carryover of $137.2 million will begin to expire in 2040.

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, 2024, the Company also has federal and state tax research and development credit carryforwards of approximately $12.2 million and $3.6 million, respectively, to offset future income taxes, which will begin to expire in 2040. As of December 31, 2023, the Company had federal and state tax research and development credit carryforwards of approximately $7.8 million and $2.2 million, respectively, to offset future income taxes.

The Company's valuation allowance increased by $26.6 million and $26.9 million during the years ended December 31, 2024 and December 31, 2023, 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 various state jurisdictions. 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, 2024, 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, 2024, 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 with rent commencing in the third quarter of 2021. The lease included an option to purchase the equipment at fair market value at the end of the lease term, which was exercised during the third quarter of 2023 when the lease term ended.

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 initial determination of the lease term. In 2022, the Company further extended the lease term through February 28, 2023 and terminated the lease as of February 28, 2023 due to the Company's move to Watertown, Massachusetts as noted below.

In October 2021, the Company entered into a lease for its corporate headquarters in Cambridge, Massachusetts with an initial term of 14 months. In 2022, the Company extended the lease through January 31, 2023 and terminated the lease as of January 31, 2023 due to the Company's move to Watertown, Massachusetts as noted below. The lease payments during the year ended December 31, 2023 were $74 thousand. The Company received their security deposit of approximately $49 thousand in the second quarter of 2023.

Watertown, MA Lease

In September 2021, the Company entered into a lease for laboratory and office space in Watertown, Massachusetts with an initial term of ten years from the rent commencement date of December 2022, and a five-year renewal option. The lease commenced for accounting purposes in January 2023 when the leased space was made available for the Company's use. As of the lease commencement date, the Company has determined that it is not reasonably certain to exercise the option to extend the lease and has not included the extension period in the 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. At the lease commencement date, the Company recorded an initial lease liability of $14.3 million and a right-of-use asset of $17.3 million.

Operating lease expense was $2.4 million for each of the years ended December 31, 2024 and 2023. Variable lease expense was $1.0 million and $0.8 million for the year ended December 31, 2024 and 2023, respectively. Variable lease expense generally includes common area maintenance, property taxes, and utilities.

The components of lease expense are as follows:

	Year Ended December 31, 2024	Year Ended December 31, 2023
Operating lease cost	$ 2,412	$ 2,435
Short term lease cost	—	—
Variable lease cost	974	755
Finance lease cost:		
Amortization of right-to-use assets	21	21
Interest on lease liabilities	—	—
Total finance lease cost	$ 21	$ 21

Supplemental cash flow information related to leases are as follows:

	Year Ended December 31, 2024	Year Ended December 31, 2023
Cash paid for amounts included in the measurement of lease liabilities		
Operating cash flows from operating leases	$ (1,911)	$ (1,707)
Operating cash flows from finance leases	$ —	$ —
Financing cash flows from finance leases	$ —	$ (23)

At December 31, 2024, the weighted-average remaining lease terms related to the operating leases are 7.9 years.

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 7.57% for the operating leases that were still active as of December 31, 2024.

Future minimum lease payments due under the Company's operating and finance lease liabilities as of December 31, 2024 are as follows:

Years ended December 31,	Operating Leases
2025	$ 1,968
2026	2,027
2027	2,088
2028 and thereafter	11,269
Total lease payments	17,352
Less: imputed interest	(4,407)
Total future minimum lease payments	$ 12,945

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.

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 recognized changes in the fair value of the anti-dilution rights at each subsequent reporting period until its settlement in May 2021.

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.

The Company did not have any expenses, prepaid expenses, or payables related to the Amgen Agreement for the years ended December 31, 2024 and December 31, 2023, respectively.

13. Related Party Transactions

Atlas

The Company entered into a lab lease agreement with Atlas Venture Fund XII, L.P., a principal stockholder of the Company, and incurred lease costs of $50 thousand for the year ended December 31, 2023. The lease payments are included in research and development expenses in the consolidated statements of operations and comprehensive loss. The Company terminated the lease for the laboratory space as of February 28, 2023 due to the Company's move to Watertown, Massachusetts, and therefore had no operating lease right-of-use asset or lease liability recorded as of December 31, 2024. As of December 31, 2024, the Company has no costs in accrued expenses associated with the leases.

14. Commitments and Contingencies

License Agreement

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

In connection with the SPA, the Company granted Sanofi the ROFN for an exclusive license, grant or transfer of rights to research, develop, manufacture and commercialize the Company’s small molecule TREM2 agonist program, including its clinical candidate, VG-3927. On July 1, 2024, the Company recognized $20.0 million as a contract liability in the condensed consolidated balance sheet until a new contract is executed following the ROFN negotiation period, Sanofi does not elect to exercise its ROFN, or the agreement expires. (see Note 7).

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 expired on September 10, 2022 and automatically renews 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 December 31, 2024. The Company did not recognize a liability in the consolidated balance sheet.

Contingencies

From time to time, the Company may have certain contingent liabilities that arise in the ordinary course of business. The Company accrues a liability for such matters when it is probable that future expenses will be incurred and can be reasonably estimated. As of December 31, 2024, the Company does not have any significant legal disputes that require a loss liability to be recorded.

401(k) Plan

The Company has a defined-contribution plan under Section 401(k) of the Internal Revenue Code of 1986 (the “401(k) Plan”). The 401(k) Plan covers all employees who meet defined minimum age and service requirements and allows participants to defer a portion of their annual compensation on a pre-tax basis. Company contributions are discretionary and contributions in the amount of $0.7 million and $0.5 million were made during the years ended December 31, 2024 and 2023, respectively.

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. Segment Reporting

The Company operates and is managed as a single operating segment. The measure of segment assets is reported on the consolidated balance sheets as total assets. All assets are in the United States and there has been no revenue generated through December 31, 2024. The accounting policies of the segment are the same as those described in Note 2.

The determination of a single operating segment is consistent with the consolidated financial information regularly reviewed by the CODM, which is used in assessing segment performance and deciding how to allocate resources on a consolidated basis. The CODM assesses segment performance and makes decisions on how to allocate resources based on consolidated net loss reported on the consolidated statements of operations and comprehensive loss. In assessing performance, the CODM reviews net loss in comparison to budget.

The following table presents information about reported significant segment expenses:

	Year Ended December 31, 2024	Year Ended December 31, 2023
Research and development external expenses		
Iluzanebart	$ 13,057	$ 19,716
Small molecule TREM2	21,444	17,614
Research and development - other	4,553	2,790
Total research and development external expenses	39,054	40,120
General and administrative external expenses	8,472	11,070
Facilities, personnel-related, and other	42,157	37,676
Loss from operations	(89,683)	(88,866)
Other income (expense), net	5,427	6,228
Net loss	$ (84,256)	$ (82,638)

EXHIBIT INDEX

Exhibit Number	Description
3.1	Third Amended and Restated Certificate of Incorporation of the Registrant (incorporated by reference to Exhibit 3.1 of the Registrant's Current Report on Form 8-K (File No. 001-41200) filed on January 11, 2022).
3.2	Certificate of Amendment to the Third Amended and Restated Certificate of Incorporation (incorporated by reference to Exhibit 3.1 to the Registrant's Form 8-K (File No. 001-41200) filed on June 6, 2024).
3.3	Certificate of Designation of Preferences, Rights and Limitations, of Series A Non-Voting Convertible Preferred Stock, dated June 27, 2024. (incorporated by reference to Exhibit 3.1 to the Registrant's Form 8-K (File No. 001-41200) filed on June 27, 2024).
3.4	Amended and Restated Bylaws of the Registrant. (incorporated by reference to Exhibit 3.2 to the Registrant's Form 8-K (File No. 001-41200) filed on June 6, 2024).
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
4.4	Form of Pre-Funded Warrant (incorporated by reference to Exhibit 4.1 of the Registrant's Current Report on Form 8-K filed on August 12, 2022).
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#	Amended and Restated Non-Employee Director Compensation Policy (incorporated by reference to Exhibit 10.1 of the Registrant's Quarterly Report on Form 10-Q filed on August 13, 2024).
10.8†	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).
10.9†	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).

10.10	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).
10.11	Securities Purchase Agreement, by and among the Registrant and the persons party thereto, dated as of August 12, 2022 (incorporated by reference to Exhibit 10.1 of the Registrant's Current Report on Form 8-K filed on August 12, 2022).
10.12	Securities Purchase Agreement, dated June 27, 2024, by and between Vigil Neuroscience, Inc. and Aventis Inc. (incorporated by reference to Exhibit 10.1 to the Registrant's Form 8-K (File No. 001-41200) filed on June 27, 2024).
19*	Amended and Restated Insider Trading Policy
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.
97	Compensation Recovery Policy (incorporated by reference to Exhibit 97 of the Registrant's Annual Report on Form 10-K filed on March 26, 2024).
101.INS	Inline XBRL Instance Document-the instance document does not appear in the Interactive Data File as its XBRL tags are embedded within the Inline XBRL document
101.SCH	Inline XBRL Taxonomy Extension Schema With Embedded Linkbase Documents
104	Cover page formatted as Inline XBRL and contained in Exhibit 101

* 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 13, 2025

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 Magovčević-Liebisch, PhD, JD	President and Chief Executive Officer *(Principal Executive Officer)*	March 13, 2025
/s/ Jennifer Ziolkowski Jennifer Ziolkowski, CPA	Chief Financial Officer *(Principal Financial Officer and Principal Accounting Officer)*	March 13, 2025
/s/ Bruce Booth Bruce Booth, D.Phil	Director, Chairperson	March 13, 2025
/s/ Cheryl Renee Blanchard Cheryl Renee Blanchard, PhD	Director	March 13, 2025
/s/ Gerhard Koenig Gerhard Koenig, PhD	Director	March 13, 2025
/s/ Mary Thistle Mary Thistle	Director	March 13, 2025
/s/ Stefan Vitorovic Stefan Vitorovic, MS, MBA	Director	March 13, 2025
/s/ Suzanne Bruhn Suzanne Bruhn, PhD	Director	March 13, 2025
/s/ Samantha Budd Haeberlein Samantha Budd Haeberlein, PhD	Director	March 13, 2025

EXECUTIVE OFFICERS

Ivana Magovčević-Liebisch, Ph.D., J.D.
President and Chief Executive Officer

Jennifer Ziolkowski, CPA
Chief Financial Officer

David Gray, Ph.D.
Chief Science Officer

Petra Kaufmann, M.D., F.A.A.N.
Chief Medical Officer

BOARD OF DIRECTORS

Bruce Booth, D.Phil
Chairman of the Board, Vigil Neuroscience, Inc.
Partner, Atlas Venture

Suzanne Bruhn, Ph.D.
Chief Executive Officer, Charcot-Marie-Tooth Association

Gerhard Koenig, Ph.D.
Executive Chairman, Augustine Therapeutics

Mary Thistle
Former Special Advisor to the Bill & Melinda Gates Medical Research Institute

Cheryl Blanchard, Ph.D.
President and Chief Executive Officer, Anika Therapeutics, Inc.

Samantha Budd Haeberlein, Ph.D.
Chief Medical Officer, Enigma Biomedical USA

Ivana Magovčević-Liebisch, Ph.D., J.D.
President and Chief Executive Officer, Vigil Neuroscience, Inc.

Stefan Vitorovic, MS, MBA
Co-Founder and Former Managing Director, Vida Ventures

CORPORATE INFORMATION

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