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, 2023

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 001-38938

Stoke Therapeutics, Inc.

(Exact name of Registrant as specified in its Charter)

Delaware	**47-1144582**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
45 Wiggins Ave Bedford, Massachusetts	**01730**
(Address of principal executive offices)	**(Zip Code)**

Registrant's telephone number, including area code: (781) 430-8200

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

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

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

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

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

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

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

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

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

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

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

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

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). ☐

The aggregate market value of the voting and non-voting common equity held by non-affiliates of the Registrant, based on the closing price of the shares of common stock on The NASDAQ Stock Market as of the last business day of the registrant's most recently completed second fiscal quarter, was approximately $290 million. The number of shares of Registrant's Common Stock outstanding as of March 15, 2024 was 46,303,743.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's Definitive Proxy Statement relating to the 2024 Annual Meeting of Stockholders are incorporated by reference into Part III of this Annual Report on Form 10-K to the extent stated herein. The Definitive Proxy Statement will be filed within 120 days of the Registrant's fiscal year ended December 31, 2023. Except with respect to information specifically incorporated by reference in this Form 10-K, the Definitive Proxy Statement is not deemed to be filed as part of this Form 10-K.

Auditor Firm Id: 185 Auditor Name: KPMG LLP Auditor Location: Boston, MA USA

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FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K contains forward-looking statements within the safe harbor provisions for forward-looking statements contained in Section 27A of the Securities Act of 1933, as amended (the "Securities Act") and Section 21E of the Securities Exchange Act of 1934, as amended (the "Exchange Act"). All statements other than statements of present and historical facts contained in this Annual Report on Form 10-K, including, but not limited to, statements regarding the ability of STK-001 to treat the underlying causes of Dravet syndrome and reduce seizures or show improvements in behavior or cognition at the indicated dosing levels or at all, the timing and expected progress of clinical trials, our future results of operations and financial position, business strategy, prospective products, planned preclinical studies and clinical or field trials, regulatory approvals, research and development costs, and timing and likelihood of success, as well as plans and objectives of management for future operations, may be forward-looking statements. In some cases, you can identify forward-looking statements by terms such as "may," "will," "should," "expect," "plan," "anticipate," "could," "intend," "target," "project," "contemplate," "believe," "estimate," "predict," "potential" or "continue" or the negative of these terms or other similar expressions, although not all forward-looking statements contain these words.

Forward-looking statements are based on our management's beliefs and assumptions and on information currently available to us. Such statements are subject to a number of known and unknown risks, uncertainties and assumptions, and actual results may differ materially from those expressed or implied in the forward-looking statements due to various factors, including, but not limited to, those identified in Part II. Item 7. "Management's Discussion and Analysis of Financial Condition and Results of Operations" and Part I. Item 1A "Risk Factors." These risks and uncertainties include, but are not limited to:

- our ability to become profitable;
- our ability to procure sufficient funding;
- our limited operating history;
- the direct and indirect impact of inflation, interest rates, foreign currency exchange rates, instability in the global banking system, geopolitical conflict and macroeconomic conditions, including as a result of a potential temporary federal government shutdown, on our business, financial condition and operations, including on our expenses, supply chain, strategic partners, research and development costs, clinical trials and employees;
- our ability to develop, obtain regulatory approval for and commercialize STK-001, STK-002 and our future product candidates;
- our success in early preclinical studies or clinical trials, which may not be indicative of results obtained in later studies or trials;
- the success of our collaboration with Acadia Pharmaceuticals and our ability to enter into successful collaborations in the future;
- the availability of coverage and adequate reimbursement from third party payors for STK-001, STK-002 and our future product candidates, if such products are approved;
- our ability to identify patients with the diseases treated by STK-001, STK-002 or our future product candidates, and to enroll patients in trials;
- the success of our efforts to use TANGO to expand our pipeline of product candidates and develop marketable products;
- our ability to obtain, maintain and protect our intellectual property;
- our reliance upon intellectual property licensed from third parties;
- our ability to identify, recruit and retain key personnel;
- our financial performance; and
- developments or projections relating to our competitors or our industry.

You should read this Annual Report on Form 10-K and the documents that we reference herein completely and with the understanding that our actual future results may be materially different from what we expect. We qualify all of our forward-looking statements by these cautionary statements. Except as required by applicable law, we do not plan to publicly update or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise.

PART I

Item 1. Business.

Overview

We are a clinical-stage company dedicated to addressing the underlying causes of severe diseases by upregulating protein expression with RNA-based medicines. Using our proprietary TANGO (Targeted Augmentation of Nuclear Gene Output) approach, we are developing antisense oligonucleotides ("ASOs") to selectively restore protein levels. Our first compound, STK-001, is in clinical testing for the treatment of Dravet syndrome, a severe and progressive genetic epilepsy. Dravet syndrome is characterized by frequent, prolonged and refractory seizures beginning within the first year of life. The disease is classified as a developmental and epileptic encephalopathy due to the developmental delays and cognitive impairment associated with it.

Dravet syndrome is one of many diseases caused by a haploinsufficiency, in which a loss of approximately 50% of normal protein levels leads to disease. We are also pursuing treatment for a second haploinsufficient disease, autosomal dominant optic atrophy ("ADOA"), the most common inherited optic nerve disorder. Our initial focus is on haploinsufficiencies and diseases of the central nervous system and the eye, although proof of concept has been demonstrated in other organs, tissues, and systems, supporting our belief in the broad potential for our proprietary approach.

Our executive management team has extensive collective expertise in human genetics and modulation of RNA processes using ASOs, as well as a track record of success in rare disease drug development. Our executive team and co-founders have been previously involved with other companies in the discovery, development and commercialization of many treatments for rare diseases, including Sarepta's Exondys 51 (eteplirsen) and Biogen's SPINRAZA. Our scientific and clinical advisory boards are comprised of leading experts in the fields of human genetics, pre-mRNA splicing and ASOs, and neurodevelopmental and neurodegenerative diseases. Their involvement in both academic research and clinical practice allows us to gain proprietary and early insight into emerging biology and clinical practice that informs our business strategy.

Our strategy

We are using our proprietary RNA therapeutics platform to create ASOs for the treatment of severe diseases. The critical components of our strategy include the following activities:

- *Rapidly advance our lead program, STK-001, to clinical proof-of-concept, approval and commercialization.* Following our announcement in March 2024 of end of study data from our Phase 1/2a open-label studies of STK-001 in the United States (MONARCH) evaluating children and adolescents ages 2 to 18 with Dravet syndrome and in the United Kingdom (ADMIRAL) evaluating children and adolescents ages 2 to up to 18 with Dravet syndrome, we plan to meet with global regulatory authorities to discuss late-stage clinical development of STK-001. We are leveraging previously-validated ASO chemistry, a modality that has been successfully utilized for other diseases, a well-defined patient population based on routine genetic testing and learnings from approved drugs for the treatment of Dravet syndrome to inform the clinical and regulatory pathways for STK-001 and minimize potential safety concerns and development risk. We believe STK-001 has the potential to significantly reduce both the occurrence and frequency of seizures and also non-seizure comorbidities. If approved, we intend to leverage a lean, targeted internal commercial organization to bring STK-001 to patients.
- *Advance STK-002 to the clinic, for the potential treatment of ADOA.* STK-002 is a proprietary ASO in preclinical development for the treatment of ADOA, the most common inherited optic nerve disorder. ADOA represents a second haploinsufficiency disease addressed by TANGO and our first treatment for diseases of the eye. STK-002 is designed to upregulate OPA1 protein expression by leveraging the non-mutant (wild-type) copy of the *OPA1* gene. We have received authorization in the United Kingdom to proceed with a Phase 1 open-label study (OSPREY) of STK-002 and we expect the study to start in 2024.

- *Expand our pipeline through internal discovery and collaboration to fully exploit the potential of our proprietary platform (TANGO).* We have built a target discovery process utilizing proprietary bioinformatics algorithms and extensive in-house expertise in whole transcriptome RNA sequencing to rapidly and systematically identify diseases that we believe can be addressed using our platform. We are also advancing additional early programs focused on multiple targets, including haploinsufficiency diseases of the central nervous system (the "CNS") and eye. In January 2022, we announced a collaboration with Acadia Pharmaceuticals to pursue RNA-based treatments for severe and rare genetic neurodevelopmental diseases of the CNS. The collaboration combines our TANGO research platform with Acadia's expertise in neurology drug development and commercialization. Longer-term, we believe that our ASOs may have the potential to upregulate non-mutated genes in biological pathways to treat diseases or conditions that are caused by multiple genes or are multifactorial.

- *Maintain broad commercial rights to our product candidates where we believe we can realize maximum value.* We intend to build a fully integrated biotechnology company and independently pursue the development and commercialization of our key product candidates, if approved. We own commercial rights to our technologies and our lead product candidates, STK-001 and STK-002. As we continue to advance our programs, we expect to pursue strategic collaborations to share risk and upside in programs with higher inherent biology risk, larger clinical trial sizes or longer or more complex clinical, regulatory or commercial paths. Our current collaboration with Acadia is an example of where we believe that the development of treatments for severe and rare genetic neurodevelopmental diseases of the CNS is well served by a strategic collaboration.

- *Continue to strengthen and expand our intellectual property portfolio.* We have an intellectual property estate that includes multi-national issued and pending claims for the TANGO mechanisms, as well as multi-national issued and pending claims relating to compositions of matter of oligonucleotides designed to target specific TANGO elements in genes for many genetic diseases that we believe are amenable to upregulation of target protein expression using TANGO. Our proprietary position is reinforced by additional technical know-how and trade secrets. We continually assess and refine our intellectual property strategy as we identify new targets amenable to TANGO, and we will file additional patent applications as appropriate.

Our proprietary RNA therapeutics platform (TANGO)

TANGO (Targeted Augmentation of Nuclear Gene Output) is our proprietary research platform. Our initial applications for this technology are diseases in which one copy of a gene functions normally and the other is mutated, also called haploinsufficiencies. In these cases, the mutated gene does not produce its share of protein, so the body does not function normally. Using the TANGO approach and a deep understanding of RNA science, Stoke researchers design ASOs that bind to pre-mRNA and help the target genes produce more protein. TANGO aims to restore missing proteins by increasing – or stoking – protein output from healthy genes, thus compensating for the non-functioning copy of the gene.

TANGO exploits unique mechanisms for modulation of splicing to prevent the synthesis of naturally occurring non-productive mRNA and increase the synthesis of productive mRNA, resulting in increased production of functional protein.

Human cells naturally regulate protein production to maintain health. Pre-mRNA splicing, including alternative splicing, is an important mechanism used to regulate how much protein and which protein variant is produced. During splicing, introns are removed and exons are joined together to generate the mRNA template that carries the code to synthesize proteins. More than one third of alternative splicing events in mammals do not produce functional proteins and lead to mRNA degradation through nonsense-mediated mRNA decay ("NMD"). TANGO ASOs act at the pre-mRNA level and prevent non-productive alternative splicing so that the body produces more protein-coding mRNA and thus more protein. This approach is particularly applicable to diseases that are caused by insufficient protein production.

In July 2020, we published data in the journal Nature Communications that support our proprietary approach to precisely upregulate protein expression using TANGO ASOs. To evaluate the approach broadly, Stoke researchers selected four gene targets that vary in type and abundance of non-productive splicing events, gene size and protein function: *PCCA* (propionic acidemia); *SYNGAP1* (autosomal dominant mental retardation 5); *CD274* (autoimmune diseases, including uveitis); and *SCN1A* (Dravet syndrome). Stoke researchers designed TANGO ASOs to target the non-productive splicing events in these genes and their activity was evaluated. Dose-dependent reductions of non-productive mRNA were observed to lead to increases in both productive mRNA and protein levels for each of the target genes.

Treatment of autosomal dominant haploinsufficiency diseases with TANGO ASOs

We are initially focused on applying the transformative potential of our platform to developing precision medicines for autosomal dominant haploinsufficiencies, or disorders in which only one allele of a gene is mutated, resulting in approximately 50% of normal protein expression.

Exhibits 1 and 2 shown below illustrate the TANGO mechanism for increasing protein synthesis in a prospective patient with a haploinsufficiency. Exhibit 1 illustrates the prospective patient with a haploinsufficiency possessing one wild-type allele and one mutant allele. The mutant allele is translated into non-functional protein and results in approximately 50% of normal protein expression. Exhibit 2 illustrates treatment with our ASO would prevent the synthesis of naturally occurring non-productive mRNA and would increase the synthesis of productive mRNA, thereby restoring the target protein to near normal levels. Our preclinical studies show that any increase in mutant mRNA would have no effect on the net protein level.

Exhibit 1: Haploinsufficiency without TANGO-ASO

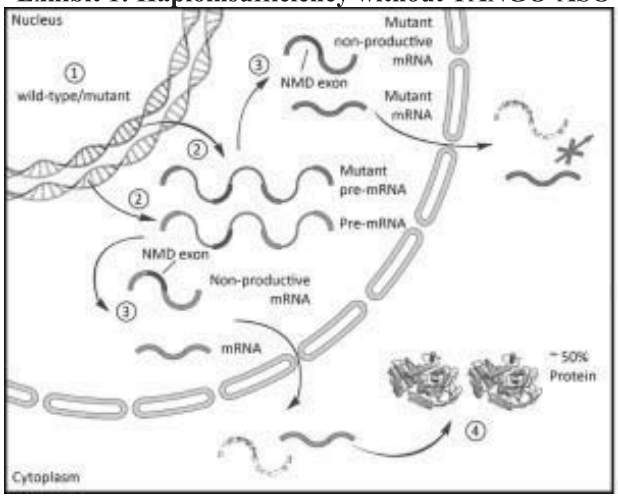
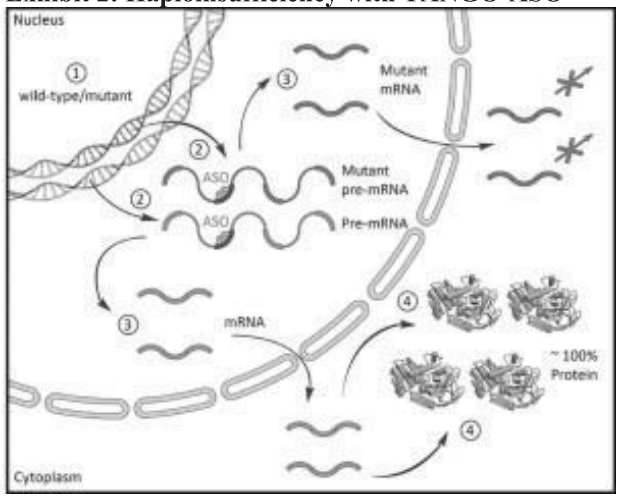


Exhibit 2: Haploinsufficiency with TANGO-ASO



TANGO mechanisms of action

Our ASOs are specifically designed to bind to a desired RNA sequence inside the nuclei of patients' cells to prevent the occurrence of non-productive splicing. By doing so, our ASOs decrease the amount of non-productive mRNA and increase the level of productive mRNA, leading to the generation of more protein. TANGO operates in a mutation-independent manner, given it utilizes one wild-type allele, and does not alter protein coding splicing isoforms. The net effect is increased expression of functional protein from the wild-type allele.

One category of non-productive splicing events amenable to TANGO is alternative splicing that leads to nonsense-mediated mRNA decay, or NMD, of the resulting mRNA. An example of an NMD event is an NMD exon, which is found in over 25% of gene transcripts. NMD exons are part of the wild-type sequence of the genes. In some cases, NMD exons are part of normal gene regulation. Non-productive mRNA, which includes these NMD exons, is degraded in the cytoplasm of the cell by nonsense-mediated mRNA decay and is not translated into protein. Our ASOs bind to the pre-mRNA and redirect the splicing machinery to prevent inclusion of the NMD exon. This splice-switching decreases non-productive mRNA and increases productive mRNA, which is translated into increased protein expression from the wild-type allele. In contrast to current exon skipping therapies, which remove a coding exon and result in a truncated protein, our TANGO mechanism skips out a non-coding NMD exon and yields a full-length functional protein. Our lead product candidates, STK-001 and STK-002, target an NMD exon and the general mechanism is shown in exhibits 3 and 4 below, with the left panel showing the non-

productive mRNA failing to be translated into protein and the right panel showing our ASOs binding to the pre-mRNA and redirecting the splicing machinery.

Exhibit 3: NMD exon without TANGO-ASO

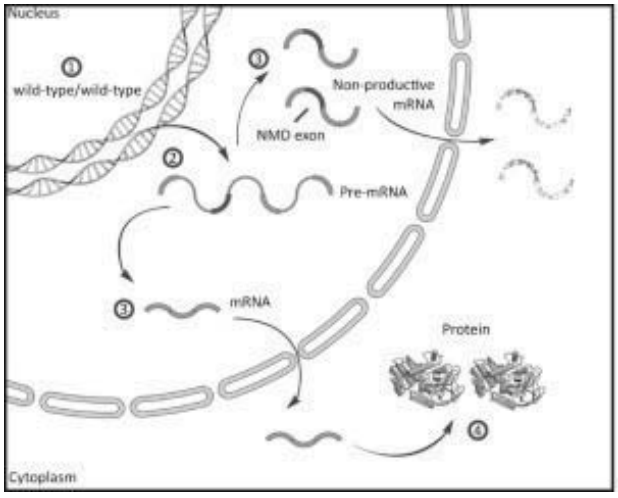
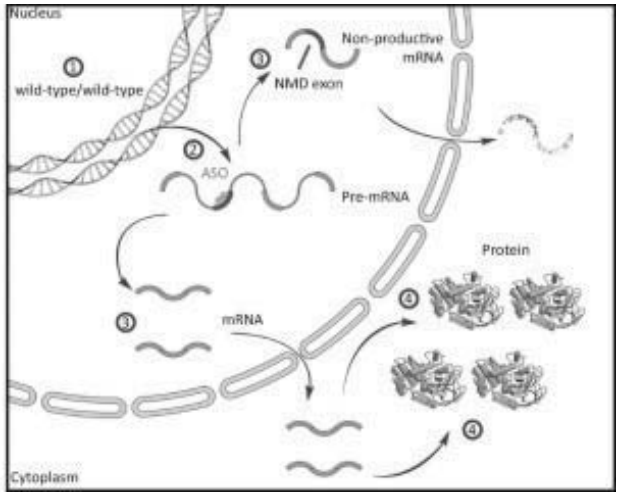


Exhibit 4: NMD exon with TANGO-ASO



Source: Stoke data

Advantages of TANGO

We believe TANGO has the ability to address the underlying genetic cause of disease may have several key advantages versus other genetic approaches, including:

- *Selectively boosts expression only in tissues where the protein is normally expressed*. The activities of our ASOs are inherently tissue-specific. TANGO-mediated upregulation of protein expression only occurs where the gene is being naturally transcribed, limiting the likelihood of expression in non-native tissues.
- *No observed unwanted off-target effects.* Our ASOs are designed to bind to a specific RNA region to modulate splicing with no observed activity on global or closely related genes and minimal off-target cross reactivity to the RNAs from other human genes.
- *Utility across small and large gene targets and mutations.* Our ASOs upregulate protein expression regardless of gene size and are not constrained to smaller gene targets. Our ASOs also upregulate expression of the wild-type allele, meaning the TANGO mechanism does not rely on targeting a specific mutation. Given this, we believe our therapies are well-suited for diseases caused by multiple mutations in a single gene, such as many haploinsufficiencies, and provide a single-drug approach that can address the full spectrum of loss-of-function mutations.
- *Does not alter DNA.* Our ASOs do not create detectable changes at the DNA level and make no detectable irreversible modifications to the patient's genome.
- *Ability to control dose level and duration.* Our ASOs provide the ability for dose titration, thereby allowing for dose-dependent and reversible control of level and duration of protein expression. The ability to titrate dosage provides us with flexibility to address a variety of tissue types, and potentially enables us to deliver the right dose, at the right location, for each indication.
- *Simple and scalable manufacturing.* Our novel ASOs are synthesized by highly scalable, solid-phase chemical synthesis and we leverage a well-established contract manufacturing base. We believe the manufacturing requirements for our ASOs are much simpler, more scalable and more cost-effective than gene therapy and gene editing.

Our approach

We employ a systematic and capital-efficient approach to develop ASOs for genetically defined patient populations. We rely on our proprietary database to identify novel drug targets and corroborate these findings with existing knowledge to improve our probability of success in the clinic. We believe that leveraging our proprietary database and focusing on our core competencies of target identification and clinical and regulatory execution will allow us to reduce the time, cost and risks of drug development.

Target identification

We continue to make significant investments in our infrastructure to accelerate the pace and scale of target identification. We have built a significant bioinformatics capability, which includes proprietary bioinformatics algorithms and extensive in-house expertise in whole transcriptome RNA sequencing, also referred to as RNAseq. RNAseq uses next-generation sequencing to determine the quantity and sequences of RNA in a sample. We leverage large internal datasets of RNAseq from key tissues known to be addressable with antisense, such as the CNS, eye, liver and kidney, that are purpose-built to enhance the capture of non-productive events.

We employ machine learning to iteratively refine our search and scoring criteria for the most addressable non-productive mRNA elements based on internal target validation and hit identification data. Our technology is amenable to a large number of mutations and can thereby potentially provide a single-drug approach for diseases that are caused by many loss-of-function mutations in a single gene. We have identified approximately 1,200 monogenic, or single gene, diseases containing at least one NMD-inducing nonproductive event, which we believe may be amenable to TANGO. We believe our approach is highly predictive and enables rapid and systematic identification of those targets that are most likely to have clinical relevance, thereby increasing the probability for clinical success and accelerating the expansion of our emerging pipeline.

Hit identification

Once a TANGO target is validated in cells and tissues that are relevant to the disease, we employ cell lines to rapidly screen for hit ASOs that can increase the target protein expression by specifically preventing the occurrence of the non-productive event in the target mRNA. We have also made investments in automated equipment to efficiently screen large numbers of ASOs. ASO arrays utilize clinically translatable previously-validated ASO chemistries, such as 2’ methoxyethyl phosphorothioate and PMO. Hit compounds are evaluated in vivo to identify lead ASOs that possess suitable efficacy and safety to merit preclinical development. Lead ASOs are subsequently evaluated in animal disease models or ex vivo disease model systems.

Lead evaluation and prioritization

After we have identified lead compounds, we evaluate and prioritize the advancement of new development candidates based on both program-specific and portfolio-wide considerations. Program-specific criteria include, among other relevant factors, the severity of the unmet medical need, the likelihood of therapeutic utility, the feasibility of clinical development, the costs of development and the commercial opportunity. Portfolio-wide considerations include the ability to demonstrate technical success for our platform, thereby increasing the probability of success and learnings for subsequent programs. We believe that the learnings from our lead Dravet syndrome program will significantly reduce the uncertainty of development of subsequent programs in our pipeline, particularly those targeting the CNS.

Clinical trial and regulatory execution

We employ a multi-pronged approach to bring new product candidates forward as rapidly as possible. Our approach leverages previously-validated ASO chemistry and a modality that has been successfully utilized for other diseases, to minimize potential safety concerns and development risk. We have announced end of study data from two Phase 1/2a open-label studies of STK-001 for Dravet syndrome, MONARCH in the United States and ADMIRAL in the United Kingdom, each with primary endpoints common to the trials for approved anti-seizure medications (“ASMs”). Additionally, we plan to design clinical trials with the goal of capturing the potential disease-modifying effects of our TANGO therapies.

Commercialization

We intend to retain broad commercial rights and independently bring our therapies to patients through a lean, targeted internal commercial organization where we believe we can realize maximum value. To do this, we are focused on ensuring that we can effectively identify and access those patients who may benefit from our product candidates. We target diseases in which genetic testing is routinely performed, thereby shortening the diagnostic odyssey and enabling rapid identification of patients who harbor the relevant genetic mutations. We have partnered with Invitae, a leading genetic information company, to provide genetic testing for pediatric epilepsy at no cost to the patient. Lastly, to maximize patient access, we aim to leverage an established network of academic and tertiary centers with extensive experience with analogous drug administration.

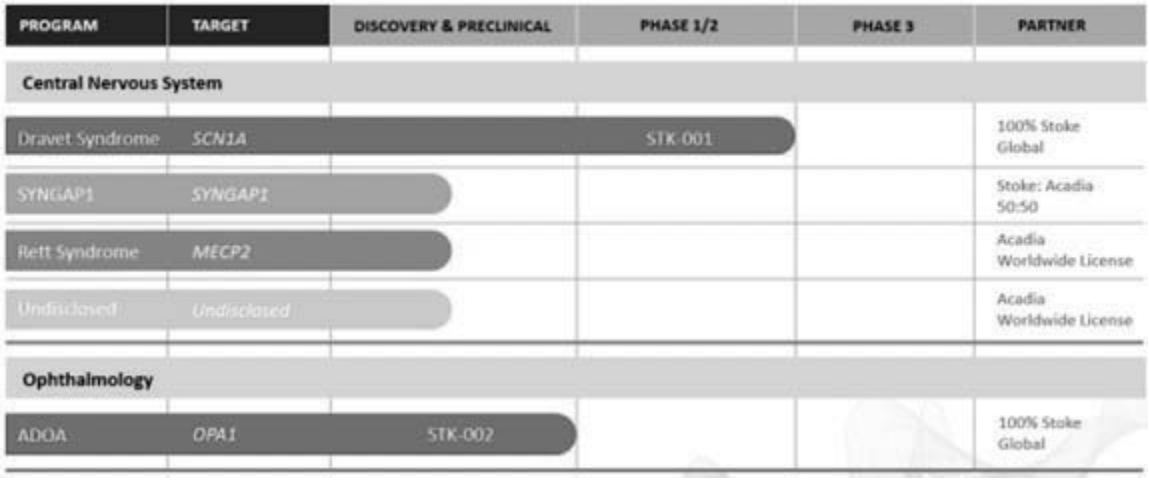
Therapeutic focus and product candidates

We believe our ASOs can be applied to treat a wide range of severe diseases, and we have carefully designed and prioritized our pipeline strategy to maximize this opportunity. We are focused on applying the transformative potential of our TANGO platform to developing medicines for patients with diseases where the genetic abnormality is known and is found in a single gene. We therefore know for a given disease precisely which gene will need to be upregulated, thus mitigating against the uncertainty of the disease biology. We are currently focused on developing product candidates to treat autosomal dominant haploinsufficiency diseases, or disorders in which one copy of a gene is mutated and results in approximately 50% of normal protein expression. Within haploinsufficiencies, we are prioritizing genetic diseases of the CNS and the eye for our near-term development efforts.

Our Development Programs

Our technology, development experience and scientific knowledge in the field of biologics, RNA splicing, and antisense oligonucleotide chemistry has enabled us to build a pipeline of programs targeting the underlying cause of severe diseases. Exhibit 5 below represents a summary of our programs, which are focused on genetic diseases of the CNS and eye.

Exhibit 5: Pipeline



Source: Stoke corporate presentation, March 2024

STK-001 for the treatment of Dravet syndrome

STK-001 is an investigational new medicine for the treatment of Dravet syndrome currently being evaluated in ongoing clinical trials. We believe that STK-001 has the potential to be the first disease-modifying therapy to address the genetic cause of Dravet syndrome. STK-001 is designed to upregulate $Na_v1.1$ protein expression by leveraging the non-mutant (wild-type) copy of the *SCN1A* gene to restore physiological $Na_v1.1$ protein levels, thereby reducing both occurrence of seizures and significant non-seizure comorbidities.

Disease Overview

Dravet syndrome is one of the most severe genetic epilepsies and affects approximately 6.4 in 100,000 people worldwide, including 5-5.5 in 100,000 people who possess a mutation in the *SCN1A* gene, according to a 2018 market research report commissioned by us and prepared by Health Advances, LLC, or the Health Advances Report. The disease is caused by a pathogenic mutation or deletion of the *SCN1A* gene in approximately 85% of patients. At least 1,700 different *de novo* mutations in the *SCN1A* gene have been identified to date in Dravet syndrome patients, including single nucleotide substitutions, small insertions or deletions and even whole gene deletions. *SCN1A* codes for the alpha subunit of the voltage-gated sodium channel, or $Na_v1.1$ protein, an ion channel that is essential for the generation and propagation of action potentials. More than 95% of the disease-causing mutations of *SCN1A* cause loss-of-function, resulting in haploinsufficiency (approximately 50% reduction) of the $Na_v1.1$ protein in select neurons in the brain. This loss of $Na_v1.1$ channels in inhibitory interneurons and other nerve cells results in Dravet syndrome.

Dravet syndrome is characterized by multiple seizure types and may progress to status epilepticus or prolonged seizures lasting more than five minutes that require immediate intervention. Patients typically experience their first seizure before 12 months of age. More than 90% of patients suffer from at least one non-seizure comorbidity, including severe intellectual and developmental disabilities, motor and speech impairment, autism, attention deficit hyperactivity disorder and behavioral difficulties. Neurologic function and cognition are usually normal in children with Dravet syndrome up to two years of age. However, nearly all Dravet syndrome patients exhibit intellectual impairment by the age of four, ranging from minor learning difficulty to global developmental delay. The time between one year and eight years of age is a critical period for intervention. After eight years of age, nearly all Dravet syndrome patients exhibit evidence of substantial developmental delay. The symptoms of the disease result in remarkably low quality of life and shortened life expectancy, and as a result impose an immense burden on individuals and families.

The cognitive impairment in Dravet syndrome is not purely a consequence of seizures. Patients with few seizures have been observed to possess severe encephalopathy, and conversely patients with frequent seizures have been observed to exhibit relatively minimal cognitive decline. In addition, there does not appear to be a correlation between cognitive outcome and *SCN1A* mutation type, whether a missense or nonsense mutation.

Importantly, patients with Dravet syndrome have an increased risk of premature death, primarily due to SUDEP, or Sudden Unexpected Death in Epilepsy. Dravet syndrome patients have the highest SUDEP rate of any epilepsy. An analysis of mortality in the Epilepsy Genetics Research Program demonstrated a Dravet syndrome-specific mortality rate of 15.84 per 1,000 patient years. SUDEP was the most common cause of premature death among Dravet syndrome patients (59%), equating to a Dravet syndrome-specific SUDEP rate of 9.32 per 1,000 patient-years. This is nearly twice the rate for adults with refractory epilepsy.

Patients with Dravet syndrome are often diagnosed by three years of age, and neither patient gender nor family history of seizures is associated with risk of Dravet syndrome. Dravet syndrome occurs worldwide and is not concentrated in any particular geographic area or ethnic group. Early diagnosis is driven by heightened awareness of Dravet syndrome and other genetic epilepsy disorders as well as an emerging consensus amongst epilepsy specialists that early diagnosis is cost-effective and beneficial for prognosis. Among pediatric Dravet syndrome patients, approximately 90% in North America and Europe undergo genetic testing as part of their diagnostic work-up, according to a 2021 market research report commissioned by Stoke and prepared by Recon Strategy.

The incidence of Dravet syndrome is approximately 64 per million births, which translates to an overall prevalence of approximately 35,000 patients across the United States, Canada, Japan, Germany, France and the United Kingdom, with approximately 16,000 patients in the United States.

Current treatments

Current treatments for Dravet syndrome only address the occurrence of seizures, not the underlying cause, and according to a 2017 study as published in the Developmental Medicine & Child Neurology Journal, more than 90% of Dravet syndrome patients still report suffering from incomplete seizure control with existing ASM regimens. As a result, the current treatment strategy involves the use of multiple ASMs, including combinations of cannabidiol, stiripentol, fenfluramine, clobazam, valproate, topiramate and others. Patients are typically treated with two to four drugs administered concomitantly, and in most cases the relief provided by polytherapy is insufficient.

Cannabidiol (Epidiolex), fenfluramine (Fintepla) and stiripentol (Diacomit) are currently the only FDA-approved ASMs for the treatment of Dravet syndrome. None of these approved ASMs address the significant non-seizure comorbidities. Moreover, patients are still likely to be affected by non-seizure comorbidities and may develop tolerance to these ASMs over time.

Patients with Dravet syndrome need a novel therapeutic that addresses the genetic basis of the disease and treats the large number of seizures and multiple seizure types that persist despite treatment with existing therapy. Importantly, additional therapy options are needed to address the disabling comorbidities that occur with Dravet syndrome. If STK-001 is approved by the FDA, we believe our precision medicine approach may have a profound impact on individuals and families.

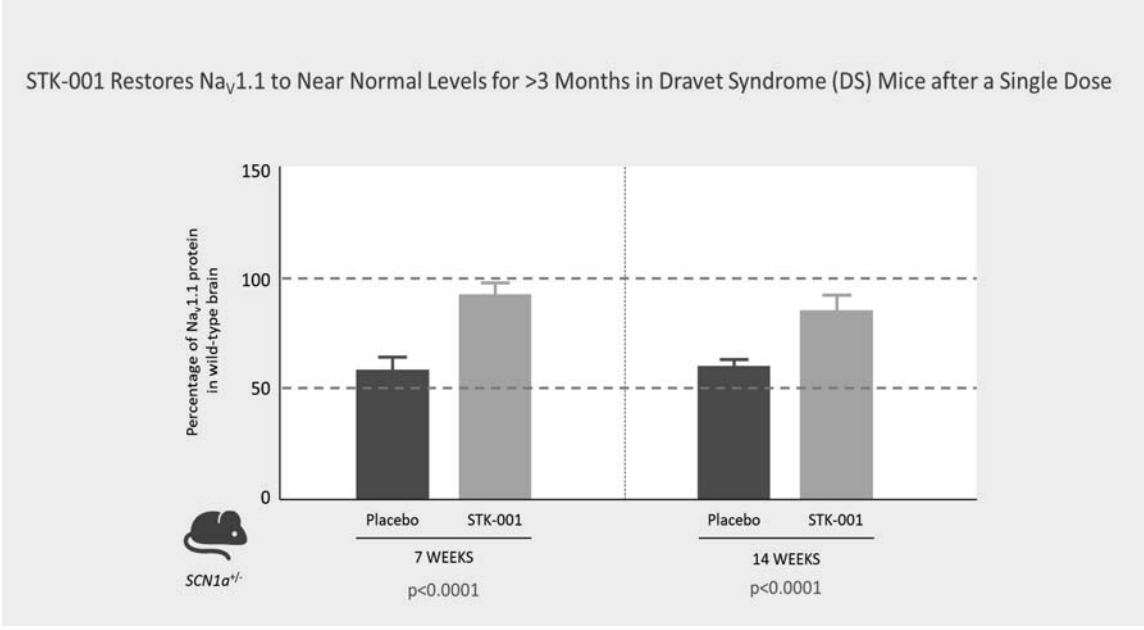
Preclinical data

We have generated compelling preclinical data that demonstrate proof-of-mechanism for STK-001. Our initial target engagement, pharmacology and efficacy studies were performed in mice, including both wild-type and a Dravet syndrome mouse model. The targeted non-productive splicing event in *SCN1A* is highly conserved across multiple species, including mouse, non-human primates and humans. The target sequence for STK-001 is also identical across species.

We evaluated STK-001 pharmacology and efficacy in transgenic mice with a heterozygous deletion of *Scn1a*. This model was created by introducing a targeted deletion in the first coding exon of the *Scn1a* gene; these mice exhibit many aspects of the Dravet syndrome phenotype including seizures and premature lethality.

Neonate (postnatal day two) Dravet syndrome mice and wild-type littermate controls were administered a single dose of either placebo (consisting of a phosphate-buffered solution), or 20 μg of STK-001 (n=~50/group) by intracerebroventricular injection. Animals from each group were monitored through day 90. Brains were collected from cohorts of these animals at approximately 7 weeks after dosing (placebo: n=11 wild-type mice, n=4 Dravet syndrome mice; STK-001: n=9 wild-type mice, n=10 Dravet syndrome mice) and 14 weeks after dosing (placebo: n=10 wild-type mice, n=10 Dravet syndrome mice; STK-001: n=10 wild-type mice, n=10 Dravet syndrome mice). Notably, a single injection of STK-001 restored $Na_v1.1$ protein in Dravet syndrome mice to levels that are near those of the wild-type mice at both 7 and 14 weeks as shown in exhibit 6. These data demonstrate that STK-001 has an impact on $Na_v1.1$ protein expression and we believe this may translate to a favorable dosing regimen in humans.

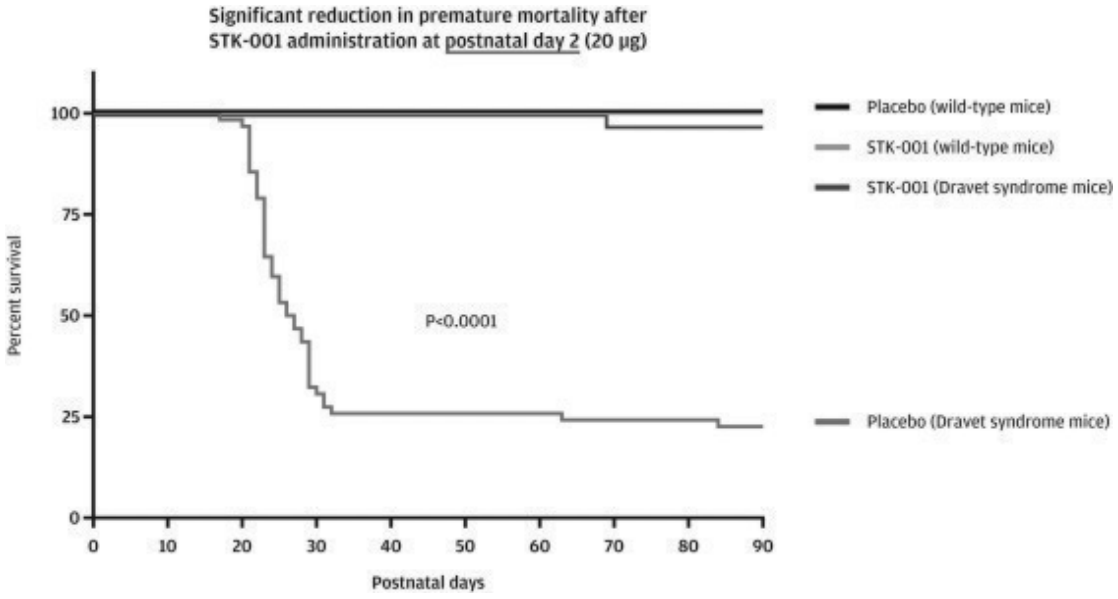
Exhibit 6. Increase of $Na_v1.1$ in Dravet Syndrome (DS) mice after a single dose of STK-001



Source: Han *et al*., Science Trans Med, 2020

In addition to an increase in the $Na_v1.1$ protein, the administration of a single dose of 20 μg of STK-001 in neonate Dravet syndrome mice (postnatal day two) resulted in a significant reduction in premature mortality. Treatment with STK-001 resulted in 97% survival of Dravet syndrome mice for the 90-day post-natal observation period (survival of 33 out of 34 mice was observed in the STK-001 Dravet syndrome mouse group) compared with 23% survival of placebo-treated mice (survival of 14 out of 62 mice). This is illustrated in exhibit 7.

Exhibit 7. Reduction in premature mortality in DS mice after administration of STK-001



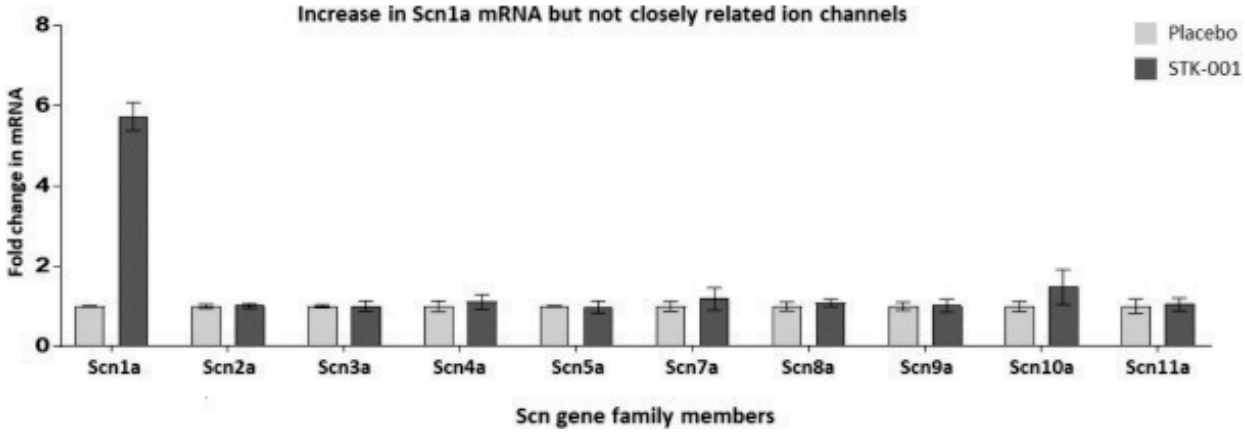
Source: Han *et al*., Science Trans Med, 2020

Further preclinical studies of STK-001 have shown significant reductions in seizure frequency in a mouse model of Dravet syndrome (DS). Data from electroencephalography (EEG) recordings showed 76% (16/21) of DS mice treated with STK-001 were seizure free compared to 48% (10/21) that were treated with a placebo. An 80% reduction in the average number of spontaneous seizures (3 seizures vs 16 seizures) was also observed among treated DS mice compared to placebo. EEG is a highly sensitive measure of seizure activity, which enables the detection of seizures that may not be otherwise visible. These data are published in Han et al., Science Trans. Med, 2020.

Analyses were also performed *in silico* to understand the specificity of STK-001. We evaluated STK-001 via bioinformatic analysis against all annotated protein-coding genes to predict potential off-target activities. Results showed no perfect 18- to 16-nucleotide match for STK-001 anywhere in the transcriptome other than *SCN1A* pre-mRNA, indicating that STK-001 recognizes a unique sequence in the human transcriptome and should possess minimal off-target bindings.

Further supporting our specificity analysis, we also evaluated brain samples of wild-type neonate mice to ensure that STK-001 does not alter levels of other channels in the highly homologous *SCN* family. Importantly, the mRNA levels of closely related ion channels were not altered in the mouse brain five days after administration of 10 µg of STK-001 (n=2/group placebo, n=4/group STK-001), as shown in the figure below. Similar analysis was performed in wild-type and Dravet syndrome mice treated with 20 µg of STK-001 at 7 and 14 weeks after dosing. As illustrated in exhibit 8, STK-001 treated samples showed an increase in expression of the *SCN1A* gene, but not any of the other *SCN* family members. These biological studies demonstrate that STK-001 is highly specific for *SCN1A* among the highly homologous family of sodium channel genes, limiting the likelihood of off-target activities.

Exhibit 8. Fold change in mRNA of Scn gene family ion channels



Source: Stoke data.

We also investigated the pharmacology, distribution and tolerability of STK-001 in a study with cynomolgus monkeys. As a pilot experiment, this study was not required to be performed under Good Laboratory Practices ("GLP"). Pre-pubescent monkeys (age 2-2.5 years old) were administered a single dose of STK-001 (n=3/group; 4 groups dosed) or control solution (n=2/group; 2 groups dosed) by intrathecal injection at a dose range that we believe coincides with the estimated therapeutic dose range and stays below the maximum tolerated dose based on tolerability in mice and published data for molecules of similar chemistry. The animals were sacrificed at 3 days (n=8) and 29 days (n=8) after dosing. An increase in $Na_V1.1$ levels was observed ranging from 1.1-fold to 2.0-fold, compared to the control group, varying by the anatomical region, dose and day of necropsy, with the greatest changes observed in the cerebral cortex. The increase in $Na_v1.1$ was also correlated with the presence of STK-001 in brain tissue. Additionally, all doses tested showed no drug-related toxicities, including no changes in platelet counts or hepatic function, no clinical signs or symptoms over the 28-day period after administration and no abnormal histopathology.

Single dose GLP toxicology studies in rats and cynomolgus monkeys, that characterized the pharmacology, exposure and tolerability of STK-001 were included in the investigational new drug application (the "IND") that was submitted to the FDA in late 2019. Additional multiple dose GLP toxicology data have subsequently been submitted to the FDA and the MHRA (U.K. regulatory agency) to support multiple dosing in the clinic, and the Company expects to receive data from a second chronic dosing GLP toxicology prior to initiating late-stage clinical development of STK-001.

Clinical program and data

We designed our lead product candidate, STK-001, to treat Dravet syndrome, a severe and progressive genetic epilepsy. This program draws on a well-defined patient population based on routine genetic testing and learnings from drugs approved for the treatment of Dravet syndrome to inform the clinical and regulatory pathways for STK-001.

We have announced end of study data from two Phase 1/2a open-label studies of STK-001, MONARCH in the United States and ADMIRAL in the United Kingdom. The MONARCH study was designed to evaluate single and multiple ascending dose levels of STK-001 administered intrathecally in children and adolescents with Dravet syndrome. Patients were eligible for the trial if they were between the ages of 2 and 18, had an established diagnosis of Dravet syndrome and had evidence of a pathogenic genetic mutation in the SCN1A gene. Requiring an SCN1A mutation for trial enrollment allows for a clear and definitive etiologic diagnosis, a more homogeneous patient population and tailored treatment based on a precision medicine approach. Eligible patients also failed at least two epilepsy treatments in the past and currently be taking at least one ASM. The protocol called for all medications and interventions to remain unchanged throughout the trials, which allows for assessment of STK-001 with a variety of ASMs.

The primary objectives were the assessment of the safety and tolerability of STK-001, as well as to characterize blood pharmacokinetics ("PK") and cerebrospinal fluid ("CSF") exposure levels. A secondary objective was to assess the efficacy of STK-001 as an adjunctive ASM treatment with respect to the percent change from baseline in convulsive seizure frequency over a 12-week treatment period. We also measured non-seizure aspects of the disease, such as quality of life as secondary endpoints.

These endpoints as well as other exploratory endpoints will be informed based on our two-year observational study (BUTTERFLY). Enrollment in BUTTERFLY is complete and final 2-year data was presented in December 2023.

BUTTERFLY was designed to evaluate seizure frequency and non-seizure comorbidities associated with the disease, including motor and speech impairment, intellectual and developmental disabilities, behavioral deficits and abnormal sleep patterns. Data from the study will support clinical development plans for STK-001. Data from BUTTERFLY suggest that commonly used cognition assessments, Vineland-III (Vineland Adaptive Behavior Scale, Third Edition), BSID-III (Bayley Scales of Infant Development, Third Edition), and WPPSI-IV (Wechsler Preschool and Primary Scale of Intelligence, Fourth Edition) may be useful for clinical studies assessing neurodevelopment and adaptive behavior in patients with Dravet syndrome. While there was heterogeneity across patient scores on clinical measures at baseline, BUTTERFLY patients did not have statistically significant change from baseline in the majority of key Vineland-III measures over the 24 months of observation. Additionally, despite treatment of BUTTERFLY patients with the best available anti-seizure medicines, on average the rate of improvement over 24 months on multiple clinical measures, including the Vineland-III, was substantially below that of neurotypical peers, and patients continued to experience convulsive seizures over the 24 months at similar frequency to that at baseline.

In March 2020, we announced the FDA had placed a partial clinical hold on doses of STK-001 above 20mg in the MONARCH study, pending additional preclinical testing to determine the safety profile of higher doses. When intrathecal doses above what the Company expects to administer in the clinic were administered to non-human primates ("NHPs"), adverse hind limb paresis was observed. This finding is known to occur following intrathecal delivery of ASOs to NHPs and is not known to translate to the human experience. When extremely high dose levels were administered, acute convulsions were observed immediately following STK-001 administration. The dose levels were well above the range of corresponding human doses that would ever be administered in the clinic and were delivered in a formulation that was at a higher concentration than would be administered in the clinic. There is no apparent correlation of these acute adverse events with the mechanism of action of STK-001.

Since March 2020, the FDA has agreed to allow us to add additional higher dose levels in the United States. Additionally, the Company announced in March 2024 that the FDA provided clearance for the evaluation of three doses of 70mg in the MONARCH study and continued dosing of 45mg in our SWALLOWTAIL Open Label Extension ("OLE") study. The FDA partial clinical hold remains in place and limits dosing in the United States to these levels.

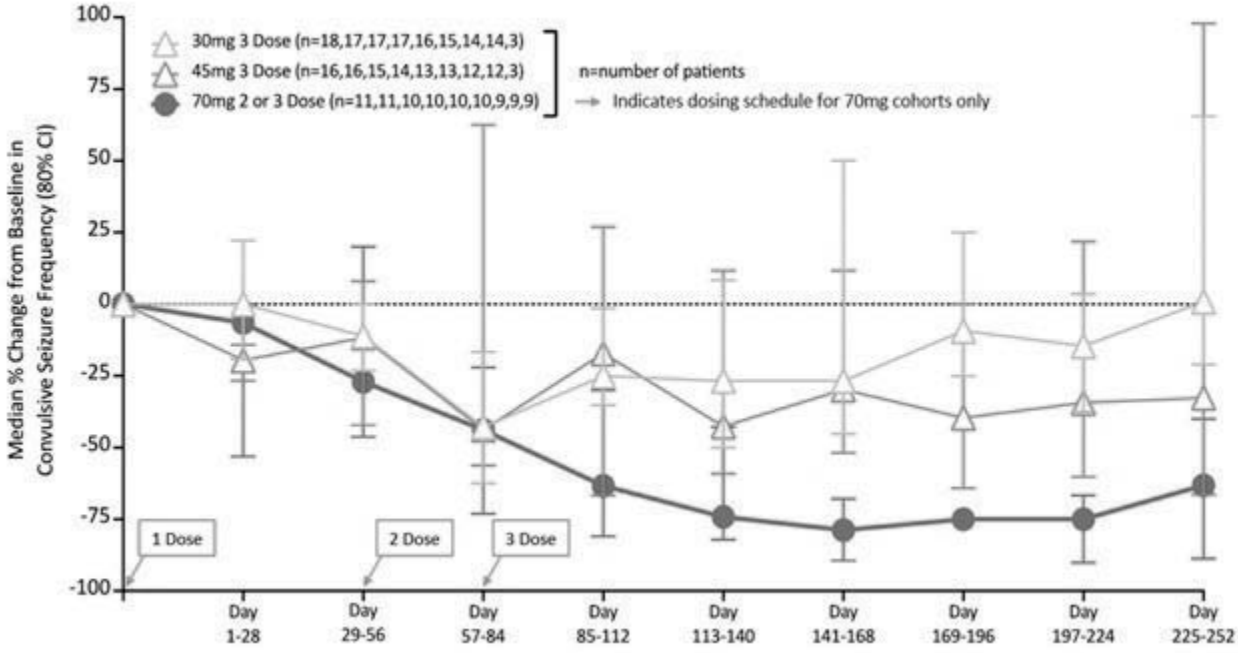
The ADMIRAL study was a Phase 1/2a open-label study of children and adolescents ages 2 to <18 who have an established diagnosis of Dravet syndrome and have evidence of a genetic mutation in the *SCN1A* gene. The primary objectives for the study were to assess the safety and tolerability of multiple doses of STK-001 up to 70mg, as well as to determine the pharmacokinetics in plasma and exposure in cerebrospinal fluid. A secondary objective was to assess the effect of multiple doses of STK-001 as an adjunctive antiepileptic treatment with respect to the percentage change from baseline in convulsive seizure frequency over a 24-week treatment period. Non-seizure aspects of the disease, such as overall clinical status and quality of life, were also measured as secondary endpoints.

Patients who participated in the MONARCH study in the United States or the ADMIRAL study in the United Kingdom and met study entry criteria are eligible to continue treatment in SWALLOWTAIL or LONGWING, respectively, both of which are designed to evaluate the long-term safety and tolerability of repeated doses of STK-001. SWALLOWTAIL and LONGWING are also providing information on the preliminary effects of STK-001 on both seizures and non-seizure aspects of the Dravet syndrome, such as behavior, cognition, and overall quality of life. Patients in LONGWING currently receive chronic dosing of 45mg of STK-001, and in March 2024, we announced that the FDA will allow chronic dosing in SWALLOWTAIL in the United States to increase to 45mg as well.

In March 2024, we announced end of study data from the Phase 1/2a open-label studies of STK-001. The pooled data from these studies demonstrated that STK-001 was generally well tolerated. 30% (24/81) of the patients experienced a treatment-emergent adverse event that was related to study drug, with the most common being CSF protein elevations and procedural vomiting. 22% (18/81) of the patients had a treatment-emergent serious adverse event, which were all assessed as unrelated to study drug except for the previously reported case of one patient who experienced Suspected Unexpected Serious Adverse Reactions.

One of several secondary endpoints for these studies was a comparison of the percent change in convulsive seizure frequency as measured by daily seizure diaries and calculated over 4-week periods: between baseline and 12 weeks after treatment; and between baseline and end of study. Data from patients treated with multiple doses of 70mg of STK-001 demonstrated the most substantial reductions in convulsive seizures on top of the standard of care, as illustrated in Exhibit 9 below.

Exhibit 9. Median reductions in convulsive seizure frequency over time



Patients who were treated with one, two or three doses of 70mg demonstrated substantial reductions in convulsive seizure frequency at three months and at six months after the last dose, as shown in Exhibit 10 below.

Exhibit 10. Reductions in convulsive seizure frequency among patients treated with 70mg doses

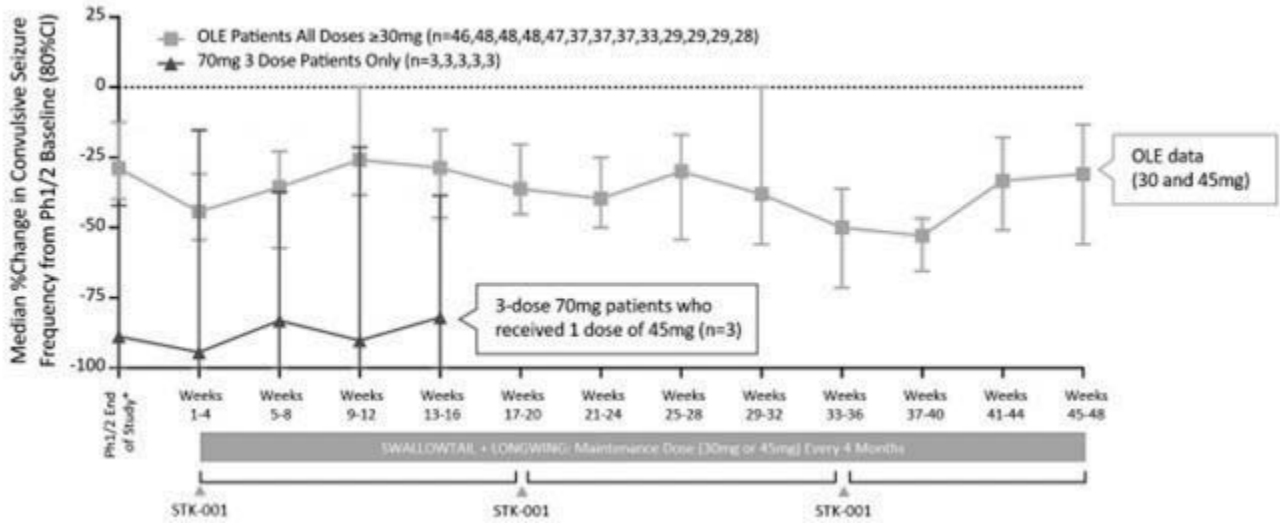
Median % Reduction from Baseline in Convulsive Seizure Frequency	70mg (1 dose)	70mg (2 or 3 doses)
At 3 Months After Last Dose	43% (n=8)	85% (n=10†)
At 6 Months After Last Dose	57% (n=7*)	74% (n=9†)

*Seizure data excluded from month 5-6 for 1 patient because >50% seizure diary was missing

†Seizure data excluded for 2 patients (1 patient prior to 3m after last dose, 1 prior to 6m after last dose) following a change in background antiseizure medicines

Additional data from patients who received cumulative doses of at least 30mg of STK-001 in the Phase 1/2a studies and then continued treatment with 30mg or 45mg doses of STK-001 every four months in one of the two OLEs demonstrated durable reductions in convulsive seizure frequency throughout the course of treatment, as shown in Exhibit 11 below.

Exhibit 11. Durable reductions in convulsive seizure frequence in OLE studies



Data from a mixed-effects model for repeated measures analysis of these patients also indicated clinically meaningful improvements from baseline over 12 months in the OLEs in multiple measures of cognition and behavior, including multiple sub-domains of the Vineland-III.

We plan to meet with regulatory authorities to discuss a registrational study design that includes initial doses of 70mg followed by continued dosing at 45mg of STK-001 and anticipate providing an update later in 2024.

STK-002 for the treatment of Autosomal Dominant Optic Atrophy (ADOA)

STK-002 is our lead clinical candidate for the treatment of ADOA. STK-002 is designed to upregulate OPA1 protein expression by leveraging the non-mutant (wild-type) copy of the *OPA1* gene to restore OPA1 protein expression with the aim to stop or slow vision loss in patients with ADOA. To date, we have generated preclinical data demonstrating proof-of-mechanism and proof-of-concept for STK-002.

Disease Overview

ADOA is the most common inherited optic nerve disorder seen in clinical practice. ADOA causes progressive and irreversible vision loss in both eyes starting in the first decade of life. Many children and adults progress to blindness. Roughly half of people with ADOA fail driving standards and up to 46% are registered as legally blind. The disease affects one in 30,000 people globally with a higher incidence of approximately one in 10,000 in Denmark due to a founder effect. 65% to 90% of ADOA is caused by mutations in one allele of the *OPA1* gene, most of which lead to haploinsufficiency and disease manifestation. More than 400 different *OPA1* mutations have been reported in people diagnosed with ADOA. Most mutations result in a severe decrease – up to 50% – of the normal amount of the OPA1 protein. There is no strong genotype-phenotype correlation.

OPA1 is a dynamin-related GTPase that plays a key role in maintaining mitochondria structure and dynamics. The OPA1 protein is imported into the mitochondria and is the crucial molecule that mediates inner mitochondria membrane fusion and cristae morphogenesis and is critical for oxidative phosphorylation and Adenosine triphosphate (“ATP”) synthesis. Insufficient OPA1 activity causes mitochondria dysfunction with consequent insufficient ATP production, excess reactive oxygen species production and eventual cell death. High energy demanding cells such as neurons and cardiomyocytes are particularly susceptible to mitochondria dysfunction, and retinal ganglion cells (“RGCs”) are a neuronal cell type most susceptible to loss of OPA1 protein as evidenced by RGC death in ADOA caused by *OPA1* haploinsufficiency.

A clinical diagnosis of ADOA is made when a patient meets some or all of the following criteria: pathogenic variant of the *OPA1* gene identified in the patient or a family member; reduced visual acuity; temporal disc pallor; visual field defect; color vision defect (acquired blue-yellow loss); thinning of retinal nerve fiber layer and abnormal visual evoked potentials. Clinical findings are based on: intraocular pressure measurement; visual field assessment; color discrimination; dilated slit lamp biomicroscopy; optical coherence tomography; or visual electrophysiology. Patients suspected of having ADOA are recommended to receive genetic testing to confirm the clinical diagnosis, help identify other family members who are

affected and ensure patients avoid stressors that could increase disease progression (e.g. smoking, alcohol). The prognosis for many patients with ADOA is poor and the rate of visual loss can be difficult to predict given significant inter- and intra-familial variability.

Current Treatments

There are currently no available treatments for ADOA. Because ADOA causes deterioration of the optic nerves, corrective aids such as glasses or contacts do not help to improve vision lost to the disease. Supportive services and low-vision aids are offered for patients with severely decreased visual acuity. Our ASOs are designed to target the underlying cause of ADOA, which is *OPA1* haploinsufficiency, by decreasing a non-productive mRNA splicing event in the *OPA1* gene to increase productive *OPA1* mRNA and OPA1 protein in the retinal ganglion cells.

Preclinical data

We previously identified a novel exon inclusion event ("Exon X") in OPA1 that leads to non-productive mRNA due to introduction of a premature termination codon ("PTC") (Exhibit 12 below). Our preclinical studies showed that our ASOs blocked the incorporation of Exon X with consequent dose-dependent increase in productive OPA1 mRNA and protein due to reduction of Exon X-directed NMD of OPA1 mRNA (Exhibit 13 below). We have now demonstrated that a single injection of ASO-14 surrogate in the rabbit eye leads to a dose-dependent increase in ASO accumulation in the retina that correlated with an increase in target engagement (removal of Exon X) and an increase in OPA1 protein (Exhibit 14 below). The study was conducted using female New Zealand white rabbits that were injected with a single dose of vehicle alone or vehicle containing ASO (n=3/group). On Days 15 and 29, the retinal tissue was collected and analyzed. Retinal exposure of ASO-14 surrogate (ST-1102) was elevated with increased dosing, dose-dependent target engagement was seen at all three time-points examined, and protein increase of OPA1 protein was observed at both Day 15 and Day 29 of the study. We further showed that in OPA1 haploinsufficient human cells, ASO-14-mediated increase in OPA1 protein translates to improved mitochondrial function as measured by the substantial restoration of ATP levels in the treated cells (Exhibit 15 below). ATP is produced by the mitochondria and is the key energy carrying molecule in cells. We observed a 20% ATP deficit in OPA1 +/- HEK293. Treatment with ASO-14 restored ATP levels to ~90% of control cells.

Exhibit 12: A representation of the non-productive mRNA splicing event in *OPA1*

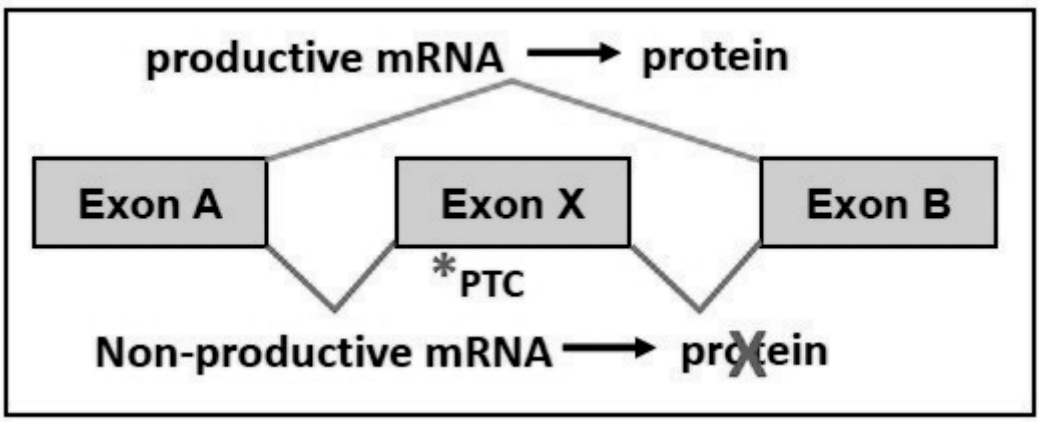


Exhibit 13: Inhibition of NMD with cycloheximide allows for evaluation of the abundance of this event in vitro

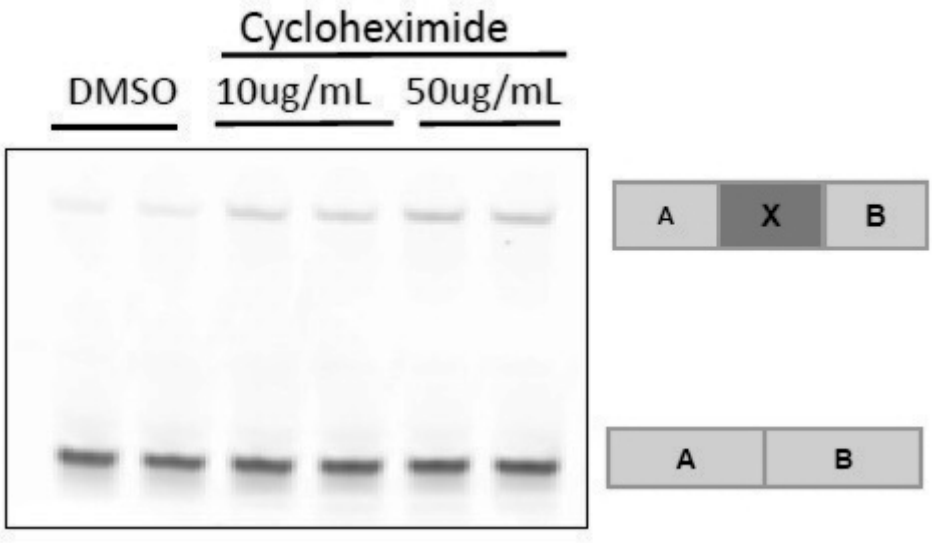
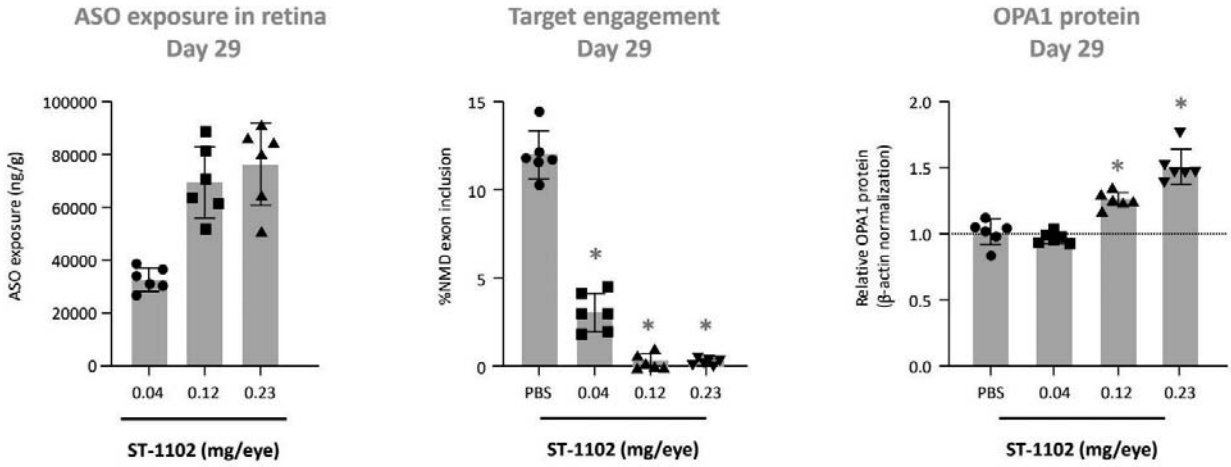
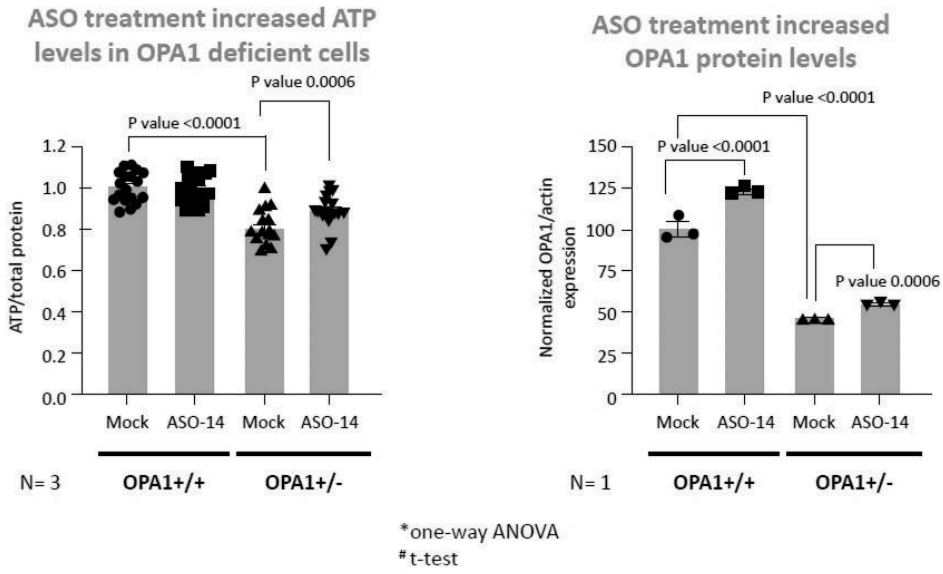


Exhibit 14: Rabbit ASO demonstrates dose-dependent OPA1 protein increase in rabbit retina



Source: Venkatesh A, et al. Antisense oligonucleotide mediated increase of OPA1 expression using TANGO technology for treatment of autosomal dominant optic atrophy. Presented at The Association for Research in Vision and Ophthalmology; May 3-7, 2020; Baltimore, MD.

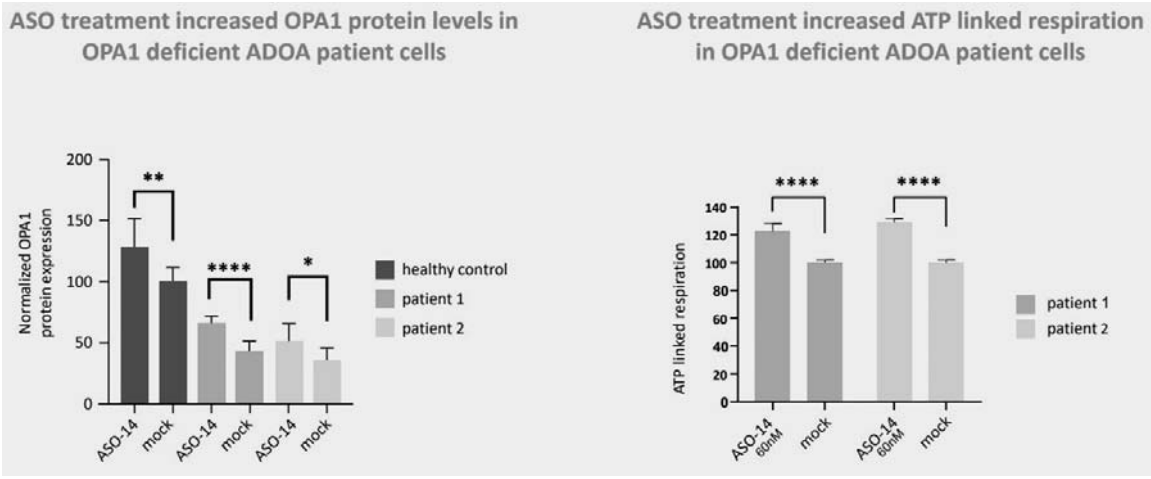
Exhibit 15: Human ASO demonstrates ATP upregulation in *OPA1* haploinsufficient HEK293 cells



Source: Stoke data

In May 2021, we presented new preclinical efficacy data at the Association for Research in Vision and Ophthalmology (ARVO) Annual Meeting demonstrating that our TANGO ASOs can increase OPA1 protein levels and improve mitochondrial function in human cells derived from ADOA patients with different OPA1 mutations. Exhibit 16 below demonstrates that our TANGO ASO increases OPA1 protein and ATP linked mitochondrial respiration in ADOA patient cells.

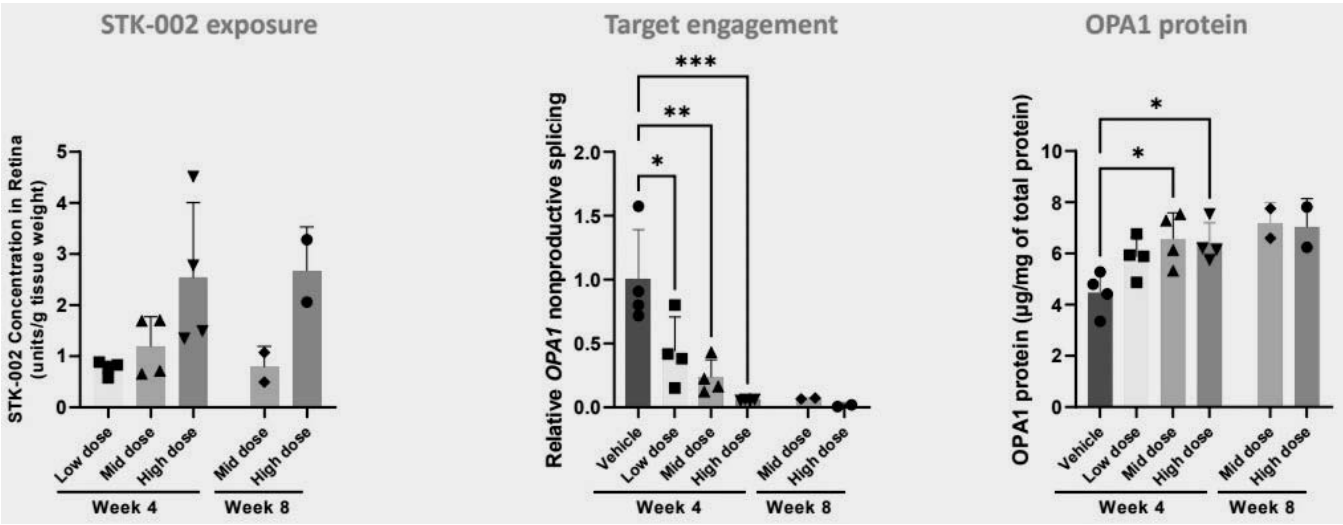
Exhibit 16: TANGO ASO increases OPA1 protein and ATP linked mitochondrial respiration in ADOA patient cells



Source (left graph): Stoke data Source (right graph): Venkatesh A, et al. Antisense oligonucleotide mediated increase in OPA1 improves mitochondrial function in fibroblasts derived from patients with autosomal dominant optic atrophy (ADOA). Presented at The Association for Research in Vision and Ophthalmology; May 1-7, 2021.

In May 2022, we presented further preclinical data for STK-002 demonstrating in-vivo, dose-related target engagement and OPA1 protein upregulation with sustained effect in NHP retinal tissue following administration of STK-002 (Exhibit 17). Additionally, a dose-related increase in OPA1 protein was detected in retinal ganglion cells of NHPs treated with STK-002.

Exhibit 17. Dose-related target engagement and OPA1 protein upregulation in retinal tissue of NHPs following IVT administration of STK-002



Source Venkatesh A, et al. STK-002, an Antisense Oligonucleotide (ASO) for the Treatment of Autosomal Dominant Optic Atrophy (ADOA), is Taken Up by Retinal Ganglion Cells (RGC) and Upregulates OPA-1 Protein Expression After Intravitreal Administration to Non-human Primates (NHPs). ASGCT; May 16-19, 2022.

Clinical Plans

We have completed enrolled (n=48) across 10 sites in the United States, United Kingdom, Italy and Denmark in our two-year prospective natural history study of people ages 8 to 60 who have a confirmed diagnosis of ADOA that is caused by an *OPA1* mutation (FALCON study). The FALCON study is designed to evaluate the rate of change in structural and functional ophthalmic assessments. Data collected from the FALCON study will support the clinical development of STK-002.

We have also received authorization in the United Kingdom to proceed with a Phase 1 open-label study (OSPREY) of children and adults ages 6 to 55 who have an established diagnosis of ADOA and have evidence of a genetic mutation in the *OPA1* gene. The primary objectives for the study are to assess the safety and tolerability of single ascending doses of STK-002, as well as to determine the exposure in blood. A secondary objective is to assess efficacy following intravitreal administration of STK-002 in one eye of each patient as measured by changes in visual function and ocular structure as well as quality of life in patients with ADOA. We expect the OSPREY study to start in 2024.

Additional product opportunities

We are also advancing additional programs focused on multiple targets, including haploinsufficiency diseases of the CNS and eye. These tissues are affected in many severe genetic diseases.

Longer-term, we believe that ASOs designed using TANGO may have the potential to upregulate non-mutated genes in biological pathways to treat both rare and non-rare diseases or conditions that are caused by multiple genes or that are multifactorial. For these diseases, we intend to opportunistically secure partnerships with biopharmaceutical partners whose scientific, development or commercial capabilities complement our own.

Acadia License and Collaboration Agreement

In January 2022, we entered into a license and collaboration agreement with Acadia Pharmaceuticals Inc. (“Acadia”) for the discovery, development and commercialization of novel RNA-based medicines for the treatment of severe and rare genetic neurodevelopmental diseases of the CNS. The agreement focuses on the targets SYNGAP1, MECP2 (Rett syndrome), and an undisclosed neurodevelopmental target of mutual interest. In connection with each target, we will collaborate with Acadia to identify potential treatments for further development and commercialization as licensed products. With respect to SYNGAP1, we have agreed with Acadia to co-develop and co-commercialize licensed products for such target globally, and in connection therewith we granted to Acadia worldwide, co-exclusive (with us) licenses for such

licensed products. With respect to MECP2 and the neurodevelopmental target, we granted to Acadia worldwide, exclusive licenses to develop and commercialize licensed products for such targets.

Pursuant to the terms of the agreement, we received an upfront payment of $60.0 million from Acadia. Acadia agreed to fund the research to identify potential licensed products for MECP2 and the neurodevelopmental target, and we will equally fund with Acadia the research to identify potential licensed products for SYNGAP1. We are eligible to receive up to $907.5 million in potential total milestone payments based upon the achievement of certain development, regulatory, first commercial sales and sales milestone events across the programs for the three targets, assuming each milestone were achieved at least once. With respect to licensed products for MECP2 and the neurodevelopmental target, we are also eligible to receive tiered royalties at percentages ranging from the mid-single digits to the mid-teens on future net sales by Acadia of licensed products worldwide. Royalties payable under the agreement are subject to standard royalty reductions. For SYNGAP1 licensed products that we are co-developing and co-commercializing, we will be responsible for 50% of the development and commercialization costs and will receive 50% of the profits from global commercialization.

With respect to each SYNGAP1 licensed product being co-developed or co-commercialized, the agreement will remain in effect, unless earlier terminated, until the parties have agreed to permanently abandon the further development and commercialization of such licensed product. With respect to licensed products for MECP2 and the neurodevelopmental target, the agreement will remain in effect, unless earlier terminated, until the expiration, on a country-by-country and licensed product-by-licensed product basis, of the applicable royalty term, at which point the license for such licensed product shall become fully paid-up, royalty-free, perpetual and irrevocable in such country.

The agreement also contains customary provisions for termination by Acadia for convenience and by either party for cause, including for material breach (subject to cure). We have standard reversion rights in connection with certain early termination events.

SYNGAP1 syndrome is a rare neurological disorder characterized by moderate to severe intellectual disability that is evident in early childhood. Mutations in the SYNGAP1 gene (which produces the SynGAP protein) were first identified in 2009 and since then, an increasing number of children with SYNGAP1 syndrome have been identified. Normal levels of SynGAP protein are essential for proper brain function and development. Mutations in the SYNGAP1 gene also play an important role in the development of epileptic encephalopathies (DEEs). The severity and onset of symptoms can vary from patient to patient. SYNGAP1 syndrome is characterized by developmental delay or intellectual disability, generalized epilepsy, and autism spectrum disorder (ASD) and other behavioral abnormalities. More than 80% of cases of SYNGAP1 syndrome are caused by a haploinsufficiency of the SYNGAP1 gene. SYNGAP1 syndrome is estimated to account for 1% to 2% of all intellectual disability cases. There are currently no approved treatments for SYNGAP1 syndrome.

Rett syndrome is a rare, debilitating neurological disorder that occurs primarily in females following apparently normal development for the first six months of life. Rett syndrome is often misdiagnosed as autism, cerebral palsy, or non-specific developmental delay. Rett syndrome is caused by mutations on the X chromosome on a gene called MECP2. There are more than 200 different mutations found on the MECP2 gene that interfere with its ability to generate a normal gene product. Rett syndrome occurs worldwide in approximately one of every 10,000 to 15,000 female births and in the United States impacts 6,000 to 9,000 patients. Rett syndrome causes problems in brain function that are responsible for cognitive, sensory, emotional, motor and autonomic function. Typically, with symptoms presenting between 6 to 18 months of age, patients experience a period of rapid decline with loss of purposeful hand use (fine motor skills), development of hand stereotypies, absent or impaired mobility (gross motor skills), loss of communication skills (including eye contact) and inability to independently conduct activities of daily living. Symptoms also include seizures, disorganized breathing patterns, an abnormal side-to-side curvature of the spine (scoliosis), and sleep disturbances. Currently, there are no FDA-approved medicines for the treatment of Rett syndrome.

Manufacturing

We currently contract with third parties to manufacture our products undergoing late-preclinical and clinical testing and anticipate using third parties for all commercial manufacturing. We do not own or operate facilities for product manufacturing, packaging, storage and distribution, or testing. We have personnel with extensive technical, manufacturing, analytical and quality experience and good project management to oversee contract manufacturing and testing activities. We will continue to expand and strengthen our network of third-party providers but may also consider investing in additional internal manufacturing capabilities in the future if there is a technical need, or a strategic or financial benefit.

Manufacturing is subject to extensive regulations that impose procedural and documentation requirements. At a minimum these regulations govern record keeping, manufacturing processes and controls, personnel, quality control and quality assurance. Our systems, procedures and contractors are required to be in compliance with these regulations and are assessed through regular monitoring and formal audits.

Drug substance

Oligonucleotide drug substance requirements for our most advanced programs can be readily met by a variety of domestic and international contractors. Many of these contractors are also able to source all the required raw materials, which allows us to consolidate raw material procurement and drug substance manufacturing activities with a single supplier. To ensure supply chain continuity, we plan to establish supply agreements with alternative suppliers as appropriate. As part of each development program, efforts will be made to invest in process changes to improve purity and yield as warranted.

Future drug substance compositions may require different manufacturing capabilities, which will be addressed through either expanded capability with existing contractors or establishing manufacturing supply relationships with new contractors. These changes in composition may also require new supply chain agreements with contractors that specialize in raw material manufacturing. Our internal personnel will work to identify and establish relationships with contractors that may be ideally suited to meeting these new manufacturing requirements.

Drug product

For the near future, we expect all our oligonucleotide drug products to consist of drug substance formulated in either saline, buffered saline, or some other diluent appropriate for intrathecal, intravitreal, subcutaneous, or intravenous injection. These types of formulations can be manufactured using common processes and readily available materials. We are establishing agreements with a variety of contractors that are suitably equipped to manufacture, package, and test these types of oligonucleotide drug product formulations for subsequent shipment to clinical sites. Several of these manufacturers would also be capable of formulation and packaging for commercial use.

Competition

The biotechnology and biopharmaceutical industries, and the genetic medicines fields, are characterized by rapid evolution of technologies, fierce competition and strong defense of intellectual property. Any product candidates that we successfully develop and commercialize will have to compete with existing therapies and new therapies that may become available in the future. While we believe that our technology, development experience and scientific knowledge in the field of biologics, RNA splicing, and antisense oligonucleotide chemistry provide us with competitive advantages, we face potential competition from many different sources, including major pharmaceutical, specialty pharmaceutical and biotechnology companies, academic institutions and governmental agencies, and public and private research institutions that conduct research, seek patent protection, and establish collaborative arrangements for research, development, manufacturing and commercialization.

While therapeutic modalities, including gene therapy, gene editing, modified RNA and protein-based drugs, are currently being developed to address monogenic diseases, most of these approaches are focused on autosomal recessive or autosomal dominant gain-of-function diseases. The nature and fundamental limitations of these approaches make them less suited for addressing the underlying cause of autosomal dominant haploinsufficiencies. Other next generation antisense oligonucleotides have also generally had limited success in upregulating gene expression of haploinsufficiencies, due to a focus on indirectly and weakly validated mechanisms of action such as targeting microRNAs or long non-coding RNAs that are associated with a gene transcript. We are pioneers in developing disease-modifying therapies to treat haploinsufficiencies and are uniquely positioned to exploit this significant opportunity with our TANGO platform.

If our current product candidate, STK-001, is approved for the treatment of Dravet syndrome, it may compete with other products currently marketed or in development. Currently marketed ASMs range from cannabidiols, such as Jazz Pharmaceuticals' Epidiolex, Fintepla® (fenfluramine) from UCB, to GABA receptor agonists, such as clobazam and stiripentol, to glutamate blockers, such as topiramate. Companies such as Ovid Therapeutics/Takeda, Xenon Pharmaceuticals, Eisai Pharmaceuticals, Epygenix, Longboard Pharmaceuticals, CAMP4, Encoded Therapeutics and others are also developing treatments for Dravet syndrome. Many of the currently marketed ASMs are available as generics. In addition, numerous compounds are in clinical development for treatment of epilepsy. To our knowledge, the clinical development pipeline for non-disease modifying therapies includes cannabinoids, 5-HT release stimulants, cholesterol 24-hydroxylase inhibitors, potassium channel openers, and sodium channel antagonists from a variety of companies. Importantly, we believe none of the drugs in clinical development address the underlying genetic cause of Dravet syndrome. However, one company (Encoded Therapeutics) has announced a clinical development plan for a gene regulation therapy program in Dravet syndrome that may address the underlying genetic cause of Dravet syndrome.

Our second product candidate, STK-002, is in development for treatment of ADOA. There are no products currently marketed or in clinical development for treatment of ADOA. To our knowledge, there are also very limited preclinical

development efforts beyond our product candidate. We believe that PYC Therapeutics is developing a cell penetrating peptide PMO conjugated to ASO for the treatment of ADOA.

Many of our competitors, either alone or with strategic partners, have substantially greater financial, technical, and human resources than we do. Accordingly, our competitors may be more successful than us in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining approval for treatments and achieving widespread market acceptance, rendering our treatments obsolete or non-competitive. Merger and acquisition activity in the biotechnology and biopharmaceutical industries may result in even more resources being concentrated among a smaller number of our competitors. These companies also compete with us in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites and patient registration for clinical trials and acquiring technologies complementary to, or necessary for, our programs. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. Our commercial opportunity could be substantially limited if our competitors develop and commercialize products that are more effective, safer, less toxic, more convenient or less expensive than our comparable products. In geographies that are critical to our commercial success, competitors may also obtain regulatory approvals before us, resulting in our competitors building a strong market position in advance of the entry of our products. In addition, our ability to compete may be affected in many cases by insurers or other third-party payors seeking to encourage the use of other drugs. The key competitive factors affecting the success of all of our programs are likely to be their efficacy, safety, convenience and availability of reimbursement.

Reimbursement

The regulations that govern pricing and reimbursement for new drugs vary widely from country to country. Some countries require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after marketing approval is granted. In some foreign markets, prescription biopharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, a drug company can obtain regulatory approval for a product in a country, but then be subject to price regulations that delay commercial launch of that product.

A drug company's ability to commercialize any products successfully will also depend in part on the extent to which coverage and adequate reimbursement for these products and related treatments will be available from third-party payors, including government authorities, such as Medicare and Medicaid, private health insurers and other organizations. Patients who are provided medical treatment for their conditions generally rely on third-party payors to reimburse all or part of the costs associated with their treatment. Coverage and adequate reimbursement from third-party payors are critical to new product acceptance. Even if one or more products are successfully brought to the market, these products may not be considered cost effective, and the amount reimbursed for such products may be insufficient to allow them to be sold on a competitive basis. Third-party payors who reimburse patients or healthcare providers, such as government plans, are requiring that drug companies provide them with predetermined discounts from list prices and are seeking to reduce the prices charged or the amounts reimbursed for biopharmaceutical products.

Significant delays can occur in obtaining reimbursement for newly-approved drugs or therapeutic biologics, and coverage may be more limited than the purposes for which the drug or therapeutic biologic is approved by the FDA or similar foreign regulatory authorities. Moreover, eligibility for reimbursement does not imply that any drug will be reimbursed in all cases or at a rate that covers a drug company's costs, including research, development, manufacture, sale and distribution.

Interim reimbursement levels for new drugs, if applicable, may also be insufficient to cover a drug company's costs and may not be made permanent. Reimbursement rates may be based on payments allowed for lower cost drugs or therapeutic biologics that are already reimbursed, may be incorporated into existing payments for other services and may reflect budgetary constraints or imperfections in Medicare data. Net prices for drugs or therapeutic biologics 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 or therapeutic biologics from countries where they may be sold at lower prices than in the United States. Further, no uniform policy for coverage and reimbursement exists in the United States. Third-party payors often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement rates, but also have their own methods and approval process apart from Medicare determinations. Therefore, coverage and reimbursement can differ significantly from payor to payor.

Intellectual Property

We strive to protect and enhance the proprietary technology, inventions and improvements that are commercially important to our business, including obtaining, maintaining and defending patent rights, whether developed internally or licensed from third parties. Our policy is to seek to protect our proprietary position by, among, other methods, pursuing and

obtaining patent protection in the United States and in jurisdictions outside of the United States related to our proprietary technology, inventions, improvements, platforms and product candidates that are important to the development and implementation of our business. Our patent portfolio, including in-licensed patents and patent applications, is intended to cover, but is not limited to, our technology platforms, product candidates and components thereof, their methods of use and processes for their manufacture, and any other inventions that are commercially important to our business. We also rely on trade secret protection of our confidential information and know-how relating to our proprietary technology, platforms and product candidates, continuing innovation, and in-licensing opportunities to develop, strengthen, and maintain our position in our TANGO platform and product candidates. Our commercial success may depend in part on our ability to obtain and maintain patent and other proprietary protection for our technology, inventions and improvements; to preserve the confidentiality of our trade secrets; to maintain our licenses to use intellectual property owned or controlled by third parties; to defend and enforce our proprietary rights, including our patents; to defend against challenges and assertions by third parties of their purported intellectual property rights; and to operate without infringement of valid and enforceable patents and other proprietary rights of third parties.

With respect to our TANGO platform, we have exclusively licensed intellectual property for our TANGO technology from the University of Southampton, which includes issued U.S. and foreign patents and pending U.S. and foreign patent applications that cover the TANGO mechanisms. As of December 31, 2023, the issued U.S. patents, issued foreign patents, pending U.S. patent applications and pending foreign patent applications that we have licensed from the University of Southampton are anticipated to expire between 2035 and 2036, absent any patent term adjustments or extensions.

Separately, we have obtained patents and filed patent applications with claims that are intended to cover compositions of matter of oligonucleotides designed to target specific elements in genes for many genetic diseases that we believe are amenable to upregulation of target protein expression using our TANGO platform. As of December 31, 2023, the issued U.S. patents, the issued foreign patents and any patents that may issue from the currently pending patent applications, including PCT international applications, U.S. patent applications, and foreign patent applications, are expected to expire between 2036 and 2044, absent any patent term adjustments or extensions.

With respect to STK-001, as of December 31, 2023, we have exclusively licensed U.S. patents that cover the mechanism of action of STK-001, as well as foreign patents and pending foreign patent applications. The issued patents and any patents that may issue from these pending patent applications are expected to expire between 2035 and 2036, absent any patent term adjustments or extensions. As of December 31, 2023, we also own U.S. patents, a pending PCT international application, pending U.S. patent applications, foreign patents and pending foreign patent applications relating to STK-001, and the U.S. patents any patents that may issue from these pending patent applications are expected to expire between 2038 and 2044, absent any patent term adjustments or extensions.

With respect to STK-002, as of December 31, 2023, we have exclusively licensed U.S. patents that cover the mechanism of action of STK-002, as well as foreign patents and pending foreign patent applications. The issued patents and any patents that may issue from these pending patent applications are expected to expire between 2035 and 2036, absent any patent term adjustments or extensions. As of December 31, 2023, we also own issued U.S. and foreign patents, a pending PCT international application, pending U.S. patent applications, and pending foreign patent applications relating to STK-002, and any patents that may issue from these pending patent applications are expected to expire between 2038 and 2044, absent any patent term adjustments or extensions.

The term of individual patents depends upon the laws of the countries in which they are obtained. In most countries in which we file, the patent term is 20 years from the earliest date of filing of a non-provisional patent application. However, the term of United States patents may be extended for delays incurred due to compliance with the FDA requirements or by delays encountered during prosecution that are caused by the United States Patent and Trademark Office (the "USPTO"). For example, for drugs that are regulated by the FDA under the Hatch-Waxman Act, it is permitted to extend the term of a patent that covers such drug for up to five years beyond the normal expiration date of the patent. For more information on patent term extensions, see "Business—Government regulation: The Hatch-Waxman Act—Patent term extension". In the future, if and when our biopharmaceutical product candidates receive FDA approval, we expect to apply for patent term extensions on patents covering those product candidates. We intend to seek patent term extensions to any of our issued patents in any jurisdiction where these are available; however, there is no guarantee that the applicable authorities, including the USPTO and FDA, will agree with our assessment of whether such extensions should be granted, and even if granted, the length of such extensions. Our currently issued patents will likely expire on dates ranging from 2035 to 2041, unless we receive patent term extension or patent term adjustment, or both. If patents are issued on our pending patent applications, the resulting patents are projected to expire on dates ranging from 2036 to 2044, unless we receive patent term extension or patent term adjustment, or both. However, the actual protection afforded by a patent varies on a product-by-product basis, from country-to-country, and depends upon many factors, including the type of patent, the scope of its coverage, the availability of regulatory-related extensions, the availability of legal remedies in a particular country and the validity and enforceability of the patent.

The patent positions of companies like ours are generally uncertain and involve complex legal and factual questions. No consistent policy regarding the scope of claims allowable in patents in the field of genetic therapy has emerged in the United States. The patent situation outside of the United States is even more uncertain. Changes in the patent laws and rules, either by legislation, judicial decisions, or regulatory interpretation in the United States and other countries may diminish our ability to protect our inventions and enforce our intellectual property rights, and more generally could affect the value of our intellectual property. In particular, our ability to stop third parties from making, using, selling, offering to sell, importing or otherwise commercializing any of our patented inventions, either directly or indirectly, will depend in part on our success in obtaining, defending and enforcing patent claims that cover our technology, inventions, and improvements. 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, nor can we be sure that any of our existing patents or any patents that may be granted to us in the future will be commercially useful in protecting our platform and product candidates and the methods used to manufacture them. Moreover, our issued patents and those that may issue in the future may not guarantee us the right to practice our technology in relation to the commercialization of our platform's product candidates. 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 TANGO platform and product candidates and practicing our proprietary technology. Our issued patents and those that may issue in the future may be challenged, narrowed, circumvented or invalidated, which could limit our ability to stop competitors from marketing related platforms or product candidates or limit the length of the term of patent protection that we may have for our TANGO platform and product candidates. In addition, the rights granted under any issued patents may not provide us with protection or competitive advantages against competitors with similar technology. Furthermore, our competitors may independently develop similar technologies. For these reasons, we expect to have competition for our TANGO platform and product candidates. Moreover, because of the extensive time required for development, testing and regulatory review of a potential product, it is possible that before any product candidate can be commercialized, any related patent may expire or remain in force for only a short period following commercialization, thereby reducing any advantage of the patent. For this and other risks related to our proprietary technology, inventions, improvements, platforms and product candidates, please see the section entitled "Risk Factors—Risks Related to our Intellectual Property."

We have filed for trademark protection of the "Stoke Therapeutics" mark with the United States Patent and Trademark Office and foreign trademark organizations. We have registered, and intend to maintain, the trademark "Stoke Therapeutics" in the United States Patent and Trademark Office and in numerous other jurisdictions, including but not limited to the European Union, China, India, and Canada.

We also rely on trade secret protection for our confidential and proprietary information. Although we take steps to protect our confidential and proprietary information as trade secrets, including through contractual means with our employees, consultants, outside scientific collaborators, sponsored researchers and other advisors, third parties may independently develop substantially equivalent proprietary information and techniques or otherwise gain access to our trade secrets or disclose our technology. Thus, we may not be able to meaningfully protect our trade secrets. It is our policy to require our employees, consultants, outside scientific collaborators, sponsored researchers and other advisors to execute confidentiality agreements under the commencement of employment or consulting relationships with us. These agreements provide that all confidential information concerning our business or financial affairs developed or made known to the individual during the individual's relationship with us is to be kept confidential and not disclosed to third parties except in specific circumstances. In the case of employees, the agreements provide that all inventions conceived by the individual, and which are related to our current or planned business or research and development or made during normal working hours, on our premises or using our equipment or proprietary information, are our exclusive property. In many cases our confidentiality and other agreements with consultants, outside scientific collaborators, sponsored researchers and other advisors require them to assign or grant us licenses to inventions they invent as a result of the work or services they render under such agreements or grant us an option to negotiate a license to use such inventions. Despite these efforts, we cannot provide any assurances that all such agreements have been duly executed, and any of these parties may breach the agreements and disclose our proprietary information, and we may not be able to obtain adequate remedies for such breaches.

We also seek to preserve the integrity and confidentiality of our proprietary technology and processes by maintaining physical security of our premises and physical and electronic security of our information technology systems. Although we have confidence in these individuals, organizations and systems, agreements or security measures may be breached, and we may not have adequate remedies for any breach. To the extent that our employees, contractors, consultants, collaborators and advisors use intellectual property owned by others in their work for us, disputes may arise as to the rights in relation to the resulting know-how or inventions. For more information, please see the section entitled "Risk Factors – Risks Related to our Intellectual Property."

License and research agreements

In July 2015, the Company entered into a worldwide license agreement with CSHL (the "CSHL Agreement"), with respect to TANGO patents. Under the CSHL Agreement, the Company received an exclusive (except with respect to certain government rights and non-exclusive licenses), worldwide license under certain patents and applications relating to TANGO. The CSHL Agreement obligated the Company to make payments that are contingent upon certain milestones being achieved. The Company was also required to pay royalties, tiered based on the scope of patent coverage for each licensed product, ranging from a low-single digit percentage to a mid-single digit percentage on annual net sales. These royalty obligations applied on a licensed product-by-licensed product and country-by-country basis until the latest of (i) the expiration of the last valid claim of a CSHL patent covering the applicable licensed product or (ii) the expiration of any regulatory exclusivity for the applicable licensed product. In addition, if the Company sublicensed the rights under the CSHL Agreement, it was required to pay a maximum of twenty percent of the sublicense revenue to CSHL, which may have been reduced to a mid-teens or a mid-single digit percentage upon achievement of certain clinical milestones for the applicable licensed product. Finally, the Company was required to pay an annual license maintenance fee of $0.01 million, which amount is creditable against any owed royalty or milestone payments. The maximum aggregate potential milestone payments payable totaled approximately $0.90 million. Additionally, certain licenses under the CSHL Agreement required the Company to reimburse CSHL for certain past and ongoing patent related expenses, however there were no expenses related to these reimbursable patent costs during the years ended December 31, 2023 and 2022. After the completion of a 90-day waiting period, in May 2023 the Company terminated the CSHL Agreement. The Company does not expect the termination of the CSHL Agreement to have a significant impact on the intellectual property underlying any of its current product candidates, including STK-001 and STK-002, or its continued development of the TANGO platform.

In April 2016, the Company entered into an exclusive, worldwide license agreement with the University of Southampton (the "Southampton Agreement"), whereby the Company acquired rights to foundational technologies related to the Company's TANGO technology. Under the Southampton Agreement, the Company receives an exclusive, worldwide license under certain licensed patents and applications relating to TANGO. Under the Southampton Agreement, the Company may be obligated to make additional payments that are contingent upon certain milestones being achieved, as well as royalties on future product sales. These royalty obligations survive until the latest of (i) the expiration of the last valid claim of a licensed patent covering a subject product or (ii) the expiration of any regulatory exclusivity for the subject product in a country. In addition, if the Company sublicenses its rights under the Southampton Agreement, the Company is required to pay a mid-single digit percentage of the sublicense revenue to the University of Southampton. As of December 31, 2023, the Company had paid $0.7 million under the Southampton Agreement as a result of entering into the Acadia Pharmaceuticals Inc. license and collaboration agreement in January 2022 (see Note 8). Additionally, certain licenses under the Southampton Agreement require the Company to reimburse the University of Southampton for certain past and ongoing patent related expenses. For the year ended December 31, 2023 these expenses were $0.2 million compared to $0.02 million for the year ended December 31, 2022.

Government Regulation

FDA approval process

In the United States, pharmaceutical products are subject to extensive regulation by FDA. The Federal Food, Drug, and Cosmetic Act (the "FDCA") and other federal and state statutes and regulations govern, among other things, the research, development, testing, manufacture, storage, recordkeeping, approval, labeling, promotion and marketing, distribution, post-approval monitoring and reporting, sampling and import and export of pharmaceutical products. Failure to comply with applicable U.S. regulations may subject a company to a variety of administrative or judicial sanctions, such as a clinical hold, FDA refusal to approve pending new drug applications, or NDAs, warning or untitled letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, civil penalties and criminal prosecution.

Pharmaceutical product development for a new product or certain changes to an approved product in the U.S. typically involves preclinical laboratory and animal testing followed by submission to the FDA of an IND which must become effective before clinical testing may commence. Data from adequate and well-controlled clinical trials are required to demonstrate the safety and effectiveness of the drug for each indication for which FDA approval is sought. Satisfaction of FDA pre-market approval requirements typically takes many years and the actual time required may vary substantially based upon the type, complexity and novelty of the product or disease.

Preclinical requirements include laboratory evaluation of product chemistry, formulation, pharmacology and toxicity studies in animal trials to assess the characteristics and potential safety and efficacy of the product. The conduct of the preclinical tests must comply with federal regulations and requirements, including GLP. The results of preclinical testing are submitted to FDA as part of an IND along with other information, including information about product chemistry,

manufacturing and controls, and a proposed clinical trial protocol. Long-term preclinical tests, such as animal tests of reproductive toxicity and carcinogenicity, may continue after the IND is submitted.

A 30-day waiting period after the submission of each IND is required prior to the commencement of clinical testing in humans. The clinical trial proposed in the IND may begin after a safe to proceed communication is received from the FDA.

Clinical trials involve the administration of the investigational new drug to healthy volunteers or patients under the supervision of a qualified investigator. Clinical trials must be conducted: (i) in compliance with federal regulations; (ii) in compliance with good clinical practice ("GCP"), an international standard designed to protect the rights and health of patients and to define the roles, qualifications and responsibilities of clinical trial sponsors, administrators and monitors; as well as (iii) under protocols detailing, among other things, the objectives of the trial, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated. Each protocol involving testing on U.S. patients and subsequent protocol amendments must be submitted to the FDA as part of the IND.

The FDA may order a clinical hold, which is the temporary, or permanent, discontinuation of a clinical trial at any time, or impose other sanctions, if it believes that the clinical trial either is not being conducted in accordance with FDA requirements or presents an unacceptable risk to the clinical trial patients. If FDA imposes a clinical hold, clinical trials cannot commence or recommence without FDA authorization and then only under terms authorized by the FDA. The study protocol and informed consent information for patients in clinical trials must also be submitted to an institutional review board ("IRB"), for approval. An IRB may also require the clinical trial at the site to be halted, either temporarily or permanently, for failure to comply with the IRB's requirements, or may impose other conditions.

Clinical trials to support NDAs for marketing approval are typically conducted in three sequential phases, but the phases may overlap. In Phase 1, the initial introduction of the drug into healthy human subjects or patients, the drug is tested to assess metabolism, pharmacokinetics, pharmacological actions, side effects associated with increasing doses, and, if possible, early evidence of effectiveness. Phase 2 usually involves trials in a limited patient population to determine the effectiveness of the drug generally for a specific indication, dosage tolerance and optimum dosage, and to identify common adverse effects and safety risks. If a compound demonstrates evidence of effectiveness and an acceptable safety profile in Phase 2 evaluations, Phase 3 trials are undertaken to obtain the additional information about clinical efficacy and safety in a larger number of patients, typically at geographically dispersed clinical trial sites, to permit FDA to evaluate the overall benefit-risk relationship of the drug and to provide adequate information for the labeling of the drug. In most cases FDA requires two adequate and well-controlled Phase 3 clinical trials to demonstrate the efficacy of the drug. A single Phase 3 trial with other confirmatory evidence may be sufficient in rare instances, including (1) where the study is a large multicenter trial demonstrating internal consistency and a statistically very persuasive finding of a clinically meaningful effect on mortality, irreversible morbidity or prevention of a disease with a potentially serious outcome and confirmation of the result in a second trial would be practically or ethically impossible or (2) when in conjunction with other confirmatory evidence.

After completion of the required clinical testing, an NDA is prepared and submitted to FDA. FDA approval of the NDA is required before marketing of the product may begin in the U.S. The NDA must include the results of all preclinical, clinical and other testing and a compilation of data relating to the product's pharmacology, chemistry, manufacture and controls. The cost of preparing and submitting an NDA is substantial. The submission of most NDAs is additionally subject to a substantial application user fee, currently $4,048,695 for fiscal year 2024, and the applicant under an approved NDA is also subject to an annual program fee, currently $416,429 for each prescription drug product. These fees are typically increased annually. Sponsors of applications for drugs granted Orphan Drug Designation are exempt from these user fees.

FDA has 60 days from its receipt of an NDA to determine whether the application will be accepted for filing based on the agency's threshold determination that it is sufficiently complete to permit substantive review. FDA may request additional information rather than file an NDA. In this event, the NDA must be resubmitted with the additional information. The resubmitted application also is subject to review before FDA files it. Once the submission is accepted for filing, FDA begins an in-depth review. FDA has agreed to certain performance goals in the review of new drug applications to encourage timeliness. Most applications for standard review drug products are reviewed within ten to twelve months of the date of submission of the new drug application to FDA; the target review period for priority review drugs is six months from the date of filing (accepted for review by the FDA) of the new drug application. Priority review can be applied to an application for a drug that treats a serious condition and if approved would provide a significant improvement in safety or effectiveness over existing treatments or provide a treatment where no adequate therapy exists. The review process for both standard and priority review may be extended by FDA for three additional months to consider certain late-submitted information, or information intended to clarify information already provided in the submission.

FDA may also refer applications for novel drug products, or drug products that present difficult questions of safety or efficacy, to an external drug advisory committee—typically a panel that includes clinicians, statisticians, patient representatives and other experts—for review, evaluation and a recommendation as to whether the application should be

approved. FDA is not bound by the recommendation of an advisory committee, but it generally follows such recommendations.

Before approving an NDA, FDA will typically inspect one or more clinical sites to assure compliance with GCP. Additionally, FDA will inspect the facility or the facilities at which the drug substance and drug product are manufactured. FDA will not approve the product unless compliance with current good manufacturing practices ("cGMPs") is satisfactory and the NDA contains data that provide substantial evidence that the drug is safe and effective in the indication studied.

After FDA evaluates the NDA and the manufacturing facilities, it issues either an approval letter or a complete response letter. A complete response letter generally outlines the deficiencies in the submission and may require substantial additional testing, or information, in order for FDA to reconsider the application. Even after an applicant submits additional information, FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval. If, or when, those deficiencies have been addressed to FDA's satisfaction in a resubmission of the NDA, FDA will issue an approval letter. FDA has committed to reviewing such resubmissions in two or six months depending on the type of information included.

An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications. As a condition of NDA approval, FDA may require a risk evaluation and mitigation strategy ("REMS") to help ensure that the benefits of the drug outweigh the potential risks. 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 patient registries. The requirement for a REMS can materially affect the potential market and profitability of the drug. FDA may also require a REMS for a drug that is already on the market if it determines, based on new safety information, that a REMS plan is necessary to ensure that the products benefits outweigh its risks.

Changes to some of the conditions established in an approved application, including changes in indications, labeling, or manufacturing processes or facilities, require submission and FDA approval of a new NDA or NDA supplement before the change can be implemented. An NDA supplement for a new indication typically requires clinical data similar to that in the original application, and FDA uses the same procedures and actions in reviewing NDA supplements as it does in reviewing NDAs.

Fast Track Designation, Breakthrough Designation, Accelerated Approval, and Priority Review

The following four FDA programs are intended to facilitate and expedite development and review of new drugs to address unmet medical need in the treatment of a serious or life-threatening condition: fast track designation, breakthrough therapy designation, accelerated approval, and priority review.

Under the Fast Track program, the sponsor of a new drug candidate may request that FDA designate the drug candidate for a specific indication as a Fast Track drug concurrent with, or after, the filing of the IND for the drug candidate. FDA must determine if the drug candidate qualifies for Fast Track Designation within 60 days of receipt of the sponsor's request. Fast Track Designation is intended to facilitate development and expedite review of drugs to treat serious and life-threatening conditions so that an approved product can reach the market expeditiously. If a submission is granted Fast Track Designation, the sponsor may engage in more frequent interactions with FDA, and FDA may review sections of the NDA before the full application is complete. This rolling review is available if, in agreement with the FDA, the applicant provides, a schedule for the submission of the remaining information. However, the FDA does not start the review clock for the application until the last section of the NDA is submitted. Fast Track Designation may be withdrawn by FDA if they believe that the designation is no longer supported by data emerging data in the development process.

Breakthrough Therapy Designation may be granted by the FDA to the development of a new drug and also for a new use or indication of an approved drug. This designation requires preliminary clinical evidence of a treatment effect that may represent substantial improvement over available therapies for the treatment of a serious condition. FDA expects that such evidence generally would be derived from early phase trials such as phase 1 or 2 trials. For purposes of Breakthrough Therapy Designation, preliminary clinical evidence refers to evidence that is sufficient to indicate that the drug may demonstrate substantial improvement in effectiveness or safety over available therapies. A Breakthrough Therapy Designation conveys more intensive FDA guidance on an efficient drug development program. FDA also has an organizational commitment to involve senior management in such guidance. Such guidance may include holding meetings with the sponsor and review team throughout the development of the drug, providing timely advice to, and interactive communication with, the sponsor regarding the development of the drug to ensure that the development program to gather the non-clinical and clinical data necessary for approval is as efficient as possible, and taking steps to ensure that the design of the clinical trials is as efficient as practicable, when scientifically appropriate, such as by minimizing the number of patients exposed to a potentially less efficacious treatment.

The FDA's accelerated approval pathway is available under FDA's accelerated approval regulations and under the FDCA for drugs that have been granted Fast Track designation. FDA may approve a drug for a serious or life-threatening illness that provides meaningful therapeutic benefit to patients over existing treatments based upon a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments.

In clinical trials, a surrogate endpoint is a measurement of laboratory or clinical signs of a disease or condition that substitutes for a direct measurement of how a patient feels, functions, or survives. Surrogate endpoints can often be measured more easily or more rapidly than clinical endpoints. A drug candidate approved on this basis is subject to rigorous and mandatory post-marketing compliance requirements, including the completion of Phase 4 or post-approval clinical trials to confirm the effect on the clinical endpoint. Failure to conduct required post-approval studies, or confirm a clinical benefit during post-marketing studies, will allow FDA to withdraw the drug from the market on an expedited basis. All promotional materials for drug candidates approved under accelerated regulations are subject to priority review by FDA. The Food and Drug Omnibus Reform Act ("FDORA") was recently enacted, which included provisions related to the accelerated approval pathway. Pursuant to FDORA, the FDA is authorized to require a post-approval study to be underway prior to approval or within a specified time period following approval. FDORA also requires the FDA to specify conditions of any required post-approval study, which may include milestones such as a target date of study completion and requires sponsors to submit progress reports for required post-approval studies and any conditions required by the FDA not later than 180 days following approval and not less frequently than every 180 days thereafter until completion or termination of the study. FDORA enables the FDA to initiate enforcement action for the failure to conduct with due diligence a required post-approval study, including a failure to meet any required conditions specified by the FDA or to submit timely reports.

A drug candidate is eligible for priority review, or review within a six-month time frame from the time an NDA is filed by FDA, if the drug candidate is intended for the treatment, diagnosis or prevention of a serious or life-threatening condition, demonstrates the potential to address an unmet medical need, or provides a significant improvement compared to marketed drugs.

Orphan Drugs

Under the Orphan Drug Act, FDA may grant Orphan Drug Designation to drugs intended to treat a rare disease or condition—generally a disease or condition that affects fewer than 200,000 individuals in the U.S. Orphan Drug designation must be requested before submitting an NDA. After FDA grants Orphan Drug Designation, the generic identity of the drug and its potential orphan use are disclosed publicly by FDA. Orphan Drug Designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process. The first NDA applicant to receive FDA approval for a particular active ingredient to treat a particular disease with FDA Orphan Drug Designation is entitled to a seven-year exclusive marketing period in the U.S. for that product, for that indication. During the seven-year exclusivity period, FDA may not approve any other applications to market the same drug for the same disease, except in limited circumstances, such as a showing of clinical superiority to the product with orphan drug exclusivity. Orphan drug exclusivity does not prevent FDA from approving a different drug for the same disease or condition, or the same drug for a different disease or condition. Among the other benefits of Orphan Drug Designation are tax credits for certain research and an exemption from the NDA user fee.

Rare Pediatric Disease Priority Review Voucher program

Under the Rare Pediatric Disease Priority Review Voucher program, FDA may award a priority review voucher to the sponsor of an approved marketing application for a product that treats or prevents a rare pediatric disease. The voucher entitles the sponsor to priority review of one subsequent marketing application.

A voucher may be awarded only for an approved rare pediatric disease product application. A rare pediatric disease product application is an NDA or a Biologics License Application ("BLA") for a product that treats or prevents a serious or life-threatening disease in which the serious or life-threatening manifestations primarily affect individuals aged from birth to 18 years; in general, the disease must affect fewer than 200,000 such individuals in the U.S.; the NDA must be deemed eligible for priority review; the NDA must not seek approval for a different adult indication (i.e., for a different disease/condition); the product must not contain an active ingredient that has been previously approved by FDA; and the NDA must rely on clinical data derived from studies examining a pediatric population such that the approved product can be adequately labeled for the pediatric population. Before NDA approval, FDA may designate a product in development as a product for a rare pediatric disease, but such designation is not required to receive a voucher.

To receive a rare pediatric disease priority review voucher, a sponsor must notify FDA, upon submission of the NDA, of its intent to request a voucher. If FDA determines that the NDA is a rare pediatric disease product application, and if the NDA is approved, FDA will award the sponsor of the NDA a voucher upon approval of the NDA. FDA may revoke a rare pediatric disease priority review voucher if the product for which it was awarded is not marketed in the U.S. within 365 days of the product's approval.

The voucher, which is transferable to another sponsor, may be submitted with a subsequent NDA or biologics license application, or BLA, and entitles the holder to priority review of the accompanying NDA or BLA. The sponsor submitting the priority review voucher must notify FDA of is intent to submit the voucher with the NDA or BLA at least 90 days prior to submission of the NDA or BLA and must pay a priority review user fee in addition to any other required user fee. FDA must take action on an NDA or BLA under priority review within six months of filing the NDA or BLA by FDA.

On December 27, 2020, the Rare Pediatric Disease Priority Review Voucher Program was extended. Under the current statutory sunset provisions, after September 30, 2024, FDA may only award a voucher for an approved rare pediatric disease product application if the sponsor has rare pediatric disease designation for the drug, and that designation was granted by September 30, 2024. Without further statutory amendments, after September 30, 2026, the FDA may not award any rare pediatric disease priority review vouchers.

Post-approval requirements

Once an NDA is approved, a product will be subject to certain post-approval requirements. For instance, FDA closely regulates the post-approval marketing and promotion of drugs, including standards and regulations for direct-to-consumer advertising, off-label promotion, industry-sponsored scientific and educational activities and promotional activities involving the internet. Drugs may be marketed only for the approved indications and in accordance with the provisions of the approved labeling.

Adverse event reporting and submission of periodic reports are required following FDA approval of an NDA. FDA also may require post-marketing testing or studies, known as Phase 4 commitments, REMS and surveillance to monitor the effects of an approved product, or FDA may place conditions on an approval that could restrict the distribution or use of the product. In addition, quality control, drug manufacture, packaging and labeling procedures must continue to conform to cGMPs after approval. Drug manufacturers and certain of their subcontractors are required to register their establishments with FDA and certain state agencies. Registration with FDA subjects entities to periodic unannounced inspections by FDA, during which the Agency inspects manufacturing facilities to assess compliance with cGMPs. Accordingly, manufacturers must continue to expend time, money and effort in the areas of production and quality-control to maintain compliance with cGMPs. Regulatory authorities may withdraw product approvals or request product recalls if a company fails to comply with regulatory standards, if it encounters problems following initial marketing, or if previously unrecognized problems are subsequently discovered.

Pediatric information

Under the Pediatric Research Equity Act (the "PREA"), NDAs or supplements to NDAs must contain data to assess the safety and effectiveness of the drug for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the drug is safe and effective. FDA may grant full or partial waivers, or deferrals, for submission of data. With certain exceptions, the PREA does not apply to any drug for an indication for which orphan designation has been granted.

The Best Pharmaceuticals for Children Act (the "BPCA") provides NDA holders a six-month extension of any exclusivity—patent or nonpatent—for a drug if certain conditions are met. Conditions for exclusivity include FDA's determination that information relating to the use of a new drug in the pediatric population may produce health benefits in that population, FDA making a written request for pediatric studies, and the applicant agreeing to perform, and reporting on, the requested studies within the statutory timeframe. Applications under the BPCA are treated as priority applications, with all of the benefits that designation confers.

Disclosure of clinical trial information

Sponsors of clinical trials of FDA regulated products, including drugs, are required to register and disclose certain clinical trial information. Information related to the product, patient population, phase of investigation, study sites and investigators, and other aspects of the clinical trial is then made public as part of the registration. Sponsors are also obligated to discuss the results of their clinical trials after completion. Disclosure of the results of these trials can be delayed in certain circumstances for up to two years after the date of completion of the trial. Competitors may use this publicly available information to gain knowledge regarding the progress of development programs. The government recently released a regulation and policy to expand and enhance the requirements related to registering and reporting the results of clinical trials, which may result in greater enforcement of these requirements in the future.

The Hatch-Waxman Act

Orange Book listing

In seeking approval for a drug through an NDA, applicants are required to list with the FDA each patent whose claims cover the applicant's product. Upon approval of a drug, each of the patents listed in the application for the drug is then published in the FDA's Approved Drug Products with Therapeutic Equivalence Evaluations, commonly known as the Orange Book. Drugs listed in the Orange Book can, in turn, be cited by potential generic competitors in support of approval of an abbreviated new drug application, or ANDA. An ANDA provides for marketing of a drug product that has the same active ingredients in the same strengths and dosage form as the listed drug and has been shown through bioequivalence testing to be therapeutically equivalent to the listed drug. Other than the requirement for bioequivalence testing, ANDA applicants are not required to conduct, or submit results of, preclinical or clinical tests to prove the safety or effectiveness of their drug product. Drugs approved in this way are commonly referred to as "generic equivalents" to the listed drug and can often be substituted by pharmacists under prescriptions written for the original listed drug.

The ANDA applicant is required to certify to the FDA concerning any patents listed for the approved product in the FDA's Orange Book. Specifically, the applicant must certify that (i) the required patent information has not been filed; (ii) the listed patent has expired; (iii) the listed patent has not expired but will expire on a particular date and approval is sought after patent expiration; or (iv) the listed patent is invalid or will not be infringed by the new product. The ANDA applicant may also elect to submit a section viii statement certifying that its proposed ANDA label does not contain (or carve out) any language regarding the patented method-of-use rather than certify to a listed method-of-use patent. If the applicant does not challenge the listed patents, the ANDA application will not be approved until all the listed patents claiming the referenced product have expired. A certification that the new product will not infringe the already approved product's listed patents, or that such patents are invalid, is called a Paragraph IV certification. If the ANDA applicant has provided a Paragraph IV certification to the FDA, the applicant must also send notice of the Paragraph IV certification to the NDA and patent holders once the ANDA has been accepted for filing by the FDA. The NDA and patent holders may then initiate a patent infringement lawsuit in response to the notice of the Paragraph IV certification. The filing of a patent infringement lawsuit within 45 days of the receipt of a Paragraph IV certification automatically prevents the FDA from approving the ANDA until the earlier of 30 months, expiration of the patent, settlement of the lawsuit, or a decision in the infringement case that is favorable to the ANDA applicant.

The ANDA application also will not be approved until any applicable non-patent exclusivity listed in the Orange Book for the referenced product has expired.

Exclusivity

Upon NDA approval of a new chemical entity ("NCE"), which is a drug that contains no active moiety that has been approved by FDA in any other NDA, that drug receives five years of marketing exclusivity during which FDA cannot receive any ANDA seeking approval of a generic version of that drug. An ANDA may be submitted one year before NCE exclusivity expires if a Paragraph IV certification is filed. If there is no listed patent in the Orange Book, there may not be a Paragraph IV certification, and, thus, no ANDA may be filed before the expiration of the exclusivity period. Certain changes to a drug, such as the addition of a new indication to the package insert, can be the subject of a three-year period if the application

contains reports of new clinical investigations (other than bioavailability studies) conducted or sponsored by the sponsor that were essential to the approval of the application. FDA cannot approve an ANDA for a generic drug that includes the change during the exclusivity period.

Patent term extension

After NDA approval, owners of relevant drug patents may apply for up to a five-year patent extension. The allowable patent term extension is calculated as half of the drug's testing phase (the time between IND application and NDA submission) and all of the review phase (the time between NDA submission and approval up to a maximum of five years). The time can be shortened if FDA determines that the applicant did not pursue approval with due diligence. The total patent term after the extension may not exceed 14 years from the date of product approval. Only one patent applicable to an approved drug is eligible for extension and only those claims covering the approved drug, a method for using it, or a method for manufacturing it may be extended and the application for the extension must be submitted prior to the expiration of the patent. For patents that might expire during the application phase, the patent owner may request an interim patent extension. An interim patent extension increases the patent term by one year and may be renewed up to four times. For each interim patent extension granted, the post-approval patent extension is reduced by one year. The director of the United States Patent and Trademark Office must determine that approval of the drug covered by the patent for which a patent extension is being sought is likely. Interim patent extensions are not available for a drug for which an NDA has not been submitted.

Other healthcare laws

In addition to FDA restrictions on marketing of pharmaceutical products, several other types of state and federal laws have been applied to restrict certain general business and marketing practices in the pharmaceutical industry in recent years. These laws include anti-kickback statutes, false claims statutes and other healthcare laws and regulations.

The federal Anti-Kickback Statute prohibits, among other things, knowingly and willfully offering, paying, soliciting or receiving remuneration to induce, or in return for, purchasing, leasing, ordering or arranging for the purchase, lease or order of any healthcare item or service reimbursable under Medicare, Medicaid, or other federally financed healthcare programs. The Patient Protection and Affordable Care Act as amended by the Health Care and Education Reconciliation Act, collectively, the ACA, amended the intent element of the federal statute so that a person or entity no longer needs to have actual knowledge of the statute or specific intent to violate it in order to commit a violation. This statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand and prescribers, purchasers and formulary managers on the other. Although there are a number of statutory exceptions and regulatory safe harbors protecting certain common activities from prosecution or other regulatory sanctions, the exceptions and safe harbors are drawn narrowly, and practices that involve remuneration intended to induce prescribing, purchases or recommendations may be subject to scrutiny if they do not qualify for an exception or safe harbor.

Federal civil and criminal false claims laws, including the federal civil False Claims Act, prohibit any person or entity from knowingly presenting, or causing to be presented, a false claim for payment to the federal government, or knowingly making, or causing to be made, a false statement to have a false claim paid. This includes claims made to programs where the federal government reimburses, such as Medicaid, as well as programs where the federal government is a direct purchaser, such as when it purchases off the Federal Supply Schedule. Recently, several pharmaceutical and other healthcare companies have been prosecuted under these laws for allegedly inflating drug prices they report to pricing services, which in turn were used by the government to set Medicare and Medicaid reimbursement rates, and for allegedly providing free product to customers with the expectation that the customers would bill federal programs for the product. In addition, certain marketing practices, including off-label promotion, may also violate false claims laws. Additionally, the ACA amended the federal Anti-Kickback Statute such that a violation of that statute can serve as a basis for liability under the federal False Claims Act. Most states also have statutes or regulations similar to the federal Anti-Kickback Statute and False Claims Act, which apply to items and services reimbursed under Medicaid and other state programs, or, in several states, apply regardless of the payor.

Other federal statutes pertaining to healthcare fraud and abuse include the civil monetary penalties statute, which prohibits, among other things, the offer or payment of remuneration to a Medicaid or Medicare beneficiary that the offeror or payor knows or should know is likely to influence the beneficiary to order a receive a reimbursable item or service from a particular supplier, and the additional federal criminal statutes created by the Health Insurance Portability and Accountability Act of 1996 ("HIPAA"), which prohibits, among other things, 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 money or property owned by or under the control of any healthcare benefit program in connection with the delivery of or payment for healthcare benefits, items or services.

In addition, HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009 ("HITECH"), and their respective implementing regulations, including the Final Omnibus Rule published on January 25, 2013, impose obligations on certain healthcare providers, health plans, and healthcare clearinghouses, known as covered

entities, as well as their business associates that perform certain services involving the storage, use or disclosure of individually identifiable health information, including mandatory contractual terms, with respect to safeguarding the privacy, security, and transmission of individually identifiable health information, and require notification to affected individuals and regulatory authorities of certain breaches of security of individually identifiable health information. HITECH increased the civil and criminal penalties that may be imposed against covered entities, business associates and possibly other persons, 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 attorney's fees and costs associated with pursuing federal civil actions. In addition, many state laws govern the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, and often are not pre-empted by HIPAA. For example, the California Consumer Privacy Act of 2018 ("CCPA"), imposes obligations on businesses to which it applies, including, but not limited to, providing specific disclosures in privacy notices and affording California residents certain rights related to their personal data, although it exempts some data processed in the context of clinical trials. In addition, the California Privacy Rights Act of 2020 ("CPRA"), which went into effect on January 1, 2023, imposes additional obligations on companies covered by the legislation and significantly modifies the CCPA, including by expanding consumers' rights with respect to certain sensitive personal information. The CPRA also creates a new state agency that is vested with authority to implement and enforce the CCPA and CPRA. Virginia's Consumer Data Protection Act, which took effect on January 1, 2023, requires businesses subject to the legislation to conduct data protection assessments in certain circumstances and requires opt-in consent from consumers to acquire and process their sensitive personal information, which includes information revealing a consumer's physical and mental health diagnosis and genetic and biometric information that can identify a consumer. In addition, Colorado enacted the Colorado Privacy Act, and Connecticut enacted the Connecticut Data Privacy Act, each of which took effect on July 1, 2023, and Utah enacted the Consumer Privacy Act, which became effective on December 31, 2023, and each of these laws may increase the complexity, variation in requirements, restrictions and potential legal risks, and could require increased compliance costs and changes in business practices and policies. Other states have also enacted, proposed, or are considering proposing, data privacy laws, which could further complicate compliance efforts, increase our potential liability and adversely affect our business.

Further, pursuant to the federal Physician Payments Sunshine Act, enacted as part of the ACA, the Centers for Medicare & Medicaid Services (the "CMS") has issued a final rule that requires manufacturers of approved prescription drugs that are reimbursable under Medicare, Medicaid, or the Children's Health Insurance Program, with certain exceptions, to collect and report annually information on certain payments or transfers of value to physicians, physician assistants, certain types of advance practice nurses and teaching hospitals, or to entities or individuals at the request of, or designated on behalf of, such providers, and to report annually certain ownership and investment interests held by physicians and their immediate family members. The reported data is made available in searchable form on a public website on an annual basis. Failure to submit required information may result in civil monetary penalties.

In addition, several states now require prescription drug companies to report certain expenses relating to the marketing and promotion of drug products and to report gifts and payments to individual healthcare practitioners in these states. Other states prohibit various marketing-related activities, such as the provision of certain kinds of gifts or meals. Still other states require the posting of information relating to clinical studies and their outcomes. A growing number of states require the reporting of certain pricing information, including information pertaining to and justifying price increases and the prices of newly launched drugs, or prohibit prescription drug price gouging. In addition, certain states require pharmaceutical companies to implement compliance programs and/or marketing codes. Certain states and local jurisdictions also require the registration of pharmaceutical sales representatives. Compliance with these laws is difficult and time consuming, and companies that do not comply with these state laws face civil penalties.

Efforts to ensure that business arrangements with third parties comply with applicable healthcare laws and regulations involve substantial costs. If a drug company's operations are found to be in violation of any such requirements, it may be subject to significant penalties, including civil, criminal and administrative penalties, damages, fines, disgorgement, imprisonment, the curtailment or restructuring of its operations, loss of eligibility to obtain approvals from the FDA, exclusion from participation in government contracting, healthcare reimbursement or other federal or state government healthcare programs, including Medicare and Medicaid, integrity oversight and reporting obligations, imprisonment, and reputational harm. Although effective compliance programs can mitigate the risk of investigation and prosecution for violations of these laws, these risks cannot be entirely eliminated. Any action for an alleged or suspected violation can cause a drug company to incur significant legal expenses and divert management's attention from the operation of the business, even if such action is successfully defended.

Possible change in law or policy

Healthcare reforms that have been adopted, and that may be adopted in the future, could result in further reductions in coverage and levels of reimbursement for pharmaceutical products, increases in rebates payable under U.S. government

rebate programs and additional downward pressure on pharmaceutical product prices. Several healthcare reform proposals recently culminated in the enactment of the Inflation Reduction Act (the "IRA"), which, among other things, allows the U.S. Department of Health and Human Services ("HHS") to directly negotiate the selling price of a statutorily specified number of drugs and biologics each year that CMS reimburses under Medicare Part B and Part D. Only high-expenditure single-source drugs that have been approved for at least 7 years (11 years for single-source biologics) are eligible to be selected by CMS for negotiation, with the negotiated price taking effect two years after the selection year. Negotiations for Medicare Part D products take place in 2024 with the negotiated price taking effect in 2026, and negotiations for Medicare Part B products will begin in 2026 with the negotiated price taking effect in 2028. In August 2023, HHS announced the ten Medicare Part D drugs and biologics that it selected for negotiations. HHS will announce the negotiated maximum fair prices by September 1, 2024, and this price cap, which cannot exceed a statutory ceiling price, will go into effect on January 1, 2026. A drug or biological product that has an orphan drug designation for only one rare disease or condition will be excluded from the IRA's price negotiation requirements, but will lose that exclusion if it receives designations for more than one rare disease or condition, or if is approved for an indication that is not within that single designated rare disease or condition, unless such additional designation or such disqualifying approvals are withdrawn by the time CMS evaluates the drug for selection for negotiation. The IRA also imposes rebates on Medicare Part D and Part B drugs whose prices have increased at a rate greater than the rate of inflation. In addition, the IRA will eliminate, beginning in 2025, the coverage gap under Medicare Part D by significantly lowering the enrollee maximum out-of-pocket cost and requiring manufacturers to subsidize, through a newly established manufacturer discount program, 10% of Part D enrollees' prescription costs for brand drugs below the out-of-pocket maximum, and 20% once the out-of-pocket maximum has been reached. The IRA also extends enhanced subsidies for individuals purchasing health insurance coverage in ACA marketplaces through plan year 2025. The IRA permits the Secretary of HHS to implement many of these provisions through guidance, as opposed to regulation, for the initial years. Manufacturers that fail to comply with the IRA may be subject to various penalties, including significant civil monetary penalties. These provisions have been and may continue to be subject to legal challenges. For example, the provisions related to the negotiation of selling prices of high-expenditure single-source drugs and biologics have been challenged in multiple lawsuits brought by pharmaceutical manufacturers. Thus, while it is unclear how the IRA will be implemented, it will likely have a significant impact on the biopharmaceutical industry and the pricing of prescription drug products. It is unclear to what extent other statutory, regulatory, and administrative initiatives will be enacted and implemented.

Foreign regulation

Clinical trials

In addition to regulations in the United States, we will be subject to a variety of foreign regulations governing clinical trials and commercial sales and distribution of our product candidates to the extent we choose to sell any products outside of the United States. For clinical trials, many countries outside of the United States have a similar process that requires the submission of a clinical study application similar to the process in the United States. However, the specific requirements governing the conduct of clinical trials vary greatly from country to country. In the European Union, for example, clinical trials are governed by the new EU Regulation on Clinical Trials (Reg. EU No. 536/2014) (the "CTR") that has become applicable on January 31, 2022. The CTR stipulates the process of obtaining competent authority approval for clinical trials. Under the CTR, trial sponsors submit their application for approval via an EU Portal. While the procedure for approval is conducted in a coordinated manner among the concerned EU Member States as provided under the CTR, the approvals will still have to be granted by the competent authorities of the EU Member States where a trial takes place. The CTR has streamlined the process for the application and granting of the approvals in comparison with the predecessor legislation, Directive 2001/20/EC on clinical trials (the "CTD"). However, the process of obtaining clinical trial approval in the EU is still complex and can significantly delay the start of a multinational clinical trial.

Following the United Kingdom's exit from the European Union on December 31, 2020, different rules apply in the United Kingdom from the European Union. In the United Kingdom, clinical trials are governed by the Medicines for Human Use (Clinical Trials) Regulations 2004. These regulations are based on the predecessor EU regulations to the CTR. The CTR have not been adopted in the United Kingdom. Under the U.K. regulations, an approval is required from the MHRA together with a positive ethics committee opinion. Clinical trials which take place in the U.K. and on NHS hospital sites, typically do so on the basis of standardized documentation which set out indemnification provisions. In the UK, there are proposals to replace the current U.K. regulations with revised legislation, which will include changes with respect to transparency, approval pathways and regulatory requirements.

Approval and reimbursement

Whether or not we obtain FDA approval for a product, we must obtain approval or licensing of a product by regulatory authorities of foreign countries before we can commence marketing of the product in those countries. The approval processes

for both approval and marketing of commercial drugs vary from country to country and the time may be longer or shorter than that required for FDA approval.

The requirements governing the product licensing, pricing and reimbursement vary greatly from country to country. As in the United States, post-approval regulatory requirements, such as those regarding product manufacture, marketing, or distribution would apply to any product that is approved outside the United States.

To obtain regulatory approval of a medicinal product under EU regulatory systems, a sponsor must submit a marketing authorization application. The grant of marketing authorization in the EU is governed by Directive 2001/83/EC of the European Parliament and of the Council, commonly known as the Community Code and Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Community procedures for the authorization and supervision of medicinal products for human and veterinary use and establishing the European Medicines Agency (the "EMA"), commonly referred to as the EMA Regulation. In addition, Regulation 1394/2007/EC on advanced therapy medicinal products ("ATMP") lays down specific rules concerning the authorization, supervision and pharmacovigilance of gene therapy medicinal products, somatic cell therapy medicinal products and tissue engineered products. The EMA's Committee for Advanced Therapies ("CAT") is responsible for assessing the quality, safety and efficacy of ATMP. The role of CAT is to prepare a draft opinion on an application for marketing authorization for an ATMP candidate. EMA then provides a final opinion regarding the application for marketing authorization. The European Commission grants or refuses marketing authorization after the EMA has delivered its opinion.

Innovative medicinal products are authorized in the EU on the basis of a full marketing authorization application (as opposed to an application for marketing authorization that relies, in whole or in part, on data in the marketing authorization dossier for another, previously approved medicinal product). Applications for marketing authorization for innovative medicinal products must contain the results of pharmaceutical tests, preclinical tests and clinical trials conducted with the medicinal product for which marketing authorization is sought.

EU legislation provides for a system of regulatory data and market exclusivity. According to Article 14(11) of the EMA Regulation, and Article 10(1) of the Community Code, upon receiving marketing authorization, new chemical entities approved on the basis of complete independent data package benefit from eight years of data exclusivity and an additional two years of market exclusivity. Data exclusivity prevents regulatory authorities in the European Union from referencing the innovator's data to assess a generic (abbreviated) application. During the additional two-year period of market exclusivity, a generic marketing authorization can be submitted, and the innovator's data may be referenced, but no generic 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, or MAH, obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to their authorization, are held to bring a significant clinical benefit in comparison with existing therapies. Even if a compound is considered to be a new chemical entity and the innovator is able to gain the period of data exclusivity, another company nevertheless could also market another version of the drug if such company obtained marketing authorization based on an application with a complete independent data package of pharmaceutical tests, preclinical tests and clinical trials. Depending upon the timing and duration of the EU marketing authorization process, products may be eligible for up to five years' supplementary protection certificates, or SPC, pursuant to Regulation (EC) No 469/2009. Such SPC extend the rights under the basic patent for the drug.

Products authorized as "orphan medicinal products" in the EU are entitled to benefits additional to those granted in relation to innovative medicinal products. In accordance with Article 3 of Regulation (EC) No. 141/2000 of the European Parliament and of the Council of 16 December 1999 on orphan medicinal products, a medicinal product may be designated as an orphan medicinal product if (1) it is intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition; (2) either (a) such condition affects no more than five in 10,000 persons in the EU when the application is made, or (b) the product, without the incentives derived from orphan medicinal product status, would not generate sufficient return in the EU to justify investment; and (3) there exists no satisfactory method of diagnosis, prevention or treatment of such condition authorized for marketing in the EU, or if such a method exists, the product will be of significant benefit to those affected by the condition. Further guidance on such criteria is provided in European Commission Regulation (EC) No. 847/2000 of 27 April 2000 laying down the provisions for implementation of the criteria for designation of a medicinal product as an orphan medicinal product and definitions of the concepts "similar medicinal product" and "clinical superiority". Orphan medicinal products are eligible for financial incentives such as reduction of fees or fee waivers and following grant of a marketing authorization, EMA and the EU Member States' competent authorities are not permitted to accept another application for a marketing authorization, or grant a marketing authorization or accept an application to extend an existing marketing authorization, for the same therapeutic indication of a similar medicinal product for ten years following grant or authorization. The application for orphan drug designation must be submitted before the application for marketing authorization. The applicant may receive a fee reduction for the marketing authorization application if the orphan drug designation has been granted, but not if the designation is still pending at the time the marketing authorization is

submitted. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process.

The 10-year market exclusivity that an orphan drug enjoys may 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, for example, if the product is sufficiently profitable not to justify maintenance of market exclusivity. Additionally, marketing authorization may be granted to a similar product during the 10-year period of market exclusivity for the same therapeutic indication at any time if:

- The second applicant can establish in its application that its product, although similar to the orphan medicinal product already authorized, is safer, more effective or otherwise clinically superior;
- The holder of the marketing authorization for the original orphan medicinal product consents to a second orphan medicinal product application; or
- The holder of the marketing authorization for the original orphan medicinal product cannot supply enough orphan medicinal product.

Similar to obligations imposed in the United States, medicinal products authorized in the EU may be subject to post-authorization obligations, including the obligation to conduct Post Marketing Safety Studies ("PASS") or Post Marketing Efficacy Studies ("PAES").

In April 2023, the European Commission adopted a proposal for a new Directive and a new Regulation, which revise and replace the existing general pharmaceutical legislation. The proposed changes include the proposal to recast Directive 2001/83/EC, i.e., the Community Code and the creation of a new Regulation laying down EU marketing authorization of medicinal products that will replace Regulation (EC) No 726/2004, Regulation (EC) No 141/2000 on orphan drugs and Regulation (EC) No 1901/2006 on pediatric medicines, and amend Regulation (EC) No 1394/2007 on ATMP and Regulation 536/2014, i.e., the CTR. The proposals include significant changes, in particular with regard to the document protection and market exclusivity periods for medicinal products. In October 2023, the European Parliament proposed revisions to the European Commission proposals with diverging views on various topics. Further changes may be expected while the legislative process continues.

Reimbursement for medicinal products is still an area that is not harmonized in the EU, but largely governed by EU Member States' laws. However, there are some EU level legal frameworks that must be taken into account, including Council Directive 89/105/EEC (the "Price Transparency Directive"). The aim of the Price Transparency Directive is to ensure that pricing and reimbursement mechanisms established in EU Member States are transparent and objective, do not hinder the free movement and trade of medicinal products in the EU and do not hinder, prevent or distort competition on the market. The Price Transparency Directive does not, however, provide any guidance concerning the specific criteria based on which pricing and reimbursement decisions are to be made in individual EU Member States. Neither does it have any direct consequence for pricing or levels of reimbursement in individual EU Member States. The national authorities of the individual EU Member States are free to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices and/or reimbursement of medicinal products for human use. Individual EU Member States adopt policies according to which a specific price or level of reimbursement is approved for the medicinal product. Other EU Member States adopt a system of reference pricing, basing the price or reimbursement level in their territory either, on the pricing and reimbursement levels in other countries, or on the pricing and reimbursement levels of medicinal products intended for the same therapeutic indication. Furthermore, some EU Member States impose direct or indirect controls on the profitability of the company placing the medicinal product on the market.

Health Technology Assessment ("HTA") of medicinal products is becoming an increasingly common part of the pricing and reimbursement procedures in some EU Member States. HTA is the procedure according to which the assessment of the public health impact, therapeutic impact and the economic and societal impact of the use of a given medicinal product in the national healthcare systems of the individual country is conducted. HTA generally focuses on the clinical efficacy and effectiveness, safety, cost, and cost-effectiveness of individual medicinal products as well as their potential implications for the national healthcare system. Those elements of medicinal products are compared with other treatment options available on the market.

The outcome of HTA may influence the pricing and reimbursement status for specific medicinal products within individual EU member states. The extent to which pricing and reimbursement decisions are influenced by the HTA of a specific medicinal product vary between the EU Member States.

A new EU Regulation on HTA was adopted on December 13, 2021, Regulation (EU) 2021/2282 of the European Parliament and of the Council of 15 December 2021 on health technology assessment and amending Directive 2011/24/EU ("HTA Regulation"). It will become applicable on January 12, 2025. The HTA Regulation covers new medicines and certain new medical devices, "providing the basis for permanent and sustainable cooperation at the EU level for joint clinical

assessments in these areas." Member states will be able to use common HTA tools, methodologies and procedures across the EU, working together in four main areas: 1) joint clinical assessments focusing on the most innovative health technologies with the most potential impact for patients; 2) joint scientific consultations whereby developers can seek advice from HTA authorities; 3) identification of emerging health technologies to identify promising technologies early; and 4) continuing voluntary cooperation in other areas. Individual member states will continue to be responsible for assessing non-clinical (e.g., economic, social, ethical) aspects of health technology, and making decisions on pricing and reimbursement.

In the United Kingdom and following the United Kingdom's exit from the European Union, EU medicines regulation has been adopted as standalone United Kingdom legislation with some amendments to reflect procedural and other requirements with respect to marketing authorizations and other regulatory provisions.

In order to market a medicinal product in the United Kingdom, a license or marketing authorization must be obtained from the United Kingdom Medicines and Healthcare Products Regulatory Agency (the "MHRA"). The United Kingdom legislation includes multiple assessment routes for applications for medicinal products, including a 150-day national assessment or a rolling review application. Further, and until December 31, 2023, the MHRA could rely on a decision taken by the European Commission on the approval of a new marketing authorization in the centralized procedure ("ECDRP") and had the power to have regard to marketing authorizations approved in EU member states ("MRDCRP"). After January 1, 2024, both of those recognition procedures (the ECDRP and the MRDCRP) have been replaced by a new international recognition framework.

The MHRA reviews applications for orphan designation at the time of a marketing authorization application or as part of a subsequent variation to that authorization. To qualify for orphan designation, a medicine must meet certain criteria in the United Kingdom including that the medicine for the treatment, prevention or diagnosis of a disease that is life-threatening or chronically debilitating, the prevalence of the condition must not be more than 5 in 10,000 or it must be unlikely that the marketing would generate sufficient returns to justify investment and no satisfactory method of diagnosis, prevention or treatment must exist in Great Britain or, if such a method exists the medicine must be of significant benefit to those affected by the condition. On grant of a marketing authorization with orphan status, the medicinal product will benefit from up to 10 years of market exclusivity from similar products in the approved orphan indication starting from the date of first approval of the product in Great Britain.

The United Kingdom has adopted new legislation, the Medicines and Medical Devices Act 2021 and may make changes to the licensing or authorization of medicines in the future. The separate U.K. authorization system, albeit with international recognition procedures in the UK, may lead to additional regulatory costs. In addition, even though at the moment the United Kingdom retains acceptance of batch testing and EU certification, further regulatory costs may be incurred with respect to the lack of mutual recognition of batch testing and related regulatory measures between the European Union and the United Kingdom.

Reimbursement in the United Kingdom for use by public payors (National Health Service) organizations may depend on a positive technology assessment by the National Institute for Health and Care Excellence ("NICE"). A positive recommendation by NICE would lead to an obligation to fund, subject to terms of that approval, by NHS organizations. In assessing any new medicinal product, NICE will take into account clinical as well as the economic value of the product.

Failure to obtain positive reimbursement recommendations or failure to obtain government and third-party payor reimbursement coverage in foreign countries may affect the marketability and commercial sales of any product candidates for which regulatory approval is received.

Employees and Human Capital Resources

As of December 31, 2023, we had 110 employees, 37 of whom have an M.D. or Ph.D. We have not experienced any work stoppages. None of our employees is represented by a labor union or covered by collective bargaining agreements, and we consider our relationship with our employees to be good.

We seek to attract, hire and retain individuals of diverse backgrounds and of all ages, genders, ethnicities, religions, home countries and sexual orientation. As of December 31, 2023, approximately 59% of our employees are female, and approximately 47% of our management team (which we define as at the vice president level and above) are female. More than 36% of our employees self-identify as racially or ethnically diverse as of December 31, 2023.

Our human capital resources objectives include, as applicable, identifying, recruiting, integrating, motivating, developing, and retaining our existing and additional employees. The principal purposes of our equity incentive and cash-based performance bonus plans are to attract, retain and motivate selected employees, consultants and directors through the granting of stock-based compensation awards.

Available Information

Stoke Therapeutics, Inc. was founded in June 2014 and was incorporated under the laws of the State of Delaware. Our principal executive offices are located at 45 Wiggins Ave, Bedford, Massachusetts 01730, and our telephone number is (781) 430-8200. Our website address is www.stoketherapeutics.com. The information contained on, or that can be accessed through, our website is not part of, and is not incorporated by reference into, this Annual Report.

We file annual, quarterly and current reports, proxy statements and other documents with the Securities and Exchange Commission, or SEC, under the Securities Exchange Act of 1934, as amended, or Exchange Act. The SEC maintains an Internet website that contains reports, proxy and information statements, and other information regarding issuers, including us, that file electronically with the SEC. The public can obtain any documents that we file with the SEC at www.sec.gov. Copies of each of our filings with the SEC can also be viewed and downloaded free of charge at our website, www.stoketherapeutics.com, after the reports and amendments are electronically filed with or furnished to the SEC.

Item 1A. Risk Factors.

Investing in our common stock involves a high degree of risk. Before making your decision to invest in shares of our common stock, you should carefully consider the risks described below, together with the other information contained in this annual report, including our consolidated financial statements and the related notes and "Management's Discussion and Analysis of Financial Condition and Results of Operations". The risks and uncertainties described below are not the only ones we face. 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. We cannot assure you that any of the events discussed below will not occur. These events could have a material and adverse impact on our business, financial condition, results of operations and prospects. If that were to happen, the trading price of our common stock could decline, and you could lose all or part of your investment.

Summary of Risk Factors

An investment in our common stock involves various risks, and prospective investors are urged to carefully consider the matters discussed in the section titled "Risk Factors" prior to making an investment in our common stock. These risks include, but are not limited to, the following:

- We are early in our development efforts. If we or our collaborators are unable to develop, obtain regulatory approval for and commercialize STK-001, STK-002 and our future product candidates, or if we experience significant delays in doing so, our business will be materially harmed.
- Success in early preclinical studies or clinical trials may not be indicative of results obtained in later preclinical studies and clinical trials, including in our Dravet syndrome program or our ADOA program.
- Even if we complete the necessary preclinical studies and clinical trials, we cannot predict when, or if, we will obtain regulatory approval to commercialize a product candidate and the approval may be for a narrower indication than we seek.
- Certain of the diseases we seek to treat have low prevalence, and it may be difficult to identify patients with these diseases, which may lead to delays in enrollment for our trials or slower commercial revenue growth if STK-001, STK-002 or our future product candidates are approved.
- If clinical trials of STK-001, STK-002 or any other product candidate that we develop fail to demonstrate safety and efficacy to the satisfaction of FDA or foreign regulatory authorities or do not otherwise produce favorable results, we may incur additional costs or experience delays in completing, or ultimately may be unable to complete, the development and commercialization of such product candidate.
- We may not be successful in our efforts to use TANGO to expand our pipeline of product candidates and develop marketable products.
- Any product candidate for which we obtain marketing approval will be subject to extensive post-marketing regulatory requirements and could be subject to post-marketing restrictions or withdrawal from the market, and we may be subject to penalties if we fail to comply with regulatory requirements or if we experience unanticipated problems with our product candidates, when and if any of them are approved.
- Our failure to obtain regulatory approval in international jurisdictions would prevent us from marketing our product candidates outside the United States.
- STK-001, STK-002 or our future product candidates may cause undesirable and unforeseen side effects or be perceived by the public as unsafe, which could delay or prevent their advancement into clinical trials or regulatory approval, limit the commercial potential or result in significant negative consequences.
- A Rare Pediatric Disease designation by the FDA does not guarantee that the new drug application ("NDA") for the product will qualify for a priority review voucher upon approval, and it does not lead to a faster development or regulatory review process, or increase the likelihood that STK-001, STK-002 or our future product candidates will receive marketing approval.

- A Fast Track Designation by the FDA, even if granted for STK-001, STK-002 or our future product candidates, may not lead to a faster development or regulatory review or approval process, and would not increase the likelihood that our product candidates will receive marketing approval.
- A Breakthrough Therapy Designation by the FDA, even if granted for STK-001, STK-002 or our future product candidates may not lead to a faster development or regulatory review or approval process, and it would not increase the likelihood that the product candidates will receive marketing approval.
- Enacted and future legislation may increase the difficulty and cost for us to obtain marketing approval of and commercialize our product candidates and may affect the prices we may set.
- The commercial success of our product candidates, including STK-001 and STK-002 will depend upon their degree of market acceptance by providers, patients, patient advocacy groups, third-party payors and the general medical community.
- The pricing, insurance coverage and reimbursement status of newly approved products is uncertain. Failure to obtain or maintain adequate coverage and reimbursement for our product candidates, if approved, could limit our ability to market those products and decrease our ability to generate product revenue.
- Current and potential future healthcare reforms may adversely impact pricing, insurance coverage and reimbursement status of newly approved products.
- We have a history of operating losses, and we may not achieve or sustain profitability. We anticipate that we will continue to incur losses for the foreseeable future. If we fail to obtain additional funding to conduct our planned research and development effort, we could be forced to delay, reduce or eliminate our product development programs or commercial development efforts.
- We expect that we will need to raise additional funding before we can expect to become profitable from any potential future sales of STK-001, STK-002 or our future product candidates. This additional financing may not be available on acceptable terms or at all. Failure to obtain this necessary capital when needed may force us to delay, limit or terminate our product development efforts or other operations.
- Our limited operating history may make it difficult for you to evaluate the success of our business to date and to assess our future viability.
- Our success depends in part on our ability to obtain, maintain and protect our intellectual property. It is difficult and costly to protect our proprietary rights and technology, and we may not be able to ensure their protection.
- The market price of our stock may be volatile, and you could lose all or part of your investment.

Risks Related to Product Development and Regulatory Approval

We are early in our development efforts. If we are unable to develop, obtain regulatory approval for and commercialize STK-001, STK-002 and our future product candidates, or if we experience significant delays in doing so, our business will be materially harmed.

We have invested substantially all of our efforts and financial resources in the development of our Targeted Augmentation of Nuclear Gene Output ("TANGO") technology and our current lead product candidate, STK-001, for the treatment of Dravet syndrome. We submitted an investigational new drug application ("IND") for STK-001 to the U.S. Food and Drug Administration (the "FDA") in late 2019. In August 2020, we dosed the first patient with STK-001 in the single ascending dose portion of the MONARCH Phase 1/2a Study at the 10mg dose level.

In addition, in November 2020, we announced the nomination of OPA1 as our next target for preclinical development to treat Autosomal Dominant Optic Atrophy ("ADOA"). In November 2021, we announced the nomination of STK-002 as the lead product candidate for the treatment of ADOA and intend to invest significant efforts and financial resources in its development. We submitted a Clinical Trial Authorization ("CTA") application for STK-002 to the United Kingdom Medicines and Healthcare Products Regulatory Agency (the "MHRA") in early 2023, and the MHRA authorized such CTA in April 2023, but enrollment and dosing of patients has not yet commenced. 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 TANGO and our product candidates, which may never occur. We currently generate no revenue from sales of any product, and we may never be able to develop or commercialize a marketable product.

Each of our programs and product candidates will require preclinical and clinical development, regulatory approval in multiple jurisdictions, obtaining preclinical, clinical and commercial manufacturing supply, capacity and expertise, building of a commercial organization, substantial investment and significant marketing efforts before we generate any revenue from product sales. STK-001, STK-002 and our future product candidates must be authorized for marketing by the FDA or certain other foreign regulatory agencies, such as the European Medicines Agency (the "EMA") or the MHRA, before we may commercialize any of our product candidates.

The success of STK-001, STK-002 and our future product candidates depends on multiple factors, including:

- effective INDs and CTAs that allow commencement of our planned clinical trials or future clinical trials for our product candidates in relevant territories;
- our ability to obtain approval from institutional review boards ("IRBs") or ethics committees to conduct clinical trials at their respective sites;
- potential delays in enrollment, site visits, evaluations, or dosing of patients participating in clinical trials as hospitals face staffing shortages, whether due to labor relations or otherwise, or patients decide not to enroll in the study as a result of such staffing shortages;
- the direct and indirect impact of general economic, industry and market conditions, including fluctuating interest rates, inflation, market volatility, potential recessions, a potential federal government shutdown, and any health pandemic on our business and operations, third party vendors, supply chain, and regulatory approvals;
- successful completion of preclinical studies, including those compliant with Good Laboratory Practices ("GLP") toxicology studies, biodistribution studies and minimum effective dose studies in animals;
- our ability to reach agreements on acceptable terms with prospective third-party contract research organizations ("CROs") and trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among CROs and trial sites;
- successful enrollment and completion of clinical trials compliant with current Good Clinical Practices ("GCPs");
- positive results from our clinical programs that demonstrate safety and efficacy and provide an acceptable risk-benefit profile for our product candidates in the intended patient populations;
- receipt of regulatory approvals from applicable regulatory authorities;
- establishment of arrangements with third-party contract manufacturing organizations ("CMOs") for key materials used in our manufacturing processes and to establish backup sources for clinical and large-scale commercial supply;
- establishment and maintenance of patent and trade secret protection and regulatory exclusivity for our product candidates;
- commercial launch of our product candidates, if and when approved, whether alone or in collaboration with others;
- acceptance of our product candidates, if and when approved, by patients, patient advocacy groups, third-party payors and the general medical community;
- our effective competition against other therapies available in the market;
- establishment and maintenance of adequate reimbursement from third-party payors for our product candidates;
- our ability to acquire or in-license additional product candidates;
- prosecution, maintenance, enforcement and defense of intellectual property rights and claims; and
- maintenance of a continued acceptable safety profile of our product candidates following approval.

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 our product candidates, which would materially harm our business. If we do not receive regulatory approvals for our product candidates, we may not be able to continue our operations.

Success in early preclinical studies or clinical trials may not be indicative of results obtained in later preclinical studies and clinical trials, including in our Dravet syndrome program or our ADOA program.

STK-001 is currently being evaluated in human clinical trials, and we may experience unexpected or negative results in the future. We will be required to demonstrate through adequate and well-controlled clinical trials that our product candidates are safe and effective, with a favorable benefit-risk profile, for use in their target indications before we can seek regulatory approvals for their commercial sale. The positive results we have observed for our product candidates in preclinical animal models may not be predictive of our future clinical trials in humans, as mouse models carry inherent limitations relevant to all preclinical studies. In particular, the Dravet syndrome mouse model is more severe than the human disease and provides a shorter post-symptomatic observation period. Trial designs and results from early-phase trials are not necessarily predictive of future clinical trial designs or results, and initial positive results we may observe may not be confirmed in later-phase clinical trials. For example, although we recently reported end of study data from our Phase 1/2a open-label studies of STK-001 demonstrating a reduction in median convulsive seizure frequency compared to baseline, these results were based on pooling data from the Phase 1/2a open-label studies of STK-001 in the United States (MONARCH) and in the United Kingdom (ADMIRAL) and additional trials may not confirm these results. Our product candidates may also fail to show the desired safety and efficacy in later stages of clinical development even if they successfully advance through initial clinical trials, and preliminary interim data readouts of ongoing trials may show results that change when such trials are completed. We may not be able to demonstrate a disease-modifying effect of STK-001 in our clinical trials in Dravet syndrome patients, even if we are able to demonstrate efficacy on seizure reduction, and we may be similarly unable to demonstrate the efficacy of STK-002 in our ADOA program or other future programs. In addition, our clinical trials to date have necessarily involved relatively small numbers of participants. Therefore, conclusions we draw based upon trial results to date may not be repeatable across larger cohorts of participants or patients with different characteristics. Moreover, even if our clinical trials demonstrate acceptable safety and efficacy of STK-001, STK-002 or our future product candidates, the labeling we obtain through negotiations with the FDA or foreign regulatory authorities may not include data on secondary endpoints and may not provide us with a competitive advantage over other products approved for the same or similar indications.

Many companies in the biotechnology industry have suffered significant setbacks in late-stage clinical trials after achieving positive results in early-stage development and there is a high failure rate for product candidates proceeding through clinical trials. In addition, different methodologies, assumptions and applications we utilize to assess particular safety or efficacy parameters may yield different statistical results. Even if we believe the data collected from clinical trials of our product candidates are promising, these data may not be sufficient to support approval by the FDA or foreign regulatory authorities. Preclinical and clinical data can be interpreted in different ways. Accordingly, the FDA or foreign regulatory authorities could interpret these data in different ways from us or our partners, which could delay, limit or prevent regulatory approval. If our study data do not consistently or sufficiently demonstrate the safety or efficacy of any of our product candidates, including STK-001 for Dravet syndrome or STK-002 for ADOA, then the regulatory approvals for such product candidates could be significantly delayed as we work to meet approval requirements, or, if we are not able to meet these requirements, such approvals could be withheld or withdrawn. Regulatory delays or rejections may be encountered as a result of many factors, including changes in regulatory policy during the period of product development. We cannot be certain that we will not face similar setbacks.

If clinical trials of STK-001, STK-002 or any other product candidate that we develop fail to demonstrate safety and efficacy to the satisfaction of FDA or foreign regulatory authorities or do not otherwise produce favorable results, we may incur additional costs or experience delays in completing, or ultimately may be unable to complete, the development and commercialization of such product candidate.

Before obtaining marketing approval from regulatory authorities for the sale of any product candidate, including STK-001 and STK-002, we must complete preclinical development and then conduct extensive clinical trials to demonstrate the safety and efficacy of our product candidates in humans. Clinical testing is expensive, difficult to design and implement, can take many years to complete and is uncertain as to outcome. A failure of one or more clinical trials can occur at any stage of testing.

Clinical trials may be placed on a full or partial clinical hold by the FDA, foreign regulatory authorities, or us for various reasons, including but not limited to: deficiencies in the conduct of the clinical trials, including failure to conduct the clinical trial in accordance with regulatory requirements or clinical protocols; deficiencies in the clinical trial operations or trial sites; deficiencies in the trial designs necessary to demonstrate efficacy; fatalities or other adverse effects arising during a clinical trial due to medical problems that may or may not be related to clinical trial treatments; the product candidates may not appear to be more effective than current therapies; the quality or stability of the product candidates may fall below acceptable standards; or the data from animal studies are not sufficient to support the anticipated exposure (dose, route of administration, and duration) for the proposed clinical trial. For example, in March 2020, we announced that the FDA had placed a partial clinical hold on doses of STK-001 above 20mg in the MONARCH study based on observations of adverse

hind limb paresis in non-human primates, pending additional preclinical testing. The partial clinical hold remains in place in the MONARCH study for single and multiple doses above 70mg, and in the SWALLOWTAIL open-label extension study for chronic doses above 45mg. Although we have now announced end of study data from the MONARCH study, if the partial clinical hold is not lifted, our ability to successfully conclude other studies related to STK-001, and our business, results of operations and financial condition, may be adversely affected.

In addition, we, the FDA, foreign regulatory authorities, or an IRB or similar foreign review board or committee, may delay initiation of, suspend or limit dose escalation of clinical trials of a product candidate at any time for various reasons, including if we or they believe the healthy volunteer subjects or patients participating in such trials are being exposed to unacceptable health risks. Among other reasons, adverse side effects of a product candidate or a related product in preclinical trials or on healthy volunteer subjects or patients in a clinical trial could result in such a decision. For example, in November 2022, we announced our decision to limit chronic dosing in the open-label extension studies to 30mg in SWALLOWTAIL in the U.S. and 45mg in LONGWING in the U.K. Our decision at that time was based on interactions with regulatory agencies and a review of interim chronic toxicology data from a study in NHPs in which the total drug administered to NHPs over a 1-year period was substantially higher than what we would anticipate giving to participants in clinical trials.

Even if we complete the necessary preclinical studies and clinical trials, we cannot predict when, or if, we will obtain regulatory approval to commercialize a product candidate and the approval may be for a narrower indication than we seek.

Prior to commercialization, STK-001, STK-002, and our other future product candidates must be approved by the FDA pursuant to an NDA in the United States and pursuant to similar marketing applications by the EMA and similar regulatory authorities outside the United States. The process of obtaining marketing approvals, both in the United States and abroad, is expensive and takes many years, if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity and novelty of the product candidates involved. Failure to obtain marketing approval for a product candidate will prevent us from commercializing the product candidate. We have not received approval to market STK-001, STK-002 or any of our other future product candidates from regulatory authorities in any jurisdiction. We have no experience in submitting and supporting the applications necessary to gain marketing approvals, and, in the event regulatory authorities indicate that we may submit such applications, we may be unable to do so as quickly and efficiently as desired. Securing marketing approval requires the submission of extensive preclinical and clinical data and supporting information to regulatory authorities for each therapeutic indication to establish the product candidate's safety and efficacy. Securing marketing approval also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities by, the regulatory authorities. Our product candidates may not be effective, may be only moderately effective or may prove to have undesirable or unintended side effects, toxicities or other characteristics that may preclude our obtaining marketing approval or prevent or limit commercial use. Regulatory authorities have substantial discretion in the approval process and may refuse to accept or file any application or may decide that our data are insufficient for approval and require additional preclinical, clinical or other studies. In addition, varying interpretations of the data obtained from preclinical and clinical testing could delay, limit or prevent marketing approval of a product candidate.

Approval of STK-001, STK-002 and our other future product candidates may be delayed or refused for many reasons, including:

- the FDA or comparable foreign regulatory authorities may disagree with the design or implementation of our clinical trials;
- we may be unable to demonstrate, to the satisfaction of the FDA or comparable foreign regulatory authorities, that our product candidates are safe and effective for any of their proposed indications;
- the results of clinical trials may not meet the level of statistical significance or clinical meaningfulness required by the FDA or comparable foreign regulatory authorities for approval;
- we may be unable to demonstrate that our product candidates' clinical and other benefits outweigh their safety risks;
- the FDA or comparable foreign regulatory authorities may disagree with our interpretation of data from preclinical programs or clinical trials;
- the data collected from clinical trials of our product candidates may not be sufficient to support the submission of an NDA or other comparable submission in foreign jurisdictions or to obtain regulatory approval in the United States or elsewhere;

- the facilities of third-party manufacturers with which we contract or procure certain service or raw materials may not be adequate to support approval of our product candidates;
- the approval policies or regulations of the FDA or comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval; and
- potential delays in enrollment, site visits, evaluations, or dosing of patients participating in the clinical trial as hospitals face staffing shortages, whether due to labor relations or otherwise, or patients decide to not enroll in the study as a result of or such staffing shortages.

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

Regulatory authorities also may approve a product candidate for more limited indications than requested or they may impose significant limitations in the form of narrow indications, warnings or a risk evaluation and mitigation strategy ("REMS"). These regulatory authorities may require precautions or contra-indications with respect to conditions of use or they may grant approval subject to the performance of costly post-marketing clinical trials. In addition, regulatory authorities may not approve the labeling claims that are necessary or desirable for the successful commercialization of our product candidates. Any of the foregoing scenarios could materially harm the commercial prospects for our product candidates and adversely affect our business, financial condition, results of operations and prospects. While currently we are not experiencing any significant delays or disruptions to our clinical trials as a result of hospital staffing shortages or global macroeconomic conditions, we take into consideration such shortages and conditions may directly or indirectly impact our clinical trial enrollment, dosing, and regulatory approval timelines.

Certain of the diseases we seek to treat have low prevalence, and it may be difficult to identify patients with these diseases, which may lead to delays in enrollment for our trials or slower commercial revenue growth if STK-001, STK-002 or our future product candidates are approved.

Genetically defined diseases generally, and especially those for which our product candidates are targeted, have low incidence and prevalence. We estimate that the worldwide incidence of Dravet syndrome is approximately one in 16,000 births, and the incidence of ADOA is approximately one in 30,000 births. This could pose obstacles to the timely recruitment and enrollment of a sufficient number of eligible patients into our trials or limit a product candidate's commercial potential. Patient enrollment may be affected by other factors including:

- the ability to identify and enroll patients that meet study eligibility criteria in a timely manner for clinical trials;
- the severity of the disease under investigation;
- design of the study protocol;
- the perceived risks, benefits and convenience of administration of the product candidate being studied;
- the patient referral practices of providers; and
- the proximity and availability of clinical trial sites to prospective patients.

Any inability to enroll a sufficient number of patients with these diseases for our planned clinical trials would result in significant delays and could cause us to not initiate or abandon one or more clinical trials altogether. Enrollment delays in our clinical trials may result in increased development costs for our product candidate, which would cause the value of our company to decline and limit our ability to obtain additional financing.

Additionally, our projections of both the number of people who have Dravet syndrome or ADOA, as well as the people with this disease who have the potential to benefit from treatment with our product candidates, are based on estimates derived from a market research study that we commissioned, which may not accurately identify the size of the market for our product candidates. The total addressable market opportunity for STK-001, STK-002 and our future product candidates will ultimately depend upon, among other things, the final labeling for our product candidates, if our product candidates are approved for sale in our target indications, acceptance by the medical community and patient access, drug pricing and reimbursement. The number of patients globally may turn out to be lower than expected, patients may not be otherwise amenable to treatment with our product candidates, or new patients may become increasingly difficult to identify or gain access to, all of which would adversely affect our results of operations and our business.

Moreover, in light of the limited number of potential patients impacted by Dravet syndrome and ADOA, our per-patient therapy pricing of STK-001, STK-002 and our future product candidates, if approved, must be high in order to recover our development and manufacturing costs, fund additional research and achieve profitability. We may also need to fund patient support programs upon the marketing of a product candidate, which would negatively affect our product revenue. We may be unable to maintain or obtain sufficient therapy sales volumes at a price high enough to justify our development efforts and our sales, marketing and manufacturing expenses.

We may not be successful in our efforts to use TANGO to expand our pipeline of product candidates and develop marketable products.

Because we have limited financial and managerial resources, we focus on research programs and product candidates that we identify for specific indications. Our business depends on our successful development and commercialization of the limited number of internal product candidates we are researching or have in preclinical development. Even if we are successful in continuing to build our pipeline, development of the potential product candidates that we identify will require substantial investment in additional clinical development, management of clinical, preclinical and manufacturing activities, regulatory approval in multiple jurisdictions, obtaining manufacturing supply capability, building a commercial organization, and significant marketing efforts before we generate any revenue from product sales. Furthermore, such product candidates may not be suitable for clinical development, including as a result of their harmful side effects, limited efficacy or other characteristics that indicate that they are unlikely to be products that will receive marketing approval and achieve market acceptance. If we cannot validate TANGO by successfully developing and commercializing product candidates based upon our technological approach, we may not be able to obtain product revenue in future periods, which would adversely affect our business, prospects, financial condition and results of operations.

In November 2021, we announced the nomination of STK-002 as our lead product candidate for in the treatment of ADOA; however, we are primarily focused on our lead product candidate for Dravet syndrome, STK-001, and we may forego or delay pursuit of opportunities with other product candidates or for other indications that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs and product candidates for specific indications may not yield any commercially viable products. Our understanding and evaluation of biological targets for the discovery and development of new product candidates may fail to identify challenges encountered in subsequent preclinical and clinical development. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights.

Any product candidate for which we obtain marketing approval will be subject to extensive post-marketing regulatory requirements and could be subject to post-marketing restrictions or withdrawal from the market, and we may be subject to penalties if we fail to comply with regulatory requirements or if we experience unanticipated problems with our product candidates, when and if any of them are approved.

Our product candidates and the activities associated with their development and potential commercialization, including their testing, manufacturing, recordkeeping, labeling, storage, approval, advertising, promotion, sale and distribution, are subject to comprehensive regulation by the FDA and other U.S. and international regulatory authorities. These requirements include submissions of safety and other post-marketing information and reports, registration and listing requirements, requirements relating to manufacturing, including current Good Manufacturing Practices (“GMPs”), quality control, quality assurance and corresponding maintenance of records and documents, including periodic inspections by the FDA and other regulatory authorities and requirements regarding the distribution of samples to providers and recordkeeping.

The FDA may also impose requirements for costly post-marketing studies or clinical trials and surveillance to monitor the safety or efficacy of any approved product. The FDA closely regulates the post-approval marketing and promotion of drugs and biologics to ensure they are marketed only for the approved indications and in accordance with the provisions of the approved labeling. The FDA imposes stringent restrictions on manufacturers' communications regarding use of their products. If we promote our product candidates in a manner inconsistent with FDA-approved labeling or otherwise not in compliance with FDA regulations, we may be subject to enforcement action. Moreover, while we believe our product candidates may provide improved safety profiles over existing products, unless we conduct head-to-head studies, we will not be able to make comparative claims for products, if approved. Violations of the Federal Food, Drug, and Cosmetic Act (the "FDCA") relating to the promotion of prescription drugs may lead to investigations alleging violations of federal and state healthcare fraud and abuse laws, as well as state consumer protection laws and similar laws in international jurisdictions.

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

- restrictions on such product candidates, manufacturers or manufacturing processes;
- restrictions on the labeling or marketing of a product;
- restrictions on product distribution or use;
- requirements to conduct post-marketing studies or clinical trials;
- warning or untitled letters;
- withdrawal of any approved product from the market;
- refusal to approve pending applications or supplements to approved applications that we submit;
- recall of product candidates;
- fines, restitution or disgorgement of profits or revenues;
- suspension or withdrawal of marketing approvals;
- refusal to permit the import or export of our product candidates;
- product seizure; or
- injunctions or the imposition of civil or criminal penalties.

Non-compliance with European requirements regarding safety monitoring or pharmacovigilance, and with requirements related to the development of products for the pediatric population, can also result in significant financial penalties. Similarly, failure to comply with Europe's requirements regarding the protection of personal information can also lead to significant penalties and sanctions.

Our failure to obtain regulatory approval in international jurisdictions would prevent us from marketing our product candidates outside the United States.

To market and sell STK-001, STK-002 and our future product candidates, 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. The regulatory approval process outside the United States generally includes all of the risks associated with obtaining FDA approval. In addition, in many countries outside the United States, we must secure product reimbursement approvals before regulatory authorities will approve the product for sale in that country. Failure to obtain foreign regulatory approvals or non-compliance with foreign regulatory requirements could result in significant delays, difficulties and costs for us and could delay or prevent the introduction of our product candidates in certain countries. The United Kingdom's exit from the European Union (the "EU"), which is referred to as "Brexit," became fully effective on December 31, 2020. Brexit continues to create political and economic uncertainty, particularly in the United Kingdom and the EU. Prior to Brexit, a significant proportion of the regulatory framework in the United Kingdom was derived from EU directives and regulations. Following Brexit, the United Kingdom retained the EU regulatory regime with certain modifications as standalone U.K. legislation. Therefore, the U.K. regulatory regime is currently similar to EU regulations, but the United Kingdom has enacted new legislation, the Medicines and Medical Devices Act. Under this legislation, the U.K. may adopt changed regulations that may diverge from the EU legislative regime for medicines, including their research, development and commercialization and has issued a consultation document with respect to future changes. Brexit may lead to additional regulatory costs and could materially impact the regulatory regime with respect to the approval of our product candidates in the United Kingdom or the EU.

If we fail to comply with the regulatory requirements in international markets and receive applicable marketing approvals, our target market will be reduced and our ability to realize the full market potential of our product candidates will be harmed and our business will be adversely affected. We may not obtain foreign regulatory approvals on a timely basis, if at all. Our failure to obtain approval of any of our product candidates by regulatory authorities in another country may significantly diminish the commercial prospects of that product candidate and our business prospects could decline.

STK-001, STK-002 or our future product candidates may cause undesirable and unforeseen side effects or be perceived by the public as unsafe, which could delay or prevent their advancement into clinical trials or regulatory approval, limit the commercial potential or result in significant negative consequences.

Although other ASOs have received regulatory approval, our method of seeking to upregulate protein expression by targeting the underlying genetic causes of haploinsufficiencies presents a new approach to disease treatment, which means there is uncertainty associated with the safety profile of STK-001, STK-002 or our future product candidates and drugs in the antisense oligonucleotide class.

In addition to side effects caused by our product candidates, the intrathecal or intravitreal administration process or related procedures also can cause adverse side effects. If any such adverse events occur, our clinical trials could be suspended or terminated. If we are unable to demonstrate that any adverse events were caused by the administration process or related procedures, the FDA, the European Commission, the EMA, the U.K. MHRA or other regulatory authorities could order us to cease further development of, or deny approval of, our product candidates for any or all targeted indications. Even if we can demonstrate that all future serious adverse events are not product-related, such occurrences could affect patient recruitment or the ability of enrolled patients to complete the trial. Moreover, if we elect, or are required, to not initiate, delay, suspend or terminate any future clinical trial of any of our product candidates, the commercial prospects of such product candidates may be harmed and our ability to generate product revenues from any of these product candidates may be delayed or eliminated. Any of these occurrences may harm our ability to develop other product candidates, and may adversely affect our business, financial condition, results of operations and prospects significantly. Finally, SPINRAZA, which is produced by Biogen Inc., is an ASO therapy utilizing intrathecal delivery, and if SPINRAZA is found to cause undesirable side effects or to be unsafe due to a potential class effect, it may adversely affect demand for STK-001 and our other future product candidates. Other ASOs in clinical development utilizing intrathecal delivery could also generate data that could adversely affect the clinical, regulatory or commercial perception of STK-001 and our other future product candidates.

Additionally, if any of our product candidates receives marketing approval, the FDA could require us to adopt a REMS to ensure that the benefits of the product outweigh its risks, which may include, for example, a Medication Guide outlining the risks of the product for distribution to patients and a communication plan to health care practitioners, or other elements to assure safe use of the product. Furthermore, if we or others later identify undesirable side effects caused by our product candidate, several potentially significant negative consequences could result, including:

- regulatory authorities may suspend or withdraw approvals of such product candidate;
- regulatory authorities may require additional warnings in the labeling;
- we may be required to change the way a product candidate is administered or conduct additional clinical trials;
- we could be sued and held liable for harm caused to patients; and
- our reputation may suffer.

Any of these occurrences may harm our business, financial condition, results of operations and prospects significantly.

A Rare Pediatric Disease designation by the FDA does not guarantee that the NDA for the product will qualify for a priority review voucher upon approval, and it does not lead to a faster development or regulatory review process, or increase the likelihood that STK-001, STK-002 or our future product candidates will receive marketing approval.

Under the Rare Pediatric Disease Priority Review Voucher program, upon the approval of a qualifying NDA for the treatment of a rare pediatric disease, the sponsor of such an application would be eligible for a rare pediatric disease priority review voucher that can be used to obtain priority review for a subsequent Biologics License Application or NDA. As part of our business strategy for STK-001, we received Rare Pediatric Disease Designation in October 2022. We may also seek Rare Pediatric Disease designations for any other future product candidates. If a product candidate is designated before September 30, 2024, it is eligible to receive a voucher if it is approved before September 30, 2026. However, there is no expectation that STK-001, STK-002 or our future product candidates will be designated, other than STK-001, or approved by those dates, or at all, or that the program will be further extended, and, therefore, we may not be in a position to obtain any priority review vouchers. Additionally, designation of a drug for a rare pediatric disease does not guarantee that an NDA will meet the

eligibility criteria for a rare pediatric disease priority review voucher at the time the application is approved. Finally, a Rare Pediatric Disease Designation does not lead to faster development or regulatory review of the product or increase the likelihood that it will receive marketing approval.

A Fast Track Designation by the FDA, even if granted for STK-001, STK-002 or any of our future product candidates, or any use of the accelerated approval pathway, may not lead to a faster development or regulatory review or approval process, and would not increase the likelihood that our product candidates will receive marketing approval.

If a drug is intended for the treatment of a serious or life-threatening condition and the drug demonstrates the potential to address unmet medical needs for this condition, the drug sponsor may apply to the FDA for Fast Track Designation. The FDA has broad discretion whether to grant this designation. Even if we believe a particular product candidate is eligible for this designation, we cannot assure you that the FDA would decide to grant it. Even if we do receive Fast Track Designation for any of our product candidates, we may not experience a faster development process, review or approval compared to conventional FDA procedures. The FDA may withdraw Fast Track Designation if it believes that the designation is no longer supported by data from our clinical development program. Many drugs that have received Fast Track Designation have failed to obtain approval.

We may also seek accelerated approval for our product candidates. Under the FDA's accelerated approval program, the FDA may approve a drug for a serious or life-threatening illness that provides meaningful therapeutic benefit to patients over existing treatments based upon a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity or prevalence of the condition and the availability or lack of alternative treatments. Full approval of another product for the same indication as any of our product candidates for which we are seeking accelerated approval may make accelerated approval of our product candidates more difficult. For drugs granted accelerated approval, post-marketing confirmatory trials are required to describe the anticipated effect on irreversible morbidity or mortality or other clinical benefit. These confirmatory trials must be completed with due diligence and in general the FDA may require that the trial be designed and/or initiated prior to approval. The Food and Drug Omnibus Reform Act ("FDORA") was recently enacted, which included provisions related to the accelerated approval pathway. Pursuant to FDORA, the FDA is authorized to require a post-approval study to be underway prior to approval or within a specified time period following approval. FDORA also requires the FDA to specify conditions of any required post-approval study, which may include milestones and requires sponsors to submit progress reports for required post-approval studies and any conditions required by the FDA. FDORA enables the FDA to initiate enforcement action for the failure to conduct with due diligence a required post-approval study, including a failure to meet any required conditions specified by the FDA or to submit timely reports. All promotional materials for product candidates approved via accelerated approval are subject to prior review by the FDA. Moreover, the FDA may withdraw approval of any product candidate or indication approved under the accelerated approval pathway if, for example:

- the trial or trials required to verify the predicted clinical benefit of the product candidate fail to verify such benefit or do not demonstrate sufficient clinical benefit to justify the risks associated with the drug;
- other evidence demonstrates that the product candidate is not shown to be safe or effective under the conditions of use;
- we fail to conduct any required post-approval trial of the product candidate with due diligence; or
- we disseminate false or misleading promotional materials relating to the product candidate.

A Breakthrough Therapy Designation by the FDA, even if granted for STK-001, STK-002 or any of our future product candidates, may not lead to a faster development or regulatory review or approval process, and it would not increase the likelihood that the product candidate will receive marketing approval.

We may seek a Breakthrough Therapy Designation for STK-001, STK-002 or one or more of our future product candidates. A breakthrough therapy is defined as a drug that is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. For drugs 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. Drugs designated as breakthrough therapies by the FDA are also eligible for priority review if supported by clinical data at the time of the submission of the NDA.

Designation as a breakthrough therapy is at the discretion of the FDA. Accordingly, even if we believe that one of our product candidates meets the criteria for designation as a breakthrough therapy, the FDA may disagree and instead determine not to make such designation. In any event, the receipt of a Breakthrough Therapy Designation for a drug may not result in a faster development process, review, or approval compared to drugs considered for approval under conventional FDA procedures and it would not assure ultimate approval by the FDA. In addition, even if one or more of our product candidates qualify as breakthrough therapies, the FDA may later decide that the product candidate no longer meets the conditions for qualification or it may decide that the time period for FDA review or approval will not be shortened.

Enacted and future legislation may increase the difficulty and cost for us to obtain marketing approval of and commercialize our product candidates and may affect the prices we may set.

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

In addition, in the United States, there have been and continue to be a number of legislative initiatives to contain healthcare costs. The pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major legislative initiatives. Previously, in March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010 (collectively, the "ACA") was enacted, which was intended to broaden access to health insurance, reduce or constrain the growth of healthcare spending, enhance remedies against fraud and abuse, add new transparency requirements for health care and health insurance industries, impose new taxes and fees on the health industry and impose additional health policy reforms.

Healthcare reform initiatives recently culminated in the enactment of the Inflation Reduction Act ("IRA") in August 2022, which, among other things, allows U.S. Department of Health and Human Services ("HHS") to directly negotiate the selling price of a statutorily specified number of drugs and biologics each year that the Centers for Medicare & Medicaid Services ("CMS") reimburses under Medicare Part B and Part D. Only high-expenditure single-source drugs that have been approved for at least 7 years (11 years for single-source biologics) are eligible be selected by CMS for negotiation, with the negotiated price taking effect two years after the selection year. Negotiations for Medicare Part D products take place in 2024 with the negotiated price taking effect in 2026, and negotiations for Medicare Part B products will begin in 2026 with the negotiated price taking effect in 2028. In August 2023, HHS announced the ten Medicare Part D drugs and biologics that it selected for negotiations. HHS will announce the negotiated maximum fair prices by September 1, 2024, and this price cap, which cannot exceed a statutory ceiling price, will go into effect on January 1, 2026. A drug or biological product that has an orphan drug designation for only one rare disease or condition will be excluded from the IRA's price negotiation requirements, but will lose that exclusion if it receives designations for more than one rare disease or condition, or if is approved for an indication that is not within that single designated rare disease or condition, unless such additional designation or such disqualifying approvals are withdrawn by the time CMS evaluates the drug for selection for negotiation. The negotiated prices will represent a significant discount from average prices to wholesalers and direct purchasers. The law also imposes rebates on Medicare Part D and Part B drugs whose prices have increased at a rate greater than the rate of inflation. In addition, the law eliminates the "donut hole" under Medicare Part D beginning in 2025 by significantly lowering the beneficiary maximum out-of-pocket cost through a newly established manufacturer discount program which requires manufacturers to subsidize 10% of Part D enrollees' prescription costs for brand drugs below the out-of-pocket maximum, and 20% once the out-of-pocket maximum has been reached. The IRA also extends enhanced subsidies for individuals purchasing health insurance coverage in ACA marketplaces through plan year 2025. The IRA permits the Secretary of HHS to implement many of these provisions through guidance, as opposed to regulation, for the initial years. Manufacturers that fail to comply with the IRA may be subject to various penalties, including civil monetary penalties. These provisions may be subject to legal challenges. For example, the provisions related to the negotiation of selling prices of high-expenditure single-source drugs and biologics have been challenged in multiple lawsuits brought by pharmaceutical manufacturers. Thus, while it is unclear how the IRA will be implemented, it will likely have a significant impact on the pharmaceutical industry.

In addition, other legislative changes have been proposed and adopted. These changes included aggregate reductions of Medicare payments to providers of up to 2% per fiscal year, which went into effect in 2013, and will remain in effect through 2031, with the exception of a temporary suspension implemented under various COVID-19 relief legislation from May 1, 2020 through March 31, 2022, unless additional Congressional action is taken. In January 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, reduced Medicare payments to several providers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These new laws may result in additional reductions in Medicare and other healthcare funding, which could have a material

adverse effect on customers for our drugs, if approved, and accordingly, our financial operations. Additionally, on May 30, 2018, the Trickett Wendler, Frank Mongiello, Jordan McLinn, and Matthew Bellina Right to Try Act of 2017 was signed into law. The law, among other things, provides a federal framework for certain patients to access certain investigational new drug products that have completed a Phase 1 clinical trial and that are undergoing investigation for FDA approval. Under certain circumstances, eligible patients can seek treatment without enrolling in clinical trials and without obtaining FDA authorization under an FDA expanded access program; however, manufacturers are not obligated to provide investigational new drug products under the current federal right to try law. We may choose to seek an expanded access program for our product candidates, or to utilize comparable rules in other countries that allow the use of a drug, on a named patient basis or under a compassionate use program.

Furthermore, there have been, and continue to be, a number of other initiatives at the United States federal and state levels that seek to reduce healthcare costs. For example, in December 2020, CMS issued a final rule implementing significant manufacturer price reporting changes under the Medicaid Drug Rebate Program, including an alternative rebate calculation for line extensions that is tied to the price increases of the original drug, and Best Price reporting related to certain value-based purchasing arrangements. Additionally, under the American Rescue Plan Act of 2021, effective January 1, 2024, the statutory cap on Medicaid Drug Rebate Program rebates that manufacturers pay to state Medicaid programs on a unit of drug is eliminated. Elimination of this cap may, in some cases, require pharmaceutical manufacturers to pay more in rebates than they receive on the sale of products. Further, the Infrastructure Investment and Jobs Act added a requirement, effective January 1, 2023, for manufacturers of certain single-source drugs separately paid for under Medicare Part B for at least 18 months and marketed in single-dose containers or packages (known as refundable single-dose containers or single-use package drugs) to provide annual refunds for any portions of the dispensed drug that are unused and discarded if those unused or discarded portions exceed an applicable percentage defined by statute or regulation. Manufacturers are subject to periodic audits and those that fail to pay refunds for their refundable single-dose containers or single-use package drugs shall be subject to civil monetary penalties. Healthcare reforms that have been adopted, and that may be adopted in the future, could result in further reductions in coverage and levels of reimbursement for pharmaceutical products, increases in rebates payable under U.S. government rebate programs and additional downward pressure on pharmaceutical product prices.

We expect that the ACA, the IRA, as well as other 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. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our product candidates.

At the state level in the United States, legislatures are increasingly enacting laws and implementing regulations designed to control pharmaceutical and biologic product pricing, including price constraints, restrictions on certain product access, reporting on price increases and the introduction of high-cost drugs.

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 FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals of our product candidates, if any, may be. In addition, increased scrutiny by the U.S. Congress of the FDA's approval process may significantly delay or prevent marketing approval, as well as subject us to more stringent product labeling and post-marketing testing and other requirements.

We may be unsuccessful in obtaining Orphan Drug Designation or transfer of designations obtained by others for future product candidates. And, even if we obtain such designation, we may be unable to maintain the benefits associated with Orphan Drug Designation, including the potential for market exclusivity, for STK-001, STK-002 or our future product candidates.

As part of our business strategy for STK-001, we received Orphan Drug Designation for the treatment of Dravet syndrome in the United States in 2019 and also in the EU in 2022. As part of our business strategy for STK-002, we received Orphan Drug Designation for the treatment of autosomal dominant optic atrophy (ADOA) in the United States in 2022. We may seek such designations for our product candidates in other countries as well. However, Orphan Drug Designation does not guarantee future orphan drug marketing exclusivity, and there is no guarantee that we will be successful in obtaining such designation for our future product candidates.

Regulatory authorities in some jurisdictions, including the United States and Europe, may designate drugs intended to treat relatively small patient populations as orphan drugs. Under the Orphan Drug Act, the FDA may designate a drug as an orphan drug if it is intended to treat a rare disease or condition, which is defined as a patient population of fewer than 200,000 individuals in the United States. In the United States, Orphan Drug Designation entitles a party to financial incentives such as opportunities for tax credits for qualified clinical research costs and exemption from prescription drug user

fees. Similarly, in the EU, the European Commission grants Orphan Drug Designation after receiving the opinion of the EMA's Committee for Orphan Medicinal Products on an Orphan Drug Designation application. In the EU, Orphan Drug Designation is intended to promote the development of drug that are intended for the diagnosis, prevention or treatment of life-threatening or chronically debilitating conditions affecting not more than five in 10,000 persons in the EU and for which no satisfactory method of diagnosis, prevention or treatment has been authorized (or the product would be a significant benefit to those affected). In the EU, Orphan Drug Designation entitles a party to financial incentives such as reduction of fees or fee waivers.

Generally, if a drug with an Orphan Drug Designation subsequently receives the first marketing approval for the indication for which it has such designation, the drug is entitled to a period of marketing exclusivity, which precludes EMA or the FDA from approving another marketing application for the same drug and indication for that time period, except in limited circumstances. If a competitor is able to obtain orphan drug exclusivity prior to us for a product that constitutes the same active moiety and treats the same indications as our product candidates, we may not be able to obtain approval of our drug by the applicable regulatory authority for a significant period of time unless we are able to show that our drug is clinically superior to the approved drug. The applicable period is seven years in the United States and ten years in the EU. The EU exclusivity period can be reduced to six years if a drug no longer meets the criteria for Orphan Drug Designation or if the drug is sufficiently profitable so that market exclusivity is no longer justified.

Even after an orphan drug is approved, the FDA can also subsequently approve a later application for the same drug for the same condition if the FDA concludes that the later drug is clinically superior in that it is shown to be safer in a substantial portion of the target populations, more effective or makes a major contribution to patient care. In addition, a designated orphan drug may not receive orphan drug exclusivity if it is approved for a use that is broader than the indication for which it received orphan designation. Moreover, orphan drug exclusive marketing rights in the United States may be lost if the FDA later determines that the request for designation was materially defective or if we are unable to manufacture sufficient quantities of the product to meet the needs of patients with the rare disease or condition. Orphan Drug Designation neither shortens the development time or regulatory review time of a drug nor gives the drug any advantage in the regulatory review or approval process.

The orphan drug exclusivity contained in the Orphan Drug Act has been the subject of recent scrutiny from the press, from some members of Congress and from some in the medical community. Furthermore, the FDA's interpretations of the Orphan Drug Act have not been successfully challenged in court and future court decisions could continue that trend. There can be no assurances that the exclusivity granted to orphan drugs approved by the FDA will not be modified in the future, or as to how any such changes might affect our products, if approved.

The FDA's and the MHRA's ability to review and approve new products may be hindered by a variety of factors, including budget and funding levels, government shutdowns, ability to hire and retain key personnel, and statutory, regulatory and policy changes.

The ability of the FDA and the MHRA to review and approve new products can be affected by a variety of factors, including budget and funding levels, government shutdowns, ability to hire and retain key personnel, and statutory, regulatory, and policy changes. In addition, government funding of other government agencies that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable.

The ability of the FDA, the MHRA and other government agencies to properly administer their functions is highly dependent on the levels of government funding and the ability to fill key leadership appointments, among various factors. Delays in filling or replacing key positions could significantly impact the ability of the FDA, the MHRA and other agencies to fulfill their functions and could greatly impact healthcare and the pharmaceutical industry.

In December 2016, the 21st Century Cures Act was signed into law, and was designed to advance medical innovation and empower the FDA with the authority to directly hire positions related to drug and device development and review. In the past, the FDA was often unable to offer key leadership candidates (including scientists) competitive compensation packages as compared to those offered by private industry. The 21st Century Cures Act is designed to streamline the agency's hiring process and enable the FDA to compete for leadership talent by expanding the narrow ranges that are provided in the existing compensation structures.

Disruptions at the FDA, the MHRA and other governmental agencies may also slow the time necessary for new drugs to be reviewed or approved by necessary government agencies, which would adversely affect our operating results and business.

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

Healthcare providers and third-party payors will play a primary role in the recommendation and prescription of any product candidates for which we obtain marketing approval. Our future arrangements with providers, third-party payors and customers will subject us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell and distribute any product candidates for which we obtain marketing approval.

Restrictions under applicable U.S. federal and state healthcare laws and regulations include the following:

- the federal Anti-Kickback Statute prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made under government healthcare programs such as Medicare and Medicaid, and 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;
- federal false claims laws, including the federal False Claims Act, imposes criminal and civil penalties, including through civil whistleblower or qui tam actions, against individuals or entities for knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent (including claims for items and services resulting from a violation of the federal Anti-Kickback Statute) or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government, and certain marketing practices, including off-label promotion, may also violate false claims laws;
- the federal Health Insurance Portability and Accountability Act of 1996 ("HIPAA") imposes criminal and civil liability for, among other things, knowingly and willfully executing or attempting to execute a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act ("HITECH") and its implementing regulations, also imposes obligations, including mandatory contractual terms, on certain types of people and entities with respect to safeguarding the privacy, security and transmission of individually identifiable health information;
- the federal Physician Payment Sunshine Act requires applicable manufacturers of covered drugs, devices, biologics, and medical supplies for which payment is available under Medicare, Medicaid, or the Children's Health Insurance Program, with specific exceptions, to report annually payments and other transfers of value to physicians, physician assistants, certain types of advance practice nurses and teaching hospitals, or to entities or individuals at the request of, or designated on behalf of, such providers, and to report annually certain ownership and investment interests held by physicians and their immediate family, which includes annual data collection and reporting obligations; and
- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers.

Some state and local laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government and may require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers. Other state laws require pharmaceutical companies to report marketing expenditures or price increases that exceed a statutory threshold, as well as information on the reasons for the price increase, or to report the introduction into the market of costly drugs. State and foreign 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.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, imprisonment, exclusion of product candidates from government-funded healthcare programs, such as Medicare and Medicaid, disgorgement, contractual damages, reputational harm, diminished profits and future earnings, and the curtailment

or restructuring of our operations. If any of the physicians or other healthcare providers or entities with whom we expect to do business is found to be not in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government-funded healthcare programs.

Risks Related to Commercialization and Manufacturing

The commercial success of our product candidates, including STK-001 and STK-002, will depend upon their degree of market acceptance by providers, patients, patient advocacy groups, third-party payors and the general medical community.

Ethical, social and legal concerns about genetic treatments generally could result in additional regulations restricting or prohibiting our product candidates. Even with the requisite approvals from the FDA, the MHRA, the EMA and other regulatory authorities internationally, the commercial success of our product candidates will depend, in part, on the acceptance of providers, patients and third-party payors of drugs designed to increase protein expression in general, and our product candidates in particular, as medically necessary, cost-effective and safe. In addition, we may face challenges in seeking to establish and grow sales of STK-001, STK-002 and any future product candidates, including acceptance of intravitreal injection, the lumbar puncture and intrathecal administration, which carries risks of infection or other complications. Any product that we commercialize may not gain acceptance by providers, patients, patient advocacy groups, third-party payors and the general medical community. If these products do not achieve an adequate level of acceptance, we may not generate significant product revenue and may not become profitable. The degree of market acceptance of genetic medicines and, in particular, STK-001, STK-002 and our future product candidates, if approved for commercial sale, will depend on several factors, including:

- the efficacy, durability and safety of such product candidates as demonstrated in clinical trials;
- the potential and perceived advantages of product candidates over alternative treatments;
- the cost of treatment relative to alternative treatments;
- the clinical indications for which the product candidate is approved by the FDA, the MHRA or the European Commission;
- the willingness of providers to prescribe new therapies;
- the willingness of the target patient population to try new therapies;
- the prevalence and severity of any side effects;
- product labeling or product insert requirements of the FDA, MHRA, EMA or other regulatory authorities, including any limitations or warnings contained in a product's approved labeling;
- the willingness of providers to prescribe, and of patients to receive, intrathecal injections;
- the strength of marketing and distribution support;
- the timing of market introduction of competitive products;
- the quality of our relationships with patient advocacy groups;
- publicity concerning our product candidates or competing products and treatments; and
- sufficient third-party payor coverage and adequate reimbursement.

Even if a potential product displays a favorable efficacy and safety profile in preclinical studies and clinical trials, market acceptance of the product will not be fully known until after it is launched.

The pricing, insurance coverage and reimbursement status of newly approved products is uncertain. Failure to obtain or maintain adequate coverage and reimbursement for our product candidates, if approved, could limit our ability to market those products and decrease our ability to generate product revenue.

Our target indications, including Dravet syndrome and ADOA, are indications with small patient populations. For product candidates that are designed to treat smaller patient populations to be commercially viable, the reimbursement for such product candidates must be higher, on a relative basis, to account for the lack of volume. Accordingly, we will need to implement a coverage and reimbursement strategy for any approved product candidate that accounts for the smaller potential market size. If we are unable to establish or sustain coverage and adequate reimbursement for any future product candidates from third-party payors, the adoption of those product candidates and sales revenue will be adversely affected, which, in turn, could adversely affect the ability to market or sell those product candidates, if approved.

We expect that coverage and reimbursement by third-party payors will be essential for most patients to be able to afford these treatments. Accordingly, sales of STK-001, STK-002 and our future product candidates will depend substantially, both domestically and internationally, on the extent to which the costs of our product candidates will be paid by health maintenance, managed care, pharmacy benefit and similar healthcare management organizations, or will be reimbursed by government authorities, private health coverage insurers and other third-party payors. 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.

There is significant uncertainty related to the insurance coverage and reimbursement of newly approved products. In the United States, the principal decisions about reimbursement by government authorities for new products are typically made by the CMS since it decides whether and to what extent a new product will be covered and reimbursed under Medicare. Private payors tend to follow CMS to a substantial degree. However, one payor's determination to provide coverage for a drug product does not assure that other payors will also provide coverage for the drug product. Further, a payor's decision to provide coverage for a drug product does not imply that an adequate reimbursement rate will be approved. Reimbursement agencies in Europe may be more conservative than CMS. For example, a number of cancer drugs have been approved for reimbursement in the United States and have not been approved for reimbursement in certain European countries.

Outside the United States, 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, Canada and other countries has and will continue to put pressure on the pricing and usage of therapeutics such as our product candidates. In many countries, particularly the countries of the EU, the prices of medical products are subject to varying price control mechanisms as part of national health systems. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. To obtain reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of our product candidate to other available therapies. In general, the prices of products under such systems are substantially lower than in the United States. Other countries allow companies to fix their own prices for products, but monitor and control company profits. Additional foreign price controls or other changes in pricing regulation could restrict the amount that we are able to charge for our product candidates. Accordingly, in markets outside the United States, the reimbursement for our product candidates may be reduced compared with the United States and may be insufficient to generate commercially reasonable revenues and profits.

Moreover, increasing efforts by governmental and third-party payors, in the United States and internationally, to cap or reduce healthcare costs may cause such organizations to limit both coverage and level of reimbursement for new products approved and, as a result, they may not cover or provide adequate payment for our product candidates. We expect to experience pricing pressures in connection with the sale of any of our product candidates due to the trend toward managed healthcare, the increasing influence of certain third-party payors, such as health maintenance organizations, and additional legislative changes. The downward pressure on healthcare costs in general, particularly prescription drugs and surgical procedures and other treatments, has become very intense. As a result, increasingly high barriers are being erected to the entry of new products into the healthcare market. Recently there have been instances in which third-party payors have refused to reimburse treatments for patients for whom the treatment is indicated in the FDA-approved product label. Even if we are successful in obtaining FDA approvals to commercialize our product candidates, we cannot guarantee that we will be able to secure reimbursement for all patients for whom treatment with our product candidates is indicated.

In addition to CMS and private payors, professional organizations such as the American Medical Association can influence decisions about reimbursement for new products by determining standards for care. In addition, many private payors contract with commercial vendors who sell software that provide guidelines that attempt to limit utilization of, and therefore reimbursement for, certain products deemed to provide limited benefit to existing alternatives. Such organizations may set guidelines that limit reimbursement or utilization of our product candidates. Even if favorable coverage and reimbursement status is attained for one or more product candidates for which we or our collaborators receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

If third parties on which we depend to conduct our planned preclinical studies, any future clinical trials, or manufacturing of our product candidates do not perform as contractually required, fail to satisfy regulatory or legal requirements or miss expected deadlines, our development program could be delayed with adverse effects on our business, financial condition, results of operations and prospects.

We rely on third parties for genetic testing, and on third-party CROs, CMOs, consultants and others to design, conduct, supervise and monitor key activities relating to, discovery, manufacturing, preclinical studies and clinical trials of our product candidates, and we intend to do the same for future activities relating to existing and future programs. Because we rely on third parties and do not have the ability to conduct all required testing, discovery, manufacturing, preclinical studies or clinical trials independently, we have less control over the timing, quality and other aspects of discovery, manufacturing, preclinical studies and clinical trials than we would if we conducted them on our own. These investigators, CROs, CMOs and consultants are not our employees and we have limited control over the amount of time and resources that they dedicate to our programs. These third parties may have contractual relationships with other entities, some of which may be our competitors, which may draw time and resources from our programs. The third parties we contract with might not be diligent, careful or timely in conducting our discovery, manufacturing, preclinical studies or clinical trials, resulting in testing, discovery, manufacturing, preclinical studies or clinical trials being delayed or unsuccessful, in whole or in part. In addition, these third parties may be subject to macroeconomic conditions, such as staffing shortages and supply chain or inflationary pressures that limit their ability to achieve anticipated timelines or result in a greater cost to us. For example, we are aware of a shortage of NHPs available for preclinical studies and although that is not expected to impact our current business, if we begin new product development programs we could be subject to longer development times or difficulty completing necessary research.

If we cannot contract with acceptable third parties on commercially reasonable terms, or at all, or if these third parties do not carry out their contractual duties, satisfy legal and regulatory requirements for the conduct of preclinical studies or clinical trials or meet expected deadlines, our clinical development programs could be delayed and otherwise adversely affected. In all events, we are responsible for ensuring that each of our preclinical studies and clinical trials is conducted in accordance with the general investigational plan and protocols for the trial as well as regulatory requirements. Our reliance on third parties that we do not control does not relieve us of these responsibilities and requirements. Any such event could have an adverse effect on our business, financial condition, results of operations and prospects.

We face significant competition in an environment of rapid technological change and it is possible that our competitors may achieve regulatory approval before us or develop therapies that are more advanced or effective than ours, which may harm our business, financial condition and our ability to successfully market or commercialize STK-001, STK-002 and our future product candidates.

The biotechnology and pharmaceutical industries, including the genetic medicine and antisense oligonucleotide fields, are characterized by rapidly changing technologies, competition and a strong emphasis on intellectual property. We are aware of several companies focused on developing RNA-based treatments in various indications as well as several companies addressing other methods for modifying genes and regulating protein expression. We also expect to face competition from large and specialty pharmaceutical and biotechnology companies, academic research institutions, government agencies and public and private research institutions.

Numerous treatments for epilepsy exist, including 5-HT agonists, such as UCB's Fintepla, cannabidiols, such as Jazz Pharmaceuticals' Epidiolex, GABA receptor agonists, such as clobazam and stiripentol, and glutamate blockers, which is one of the mechanisms of action of topiramate. In addition, numerous compounds are in clinical development for treatment of epilepsy. We believe the clinical development pipeline includes cannabinoids, 5-HT release stimulants, cholesterol 24-hydroxylase inhibitors, potassium channel openers, and sodium channel agonists from a variety of companies. In addition to competition from these small molecule drugs, any products we may develop may also face competition from other types of therapies, such as gene therapy, gene editing, tRNA therapies, modified mRNA therapies or other ASO approaches. For example, one company (Encoded Therapeutics) has announced a clinical development plan for a gene regulation therapy in Dravet syndrome that may address the underlying genetic cause of the disease.

Many of our potential competitors, alone or with their strategic partners, have substantially greater financial, technical and other resources than we do, such as larger research and development, clinical, marketing and manufacturing organizations. Mergers and acquisitions in the biotechnology and pharmaceutical industries may result in even more resources being concentrated among a smaller number of competitors. Our commercial opportunity could be reduced or eliminated if competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than any product candidates that we may develop. Competitors also may obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market, if ever. Additionally,

new or advanced technologies developed by our competitors may render our current or future product candidates uneconomical or obsolete, and we may not be successful in marketing our product candidates against competitors.

To become and remain profitable, we must develop and eventually commercialize product candidates with significant market potential, which will require us to be successful in a range of challenging activities. These activities include, among other things, completing preclinical studies and initiating and completing clinical trials of our product candidates, obtaining marketing approval for these product candidates, manufacturing, marketing and selling those products that are approved and satisfying any post marketing requirements. We may never succeed in any or all of these activities and, even if we do, we may never generate revenues that are significant or large enough to achieve profitability. If we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would decrease the value of our company and could impair our ability to raise capital, maintain our research and development efforts, expand our business or continue our operations. A decline in the value of our company also could cause you to lose all or part of your investment.

The manufacture of drugs is complex and our third-party manufacturers may encounter difficulties in production. If any of our third-party manufacturers encounter such difficulties, our ability to provide supply of STK-001, STK-002 or our future product candidates for clinical trials, our ability to obtain marketing approval, or our ability to provide supply of our product candidates for patients, if approved, could be delayed or stopped.

We have established manufacturing relationships with a limited number of suppliers to manufacture raw materials and the drug substance of any product candidate for which we are responsible for preclinical or clinical development. Each supplier may require licenses to manufacture such components if such processes are not owned by the supplier or in the public domain. As part of any marketing approval, a manufacturer and its processes are required to be qualified by the FDA prior to commercialization. If supply from the approved vendor is interrupted, there could be a significant disruption in commercial supply. An alternative vendor would need to be qualified through an NDA supplement which could result in further delay. The FDA or other regulatory agencies outside of the United States may also require additional studies if a new supplier is relied upon for the manufacture of clinical trial materials or commercial production. Switching vendors may involve substantial costs and is likely to result in a delay in our desired clinical and commercial timelines.

The process of manufacturing drugs is complex, highly-regulated and subject to multiple risks. Manufacturing drugs is highly susceptible to product loss due to contamination, equipment failure, improper installation or operation of equipment, vendor or operator error, inconsistency in yields, variability in product characteristics and difficulties in scaling the production process. Even minor deviations from normal manufacturing processes could result in reduced production yields, product defects and other supply disruptions. If microbial, viral or other contaminations are discovered at the facilities of our manufacturers, such facilities may need to be closed for an extended period of time to investigate and remedy the contamination, which could delay clinical trials and adversely harm our business. Moreover, if the FDA determines that our manufacturers are not in compliance with FDA laws and regulations, including those governing CGMPs, the FDA may deny NDA approval until the deficiencies are corrected or we replace the manufacturer in our NDA with a manufacturer that is in compliance.

In addition, there are risks associated with large scale manufacturing for clinical trials or commercial scale including, among others, cost overruns, potential problems with process scale-up, process reproducibility, stability issues, compliance with good manufacturing practices, lot consistency and timely availability of raw materials. Even if we or our collaborators obtain regulatory approval for any of our product candidates, there is no assurance that manufacturers will be able to manufacture the approved product to specifications acceptable to the FDA or other regulatory authorities, to produce it in sufficient quantities to meet the requirements for the potential launch of the product or to meet potential future demand. If our manufacturers are unable to produce sufficient quantities for clinical trials or for commercialization, research and commercialization efforts would be impaired, which would have an adverse effect on our business, financial condition, results of operations and prospects.

Our reliance on a limited number of manufacturers, the complexity of drug manufacturing and the difficulty of scaling up a manufacturing process could cause the delay of clinical trials, regulatory submissions, required approvals or commercialization of our product candidates, cause us to incur higher costs and prevent us from commercializing our product candidates successfully. Furthermore, if our suppliers fail to deliver the required commercial quantities of materials on a timely basis and at commercially reasonable prices, and we are unable to secure one or more replacement suppliers capable of production in a timely manner at a substantially equivalent cost, our clinical trials may be delayed or we could lose potential revenue.

If we are unable to establish sales and marketing capabilities or enter into agreements with third parties to market and sell STK-001, STK-002 and our future product candidates, we may be unable to generate any revenues.

We currently do not have an organization for the sales, marketing and distribution of STK-001, STK-002 and our future product candidates and the cost of establishing and maintaining such an organization may exceed the cost-effectiveness of doing so. To market any products that may be approved, we must build our sales, marketing, managerial and other non-technical capabilities or make arrangements with third parties to perform these services. With respect to certain of our current programs as well as future programs, we may rely completely on an alliance partner for sales and marketing. In addition, although we intend to establish a sales organization if we are able to obtain approval to market any product candidates, we may enter into strategic alliances with third parties to develop and commercialize STK-001, STK-002 and other future product candidates, including in markets outside of the United States or for other large markets that are beyond our resources. This will reduce the revenue generated from the sales of these products.

Any future strategic alliance partners may not dedicate sufficient resources to the commercialization of our product candidates or may otherwise fail in their commercialization due to factors beyond our control. If we are unable to establish effective alliances to enable the sale of our product candidates to healthcare professionals and in geographical regions, including the United States, that will not be covered by our own marketing and sales force, or if our potential future strategic alliance partners do not successfully commercialize the product candidates, our ability to generate revenues from product sales will be adversely affected.

If we are unable to establish adequate sales, marketing and distribution capabilities, whether independently or with third parties, we may not be able to generate sufficient product revenue and may not become profitable. We will be competing with many companies that currently have extensive and well-funded marketing and sales operations. Without an internal team or the support of a third party to perform marketing and sales functions, we may be unable to compete successfully against these more established companies.

We may expend our limited resources to pursue a particular product candidate or indication and fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success.

Because we have limited financial and managerial resources, we focus on research programs and product candidates that we identify for specific indications. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to timely capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs and product candidates for specific indications may not yield any commercially viable products. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate.

We have entered into a collaboration with Acadia Pharmaceuticals and may, in the future, seek to enter into collaborations with other third parties for the discovery, development and commercialization of our product candidates. If our collaborators cease development efforts under our collaboration agreements, or if any of those agreements are terminated, these collaborations may fail to lead to commercial products and we may never receive milestone payments or future royalties under these agreements.

We have entered into a collaboration with Acadia Pharmaceuticals to discover or develop certain novel RNA-based medicines for the potential treatment of severe and rare genetic neurodevelopmental diseases of the central nervous system (“CNS”). The collaboration includes SYNGAP1 syndrome, Rett syndrome (MECP2), and an undisclosed neurodevelopmental target of mutual interest, and such collaboration could represent a significant portion of our product pipeline. We may derive a significant portion of our future revenue from these agreements or other similar agreements into which we may enter in the future. Revenue from research and development collaborations depends upon continuation of the collaborations, payments for research and development services and resulting options to acquire any licenses of successful product candidates, and the achievement of milestones, contingent payments and royalties, if any, derived from future products developed from our research.

Collaborations involving our product candidates currently pose, and will continue to pose, the following risks to us:

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

As a result of the foregoing, our current and any future collaboration agreements may not lead to development or commercialization of our product candidates in the most efficient manner or at all. If a collaborator of ours were to be involved in a business combination, the continued pursuit and emphasis on our product development or commercialization program could be delayed, diminished or terminated. Any failure to successfully develop or commercialize our product candidates pursuant to our current or any future collaboration agreements could have a material and adverse effect on our business, financial condition, results of operations and prospects.

Moreover, to the extent that any of our existing or future collaborators were to terminate a collaboration agreement, we may be forced to independently develop these product candidates, including funding preclinical studies or clinical trials, assuming marketing and distribution costs and defending intellectual property rights, or, in certain instances, abandon product candidates altogether, any of which could result in a change to our business plan and have a material adverse effect on our business, financial condition, results of operations and prospects.

We may not be successful in finding strategic collaborators for continuing development of certain of our future product candidates or successfully commercializing or competing in the market for certain indications.

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

that we may establish may not be favorable to us. Collaborations are complex and time-consuming to negotiate and document. In addition, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators.

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

The success of any potential collaboration arrangements will depend heavily on the efforts and activities of our collaborators. Collaborators generally have significant discretion in determining the efforts and resources that they will apply to these collaborations. Disagreements between parties to a collaboration arrangement regarding clinical development and commercialization matters can lead to delays in the development process or commercializing the applicable product candidate and, in some cases, termination of such collaboration arrangements. These disagreements can be difficult to resolve if neither of the parties has final decision-making authority. Collaborations with pharmaceutical or biotechnology companies and other third parties often are terminated or allowed to expire by the other party. Any such termination or expiration would adversely affect us financially and could harm our business reputation.

Risks Related to our Financial Position

We have a history of operating losses, and we may not achieve or sustain profitability. We anticipate that we will continue to incur losses for the foreseeable future. If we fail to obtain additional funding to conduct our planned research and development effort, we could be forced to delay, reduce or eliminate our product development programs or commercial development efforts.

We are an early-stage biotechnology company with a limited operating history on which to base your investment decision. Biotechnology product development is a highly speculative undertaking and involves a substantial degree of risk. Our operations to date have been limited primarily to organizing and staffing our company, business planning, raising capital, acquiring and developing product and technology rights, manufacturing, and conducting research and development activities for our product candidates. We have never generated any revenue from product sales. We have not obtained regulatory approvals for any of our product candidates, and have funded our operations to date through proceeds from sales of our preferred stock and common stock.

We have incurred net losses in each year since our inception. We incurred net losses of $104.7 million and $101.1 million, for the years ended December 31, 2023 and 2022, respectively. As of December 31, 2023, we had accumulated deficits of $401.8 million. Substantially all of our operating losses have resulted from costs incurred in connection with our research and development programs and from general and administrative costs associated with our operations. We expect to continue to incur significant expenses and operating losses over the next several years and for the foreseeable future as we intend to continue to conduct research and development, clinical testing, regulatory compliance activities, manufacturing activities, and, if any of our product candidates is approved, sales and marketing activities that, together with anticipated general and administrative expenses, will likely result in us incurring significant losses for the foreseeable future. Our prior losses, combined with expected future losses, have had and will continue to have an adverse effect on our stockholders' equity and working capital.

We expect that we will need to raise additional funding before we can expect to become profitable from any potential future sales of STK-001, STK-002 or our future product candidates. This additional financing may not be available on acceptable terms or at all. Failure to obtain this necessary capital when needed may force us to delay, limit or terminate our product development efforts or other operations.

We will require substantial future capital in order to complete planned and future preclinical and clinical development for STK-001, STK-002 and other future product candidates, if any, and potentially commercialize these product candidates. Based upon our current operating plan, we believe that our cash, cash equivalents and marketable securities of $201.4 million as of December 31, 2023 will enable us to fund our operating expenses and capital expenditure requirements to the end of 2025. We expect our spending levels to increase in connection with our preclinical studies and clinical trials of our product candidates. In addition, if we obtain marketing approval for any of our product candidates, we expect to incur significant expenses related to commercial launch, product sales, medical affairs, marketing, manufacturing and distribution.

Furthermore, we expect to incur additional costs associated with operating as a public company. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. If we are unable to raise capital when needed or on attractive terms, we would be forced to delay, reduce or eliminate certain of our licensing activities, our research and development programs or other operations.

Additional capital might not be available when we need it and our actual cash requirements might be greater than anticipated. If we require additional capital at a time when investment in our industry or in the marketplace in general is limited, we might not be able to raise funding on favorable terms if at all. If we are not able to obtain financing on terms favorable to us, we may need to cease or reduce development or commercialization activities, sell some or all of our assets or merge with another entity, which could result in a loss of all or part of your investment.

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

- the costs associated with the scope, progress and results of discovery, preclinical development, laboratory testing and clinical trials for our product candidates;
- the costs associated with the development of our internal manufacturing facility and processes;
- the costs related to the extent to which we enter into partnerships or other arrangements with third parties to further develop our product candidates;
- the costs and fees associated with the discovery, acquisition or in-license of product candidates or technologies;
- our ability to establish collaborations on favorable terms, if at all;
- the costs of future commercialization activities, if any, including product sales, marketing, manufacturing and distribution, for any of our product candidates for which we receive marketing approval;
- revenue, if any, received from commercial sales of our product candidates, should any of our product candidates receive marketing approval; and
- the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims.

Our product candidates, if approved, may not achieve commercial success. Our commercial revenues, if any, will be derived from sales of product candidates 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, which may not be available to us on acceptable terms, or at all.

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

We are a clinical stage biotechnology company formed in June 2014. Our operations to date have been limited to organizing and staffing our company, business planning, raising capital, acquiring our technology, identifying potential product candidates, undertaking research, preclinical and clinical development of our product candidates, manufacturing, and establishing licensing arrangements. We have not yet demonstrated the ability to complete clinical trials of our product candidates, obtain marketing approvals, manufacture a commercial scale product or conduct sales and marketing activities necessary for successful commercialization. Consequently, any predictions you make about our future success or viability may not be as accurate as they could be if we had a longer operating history.

In addition, as a new business, we may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown factors. We will need to transition from a company with a licensing and research focus to a company that is also capable of supporting clinical development and commercial activities. We may not be successful in such a transition.

Our ability to utilize our net operating loss carryforwards may be subject to limitations.

We have incurred substantial losses during our history. We do not expect to be profitable soon and may never achieve profitability. As of December 31, 2023, we had federal and state net operating loss carryforwards, or NOLs, of approximately $189.5 million and $199.4 million, respectively, and as of December 31, 2022, we had federal and state NOLs of approximately $210.9 million and $212.8 million, respectively. Our pre-2018 NOLs expire at various dates beginning in 2034. In general, NOLs generated in and after 2018 have no expiration. To the extent that we continue to generate NOLs, unused NOLs carry forward to offset future taxable income until such NOLs expire. Under Sections 382 and 383 of the Internal Revenue Code of 1986 ("IRC"), as amended, or the Code, if a corporation undergoes an “ownership change,”

generally defined as a greater than 50% change (by value) in its equity ownership over a three-year period, the corporation's ability to use its pre-change NOLs and other pre-change tax attributes (such as research tax credits) to offset its post-change income may be limited. The Company recently performed an IRC 382 study and identified ownership changes in prior years. Based on existing Section 382 limitations, $0.9 million of the existing federal NOL will not be utilizable due to restrictive limitations. We may experience additional ownership changes in the future because of subsequent shifts in our stock ownership. As a result, our ability to use our pre-change NOLs to offset U.S. federal taxable income, if any, is subject to limitations, which could potentially result in increased future tax liability. In addition, at the state level, there may be periods during which the use of NOLs is suspended or otherwise limited, which could accelerate or permanently increase state taxes owed.

U.S. federal income tax reform and changes in other tax laws could adversely affect us.

In December 2017, U.S. federal tax legislation, commonly referred to as the Tax Cuts and Jobs Act (the "TCJA") was signed into law, significantly reforming the Code. The TCJA, among other things, includes changes to U.S. federal tax rates, imposes significant additional limitations on the deductibility of business interest, allows for the expensing of capital expenditures, puts into effect the migration from a "worldwide" system of taxation to a partial "territorial" system, and modifies or repeals many business deductions and credits. Beginning in 2022, the TCJA also eliminated the option to immediately deduct research and development expenditures and required taxpayers to amortize domestic expenditures over five years and foreign expenditures over fifteen years.

We continue to examine the impact the TCJA may have on our business. The TCJA is a far-reaching and complex revision to the U.S. federal income tax laws with disparate and, in some cases, countervailing impacts on different categories of taxpayers and industries, and will require subsequent rulemaking and interpretation in a number of areas. The long-term impact of the TCJA on the overall economy, the industries in which we operate and our and our partners' businesses cannot be reliably predicted at this early stage of the new law's implementation. There can be no assurance that the TCJA will not negatively impact our operating results, financial condition, and future business operations. The estimated impact of the TCJA is based on our management's current knowledge and assumptions, following consultation with our tax advisors.

Because of our valuation allowance in the U.S., ongoing tax effects of the Act are not expected to materially change our effective tax rate in future periods.

Risks Related to our Intellectual Property

Our success depends in part on our ability to obtain, maintain and protect our intellectual property. It is difficult and costly to protect our proprietary rights and technology, and we may not be able to ensure their protection.

Our commercial success will depend in large part on obtaining and maintaining patent, trademark, trade secret and other intellectual property protection of our proprietary technologies and product candidates, which include TANGO, STK-001, STK-002 and the additional gene targets identified by TANGO, their respective components, formulations, combination therapies, methods used to manufacture them and methods of treatment, as well as successfully defending our patents and other intellectual property rights against third-party challenges. Our ability to stop unauthorized third parties from making, using, selling, offering to sell, importing or otherwise commercializing our product candidates is dependent upon the extent to which we have rights under valid and enforceable patents or trade secrets that cover these activities. If we are unable to secure and maintain patent protection for any product or technology we develop, or if the scope of the patent protection secured is not sufficiently broad, our competitors could develop and commercialize products and technology similar or identical to ours, and our ability to commercialize any product candidates we may develop may be adversely affected. The patenting process is expensive and time-consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. In addition, we may not pursue or obtain patent protection in all relevant markets. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. Moreover, in some circumstances, we may not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the patents, covering technology that we license from or license to third parties and are reliant on our licensors or licensees to do so. Our pending and future patent applications may not result in issued patents. Even if patent applications we license or own currently or in the future issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors or other third parties from competing with us, or otherwise provide us with any competitive advantage. Any patents that we hold or in-license may be challenged, narrowed, circumvented, or invalidated by third parties. Consequently, we do not know whether any of our platform advances and product candidates will be protectable or remain protected by valid and enforceable patents. In addition, our existing patents and any future patents we obtain may not be sufficiently broad to prevent others from using our technology or from developing competing products and technologies.

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

We are dependent on patents, know-how and proprietary technology licensed from others. Our licenses to such patents, know-how and proprietary technology may not provide exclusive rights in all relevant fields of use and in all territories in which we may wish to develop or commercialize our products in the future. The agreements under which we license patents, know-how and proprietary technology from others are complex, and certain provisions in such agreements may be susceptible to multiple interpretations.

For example, we are a party to a license agreement with the University of Southampton, pursuant to which we in-license key patents and patent applications for our TANGO platform, STK-001, STK-002 and our future product candidates. For more information regarding the agreement, please see "Business—License and research agreements." The agreement imposes various diligence, milestone payment, royalty, insurance and other obligations on us. If we fail to comply with these obligations, our licensor may have the right to terminate our license, in which event we would not be able to develop or market our TANGO platform, STK-001, STK-002 or any other technology or product candidates covered by the intellectual property licensed under the agreement. In addition, we may need to obtain additional licenses from our existing licensor and others to advance our research or allow commercialization of product candidates we may develop. It is possible that we may be unable to obtain any additional licenses at a reasonable cost or on reasonable terms, if at all. In either event, we may be required to expend significant time and resources to redesign our technology, product candidates, or the methods for manufacturing them or to develop or license replacement technology, all of which may not be feasible on a technical or commercial basis. If we are unable to do so, we may be unable to develop or commercialize the affected technology or product candidates.

If we or our existing or future licensors fail to adequately protect our licensed intellectual property, our ability to commercialize product candidates could suffer. We do not have complete control over the maintenance, prosecution and litigation of our in-licensed patents and patent applications and may have limited control over future intellectual property that may be in-licensed. For example, we cannot be certain that activities such as the maintenance and prosecution by our existing or future licensors have been or will be conducted in compliance with applicable laws and regulations or will result in valid and enforceable patents and other intellectual property rights. It is possible that our existing or future licensors' infringement proceedings or defense activities may be less vigorous than had we conducted them ourselves, or may not be conducted in accordance with our best interests.

Furthermore, inventions contained within some of our existing or future in-licensed patents and patent applications may be made using U.S. government funding or other non-governmental funding. We rely on our existing or future licensors to ensure compliance with applicable obligations arising from such funding, such as timely reporting, an obligation associated with in-licensed patents and patent applications. The failure of our existing or future licensors to meet their obligations may lead to a loss of rights or the unenforceability of relevant patents. For example, the government could have certain rights in such in-licensed patents, including a non-exclusive license authorizing the government to use the invention or to have others use the invention on its behalf for non-commercial purposes. If the U.S. government then decides to exercise these rights, it is not required to engage us as its contractor in connection with doing so. These rights may also permit the government to exercise march-in rights to use or allow third parties to use the technology covered by such in-licensed patents. The government may also exercise its march-in rights if it determines that action is necessary because we or our licensors failed to achieve practical application of the government-funded technology, because action is necessary to alleviate health or safety needs, to meet requirements of federal regulations, or to give preference to U.S. industry. In addition, our rights in such in-licensed government-funded inventions may be subject to certain requirements to manufacture products embodying such inventions in the United States. Any of the foregoing could harm our business, financial condition, results of operations, and prospects significantly.

In addition, 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 patents, know-how and proprietary technology, or increase what we believe to be our financial or other obligations under the relevant agreement. Disputes that may arise between us and our existing or future licensors regarding intellectual property subject to a license agreement could include disputes regarding:

- 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 product candidates 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.

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 technology or product candidates. As a result, any termination of or disputes over our intellectual property licenses could result in the loss of our ability to develop and commercialize our TANGO platform, STK-001, or STK-002, or we could lose other significant rights, any of which could have a material adverse effect on our business, financial condition, results of operations, and prospects.

Moreover, our agreements with certain of our third-party research partners provide that improvements developed in the course of our relationship may be owned solely by either us or our third-party research partner, or jointly between us and the third party. If we determine that rights to such improvements owned solely by a research partner or other third party with whom we collaborate are necessary to commercialize our drug candidates or maintain our competitive advantage, we may need to obtain a license from such third party in order to use the improvements and continue developing, manufacturing or marketing our drug candidates. We may not be able to obtain such a license on an exclusive basis, on commercially reasonable terms, or at all, which could prevent us from commercializing our drug candidates or allow our competitors or others the chance to access technology that is important to our business. We also may need the cooperation of any co-owners of our intellectual property in order to enforce such intellectual property against third parties, and such cooperation may not be provided to us.

Our owned and in-licensed patents and patent applications may not provide sufficient protection of our TANGO platform, our STK-001 and STK-002 product candidates, and our future product candidates or result in any competitive advantage.

We own an issued U.S. patent covering STK-001 and related compositions, an issued U.S. patent covering the mechanism of action of STK-001 and use of STK-001 for treating diseases, and a pending PCT international application and five pending U.S. patent applications covering STK-001 and related compositions, and use of STK-001 for treating diseases. We have also in-licensed two issued U.S. patents and at least six issued foreign patents that cover the mechanism of action of STK-001, use of the mechanism for treating diseases, and related compositions. We have obtained at least fifteen issued foreign patents covering STK-001, related compositions and its uses and are currently pursuing patent protection for STK-001, related compositions, and its uses in several economically significant countries. With respect to STK-002, we have applied for and are currently pursuing patent protection for the mechanism of action, compositions related to STK-002, and uses of those compositions in several economically significant countries. We own an issued U.S. patent and an issued foreign patent covering STK-002 and related compositions. We also own a pending PCT international application and numerous pending U.S. and foreign patent applications covering STK-002 and related compositions, mechanism of action and use of STK-002 for treating diseases. Furthermore, our in-licensed issued U.S. patents and foreign patents (mentioned above) cover the mechanism of action of STK-002. We cannot be certain that any of these pending patent applications will issue as patents, and if they do, that such patents will cover or adequately protect STK-001, STK-002 and other programs or that such patents will not be challenged, narrowed, circumvented, invalidated or held unenforceable.

In addition to claims directed toward the technology underlying our TANGO platform, our owned and in-licensed patents and patent applications contain claims directed to compositions of matter on the active pharmaceutical ingredients ("APIs") in our product candidates, as well as methods-of-use directed to the use of an API for a specified treatment. Composition-of-matter patents on the active pharmaceutical ingredient in prescription drug products provide protection without regard to any particular method of use of the API used. Method-of-use patents do not prevent a competitor or other third party from developing or marketing an identical product for an indication that is outside the scope of the patented method. Moreover, with respect to method-of-use patents, even if competitors or other third parties do not actively promote their product for our targeted indications or uses for which we may obtain patents, providers may recommend that patients use these products off-label, or patients may do so themselves. Although off-label use may infringe or contribute to the infringement of method-of-use patents, the practice is common and this type of infringement is difficult to prevent or prosecute.

The strength of patents in the biotechnology and pharmaceutical field involves complex legal and scientific questions and can be uncertain. The patent applications that we own or in-license may fail to result in issued patents with claims that cover our product candidates or uses thereof in the United States or in other foreign countries. For example, while our patent applications are pending, we may be subject to a third party preissuance submission of prior art to the United States Patent and Trademark Office (the "USPTO") or become involved in interference or derivation proceedings, or equivalent proceedings in foreign jurisdictions. Even if patents do successfully issue, third parties may challenge their inventorship,

validity, enforceability or scope, including through opposition, revocation, reexamination, post-grant and *inter partes* review proceedings. An adverse determination in any such submission, proceeding or litigation may result in loss of patent rights, loss of exclusivity, or in patent claims being narrowed, invalidated, or held unenforceable, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology and product candidates. Furthermore, even if they are unchallenged, our patents and patent applications may not adequately protect our intellectual property or prevent others from designing around our claims. Moreover, some of our owned and in-licensed patents and patent applications may be co-owned with third parties. If we are unable to obtain an exclusive license to any such third-party co-owners' interest in such patents or patent applications, such 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. In addition, we may need the cooperation of any such co-owners of our patents in order to enforce such patents against third parties, and such cooperation may not be provided to us. If the breadth or strength of protection provided by the patent applications we hold with respect to our product candidates is threatened, it could dissuade companies from collaborating with us to develop, and threaten our ability to commercialize, our product candidates. Further, if we encounter delays in development, testing, and regulatory review of new product candidates, the period of time during which we could market our product candidates under patent protection would be reduced.

Since patent applications in the United States and other countries are confidential for a period of time after filing, at any moment in time, we cannot be certain that we were in the past or will be in the future the first to file any patent application related to our product candidates. In addition, some patent applications in the United States may be maintained in secrecy until the patents are issued. As a result, there may be prior art of which we are not aware that may affect the validity or enforceability of a patent claim, and we may be subject to priority disputes. We may be required to disclaim part or all of the term of certain patents or all of the term of certain patent applications. There may be prior art of which we are not aware that may affect the validity or enforceability of a patent claim. There also may be prior art of which we are aware, but which we do not believe affects the validity or enforceability of a claim, which may, nonetheless, ultimately be found to affect the validity or enforceability of a claim. No assurance can be given that, if challenged, our patents would be declared by a court, patent office or other governmental authority to be valid or enforceable or that even if found valid and enforceable, a competitor's technology or product would be found by a court to infringe our patents. We may analyze patents or patent applications of our competitors that we believe are relevant to our activities, and consider that we are free to operate in relation to our product candidates, but our competitors may achieve issued claims, including in patents we consider to be unrelated, that block our efforts or potentially result in our product candidates or our activities infringing such claims. It is possible that our competitors may have filed, and may in the future file, patent applications covering our products or technology similar to ours. Those patent applications may have priority over our owned and in-licensed patent applications or patents, which could require us to obtain rights to issued patents covering such technologies. The possibility also exists that others will develop products that have the same effect as our product candidates on an independent basis that do not infringe our patents or other intellectual property rights, or will design around the claims of patents that we have had issued that cover our product candidates.

Likewise, our currently owned and in-licensed patents and patent applications, if issued as patents, directed to our proprietary technologies and our product candidates are expected to expire from 2035 through 2044, without taking into account any possible patent term adjustments or extensions. Our earliest in-licensed patents may expire before, or soon after, our first product achieves marketing approval in the United States or foreign jurisdictions. Additionally, we cannot be assured that the USPTO or relevant foreign patent offices will grant any of the pending patent applications we own or in-license currently or in the future. Upon the expiration of our current patents, we may lose the right to exclude others from practicing these inventions. The expiration of these patents could also have a similar material adverse effect on our business, financial condition, results of operations and prospects.

The degree of future protection for our proprietary rights is uncertain because legal means afford only limited protection and may not adequately protect our rights or permit us to gain or keep our competitive advantage. For example:

- others may be able to make or use compounds that are similar to the active compositions of our product candidates but that are not covered by the claims of our patents;
- the active pharmaceutical ingredients in our current product candidates will eventually become commercially available in generic drug products, and no patent protection may be available with regard to formulation or method of use;
- we or our licensors, as the case may be, may fail to meet our obligations to the U.S. government regarding any in-licensed patents and patent applications funded by U.S. government grants, leading to the loss or unenforceability of patent rights;

- we or our licensors, as the case may be, might not have been the first to file patent applications for certain inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies;
- it is possible that our pending patent applications will not result in issued patents;
- it is possible that there are prior public disclosures that could invalidate our owned or in-licensed patents, as the case may be, or parts of our owned or in-licensed patents;
- it is possible that others may circumvent our owned or in-licensed patents;
- it is possible that there are unpublished applications or patent applications maintained in secrecy that may later issue with claims covering our product candidates or technology similar to ours;
- the laws of foreign countries may not protect our or our licensors', as the case may be, proprietary rights to the same extent as the laws of the United States;
- the claims of our owned or in-licensed issued patents or patent applications, if and when issued, may not cover our product candidates;
- our owned or in-licensed issued patents may not provide us with any competitive advantages, may be narrowed in scope, or be held invalid or unenforceable as a result of legal challenges by third parties;
- the inventors of our owned or in-licensed patents or patent applications may become involved with competitors, develop products or processes that design around our patents, or become hostile to us or the patents or patent applications on which they are named as inventors;
- it is possible that our owned or in-licensed patents or patent applications omit individual(s) that should be listed as inventor(s) or include individual(s) that should not be listed as inventor(s), which may cause these patents or patents issuing from these patent applications to be held invalid or unenforceable;
- we have engaged in scientific collaborations in the past and will continue to do so in the future and our collaborators may develop adjacent or competing products that are outside the scope of our patents;
- we may not develop additional proprietary technologies for which we can obtain patent protection;
- it is possible that product candidates or diagnostic tests we develop may be covered by third parties' patents or other exclusive rights; or
- the patents of others may have an adverse effect on our business.

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

Our strategy of obtaining rights to key technologies through in-licenses may not be successful.

We seek to expand our product candidate pipeline in part by in-licensing the rights to key technologies, including those related to specific gene targets which may be upregulated by TANGO. The future growth of our business will depend in part on our ability to in-license or otherwise acquire the rights to additional product candidates and technologies. Although we have succeeded in licensing technologies from the University of Southampton in the past, we cannot assure you that we will be able to in-license or acquire the rights to any product candidates or technologies from third parties on acceptable terms or at all.

For example, our agreements with certain of our third-party research partners provide that improvements developed in the course of our relationship may be owned solely by either us or our third-party research partner, or jointly between us and the third party. If we determine that exclusive rights to such improvements owned solely by a research partner or other third party with whom we collaborate are necessary to commercialize our drug candidates or maintain our competitive advantage, we may need to obtain an exclusive license from such third party in order to use the improvements and continue developing, manufacturing or marketing our drug candidates. We may not be able to obtain such a license on an exclusive basis, on commercially reasonable terms, or at all, which could prevent us from commercializing our drug candidates or allow our competitors or others the opportunity to access technology that is important to our business. We also may need the cooperation of any co-owners of our intellectual property in order to enforce such intellectual property against third parties, and such cooperation may not be provided to us.

In addition, the in-licensing and acquisition of these technologies is a highly competitive area, and a number of more established companies are also pursuing strategies to license or acquire product candidates or technologies that we may consider attractive. These established companies may have a competitive advantage over us due to their size, cash resources and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to license rights to us. Furthermore, we may be unable to identify suitable product candidates or technologies within our area of focus. If we are unable to successfully obtain rights to suitable product candidates or technologies, our business and prospects could be materially and adversely affected.

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

In addition to patent protection, we rely upon know-how and trade secret protection, as well as non-disclosure agreements and invention assignment agreements with our employees, consultants and third-parties, to protect our confidential and proprietary information, especially where we do not believe patent protection is appropriate or obtainable.

It is our policy to require our employees, consultants, outside scientific collaborators, sponsored researchers and other advisors to execute confidentiality agreements upon the commencement of employment or consulting relationships with us. These agreements provide that all confidential information concerning our business or financial affairs developed or made known to the individual or entity during the course of the party's relationship with us is to be kept confidential and not disclosed to third parties, except in certain specified circumstances. In the case of employees, the agreements provide that all inventions conceived by the individual, and that are related to our current or planned business or research and development or made during normal working hours, on our premises or using our equipment or proprietary information, are our exclusive property. In the case of consultants and other third parties, the agreements provide that all inventions conceived in connection with the services provided are our exclusive property. However, we cannot guarantee that we have entered into such agreements with each party that may have or have had access to our trade secrets or proprietary technology and processes. We have also adopted policies and conduct training that provides guidance on our expectations, and our advice for best practices, in protecting our trade secrets. Despite these efforts, any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches.

In addition to contractual measures, we try to protect the confidential nature of our proprietary information through other appropriate precautions, such as physical and technological security measures. However, trade secrets and know-how can be difficult to protect. These measures may not, for example, in the case of misappropriation of a trade secret by an employee or third party with authorized access, provide adequate protection for our proprietary information. Our security measures may not prevent an employee or consultant from misappropriating our trade secrets and providing them to a competitor, and any recourse we might take against this type of misconduct may not provide an adequate remedy to protect our interests fully. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret can be difficult, expensive, and time-consuming, and the outcome is unpredictable. In addition, trade secrets may be independently developed by others in a manner that could prevent us from receiving legal recourse. If any of our confidential or proprietary information, such as our trade secrets, were to be disclosed or misappropriated, or if any of that information was independently developed by a competitor, our competitive position could be harmed.

In addition, courts outside the United States are sometimes less willing to protect trade secrets. If we choose to go to court to stop a third party from using any of our trade secrets, we may incur substantial costs. Even if we are successful, these types of lawsuits may consume our time and other resources. Although we take steps to protect our proprietary information and trade secrets, third parties may independently develop substantially equivalent proprietary information and techniques or otherwise gain access to our trade secrets or disclose our technology. As a result, we may not be able to meaningfully protect our trade secrets. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations and prospects.

Third-party claims of intellectual property infringement may prevent, delay or otherwise interfere with our product discovery and development efforts.

Our commercial success depends in part on our ability to develop, manufacture, market and sell our product candidates and use our proprietary technologies without infringing, misappropriating or otherwise violating the intellectual property or proprietary rights of third parties. There is a substantial amount of 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, *inter partes* review, post grant review, and reexamination proceedings before the USPTO or oppositions and other comparable proceedings in foreign jurisdictions. We may be exposed to, or threatened with, future litigation by third parties having patent or other intellectual property rights alleging that our product candidates and/or proprietary technologies infringe, misappropriate or otherwise violate their intellectual property rights. Numerous U.S. and

foreign issued patents and pending patent applications that are owned by third parties, such as Ionis Pharmaceuticals, exist in the fields in which we are developing our product candidates. As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our product candidates may give rise to claims of infringement of the patent rights of others. Moreover, it is not always clear to industry participants, including us, which patents cover various types of drugs, products or their methods of use or manufacture. Thus, because of the large number of patents issued and patent applications filed in our field, third parties may allege they have patent rights encompassing our product candidates, technologies or methods.

If a third party claims that we infringe, misappropriate or otherwise violate its intellectual property rights, we may face a number of issues, including, but not limited to:

- infringement and other intellectual property claims that, regardless of merit, may be expensive and time-consuming to litigate and may divert our management's attention from our core business;
- substantial damages for infringement, which we may have to pay if a court decides that the product candidate or technology at issue infringes on or violates the third party's rights, and, if the court finds that the infringement was willful, we could be ordered to pay treble damages plus the patent owner's attorneys' fees;
- a court prohibiting us from developing, manufacturing, marketing or selling our product candidates, or from using our proprietary technologies, unless the third party licenses its product rights to us, which it is not required to do, on commercially reasonable terms or at all;
- if a license is available from a third party, we may have to pay substantial royalties, upfront fees and other amounts, and/or grant cross-licenses to intellectual property rights for our product candidates;
- the requirement that we redesign our product candidates or processes so they do not infringe, which may not be possible or may require substantial monetary expenditures and time; and
- 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.

Some of our competitors may be able to sustain the costs of complex patent litigation more effectively than we can because they have substantially greater resources. In addition, any uncertainties resulting from the initiation and continuation of any litigation could have a material adverse effect on our ability to raise the funds necessary to continue our operations or could otherwise have a material adverse effect on our business, financial condition, results of operations and prospects.

Third parties may assert that we are employing their proprietary technology without authorization, including by enforcing its patents against us by filing a patent infringement lawsuit against us. In this regard, patents issued in the United States by law enjoy a presumption of validity that can be rebutted only with evidence that is "clear and convincing," a heightened standard of proof.

There may be third-party patents of which we are currently unaware with claims to materials, formulations, methods of manufacture or methods for treatment related to the use or manufacture of our product candidates. Because patent applications can take many years to issue, there may be currently pending patent applications that may later result in issued patents that our product candidates may infringe. In addition, third parties may obtain patents in the future and claim that use of our technologies infringes upon these patents.

If any third-party patents were held by a court of competent jurisdiction to cover the manufacturing process of our product candidates, or materials used in or formed during the manufacturing process, or any final product itself, the holders of those patents may be able to block our ability to commercialize our product candidate unless we obtain a license under the applicable patents, or until those patents were to expire or those patents are finally determined to be invalid or unenforceable. Similarly, if any third-party patent were held by a court of competent jurisdiction to cover aspects of our formulations, processes for manufacture or methods of use, including combination therapy or patient selection methods, the holders of that patent may be able to block our ability to develop and commercialize the product candidate unless we obtain a license or until such patent expires or is finally determined to be invalid or unenforceable. In either case, a license may not be available on commercially reasonable terms, or at all, particularly if such patent is owned or controlled by one of our primary competitors. If we are unable to obtain a necessary license to a third-party patent on commercially reasonable terms, or at all, our ability to commercialize our product candidates may be impaired or delayed, which could significantly harm our business. Even if we obtain a license, it may be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. In addition, if the breadth or strength of protection provided by our patents and patent applications is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates.

Parties making claims against us may seek and obtain injunctive or other equitable relief, which could effectively block our ability to further develop and commercialize our product candidates. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee time and resources from our business. In the event of a successful claim of infringement against us, 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 or redesign our infringing products, which may be impossible or require substantial time and monetary expenditure. We cannot predict whether any license of this nature would be available at all or whether it would be available on commercially reasonable terms. Furthermore, even in the absence of litigation, we may need to obtain licenses from third parties to advance our research or allow commercialization of our product candidates and we may fail to obtain any of these licenses at a reasonable cost or on reasonable terms, if at all. In that event, we would be unable to further develop and commercialize our product candidates, which could significantly harm our business.

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

Competitors may infringe our patents or the patents of our licensors. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time-consuming. In addition, in an infringement proceeding, a court may decide that one or more of our patents is not valid or is unenforceable, or may refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question.

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

Conversely, we may choose to challenge the patentability of claims in a third party's U.S. patent by requesting that the USPTO review the patent claims in re-examination, post-grant review, *inter partes* review, interference proceedings, derivation proceedings, and equivalent proceedings in foreign jurisdictions (e.g., opposition proceedings), or we may choose to challenge a third party's patent in patent opposition proceedings in the European Patent Office (the "EPO") or another foreign patent office. Even if successful, the costs of these opposition proceedings could be substantial, and may consume our time or other resources. If we fail to obtain a favorable result at the USPTO, the EPO or other patent office then we may be exposed to litigation by a third party alleging that the patent may be infringed by our product candidates or proprietary technologies.

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, that perception could have a substantial adverse effect on the price of our common stock. Any of the foregoing could have a material adverse effect on our business financial condition, results of operations and prospects.

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

We have limited intellectual property rights outside the United States. Filing, prosecuting and defending patents on product candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States can be less extensive than those in the United States. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the United States. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we have patent protection but where enforcement is not as strong as that in the United States. These products may compete with our product candidates in jurisdictions where we do not have any issued patents and our patent claims or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets and other intellectual property protection, particularly those relating to biopharmaceutical products, which could make it difficult for us to stop the infringement of our patents or marketing of competing products against third parties in violation of our proprietary rights generally. The initiation of proceedings by third parties to challenge the scope or validity of our patent rights in foreign jurisdictions could result in substantial cost and divert our efforts and attention from other aspects of our business. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly and our patent applications at risk of not issuing and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded, if any, may not be commercially meaningful. 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.

Geopolitical actions in the United States and in foreign countries could increase the uncertainties and costs surrounding the prosecution or maintenance of our patent applications or those of any current or future licensors and the maintenance, enforcement or defense of our issued patents or those of any current or future licensors. For example, the United States and foreign government actions related to Russia's invasion of Ukraine may limit or prevent filing, prosecution and maintenance of patent applications in Russia. Government actions may also prevent maintenance of issued patents in Russia. These actions could result in abandonment or lapse of our patents or patent applications, resulting in partial or complete loss of patent rights in Russia. In addition, a decree was adopted by the Russian government in March 2022, allowing Russian companies and individuals to exploit inventions owned by patentees that have citizenship or nationality in, are registered in, or have predominately primary place of business or profit-making activities in the United States and other countries that Russia has deemed unfriendly without consent or compensation. Consequently, we would not be able to prevent third parties from practicing our inventions in Russia or from selling or importing products made using our inventions in and into Russia. Similarly, the ongoing conflict in Israel could result in regulatory delays or the inability to secure intellectual property or commercialize our products there. Accordingly, our competitive position may be impaired, and our business, financial condition, results of operations and prospects may be adversely affected.

Our use of open source software could impose limitations on our ability to commercialize our product candidates.

Our use of open source software could impose limitations on our ability to commercialize our product candidates. Our technology utilizes open source software that contains modules licensed for use from third-party authors under open source licenses. In particular, some of the software that powers TANGO may be provided under license arrangements that allow use of the software for research or other non-commercial purposes. As a result, in the future, as we seek to use our platform in connection with commercially available products, we may be required to license that software under different license terms, which may not be possible on commercially reasonable terms, if at all. If we are unable to license software components on terms that permit its use for commercial purposes, we may be required to replace those software components, which could result in delays, additional cost and additional regulatory approvals.

Use and distribution of open source software may entail greater risks than use of third-party commercial software, as open source licensors generally do not provide warranties or other contractual protections regarding infringement claims or the quality of the software code. Some open source licenses contain requirements that we make available source code for modifications or derivative works we create based upon the type of open source software we use. If we combine our proprietary software with open source software in a certain manner, we could, under certain of the open source licenses, be required to release the source code of our proprietary software to the public. This could allow our competitors to create similar products with lower development effort and time, and ultimately could result in a loss of product sales for us. Although we monitor our use of open source software, the terms of many open source licenses have not been interpreted by

U.S. courts, and there is a risk that those licenses could be construed in a manner that could impose unanticipated conditions or restrictions on our ability to commercialize our product candidates. We could be required to seek licenses from third parties in order to continue offering our product candidates, to re-engineer our product candidates or to discontinue the sale of our product candidates in the event re-engineering cannot be accomplished on a timely basis, any of which could materially and adversely affect our business, financial condition, results of operations and prospects.

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

As is common in the biotechnology and pharmaceutical industries, we employ individuals who were previously employed at universities or other biopharmaceutical or pharmaceutical companies, including our competitors or potential competitors. Although no misappropriation or improper disclosure claims against us are currently pending, and although we try to ensure that our employees and consultants do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that we or our employees, consultants or independent contractors have inadvertently or otherwise used or disclosed intellectual property, including trade secrets or other proprietary information, of a former employer or other third parties. We may then have to pursue litigation to defend against these claims. If we fail in defending any claims of this nature in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Even if we are successful in defending against these types of claims, litigation or other legal proceedings relating to intellectual property claims 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, that perception could have a substantial adverse effect on the price of our common stock. This type of litigation or proceeding could substantially increase our operating losses and reduce our resources available for development activities, and we may not have sufficient financial or other resources to adequately conduct this type of litigation or proceedings. For example, some of our competitors may be able to sustain the costs of this type of litigation or proceedings more effectively than we can because of their substantially greater financial resources. In any case, uncertainties resulting from the initiation and continuation of intellectual property litigation or other intellectual property related proceedings could adversely affect our ability to compete in the marketplace.

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 product candidates may require specific formulations to work effectively and efficiently, we may develop product 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 product candidates, any of which could require us to obtain rights to use intellectual property held by third parties. In addition, with respect to any patents we may co-own with third parties, we may require licenses to such co-owners interest to such patents. 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. Even if we are able to obtain a license, it may be non-exclusive, which means that our competitors may also receive access to the same technologies licensed to us. In that event, we may be required to expend significant time and resources to develop or license replacement technology.

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

The licensing and acquisition of third-party intellectual property rights is a competitive area, and companies that may be more established or have greater resources than we do may also be pursuing strategies to license or acquire third-party intellectual property rights that we may consider necessary or attractive in order to commercialize our product candidates. More established companies may have a competitive advantage over us due to their size, cash 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. There can be no assurance that we will be able to successfully complete these types of negotiations and ultimately acquire the rights to the intellectual property surrounding the additional product candidates that we may seek to develop or market. If we are unable to successfully obtain rights to required third-party intellectual property or to maintain the existing intellectual property rights we have, we may have to abandon development of certain programs and our business financial condition, results of operations and prospects could suffer.

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

Periodic maintenance fees on any issued patent are due to be paid to the USPTO and foreign patent agencies in several stages over the lifetime of the patent. The USPTO and various foreign patent agencies also require compliance with a number of procedural, documentary, fee payment and other provisions during the patent application process and following the issuance of a patent. While an inadvertent lapse can in many cases be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. Noncompliance events that could result in abandonment or lapse of a patent or patent application include, but are not limited to, failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. Were a noncompliance event to occur, our competitors might be able to enter the market, which would have a material adverse effect on our business financial condition, results of operations and prospects.

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

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

Past or future patent reform legislation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents. For example, in March 2013, under the Leahy-Smith America Invents Act (the "America Invents Act") the United States moved from a "first to invent" to a "first-to-file" patent system. Under a "first-to-file" system, assuming the other requirements for patentability are met, the first inventor to file a patent application generally will be entitled to a patent on the invention regardless of whether another inventor had made the invention earlier. The America Invents Act includes a number of other significant changes to U.S. patent law, including provisions that affect the way patent applications are prosecuted, redefine prior art and establish a new post-grant review system. The effects of these changes are currently unclear as the USPTO continues to promulgate new regulations and procedures in connection with the America Invents Act and many of the substantive changes to patent law, including the "first-to-file" provisions, only became effective in March 2013. In addition, the courts have yet to address many of these provisions and the applicability of the act and new regulations on the specific patents discussed in this filing have not been determined and would need to be reviewed. However, the America Invents Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents.

Additionally, recent U.S. Supreme Court rulings have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on decisions by the U.S. Congress, the federal courts and the USPTO, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future. For 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. While we do not believe that any of our owned or in-licensed patents will be found invalid based on this decision, we cannot predict how future decisions by the courts, the U.S. Congress or the USPTO may impact the value of our patents. Any similar adverse changes in the patent laws of other jurisdictions could also have a material adverse effect on our business, financial condition, results of operations and prospects.

Additionally, starting from June 1, 2023, European applications have the option, upon grant of a patent, of becoming a Unitary Patent which will be subject to the jurisdiction of the Unitary Patent Court ("UPC"). This is a significant change in European patent practice. As the UPC is a new court system, there is no precedent for the court, increasing the uncertainty of any litigation.

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

Patents have a limited lifespan. In the United States, if all maintenance fees are timely paid, the natural expiration of a patent is generally 20 years from its earliest U.S. non-provisional filing date. Various extensions may be available, but the life of a patent, and the protection it affords, is limited. Even if patents covering our product candidates are obtained, once the patent life has expired, we may be open to competition from competitive products, including generics. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting our product candidates might expire before or shortly after we or our partners commercialize those candidates. As a result, our owned and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

If we do not obtain patent term extension for any product candidates we may develop, our business may be materially harmed.

Depending upon the timing, duration and specifics of any FDA marketing approval of any product candidates we may develop, one or more of our U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984 (the "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 per product may be extended and only those claims covering the approved drug, a method for using it, or a method for manufacturing it may be extended. However, even if we were to seek a patent term extension, it may not be granted because of, for example, the failure to exercise due diligence during the testing phase or regulatory review process, the failure to apply within applicable deadlines, the failure to apply prior to expiration of relevant patents, or any other failure to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. If we are unable to obtain patent term extension or term of any such extension is less than we request, our competitors may obtain approval of competing products following our patent expiration, and our business, financial condition, results of operations, and prospects could be materially harmed.

We are subject to a variety of privacy and data security laws, and our failure to comply with them could harm our business.

We maintain a large quantity of sensitive information, including confidential business and patient health information in connection with our preclinical studies, and are subject to laws and regulations governing the privacy and security of such information. In the United States, there are numerous federal and state privacy and data security laws and regulations governing the collection, use, disclosure and protection of personal information, including federal and state health information privacy laws, federal and state security breach notification laws, and federal and state consumer protection laws. Each of these laws is subject to varying interpretations and constantly evolving. In May 2018, a new privacy regime, the General Data Protection Regulation (the "GDPR") took effect in the European Economic Area (the "EEA") and the United Kingdom. The GDPR governs the collection, use, disclosure, transfer or other processing of personal data of European and United Kingdom persons. The GDPR continues to form part of law in the United Kingdom with some amendments following Brexit ("UK GDPR"), although there is a risk of divergence in the future which may increase our overall data protection compliance cost. Among other things, the GDPR and UK GDPR impose new requirements regarding the security of personal data and notification of data processing obligations to the competent national data processing authorities, changes the lawful bases on which personal data can be processed, expands the definition of personal data and requires changes to informed consent practices, as well as more detailed notices for clinical trial subjects and investigators. In addition, the GDPR and UK GDPR increase the scrutiny of transfers of personal data from clinical trial sites located in the EEA and the United Kingdom to the United States and other jurisdictions that the European Commission or the United Kingdom do not recognize as having "adequate" data protection laws, and imposes substantial fines for breaches and violations (up to the greater of €20 million or 4% of our consolidated annual worldwide gross revenue). The GDPR and UK GDPR also confer 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 or UK GDPR.

More recently, the SEC has enacted regulations requiring companies to disclose or otherwise provide notifications regarding data security breaches. For example, the SEC recently adopted cybersecurity risk management and disclosure rules, which require the disclosure of information pertaining to cybersecurity incidents and cybersecurity risk management, strategy and governance. Compliance with these and any other applicable privacy and data security laws and regulations is a rigorous and time-intensive process, and we may be required to put in place additional mechanisms ensuring compliance with the new data protection rules. If we fail to comply with any such laws or regulations, we may face significant fines and penalties that could adversely affect our business, financial condition and results of operations. Compliance with these and any other applicable privacy and data security laws and regulations is a rigorous and time-intensive process, and we may be required to put in place additional mechanisms ensuring compliance with the new data protection rules. If we fail to comply with any such laws or regulations, we may face significant fines and penalties that could adversely affect our business, financial condition and results of operations.

Risks Related to Employee Matters, Managing Growth and Other Risks Related to our Business

We expect to expand our development and regulatory capabilities, and as a result, we may encounter difficulties in managing our growth, which could disrupt our operations.

We expect to experience significant growth in the number of our employees and the scope of our operations, particularly in the areas of product candidate development and growing our capability to conduct clinical trials. To manage our anticipated future growth, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. Due to our limited financial resources and the limited experience of our management team in managing a company with such anticipated growth, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. The expansion of our operations may lead to significant costs and may divert our management and business development resources. Any inability to manage growth could delay the execution of our business plans or disrupt our operations.

We must attract and retain highly skilled employees to succeed.

To succeed, we must recruit, retain, manage and motivate qualified clinical, scientific, technical and management personnel, and we face significant competition for experienced personnel. If we do not succeed in attracting and retaining qualified personnel, particularly at the management level, it could adversely affect our ability to execute our business plan, harm our results of operations and increase our capabilities to successfully commercialize STK-001, STK-002 and our future product candidates. In particular, we believe that our future success is highly dependent upon the contributions of our senior management, including Edward M. Kaye, our Chief Executive Officer, as well as our senior scientists and other members of our senior management team. The loss of services of one or more of these individuals, who all have at-will employment arrangements with us, could delay or prevent the successful development of our product pipeline, completion of our planned clinical trials or the commercialization of our product candidates, if approved. The competition for qualified personnel in the biotechnology field is intense and as a result, we may be unable to continue to attract and retain qualified personnel necessary for the development of our business or to recruit suitable replacement personnel.

Many of the other biotechnology companies that we compete against for qualified personnel have greater financial and other resources, different risk profiles and a longer history in the industry than we do. They also may provide more diverse opportunities and better chances for career advancement. Some of these characteristics may be more appealing to high-quality candidates than what we have to offer. If we are unable to continue to attract and retain high-quality personnel, the rate and success at which we can discover and develop product candidates and our business will be limited.

Future acquisitions or strategic alliances could disrupt our business and harm our financial condition and results of operations.

We may acquire additional businesses or drugs, form strategic alliances or create joint ventures with third parties that we believe will complement or augment our existing business. If we acquire businesses with promising markets or technologies, we may not be able to realize the benefit of acquiring such businesses if we are unable to successfully integrate them with our existing operations and company culture. We may encounter numerous difficulties in developing, manufacturing and marketing any new drugs resulting from a strategic alliance or acquisition that delay or prevent us from realizing their expected benefits or enhancing our business. We cannot assure you that, following any such acquisition, we will achieve the expected synergies to justify the transaction. The risks we face in connection with acquisitions, include:

- diversion of management time and focus from operating our business to addressing acquisition integration challenges;
- coordination of research and development efforts;

- retention of key employees from the acquired company;
- changes in relationships with strategic partners as a result of product acquisitions or strategic positioning resulting from the acquisition;
- cultural challenges associated with integrating employees from the acquired company into our organization;
- the need to implement or improve controls, procedures, and policies at a business that prior to the acquisition may have lacked sufficiently effective controls, procedures and policies;
- liability for activities of the acquired company before the acquisition, including intellectual property infringement claims, violation of laws, commercial disputes, tax liabilities, and other known liabilities;
- unanticipated write-offs or charges; and
- litigation or other claims in connection with the acquired company, including claims from terminated employees, customers, former stockholders or other third parties.

Our failure to address these risks or other problems encountered in connection with our past or future acquisitions or strategic alliances could cause us to fail to realize the anticipated benefits of these transactions, cause us to incur unanticipated liabilities and harm the business generally. There is also a risk that future acquisitions will result in the incurrence of debt, contingent liabilities, amortization expenses or incremental operating expenses, any of which could harm our financial condition or results of operations.

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 will become subject to numerous environmental, health, and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment, and disposal of hazardous materials and wastes. Our operations will involve the use of hazardous and flammable materials, including chemicals and biological materials. Our operations also may produce hazardous waste products. We generally anticipate contracting with third parties for the disposal of these materials and wastes. We will not be able to eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from any use by us of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties for failure to comply with such laws and regulations.

Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities.

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

Unfavorable global economic conditions could adversely affect our business, financial condition, stock price and results of operations.

Our results of operations could be adversely affected by general conditions in the global economy and in the global financial markets. For example, the global financial crisis of 2008 caused extreme volatility and disruptions in the capital and credit markets. Similarly, the global economy has been impacted by fluctuating interest rates and inflation, as well as the possibility of a recession or further economic downturn. Moreover, adverse developments that affect financial institutions, such as events involving liquidity that are rumored or actual, have in the past and may in the future lead to market-wide liquidity problems. For example, on March 10, 2023, Silicon Valley Bank ("SVB"), one of our banking partners, was closed by the California Department of Financial Protection and Innovation, which appointed the Federal Deposit Insurance Corporation (the "FDIC") as receiver. While we only had a minimal amount of our cash directly at SVB and, since that date, the FDIC has stated that all depositors of SVB will be made whole, there is no guarantee that the federal government would guarantee all depositors in the event of future bank closures, and continued instability in the banking system may adversely impact our business and financial condition. Likewise, the capital and credit markets may be adversely affected by the ongoing conflicts in Israel and Ukraine, and the possibility of a wider Middle Eastern, European or global conflict, global sanctions imposed in response thereto, an energy crisis and potential recessions. A weak or declining economy could also strain our suppliers, possibly resulting in supply disruption, or cause our customers to delay making payments for our services. If the current equity and credit markets deteriorate, it may make any necessary debt or equity financing more

difficult, more costly, and more dilutive. Failure to secure any necessary financing in a timely manner and on favorable terms could have a material adverse effect 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 such difficult economic times, which could directly affect our ability to attain our operating goals on schedule and on budget. Also, hospitals and other medical facilitates face staffing shortages, whether due to labor relations or otherwise, which could potentially cause delays in enrollment, site visits, evaluations or other activities important to our research and development efforts. Any of the foregoing could harm our business and we cannot anticipate all of the ways in which the current economic climate and financial market conditions could adversely impact our business. Furthermore, our stock price may decline due in part to the volatility of the stock market and any general economic downturn.

We or the third parties upon whom we depend may be adversely affected by natural disasters and our business continuity and disaster recovery plans may not adequately protect us from a serious disaster.

Natural disasters could severely disrupt our operations and have a material adverse effect on our business, results of operations, financial condition and prospects. If a natural disaster, fire, hurricane, power outage or other event occurred that prevented us from using all or a significant portion of our headquarters, that damaged critical infrastructure, such as our suppliers' manufacturing facilities, or that otherwise disrupted operations, it may be difficult or, in certain cases, impossible for us to continue our business for a substantial period of time.

The disaster recovery and business continuity plans we have in place may prove inadequate in the event of a serious disaster or similar event. We may incur substantial expenses as a result of the limited nature of our disaster recovery and business continuity plans, which could have a material adverse effect on our business.

Our internal computer and information systems, or those used by our CROs, CMOs or other contractors or consultants, may fail or suffer security breaches, which could result in a material disruption of our development programs.

Despite the implementation of appropriate security measures, our internal computer and information systems and those of our current and any future CROs, CMOs and other contractors or consultants may become vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. While we have not experienced any such material system failure, or accident, and are unaware of any security breach to date, if such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our development programs and our business operations, whether due to a loss of our trade secrets or other proprietary information or other similar disruptions. For example, the loss of data from completed or future preclinical studies or clinical trials could result in significant delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability, our competitive position could be harmed and the further development and commercialization of our product candidates could be significantly delayed.

A breakdown or breach of our technology systems could subject us to liability or interrupt the operation of our business.

We are increasingly dependent upon technology systems and data to operate our business. In particular, the COVID-19 pandemic caused us to modify our business practices, including increasing the prevalence of employees working remotely. As a result, we are increasingly dependent upon our technology systems to operate our business and our ability to effectively manage our business depends on the security, reliability and adequacy of our technology systems and data, which includes use of cloud technologies, including Software as a Service (SaaS), Platform as a Service (PaaS) and Infrastructure as a Service (IaaS). A breakdown, invasion, corruption, destruction or breach of our technology systems, including the cloud technologies that we utilize, and/or unauthorized access to our data and information could subject us to liability or negatively impact the operation of our business. Our technology systems, including the cloud technologies that we utilize, continue to increase in multitude and complexity, making them potentially vulnerable to breakdown, malicious intrusion and random attack. Likewise, data privacy or security breaches by individuals authorized to access our technology systems, including the cloud technologies that we utilize, may pose a risk that sensitive data, including intellectual property, trade secrets or personal information belonging to us, our patients or other business partners, may be exposed to unauthorized persons or to the public.

Cyber-attacks and other cybersecurity incidents are increasing in their frequency, sophistication and intensity, and have become increasingly difficult to detect. They are often carried out by motivated, well-resourced, skilled and persistent actors, including nation states, organized crime groups, "hacktivists" and employees or contractors acting with malicious intent. Cyber-attacks could include the deployment of harmful malware and key loggers, ransomware, a denial-of-service attack, a

malicious website, the use of social engineering and other means to affect the confidentiality, integrity and availability of our technology systems and data. Cyber-attacks could also include supply chain attacks, which could cause a delay in the manufacturing of our products or products produced for contract manufacturing. Our key business partners face similar risks and any security breach of their systems could adversely affect our security posture. Cyber-attacks could include wrongful conduct by hostile foreign governments, industrial espionage, wire fraud and other forms of cyber fraud, the deployment of harmful malware, denial-of-service, social engineering fraud or other means to threaten data confidentiality, integrity and availability. A successful cyber-attack could cause serious negative consequences for us, including, without limitation, the disruption of operations, the misappropriation of confidential business information, including financial information, trade secrets, financial loss and the disclosure of corporate strategic plans. To date, we have not experienced a material compromise of our data or information systems. However, although we devote resources to protect our information systems, we realize that cyber-attacks are a threat, and there can be no assurance that our efforts will prevent information security breaches that would result in business, legal, financial or reputational harm to us, or would have a material adverse effect on our results of operations and financial condition.

In addition, the computer systems of various third parties on which we rely, including our CROs, CMOs and other contractors, consultants and law and accounting firms, may sustain damage from computer viruses, unauthorized access, data breaches, phishing attacks, cybercriminals, natural disasters (including hurricanes and earthquakes), terrorism, war and telecommunication and electrical failures. We rely on our third-party providers to implement effective security measures and identify and correct for any such failures, deficiencies or breaches.

Moreover, our increased use of cloud technologies and remote working arrangements could heighten these and other operational risks, and any failure by cloud technology service providers to adequately safeguard their systems and prevent cyber-attacks could disrupt our operations and result in misappropriation, corruption or loss of confidential or propriety information. Despite the implementation of appropriate security measures, our internal computer and information systems and those of our current and any future CROs, CMOs and other contractors or consultants may become vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. While we have not experienced any such material system failure, or accident, and are unaware of any security breach to date, if such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our development programs and our business operations, whether due to a loss of our trade secrets or other proprietary information or other similar disruptions. For example, the loss of data from completed or future preclinical studies or clinical trials could result in significant delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability, our competitive position could be harmed and the further development and commercialization of our product candidates could be significantly delayed. While we continue to build and improve our systems and infrastructure, including our business continuity plans, there can be no assurance that our efforts will prevent breakdowns or breaches in our systems that could adversely affect our business and operations and/or result in the loss of critical or sensitive information, which could result in financial, legal, business, operational or reputational harm to us, or loss of competitive advantage. In addition, our liability insurance may not be sufficient in type or amount to cover us against claims related to security breaches, cyber-attacks and other related breaches.

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

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

Our business entails a significant risk of product liability and our ability to obtain sufficient insurance coverage could have a material and adverse effect on our business, financial condition, results of operations and prospects.

We will face an inherent risk of product liability exposure related to the testing of STK-001, STK-002 and our future product candidates in clinical trials and will face an even greater risk if we commercialize any of our product candidates. If we cannot successfully defend ourselves against claims that our product candidates caused injuries, we could incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

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

While we currently have product liability insurance that we believe is appropriate for our stage of development, we may need to obtain higher levels prior to clinical development or marketing STK-001, STK-002 or any of our future product candidates. Any insurance we have or may obtain may not provide sufficient coverage against potential liabilities. Furthermore, clinical trial and product liability insurance is becoming increasingly expensive. As a result, we may be unable to obtain sufficient insurance at a reasonable cost to protect us against losses caused by product liability claims that could have a material and adverse effect on our business, financial condition, results of operations and prospects.

Risks Related to Ownership of our Common Stock

The market price of our stock may be volatile, and you could lose all or part of your investment.

The trading price of our common stock may be highly volatile and subject to wide fluctuations in response to various factors, some of which we cannot control. The market price for our common stock may be influenced by many factors, including the other risks described in this section and elsewhere in this report and the following:

- results of preclinical studies and clinical trials of our product candidates, or those of our competitors or our existing or future collaborators;
- regulatory or legal developments in the United States and other countries, especially changes in laws or regulations applicable to our product candidates;
- the success of competitive products or technologies;
- introductions and announcements of new products by us, our future commercialization partners, or our competitors, and the timing of these introductions or announcements;
- actions taken by regulatory agencies with respect to our product candidates, clinical studies, manufacturing process or sales and marketing terms;
- actual or anticipated variations in our financial results or those of companies that are perceived to be similar to us;
- the success of our efforts to acquire or in-license additional technologies, products or product candidates;
- developments concerning any future collaborations, including but not limited to those with our sources of manufacturing supply and our commercialization partners;
- market conditions in the pharmaceutical and biotechnology sectors;
- announcements by us or our competitors of significant acquisitions, strategic collaborations, joint ventures or capital commitments;
- developments or disputes concerning patents or other proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our product candidates and products;
- our ability or inability to raise additional capital and the terms on which we raise it;

- the recruitment or departure of key personnel;
- changes in the structure of healthcare payment systems;
- actual or anticipated changes in earnings estimates or changes in stock market analyst recommendations regarding our common stock, other comparable companies or our industry generally;
- our failure or the failure of our competitors to meet analysts' projections or guidance that we or our competitors may give to the market;
- fluctuations in the valuation of companies perceived by investors to be comparable to us;
- announcement and expectation of additional financing efforts;
- speculation in the press or investment community;
- trading volume of our common stock;
- sales of our common stock by us or our stockholders;
- the concentrated ownership of our common stock;
- changes in accounting principles;
- terrorist acts, acts of war or periods of widespread civil unrest, including the conflict in Ukraine and actions taken by third parties in response to such conflict;
- natural disasters and other calamities; and
- general economic, industry and market conditions including interest rate increases and inflation.

In addition, the stock market in general, and the markets for pharmaceutical, biopharmaceutical and biotechnology stocks in particular, have experienced extreme price and volume fluctuations that have been often unrelated or disproportionate to the operating performance of the issuer, including as a result of general economic conditions. These broad market and industry factors may seriously harm the market price of our common stock, regardless of our actual operating performance. 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 principal stockholders own a significant percentage of our stock and will be able to exert significant control over matters subject to stockholder approval.

As of December 31, 2023 entities affiliated with Skorpios Trust beneficially owned 31.46% of the voting power of all outstanding shares of our common stock. As a result, these entities will have considerable influence over the outcome of corporate actions requiring stockholder approval, including the election of directors, amendment of our organizational documents, any merger, consolidation or sale of all or substantially all of our assets and any other significant corporate transaction. The interests of such entities may not be the same as or may even conflict with your interests. For example, these entities could potentially delay or prevent a change of control of our company, even if such a change of control would benefit our other stockholders, which could deprive our stockholders of an opportunity to receive a premium for their common stock as part of a sale of our company or our assets and might affect the prevailing market price of our common stock.

In addition, Skorpios Trust received its shares from Apple Tree Partners, which previously controlled a majority of the voting power of our common stock. Seth L. Harrison, the chairman of our board of directors, serves as Managing Partner of Apple Tree Partners.

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

The trading market for our common stock will be influenced by the research and reports that industry or securities analysts publish about us or our business. We do not have any control over the analysts, or the content and opinions included in their reports. If any of the analysts who cover us issue an adverse or misleading opinion regarding us, our business model, our intellectual property or our stock performance, or if our preclinical studies and clinical trials and results of operations fail to meet the expectations of analysts, our stock price would likely decline. If one or more of such 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 a decline in our stock price or trading volume.

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 or 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 (the "JOBS Act"). For as long as we continue to be an emerging growth company, we may take advantage of exemptions from various reporting requirements that are applicable to other public companies that are not emerging growth companies, including (i) not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002, as amended (the "Sarbanes-Oxley Act"), (ii) reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements and (iii) exemptions from the requirements of holding nonbinding advisory stockholder votes on executive compensation and stockholder approval of any golden parachute payments not approved previously.

We will remain an emerging growth company until the earliest of (i) the last day of the fiscal year (a) in which we have total annual gross revenue of at least $1.235 billion or (b) in which we are deemed to be a large accelerated filer, which means the market value of our common stock that is held by non-affiliates exceeds $700.0 million as of the prior June 30th, (ii) the date on which we have issued more than $1.0 billion in non-convertible debt during the prior three-year period and (iii) December 31, 2024. We anticipate ceasing to be an emerging growth company as of December 31, 2024, which is the last day of our fiscal year following the fifth anniversary of the completion of our IPO.

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 take advantage of the benefits of this extended transition period. Our consolidated financial statements may therefore not be comparable to those of companies that comply with such new or revised accounting standards. Until the date that we are no longer an "emerging growth company" or affirmatively and irrevocably opt out of the exemption provided by Section 7(a)(2)(B) of the Securities Act, upon issuance of a new or revised accounting standard that applies to our consolidated financial statements and that has a different effective date for public and private companies, we will disclose the date on which adoption is required for non-emerging growth companies and the date on which we will adopt the recently issued accounting standard.

We are also a "smaller reporting company," meaning that the market value of our stock held by non-affiliates was less than $700.0 million and our annual revenue was less than $100.0 million during the most recently completed fiscal year. We may continue to be a smaller reporting company as long as either (i) the market value of our stock held by non-affiliates is less than $250.0 million or (ii) our annual revenue is less than $100.0 million during the most recently completed fiscal year and the market value of our stock held by non-affiliates is less than $700.0 million. If we are a smaller reporting company at the time we cease to be an emerging growth company, we may continue to rely on exemptions from certain disclosure requirements that are available to smaller reporting companies. Specifically, as a smaller reporting company we may choose to present only the two most recent fiscal years of audited financial statements in our Annual Report on Form 10-K and, similar to emerging growth companies, smaller reporting companies have reduced disclosure obligations regarding executive compensation. 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 share price may be more volatile.

Anti-takeover provisions in our charter documents and under Delaware law could make an acquisition of us, which may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current management.

Our restated certificate of incorporation and our restated bylaws contain provisions that could delay or prevent a change in control of our company. These provisions could also make it difficult for stockholders to elect directors who are not nominated by current members of our board of directors or take other corporate actions, including effecting changes in our management. These provisions:

- establish a classified board of directors so that not all members of our board are elected at one time;
- permit only the board of directors to establish the number of directors and fill vacancies on the board;
- provide that directors may only be removed "for cause" and only with the approval of two-thirds of our stockholders;
- require super-majority voting to amend some provisions in our restated certificate of incorporation and restated bylaws;
- authorize the issuance of "blank check" preferred stock that our board could use to implement a stockholder rights plan;

- eliminate the ability of our stockholders to call special meetings of stockholders;
- prohibit stockholder action by written consent, which requires all stockholder actions to be taken at a meeting of our stockholders;
- prohibit cumulative voting; and
- establish advance notice requirements for nominations for election to our board or for proposing matters that can be acted upon by stockholders at annual stockholder meetings.

The exclusive forum provision in our restated certificate of incorporation may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or any of our directors, officers, or other employees, which may discourage lawsuits with respect to such claims.

Our restated certificate of incorporation, to the fullest extent permitted by law, provides that the Court of Chancery of the State of Delaware is the exclusive forum for: any derivative action or proceeding brought on our behalf; any action asserting a breach of fiduciary duty; any action asserting a claim against us arising pursuant to the Delaware General Corporation Law (the "DGCL"), our restated certificate of incorporation, or our restated bylaws; or any action asserting a claim against us that is governed by the internal affairs doctrine. This exclusive forum provision does not apply to suits brought to enforce a duty or liability created by the Exchange Act. It could apply, however, to a suit that falls within one or more of the categories enumerated in the exclusive forum provision and asserts claims under the Securities Act, inasmuch as Section 22 of the Securities Act creates concurrent jurisdiction for federal and state courts over all suits brought to enforce any duty or liability created by the Securities Act or the rule and regulations thereunder. There is uncertainty as to whether a court would enforce such provision with respect to claims under the Securities Act, and our stockholders will not be deemed to have waived our compliance with the federal securities laws and the rules and regulations thereunder.

This choice of forum provision may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or any of our directors, officers, or other employees, which may discourage lawsuits with respect to such claims. Alternatively, if a court were to find the choice of forum provisions contained in our restated certificate of incorporation to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving such action in other jurisdictions, which could harm our business, results of operations and financial condition.

In addition, Section 203 of the DGCL may discourage, delay or prevent a change in control of our company. Section 203 imposes certain restrictions on mergers, business combinations and other transactions between us and holders of 15% or more of our common stock.

Section 22 of the Securities Act creates concurrent jurisdiction for federal and state courts over all claims brought to enforce any duty or liability created by the Securities Act or the rules and regulations thereunder. In April 2020, we amended and restated our restated bylaws to provide that the federal district courts of the United States will, to the fullest extent permitted by law, be the exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act (such provision, a "Federal Forum Provision"). Our decision to adopt a Federal Forum Provision followed a decision by the Supreme Court of the State of Delaware holding that such provisions are facially valid under Delaware law. While there can be no assurance that federal or state courts will follow the holding of the Delaware Supreme Court or determine that the Federal Forum Provision should be enforced in a particular case, application of the Federal Forum Provision means that suits brought by our stockholders to enforce any duty or liability created by the Securities Act must be brought in federal court and cannot be brought in state court.

Section 27 of the Exchange Act creates exclusive federal jurisdiction over all claims brought to enforce any duty or liability created by the Exchange Act or the rules and regulations thereunder. In addition, neither the exclusive forum provision nor the Federal Forum Provision applies to suits brought to enforce any duty or liability created by the Exchange Act. Accordingly, actions by our stockholders to enforce any duty or liability created by the Exchange Act or the rules and regulations thereunder must be brought in federal court.

Our stockholders will not be deemed to have waived our compliance with the federal securities laws and the regulations promulgated thereunder.

Any person or entity purchasing or otherwise acquiring or holding any interest in any of our securities shall be deemed to have notice of and consented to our exclusive forum provisions, including the Federal Forum Provision. These provisions may limit a stockholder's ability to bring a claim in a judicial forum of their choosing for disputes with us or our directors, officers, or other employees, which may discourage lawsuits against us and our directors, officers, and other employees.

We will incur increased costs as a result of operating as a public company, and our management will be required to devote substantial time to new compliance initiatives and corporate governance practices.

As a public company, and particularly after we are no longer an emerging growth company, we will incur significant legal, accounting and other expenses that we did not incur as a private company. The Sarbanes-Oxley Act, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of the Nasdaq Global Select Market ("Nasdaq") and other applicable securities rules and regulations impose various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our management and other personnel will need to devote a substantial amount of time to these compliance initiatives. Moreover, we expect these rules and regulations to substantially increase our legal and financial compliance costs and to make some activities more time consuming and costly. We cannot 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. Moreover, these rules and regulations are often subject to varying interpretations, in many cases due to their lack of specificity, and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. This could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices.

If we fail to maintain proper and effective internal control over financial reporting in the future, our ability to produce accurate and timely financial statements could be impaired, which could harm our operating results, investors' views of us and, as a result, the value of our common stock.

We previously were not required to independently comply with Section 404(a) of the Sarbanes-Oxley Act. Section 404(a) of the Sarbanes-Oxley Act requires annual management assessments of the effectiveness of our internal control over financial reporting, starting with the second annual report that we file with the SEC. We were required to meet these standards in the course of preparing our financial statements as of and for the year ended December 31, 2023, and our management is required to report on the effectiveness of our internal control over financial reporting for such year and annually thereafter. Additionally, once we are no longer an "emerging growth company," our independent registered public accounting firm will be required pursuant to Section 404(b) of the Sarbanes-Oxley Act to attest to the effectiveness of our internal control over financial reporting on an annual basis. The rules governing the standards that must be met for our management to assess our internal control over financial reporting are complex and require significant documentation, testing, and possible remediation.

To achieve compliance with Section 404(b) within the prescribed period, we will be engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to continue to dedicate internal resources, potentially engage outside consultants and adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, there is a risk that we will not be able to conclude, within the prescribed timeframe or at all, that our internal control over financial reporting is effective as required by Section 404. If we identify one or more material weaknesses, it could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our consolidated financial statements. In addition, if we are not able to continue to meet these requirements, we may not be able to remain listed on Nasdaq.

As we grow, we expect to hire additional personnel and may utilize external temporary resources to implement, document and modify policies and procedures to maintain effective internal controls. However, it is possible that we may identify deficiencies and weaknesses in our internal controls. If material weaknesses or deficiencies in our internal controls exist and go undetected or unremediated, our consolidated financial statements could contain material misstatements that, when discovered in the future, could cause us to fail to meet our future reporting obligations and cause the price of our common stock to decline.

Because we do not anticipate paying any cash dividends on our capital stock in the foreseeable future, capital appreciation, if any, will be your sole source of gain.

We have never declared or paid cash dividends on our capital stock. We currently intend to retain all of our future earnings, if any, to finance the growth and development of our business. As a result, capital appreciation, if any, of our common stock will be your sole source of gain for the foreseeable future.

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.

Item 1B. Unresolved Staff Comments.

None.

Item 1C. Cybersecurity

We recognize the critical importance of maintaining the trust and confidence of our all of our stakeholders. Our business increasingly depends on the efficient and uninterrupted operation of our information technology systems and those of our third-party contract research organizations, contract manufacturing organizations, or other vendors, contractors or consultants. Our board of directors and our management team are actively involved in the oversight of risk management, and cybersecurity represents an important component of our overall approach to compliance and risk management. Our cybersecurity policies, standards, processes and practices are integrated into our approach to compliance and risk management and follow recognized industry best practices. In general, we seek to address cybersecurity risks through a cross-functional approach that is focused on preserving the confidentiality, integrity, and availability of the information that we collect, process, and store by identifying, preventing and mitigating cybersecurity threats and effectively responding to cybersecurity incidents when they occur.

Cybersecurity Risk Mitigation

As one of the critical elements of our overall approach to compliance and risk management, our cybersecurity program is focused on the following key areas:

Confidentiality and Integrity: To ensure the confidentiality and integrity of data and systems, we leverage encryption of data during transfer and at rest whenever possible and as necessary, least privileged access when granting access, strong passwords and two-factor authentication, and version-controlled file systems.

Availability: To preserve the availability of data and systems, we perform daily backups with some occurring multiple times a day. Additionally, to mitigate ransomware, data is stored in version-controlled file systems. When implementing systems, architectural patterns for redundancy and failover are used.

Other Technical Safeguards: Additional technical safeguards that are designed to protect our information systems from cybersecurity threats include endpoint tools that detect and prevent threats on a computer and monitor for vulnerabilities, next generation firewalls, intrusion prevention and detection systems, and cybersecurity testing of our systems.

Monitoring: We maintain a security operations center that monitors our systems and networks for anomalous activity. Additionally, our information technology ("IT") team actively monitors different cybersecurity threat intelligence sources and responds accordingly based on risk.

Education and Awareness: We provide regular, mandatory security awareness training for personnel to educate our employees on cybersecurity threats and to communicate our evolving information security policies, standards, processes, and practices. In addition to the training, we periodically test employees with phishing emails.

Collaborative Approach: We have implemented a cross-functional approach to identifying, preventing, and mitigating cybersecurity threats and incidents, while also implementing controls and procedures that provide for the prompt escalation of certain cybersecurity incidents so that decisions regarding the public disclosure and reporting of such incidents can be made by management in a timely manner.

Incident Response and Recovery Planning: We have established and maintain comprehensive incident response and recovery plans to address our response to a cybersecurity incident.

Third-Party Risk Management: We maintain a risk-based approach to identifying cybersecurity risks presented by third parties, including vendors, service providers and other external users of our systems, as well as the systems of third parties that could adversely impact our business in the event of a cybersecurity incident affecting those third-party systems.

Policies and Processes: We engage in the periodic assessment of our policies, standards, processes, and practices that are designed to address cybersecurity threats and incidents. These efforts include a wide range of activities, including audits, penetration testing and other exercises focused on evaluating the effectiveness of our cybersecurity measures. The results of such exercises, if material, are reported to the audit committee of our board and our board of directors, and we adjust our cybersecurity policies, standards, processes and practices as necessary based on the information provided by these assessments, audits and reviews.

Governance

Our board of directors, in coordination with our audit committee, oversees our risk management process. Our audit committee receives presentations and reports on cybersecurity risks, which address a wide range of topics including recent developments, evolving standards, vulnerability assessments, the threat environment, technological trends and information security considerations arising with respect to our peers and third parties. Our board of directors and audit committee also receive prompt and timely information regarding any cybersecurity incident that meets established reporting thresholds, as well as ongoing updates regarding any such incident until it has been addressed. On a periodic basis, our board of directors and audit committee discuss our approach to cybersecurity risk management with our head of IT.

Our head of IT, in coordination and with support from our executive management team, works collaboratively across the company to implement a program designed to protect our information systems from cybersecurity threats and to promptly respond to any cybersecurity incidents in accordance with our incident response and recovery plans. Through ongoing communications with our entire employee basis and appropriate third-party contractors, the head of IT and the management team monitor the prevention, detection, mitigation and remediation of cybersecurity threats and incidents in real time and report such threats and incidents to our audit committee when appropriate.

Our head of IT has over 20 years of experience building and managing information systems with cybersecurity principles, such as least privileged access, patching and vulnerability management, encryption, etc., as part of a foundation to ensure confidentiality, integrity, and availability. Our head of IT has also served in consulting and architecture roles for cybersecurity and compliance projects ranging from design and auditing systems, red team testing, to compliance audits and remediation for the Sarbanes-Oxley Act of 2002, as amended, and the payment card industry data security standards.

No cybersecurity threats, including as a result of any previous cybersecurity incidents, have materially affected or are reasonably likely to affect us, including our business strategy, results of operations or financial condition

Item 2. Properties.

We currently occupy approximately 38,000 square feet of office and laboratory space in Bedford, Massachusetts, under a lease that expires December 31, 2026. We also occupy 4,842 square feet of office space in Cambridge, Massachusetts under a lease that expires on April 30, 2025. We believe that our facilities suffice to meet our current and near-term needs and that suitable additional space will be available as and when needed.

Item 3. Legal Proceedings.

From time to time we may be subject to various claims, complaints and legal actions that arise in the normal course of business. We are not presently party to any legal proceedings that, in the opinion of management, the outcome of which could have a material adverse effect on our business. Regardless of outcome, litigation can have an adverse impact on us due to defense and settlement costs, diversion of management resources, negative publicity and reputation harm, and other factors. There can be no assurance that future legal proceedings arising in the ordinary course of business or otherwise will not have a material adverse effect on our business, financial condition, or results of operations.

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.

Unregistered Sales of Equity Securities and Use of Proceeds.

Unregistered Sales of Equity Securities

None.

Use of Proceeds

None.

Holders of Record

As of December 31, 2023, there were 6 holders of record of our common stock. The actual number of stockholders is greater than this number of record holders and includes stockholders who are beneficial owners but whose shares are held in street name by brokers and other nominees. This number of holders of record also does not include stockholders whose shares may be held in trust by other entities.

Dividends

We have not declared or paid any cash dividends on our common stock since our inception. We do not plan to pay dividends in the foreseeable future. We currently intend to retain all available funds and any future earnings, if any, for use in the operation of our business. Any future determination to declare cash dividends will be made at the discretion of our board of directors, subject to applicable laws, and will depend on our financial condition, results of operations, capital requirements, general business conditions and other factors that our board of directors may deem relevant, and subject to the restrictions contained in future financing instruments. Consequently, stockholders will need to sell shares of our common stock to realize a return on their investment, if any.

Item 6. [Reserved]

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 consolidated results of operations together with our consolidated financial statements and related notes appearing 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. You should carefully read the sections entitled "Risk Factors" and "Special Note Regarding Forward-Looking Statements" to gain an understanding of the important factors that could cause actual results to differ materially from our forward-looking statements.

Overview

We are dedicated to addressing the underlying causes of severe diseases by upregulating protein expression with RNA-based medicines. Using our proprietary TANGO (Targeted Augmentation of Nuclear Gene Output) approach, we are developing antisense oligonucleotides ("ASOs") to selectively restore protein levels.

Our first compound, STK-001, is in clinical testing for the treatment of Dravet syndrome, a severe and progressive genetic epilepsy. Dravet syndrome is characterized by frequent, prolonged and refractory seizures beginning within the first year of life. The disease is classified as a developmental and epileptic encephalopathy due to the developmental delays and cognitive impairment associated with it. Dravet syndrome is one of many diseases caused by a haploinsufficiency, in which a loss of approximately 50% of normal protein levels leads to disease. We have announced end of study data from our two Phase 1/2a open-label studies of STK-001, MONARCH in the United States and ADMIRAL in the United Kingdom. We also have SWALLOWTAIL in the U.S. and LONGWING in the U.K., which are Open Label Extension ("OLE") studies of STK-001 for children and adolescents with Dravet syndrome. Patients who participated in the MONARCH study in the United States or the ADMIRAL study in the United Kingdom and met study entry criteria are eligible to continue treatment in SWALLOWTAIL or LONGWING, respectively, both of which are designed to evaluate the long-term safety and tolerability of repeat doses of STK-001.

We are also pursuing treatment for a second haploinsufficient disease, autosomal dominant optic atrophy ("ADOA"), the most common inherited optic nerve disorder. STK-002 is our lead clinical candidate for the treatment of ADOA. STK-002 is designed to upregulate OPA1 protein expression by leveraging the non-mutant (wild-type) copy of the *OPA1* gene to restore OPA1 protein expression with the aim to stop or slow vision loss in patients with ADOA. We have received authorization in the United Kingdom to proceed with a Phase 1 open-label study (OSPREY) of STK-002, and we expect the study to start in 2024.

In May 2022, we filed a universal Shelf Registration statement on Form S-3 (the "Registration Statement") with the SEC. The Registration Statement was declared effective by the SEC on May 31, 2022, and contains two prospectuses: a base prospectus, which covers the offering, issuance and sale by us of up to a maximum aggregate offering price of $400.0 million of our common stock, preferred stock, debt securities, warrants to purchase common stock, preferred stock or debt securities, subscription rights to purchase common stock, preferred stock or debt securities and/or units consisting of some or all of these securities; and a sales agreement prospectus covering the offering, issuance and sale by us of up to a maximum aggregate offering price of $150.0 million of common stock that may be issued and sold under a Controlled Equity Offering Sales Agreement ("Sales Agreement"). The specific terms of any securities to be offered pursuant to the base prospectus will be specified in a prospectus supplement to the base prospectus. The $150.0 million of common stock that may be offered, issued and sold under the sales agreement prospectus is included in the $400.0 million of securities that may be offered, issued and sold by us under the base prospectus. As of December 31, 2023, we had issued approximately 6.3 million shares of common stock pursuant to the Sales Agreement for net proceeds of $52.1 million. We may terminate this at-the-market program at any time, pursuant to its terms.

As of December 31, 2023 and 2022 we had $201.4 million and $229.6 million, respectively, in cash, cash equivalents and marketable securities.

Since inception, we have had operating losses, the majority of which are attributable to research and development activities. Our net losses were $104.7 million and $101.1 million for the years ended December 31, 2023 and 2022, respectively. As of December 31, 2023, we had an accumulated deficit of $401.8 million and as of December 31, 2022, we had an accumulated deficit of $297.2 million.

Our primary use of cash is to fund operating expenses, which consist primarily of research and development expenditures, and to a lesser extent, general and administrative expenditures. Cash used to fund operating expenses is impacted by the timing of when we pay these expenses, as reflected in the change in our outstanding accounts payable and accrued expenses. We expect to continue to incur net losses for the foreseeable future, and we expect our research and development expenses, general and administrative expenses, and capital expenditures will continue to increase. In particular,

we expect our expenses and losses to increase as we continue our development of, and seek regulatory approvals for, our product candidates, and begin to commercialize any approved products, as well as hire additional personnel, develop commercial infrastructure, pay fees to outside consultants, lawyers and accountants, and incur increased costs associated with being a public company such as expenses related to services associated with maintaining compliance with Nasdaq listing rules and SEC requirements, insurance and investor relations costs. Our net losses may fluctuate significantly from quarter-to-quarter and year-to-year, depending on the timing of our clinical trials and our expenditures on other research and development activities.

Based upon our current operating plan, we believe that our cash, cash equivalents and marketable securities of $201.4 million as of December 31, 2023, together with the proceeds since December 31, 2023 from the Sales Agreement of $1.3 million, will enable us to fund our operating expenses and capital expenditure requirements to the end of 2025. To date, we have not had any products approved for sale and have not generated any product sales. We do not expect to generate any revenues from product sales unless and until we successfully complete development and obtain regulatory approval for one or more of our product candidates, which we expect will take a number of years. If we obtain regulatory approval for any of our product candidates, we expect to incur significant commercialization expenses related to product sales, marketing, manufacturing and distribution. As a result, until such time, if ever, as we can generate substantial product revenue, we expect to finance our cash needs through equity offerings, debt financings or other capital sources, including potentially collaborations, licenses and other similar arrangements. However, we may be unable to raise additional funds or enter into such other arrangements when needed on favorable terms or at all. Any failure to raise capital as and when needed could have a negative impact on our financial condition and on our ability to pursue our business plans and strategies. If we are unable to raise capital, we will need to delay, reduce or terminate planned activities to reduce costs.

License and Collaboration Agreement with Acadia Pharmaceuticals Inc.

In January 2022, we entered into a license and collaboration agreement with Acadia Pharmaceuticals Inc. (“Acadia”) for the discovery, development and commercialization of novel RNA-based medicines for the treatment of severe and rare genetic neurodevelopmental diseases of the central nervous system. The agreement focuses on the targets SYNGAP1, MECP2 (Rett syndrome), and an undisclosed neurodevelopmental target of mutual interest. In connection with each target, we will collaborate with Acadia to identify potential treatments for further development and commercialization as licensed products. With respect to SYNGAP1, we have agreed with Acadia to co-develop and co-commercialize licensed products for such target globally, and in connection therewith we granted to Acadia worldwide, co-exclusive (with us) licenses for such licensed products. With respect to MECP2 and the neurodevelopmental target, we granted to Acadia worldwide, exclusive licenses to develop and commercialize licensed products for such targets.

Pursuant to the terms of the agreement, we received an upfront payment of $60.0 million from Acadia. Acadia agreed to fund the research to identify potential licensed products for MECP2 and the neurodevelopmental target, and we will equally fund with Acadia the research to identify potential licensed products for SYNGAP1. We are eligible to receive up to $907.5 million in potential total milestone payments based upon the achievement of certain development, regulatory, first commercial sales and sales milestone events across the programs for the three targets, assuming each milestone were achieved at least once. With respect to licensed products for MECP2 and the neurodevelopmental target, we are also eligible to receive tiered royalties at percentages ranging from the mid-single digits to the mid-teens on future net sales by Acadia of licensed products worldwide. Royalties payable under the agreement are subject to standard royalty reductions. For SYNGAP1 licensed products that we are co-developing and co-commercializing, we will be responsible for 50% of the development and commercialization costs and will receive 50% of the profits from global commercialization. We are provided with a co-development and co-commercialization opt out option relating to the SYNGAP1 target indication at our discretion. Such opt-out would reduce development and commercialization milestones but would provide us with royalties on an escalating basis attributable to net sales milestones.

Financial Operations Overview

Revenue

We currently do not have any products approved for sale and have not generated any revenue since inception through December 31, 2023. If we are able to successfully develop, receive regulatory approval for and commercialize any of our current or future product candidates alone or in collaboration with third parties, we may generate revenue from the sales of these product candidates.

In January 2022, we entered into a license and collaboration agreement with Acadia Pharmaceuticals Inc. (“Acadia”) for the discovery, development and commercialization of novel RNA-based medicines for the treatment of severe and rare genetic neurodevelopmental diseases of the central nervous system (the “CNS”). The agreement focuses on the targets

SYNGAP1, MECP2 (Rett syndrome), and an undisclosed neurodevelopmental target of mutual interest. In connection with each target, we will collaborate with Acadia to identify potential treatments for further development and commercialization as licensed products. With respect to SYNGAP1, we have agreed with Acadia to co-develop and co-commercialize licensed products for such target globally, and in connection therewith we granted to Acadia worldwide, co-exclusive (with us) licenses for such licensed products. With respect to MECP2 and the neurodevelopmental target, we granted to Acadia worldwide, exclusive licenses to develop and commercialize licensed products for such targets.

Pursuant to the terms of the agreement, we received an upfront payment of $60.0 million from Acadia. Acadia agreed to fund the research to identify potential licensed products for MECP2 and the neurodevelopmental target, and we will equally fund with Acadia the research to identify potential licensed products for SYNGAP1. We are eligible to receive up to $907.5 million in potential total milestone payments based upon the achievement of certain development, regulatory, first commercial sales and sales milestone events across the programs for the three targets, assuming each milestone were achieved at least once. With respect to licensed products for MECP2 and the neurodevelopmental target, we are also eligible to receive tiered royalties at percentages ranging from the mid-single digits to the mid-teens on future net sales by Acadia of licensed products worldwide. Royalties payable under the agreement are subject to standard royalty reductions. For SYNGAP1 licensed products that we are co-developing and co-commercializing, we will be responsible for 50% of the development and commercialization costs and will receive 50% of the profits from global commercialization. We are provided with a co-development and co-commercialization opt out option relating to the SYNGAP1 target indication at our discretion. Such opt-out would reduce development and commercialization milestones but would provide us with royalties on an escalating basis attributable to net sales milestones.

For the year ended, December 31, 2023, we recognized revenue related to the Acadia collaboration of $8.8 million and for the year ended, December 31, 2022, we recognized revenue related to the Acadia collaboration of $12.4 million.

See *Note 8—License and Collaboration Agreement with Acadia Pharmaceuticals, Inc.* of the notes to our consolidated financial statements included elsewhere in this Annual Report on Form 10-K.

Research and development

Research and development expenses consist primarily of costs incurred for the development of our discovery work and preclinical programs, which include:

- personnel costs, which include salaries, benefits and stock-based compensation expense;
- expenses incurred under agreements with consultants, third-party contract organizations that conduct research and development activities on our behalf, costs related to production of preclinical material and laboratory and vendor expenses related to the execution of preclinical studies;
- scientific consulting, collaboration and licensing fees;
- laboratory supplies; and
- facilities costs, depreciation and other expenses related to internal research and development activities.

We use our personnel and infrastructure resources across multiple research and development programs directed toward identifying and developing product candidates. Our direct research and development expenses are tracked on a program-by-program basis from the point a program becomes a clinical candidate for us and consists primarily of external costs, such as fees paid to consultants, central laboratories and contractors in connection with our preclinical activities. We do not allocate employee costs, costs associated with our technology or facility expenses, including depreciation or other indirect costs, to specific programs because these costs are currently deployed across multiple product development programs and, as such, are not separately classified. We use internal resources to manage our development activities and our employees work across multiple development programs and, therefore, we do not track their costs by program.

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

	Year ended December 31,	
	2023	2022
	(in thousands)	
STK-001	$ 27,078	$ 25,327
STK-002	7,997	9,087
SYNGAP1	554	405
MECP2	994	745
Non-program specific and unallocated research and development expenses	45,608	42,273
Total research and development expenses	$ 82,231	$ 77,837

We expense all research and development costs in the periods in which they are incurred. Costs for certain development activities are recognized based on an evaluation of the progress to completion of specific tasks using information and data provided to us by our vendors and third-party service providers.

We expect that our expenses will increase substantially in connection with our planned discovery work, preclinical and clinical development activities in the near term and our planned clinical trials in the future. At this time, we cannot reasonably estimate the costs for completing the preclinical and clinical development of any of our other product candidates. We expect our research and development expenses to increase substantially for the foreseeable future as we continue to invest in research and development activities related to developing our product candidates, including investments in manufacturing, as our programs advance into later stages of development and we conduct clinical trials. The process of conducting the necessary clinical research to obtain regulatory approval is costly and time-consuming, and the successful development of our product candidates is highly uncertain. As a result, we are unable to determine the duration and completion costs of our research and development projects or when and to what extent we will generate revenue from the commercialization and sale of any of our product candidates.

Because of the numerous risks and uncertainties associated with product development, we cannot determine with certainty the duration and completion costs of the current or future preclinical studies and clinical trials or if, when, or to what extent we will generate revenues from the commercialization and sale of our product candidates. We may never succeed in achieving regulatory approval for our product candidates. The duration, costs and timing of preclinical studies and clinical trials and development of our product candidates will depend on a variety of factors, including:

- successful completion of preclinical studies and investigational new drug-enabling studies;
- successful enrollment in, and completion of, clinical trials;
- receipt of regulatory approvals from applicable regulatory authorities;
- furthering our commercial manufacturing capabilities and arrangements with third-party manufacturers;
- obtaining and maintaining patent and trade secret protection and non-patent exclusivity;
- launching commercial sales of our product candidates, if and when approved, whether alone or in collaboration with others;
- acceptance of our product candidates, if and when approved, by patients, the medical community and third-party payors;
- effectively competing with other therapies and treatment options;
- a continued acceptable safety profile following approval;
- enforcing and defending intellectual property and proprietary rights and claims; and
- achieving desirable medicinal properties for the intended indications.

A change in the outcome of any of these factors could mean a significant change in the costs and timing associated with the development of our current and future preclinical and clinical product candidates. For example, if the FDA, or another regulatory authority were to require us to conduct clinical trials beyond those that we currently anticipate will be required for the completion of clinical development, or if we experience significant delays in execution of or enrollment in any of our preclinical studies or clinical trials, we could be required to expend significant additional financial resources and time on the completion of preclinical and clinical development. We expect our research and development expenses to increase for the foreseeable future as we continue the development of product candidates.

General and administrative expenses

General and administrative expenses consist primarily of personnel costs, costs related to maintenance and filing of intellectual property, expenses for outside professional services, including legal, human resources, information technology, audit and accounting services, and facilities and other expenses. Personnel costs consist of salaries, benefits and stock-based compensation expense. We expect our general and administrative expenses to increase over the next several years to support our continued research and development activities, manufacturing activities, increased costs of operating as a public company and the potential commercialization of our product candidates. These increases are anticipated to include increased costs related to the hiring of additional personnel, developing commercial infrastructure, fees to outside consultants, lawyers and accountants, and increased costs associated with being a public company such as expenses related to services associated with maintaining compliance with Nasdaq listing rules and SEC requirements, insurance and investor relations costs.

Other income (expense)

Our other income (expense), includes (i) interest income earned on cash reserves in our operating money market fund, investment accounts and on our marketable securities investments and (ii) other items of income (expense), net.

Results of Operations for the Years Ended December 31, 2023 and 2022

The following table sets forth our results of operations:

	Year ended December 31,	
	2023	2022
	(in thousands)	
Consolidated statements of operations		
Revenue	$ 8,780	$ 12,405
Operating expenses:		
Research and development	82,231	77,837
General and administrative	41,322	38,924
Total operating expenses	123,553	116,761
Loss from operations	(114,773)	(104,356)
Other income (expense):		
Interest income (expense), net	9,908	3,122
Other income (expense), net	166	167
Total other income (expense)	10,074	3,289
Net loss	$ (104,699)	$ (101,067)

Research and development expenses

Research and development expenses were $82.2 million for the year ended December 31, 2023 as compared to $77.8 million for the year ended December 31, 2022, an increase of $4.4 million. The table below summarizes our research and development expenses:

	Year Ended December 31,	
	2023	2022
	(in thousands)	
STK-001	$ 27,078	$ 25,327
STK-002	7,997	9,087
SYNGAP1	554	405
MECP2	994	745
Personnel-related expenses	31,485	29,028
Third-party services	2,085	3,409
Scientific consulting	1,093	794
Facilities and other research and development expenses	10,945	9,042
Total research and development expenses	$ 82,231	$ 77,837

The increase in research and development expenses were primarily attributable to an increase of $2.5 million in personnel costs resulting from annual compensation increases and increases in stock-based compensation expense, $1.9 million in facilities and other research and development costs, an increase of $1.8 million in expenses related to our STK-001 program, which is comprised of third-party services and scientific consulting fees, offset by a decrease of $1.1 million in expenses related to our STK-002 program, which is comprised of third-party services and scientific consulting fees, and a decrease of $0.7 million in external third-party expenses related to SYNGAP1, MECP2, and non-project specific consulting and third-party services. The increase in expenses reflects the accelerating pace of research and development activities and the increases in personnel needed to support those activities.

General and administrative expenses

General and administrative expenses were $41.3 million for the year ended December 31, 2023 as compared to $38.9 million for the year ended December 31, 2022, an increase of $2.4 million.

The increases in general and administrative expenses were primarily attributable to an increase of $2.2 million in personnel costs, including increases in stock-based compensation expense, from increases in headcount and the annual options award and an increase of $0.2 million in third-party services to support our in-house personnel in various aspects of developing and supporting the business including human resources, information technology, audit, tax, public relations, communications and other general and administrative activities.

Other income (expense)

The change in our other income (expense) for the year ended December 31, 2023 as compared to the year ended December 31, 2022 primarily reflects an increase in cash balances throughout the year as well as increased interest rates.

Liquidity and Capital Resources

Since our inception through December 31, 2023, our operations have been financed by net proceeds of $542.6 million from the sale of convertible notes payable and our convertible preferred stock, our initial public offering, follow-on offering, proceeds from the controlled equity offering sales agreements and the upfront payment from Acadia. As of December 31, 2023, we had $201.4 million in cash, cash equivalents and marketable securities. Cash in excess of immediate requirements is invested in accordance with our investment policy, primarily with a view to liquidity and capital preservation.

We have incurred losses since our inception in June 2014 and, as of December 31, 2023 and 2022, we had accumulated deficits of $401.8 million and $297.2 million, respectively. Our primary use of cash is to fund operating expenses, which consist primarily of research and development expenditures, and to a lesser extent, general and administrative expenditures. Cash used to fund operating expenses is impacted by the timing of when we pay these expenses, as reflected in the change in our outstanding accounts payable and accrued expenses.

Our product candidates may never achieve commercialization and we anticipate that we will continue to incur losses for the foreseeable future. We expect that our research and development expenses, general and administrative expenses, and capital expenditures will continue to increase. As a result, until such time, if ever, as we can generate substantial product revenue, we expect to finance our cash needs through a combination of equity offerings, debt financings or other capital sources, including potentially collaborations, licenses and other similar arrangements. Our primary uses of capital are, and we expect will continue to be, compensation and related expenses, third-party clinical research and development services, costs relating to the build-out of our headquarters and manufacturing facility, license payments or milestone obligations that may arise, laboratory and related supplies, clinical costs, manufacturing costs, legal and other regulatory expenses and general overhead costs.

Based upon our current operating plan, we believe that our cash, cash equivalents and marketable securities of $201.4 million as of December 31, 2023, together with the proceeds since December 31, 2023 from the Sales Agreement of $1.3 million, will enable us to fund our operating expenses and capital expenditure requirements to the end of 2025. We have based this estimate on assumptions that may prove to be wrong, and we could utilize our available capital resources sooner than we currently expect. We will continue to require additional financing to advance our current product candidates through clinical development, to develop, acquire or in-license other potential product candidates and to fund operations for the foreseeable future. We will continue to seek funds through equity offerings, debt financings or other capital sources, including potentially collaborations, licenses and other similar arrangements. However, we may be unable to raise additional funds or enter into such other arrangements when needed on favorable terms or at all. If we do raise additional capital through public or private equity offerings, the ownership interest of our existing stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect our stockholders' rights. If we raise additional capital through debt financing, we may be subject to covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. Any failure to raise capital as and when needed could have a negative impact on our financial condition and on our ability to pursue our business plans and strategies. If we are unable to raise capital, we will need to delay, reduce or terminate planned activities to reduce costs.

Because of the numerous risks and uncertainties associated with research, development and commercialization of pharmaceutical products, we are unable to estimate the exact amount of our operating capital requirements. Our future funding requirements will depend on many factors, including, but not limited to:

- the scope, progress, results and costs of researching and developing our lead product candidates or any future product candidates, and conducting nonclinical studies and clinical trials;
- the timing of, and the costs involved in, obtaining regulatory approvals or clearances for our lead product candidates or any future product candidates;
- the number and characteristics of any additional product candidates we develop or acquire;
- the timing of any cash milestone payments if we successfully achieve certain predetermined milestones;
- the cost of manufacturing our lead product candidates or any future product candidates and any products we successfully commercialize, including costs associated with building-out our manufacturing capabilities;
- our ability to establish and maintain strategic collaborations, licensing or other arrangements and the financial terms of any such agreements that we may enter into;
- the expenses needed to attract and retain skilled personnel;
- the costs associated with being a public company; and
- the timing, receipt and amount of sales of any future approved or cleared products, if any.

Further, our operating plans may change, and we may need additional funds to meet operational needs and capital requirements for clinical trials and other research and development activities. We currently have no credit facility or committed sources of capital. Because of the numerous risks and uncertainties associated with the development and commercialization of our product candidates, we are unable to estimate the amounts of increased capital outlays and operating expenditures associated with our current and anticipated product development programs.

Cash flows

The following table summarizes our cash flows:

	Year ended December 31,	
	2023	2022
	(in thousands)	
Net cash provided by (used in):		
Operating activities	$ (81,067)	$ (31,866)
Investing activities	105,946	(45,882)
Financing activities	53,007	46,409
Net increase (decrease) in cash, cash equivalents and restricted cash	$ 77,886	$ (31,339)

Operating activities

During the year ended December 31, 2023, cash used in operating activities was $81.1 million. This was primarily attributable to a net loss of $104.7 million and by a net change of $6.0 million in our net operating assets and liabilities, offset by non-cash charges of $29.6 million for stock-based compensation, depreciation, amortization and accretion of marketable securities, and reduction in the carrying amount of right of use assets.

During the year ended December 31, 2022, cash used in operating activities was $31.9 million. This was primarily attributable to a net loss of $101.1 million and by a net change of $8.7 million in our net operating assets and liabilities, offset by $51.7 million in deferred revenue received as part of the Acadia collaboration and to non-cash charges of $26.2 million for share-based compensation, depreciation, amortization and accretion of marketable securities, and reduction in the carrying amount of right of use assets.

Investing activities

Our investing activities during the years ended December 31, 2023 and 2022 have consisted of purchases of property and equipment and purchases and sales of marketable securities.

Financing activities

Our financing activities during year ended December 31, 2023 consisted of $0.4 million from the exercise of stock options, $0.6 million in proceeds from our Employee Stock Purchase Plan and $52.1 million of net proceeds from the controlled equity offering sales agreements.

Our financing activities during year ended December 31, 2022 consisted of $0.5 million from the exercise of stock options, $0.6 million in proceeds from our Employee Stock Purchase Plan and $45.3 million of net proceeds from the controlled equity offering sales agreements.

Contractual Obligations and Commitments

The following table summarizes our contractual obligations as of December 31, 2023 and the effects that such obligations are expected to have on our liquidity and cash flows in future periods:

	Payments Due by Period				
	Total	Less Than 1 Year	1 to 3 Years	4 to 5 Years	More than 5 Years
			(in thousands)		
Operating lease obligations	$ 7,833	$ 2,608	$ 5,225	$ —	$ —
Total	$ 7,833	$ 2,608	$ 5,225	$ —	$ —

In August 2018, we entered into an agreement to lease approximately 23,000 square feet of space for a term of three years. Lease terms are triple net lease commencing at $0.9 million per year, then with 3% annual base rent increases plus operating expenses, real estate taxes, utilities and janitorial fees. The lease commencement date was December 10, 2018.

In September 2021, we entered into an agreement to extend the initial term of the 23,000 square foot lease for a period of three years ending December 31, 2024. In addition, this agreement provides for the lease of an additional 15,000 square feet of rentable space beginning on April 1, 2022 and ending on December 31, 2024. Initial monthly lease payments are approximately $0.1 million with respect to the 23,000 square feet space, and $0.1 million with respect to the 15,000 square feet space, and in each case subject to annual rent escalations.

In December 2023, we entered into an agreement to extend the term of the 38,000 square foot lease for a period of two years commencing on January 1, 2025 and ending on December 31, 2026. In December 2023, we recognized a right-of-use asset and operating lease liability of $4.1 million.

In December 2018, we entered into an agreement to lease 2,485 square feet of space for a term of three years. The lease includes one renewal option for an additional two years. Lease terms commence at $0.2 million per year, with 2.5% annual base rent increases plus operating expenses, real estate taxes, utilities and janitorial fees. We occupied this space in May 2019.

In June 2021, we amended the agreement to extend the initial term of the 2,485 square foot lease for a period of three years ending April 30, 2025. In addition, the amendment provided for the lease of an additional 2,357 square feet of rentable space beginning on July 6, 2021 and ending on April 30, 2025. The amended lease provides us with the option to extend the term of the lease for an additional two years with a base annual rent increase of 3%.

Commitments

Our commitments primarily consist of obligations under our agreement with the University of Southampton. As of December 31, 2023, we were unable to estimate the timing or likelihood of achieving the milestones or making future product sales. For additional information regarding our agreements, see “Business—License and research agreements.”

Additionally, we have entered into agreements with third-party contract manufacturers for the manufacture and processing of certain of our product candidates for preclinical testing purposes, and we have entered and will enter into other contracts in the normal course of business with contract research organizations for clinical trials and other vendors for other services and products for operating purposes. These agreements generally provide for termination or cancellation, other than for costs already incurred.

Off-Balance Sheet Arrangements

During the periods presented, we did not have, nor do we currently have, any off-balance sheet arrangements as defined under SEC rules.

Critical Accounting Policies and Significant Judgments and Estimates

Our management’s discussion and analysis of our financial condition and results of operations is based on our consolidated financial statements, which have been prepared in accordance with generally accepted accounting principles, or GAAP. The preparation of these consolidated financial statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the consolidated financial statements, as well as the reported expenses incurred during the reporting periods. Our estimates are based on our historical experience and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions. We believe that the accounting policies discussed below are critical to understanding our historical and future performance, as these policies relate to the more significant areas involving management’s judgments and estimates.

While our significant accounting policies are more fully described in Note 2 to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K, we believe that the following accounting policies are the most critical in order to fully understand and evaluate our financial condition and results of operations.

Revenue Recognition

We recognize revenue in accordance with Accounting Standards Codification (“ASC”) Topic 606, *Revenue from Contracts with Customers* (“ASC 606”). This standard applies to all contracts with customers, except for contracts that are within the scope of other standards, such as leases, insurance, and financial instruments. Under ASC 606, an entity recognizes revenue when its customer obtains control of promised goods or services, in an amount that reflects the

consideration that the entity expects to receive in exchange for those goods or services. To determine revenue recognition for arrangements that an entity determines are within the scope of ASC 606, the entity performs the following five-step analysis: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) the entity satisfies a performance obligation. We only apply the five-step analysis to contracts when it is probable that the entity will collect the consideration to which it is entitled in exchange for the goods or services it transfers to the customer. As part of the accounting for these arrangements, we must use significant judgment to determine: (a) the number of performance obligations based on the determination under step (ii) above; (b) the transaction price under step (iii) above; and (c) the timing of satisfaction of performance obligations as a measure of progress in step (v) above.

For contracts determined to be within the scope of ASC 606, we assess whether the goods or services promised within each contract are distinct to identify those that are performance obligations. This assessment involves subjective determinations and requires management to make judgments about the individual promised goods or services and whether such are separable from the other aspects of the contractual relationship. Promised goods and services are considered distinct provided that: (i) the customer can benefit from the good or service either on its own or together with other resources that are readily available to the customer, and (ii) the entity's promise to transfer the good or service to the customer is separately identifiable from other promises in the contract. In assessing whether a promise or performance obligation is distinct from the other promises, we consider factors such as the research, development, manufacturing and commercialization capabilities of the customer and the availability of the associated expertise in the general marketplace. In addition, we consider whether the customer can benefit from a promise for its intended purpose without the receipt of the remaining promise, whether the value of the promise is dependent on the unsatisfied promise, whether there are other vendors that could provide the remaining promise, and whether it is separately identifiable from the remaining promise. For licenses that are combined with other promises, we utilize judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress for purposes of recognizing revenue.

The licenses of our intellectual property granted to Acadia were not determined to be distinct from the other promises or performance obligations, i.e., research and development services, identified in the arrangement. Accordingly, such licenses are therefore combined with research and development services in the arrangement. Payments or reimbursements resulting from our research and development efforts are recognized as the services are performed and presented on a gross basis because we are the principal for such efforts.

The transaction price (the amount of consideration we expect to be entitled to from a customer in exchange for the promised good or services) is determined and allocated to the identified performance obligations in proportion to their standalone selling prices ("SSP") on a relative SSP basis. SSP is determined at contract inception and is not updated to reflect changes between contract inception and when the performance obligations are satisfied.

We use significant judgment to determine whether milestone payments or other variable consideration, except for royalties, should be included in the transaction price. The transaction price is allocated to each performance obligation based on the relative standalone selling prices of each performance obligation in the contract, and we recognize revenue based on those amounts when, or as, the performance obligations under the contract are satisfied. Any variable consideration is constrained, and therefore, the cumulative revenue associated with this consideration is not recognized until it is deemed not to be at significant risk of reversal.

We then recognize as revenue the amount of the transaction price that is allocated to the respective performance obligation(s) when (or as) each performance obligation is satisfied, either at a point in time or over time, and if over time recognition is based on the appropriate method of measuring progress for purposes of recognizing revenue. We evaluate the measure of progress each reporting period and, if necessary, adjusts the measure of performance and related revenue recognition. Amounts received prior to being recognized as revenue are recorded as deferred revenue. Amounts expected to be recognized as revenue within the 12 months following the balance sheet date are classified as current portion of deferred revenue in the accompanying consolidated balance sheets. Amounts not expected to be recognized as revenue within the 12 months following the balance sheet date are classified as deferred revenue, net of current portion.

Customer options: If an arrangement is determined to contain customer options that allow the customer to acquire additional goods or services, the goods and services underlying the customer options are not considered to be performance obligations at the outset of the arrangement, as they are contingent upon option exercise. We evaluate the customer options for material rights, that is, the option to acquire additional goods or services for free or at a discount. If the customer options are determined to represent a material right, the material right is recognized as a separate performance obligation at the outset of the arrangement. We allocate the transaction price to material rights based on the standalone selling price. As a practical alternative to estimating the standalone selling price when the goods or services are both (i) similar to the original goods and services in the contract and (ii) provided in accordance with the terms of the original contract, we allocate the total amount of

consideration expected to be received from the customer to the total goods or services expected to be provided to the customer. Amounts allocated to any material right are not recognized as revenue until the option is exercised and the performance obligation is satisfied.

No such material rights were identified in the arrangement with Acadia. If such material rights were identified, then we would allocate the transaction price to material rights based on the relative standalone selling price, which is determined based on the identified discount and the probability that the customer will exercise the option. Amounts allocated to a material right are not recognized or begin to be recognized as revenue until, at the earliest, the option is exercised.

Milestone payments: At the inception of each arrangement that includes milestone payments, we evaluate whether a significant reversal of cumulative revenue provided in conjunction with achieving the milestones is probable and estimate the amount to be included in the transaction price using the most likely amount method. If it is probable that a significant reversal of cumulative revenue would not occur, the associated milestone value is included in the transaction price. Milestone payments that are not within the control of us or the licensee, such as regulatory approvals, are not considered probable of being achieved until those approvals are received. For other milestones, we evaluate factors such as the scientific, clinical, regulatory, commercial, and other risks that must be overcome to achieve the particular milestone in making this assessment. There is considerable judgment involved in determining whether it is probable that a significant reversal of cumulative revenue would not occur. At the end of each subsequent reporting period, we reevaluate the probability of achievement of all milestones subject to constraint and, if necessary, adjusts its estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis, which would affect revenues and earnings in the period of adjustment.

Accrued research and development expenses

As part of the process of preparing financial statements, we are required to estimate and accrue research and development expenses. This process involves the following:

- communicating with our applicable personnel to identify services that have been performed on our behalf and 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 cost;
- estimating and accruing expenses in our consolidated financial statements as of each balance sheet date based on facts and circumstances known to us at the time; and
- periodically confirming the accuracy of our estimates with selected service providers and making adjustments, if necessary.

Examples of estimated research and development expenses that we accrue include:

- fees paid to investigative sites in connection with clinical studies;
- fees paid to contract manufacturing organizations in connection with non-clinical development, preclinical research, and the production of clinical study materials; and
- professional service fees for consulting and related services.

We base our expense accruals related to non-clinical development, preclinical studies, and clinical trials on our estimates of the services received and efforts expended pursuant to contracts with organizations/consultants that conduct and manage clinical studies on our behalf. The financial terms of these agreements vary from contract to contract and may result in uneven payment flows. Payments under some of these contracts may depend on many factors, such as the successful enrollment of patients, site initiation, and the completion of clinical study milestones.

Our service providers invoice us monthly in arrears for services performed. 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 we do not identify costs that we have begun to incur, or if we underestimate or overestimate the level of services performed or the costs of these services, our actual expenses could differ from our estimates. To date, we have not experienced significant changes in our estimates of accrued research and development expenses after a reporting period. However, due to the nature of estimates, we cannot assure you that we will not make changes to our estimates in the future as we become aware of additional information about the status or conduct of our clinical trials and other research activities.

Stock-Based Compensation

Stock options

We recognize compensation costs related to awards granted to employees and directors, based on the estimated fair value of the awards on the date of grant. For stock options, we estimate the grant date fair value, and the resulting stock-based compensation, using the Black-Scholes option-pricing model. The grant date fair value of the stock-based awards is recognized on a straight-line basis over the requisite service period, which is generally the vesting period of the respective awards.

The Black-Scholes option-pricing model requires the use of subjective assumptions to determine the fair value of stock options. These key subjective assumptions include:

- *Expected term*—The expected term represents the period that stock options are expected to be outstanding. The expected term is determined using the simplified method. The simplified method deems the expected term to be the midpoint between the vesting date and the contractual life of the stock options.
- *Expected volatility*— We completed our IPO in June 2019 and accordingly, we lack sufficient company-specific historical and implied volatility information for our shares traded in the public markets commensurate with the expected term of our stock options. Therefore, we estimate our expected share price volatility based on a blend of our historical volatility and the historical volatility of publicly traded peer companies and expect to continue to do so until such time as we have adequate historical data regarding the volatility of our own traded share price. The comparable companies were chosen based on their similar size, stage in the life cycle or area of specialty.

The following table presents the weighted-average assumptions used to estimate the fair value of share-based awards granted:

	Year ended December 31,	
	2023	2022
Risk-free interest rate	3.57-3.94%	1.82-4.15%
Expected dividend yield	0%	0%
Expected life	5.5-6.25 years	5.5-6.25 years
Expected volatility	70-73%	70-71%

We will continue to use judgment in evaluating the assumptions utilized for the grant-date fair value of our stock options on a prospective basis.

Other Information

Net operating loss carryforwards

As of December 31, 2023, and 2022, the Company had federal NOL carryforwards of $189.5 million and $210.9 million, respectively, which may be available to reduce future taxable income. Federal NOLs generated prior to December 31, 2018 expire at various dates beginning in 2035 and NOLs generated after December 31, 2018 carryforward indefinitely. As of December 31, 2023, and 2022, the Company had state NOLs of $199.4 million and $212.8 million, respectively, which may be available to reduce future taxable income. The state NOLs expire at various dates beginning in 2035.

In accordance with ASC 740, *Accounting for Income Taxes*, management of the Company has evaluated the positive and negative evidence bearing upon the realizability of its deferred tax assets and has determined that it is more likely than not that the Company will not recognize the net benefits of federal and state deferred tax assets. A full valuation allowance of $133.3 million and $97.9 million was established at December 31, 2023 and 2022, respectively. The change in the valuation allowance was an increase of $35.4 million and $31.8 million in 2023 and 2022, respectively.

As of December 31, 2023 and 2022, the Company had federal research and development tax credit (“R&D Credit”) carryforwards of $12.8 million and $9.2 million, respectively, and state R&D Credit carryforwards of $5.9 million and $4.3 million, respectively. Both federal and state R&D Credit carryforwards may be available to reduce future tax liabilities and expire at various dates beginning in 2034.

The Internal Revenue Code of 1986, as amended ("IRC"), provides for a limitation of the annual use of NOLs, R&D Credits, and other tax attributes following certain ownership changes that could limit our ability to utilize NOL and R&D Credit carryforwards. Under IRC Sections 382 and 383 an ownership change is generally defined as a greater than 50% change (by value) in its equity ownership over a three-year period. The Company has experienced ownership changes in the past and based on the existing Section 382 limitations, $0.9 million and $0.02 million of existing Federal NOLs and R&D credits, respectively, will not be utilizable. The Company may experience additional ownership changes in the future because of subsequent shifts in our stock ownership. As a result, our ability to use our pre-change NOLs to offset taxable income, if any, is subject to limitations, which could potentially result in increased future tax liability. In addition, at the state level, there may be periods during which the use of NOLs is suspended or otherwise limited, which could accelerate or permanently increase state taxes owed.

Emerging Growth Company and Smaller Reporting Company Status

We are an "emerging growth company," as defined in the Jumpstart our Business Startups Act of 2012, or the JOBS Act. Under the JOBS Act, emerging growth companies can delay adopting new or revised accounting standards issued subsequent to the enactment of the JOBS Act until such time as those standards apply to private companies.

We have elected to use this extended transition period for complying with new or revised accounting standards that have different effective dates for public and private companies until the earlier of the date we (i) are no longer an emerging growth company or (ii) affirmatively and irrevocably opt out of the extended transition period provided in the JOBS Act.

As a result, our consolidated financial statements may not be comparable to companies that comply with new or revised accounting pronouncements as of public company effective dates.

We will remain an emerging growth company until the earliest of (i) the last day of our first fiscal year (a) following the fifth anniversary of the completion of our IPO, (b) in which we have total annual gross revenues of at least $1.235 billion, or (c) when we are deemed to be a large accelerated filer, which means the market value of our common stock that is held by non-affiliates exceeds $700.0 million as of the prior June 30th, and (ii) the date on which we have issued more than $1.0 billion in non-convertible debt securities during the prior three-year period. We anticipate ceasing to be an emerging growth company as of December 31, 2024, which is the last day of our fiscal year following the fifth anniversary of the completion of our IPO.

We are also a "smaller reporting company," meaning that the market value of our stock held by non-affiliates was less than $700.0 million and our annual revenue is less than $100.0 million during the most recently completed fiscal year. We will continue to be a smaller reporting company for so long as either (i) the market value of our stock held by non-affiliates is less than $250.0 million or (ii) our annual revenue is less than $100.0 million during the most recently completed fiscal year and the market value of our stock held by non-affiliates is less than $700.0 million. If we are a smaller reporting company at the time we cease to be an emerging growth company, we may continue to rely on exemptions from certain disclosure requirements that are available to smaller reporting companies. Specifically, as a smaller reporting company we may choose to present only the two most recent fiscal years of audited financial statements in our Annual Report on Form 10-K and, similar to emerging growth companies, smaller reporting companies have reduced disclosure obligations regarding executive compensation.

Recently Issued Accounting Pronouncements

In November 2023, the FASB issued ASU 2023-07, "*Segment Reporting (Topic 280): Improvements to Reportable Segment Disclosures*" ("ASU 2023-07"), which expands disclosures about a public entity's reportable segments and requires more enhanced information about a reportable segment's expenses, interim segment profit or loss, and how a public entity's chief operating decision maker uses reported segment profit or loss information in assessing segment performance and allocating resources. The standard is effective for annual reporting periods beginning after December 15, 2023, and interim periods within years beginning after December 15, 2024, with early adoption permitted. The Company is currently assessing the impact that the adoption will have on its consolidated financial statements.

In December 2023, the FASB issued ASU 2023-09, "*Income Taxes (Topic 740): Improvements to Income Tax Disclosures*" ("ASU 2023-09"). ASU 2023-09 requires that an entity disclose specific categories in the effective tax rate reconciliation as well as provide additional information for reconciling items that meet a quantitative threshold and certain disclosures of state versus federal income tax expenses and taxes paid. ASC 2023-09 is effective for fiscal years beginning after December 15, 2024. The Company does not expect the adoption of ASU 2023-09 to have a material impact on its consolidated financial statements and will adopt the standard effective January 1, 2025.

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

Interest rate risk

We are exposed to market risks in the ordinary course, primarily including interest sensitivities. As of December 31, 2023, we had cash, cash equivalents and marketable securities of $201.4 million and $229.6 million as of December 31, 2022. Our primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of U.S. interest rates. Because of the short-term maturities of our cash and cash equivalents, we do not believe that an immediate 10% increase in interest rates would have any significant impact on the realized value of our investments. Accordingly, we do not believe we are exposed to material market risk with respect to our cash and cash equivalents.

Inflation risk

Inflation generally affects us by increasing our clinical trial costs. We do not believe that inflation has had a material effect on our business, financial condition or results of operations during the years ended December 31, 2023 and 2022.

Item 8. Financial Statements and Supplementary Data.

The financial statements required to be filed pursuant to this Item 8 are appended to this report. An index of those financial statements is found in Item 15 of Part IV of this Annual Report on Form 10-K.

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

None.

Item 9A. Controls and Procedures.

Management's Evaluation of Disclosure Controls and Procedures

Under the supervision and with the participation of our management, including our Chief Financial Officer (Our principal accounting officer) and Chief Executive Officer (Our principal executive officer), we evaluated the effectiveness of the design and operation of our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended (Exchange Act)) as of December 31, 2023. The term "disclosure controls and procedures," as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act, means controls and other procedures of a company that are designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is accumulated and communicated to the company's management, including its principal executive and principal financial officers, as appropriate, to allow timely decisions regarding required disclosure. Management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Based on our management's evaluation (with the participation of our Chief Executive Officer and our Chief Financial Officer), as of the end of the period covered by this report, our Chief Executive Officer and our Chief Financial Officer have concluded that our disclosure controls and procedures were effective at the reasonable assurance level.

Management's Annual Report on Internal Control over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting as defined in Rule 13a-15(f) of the Exchange Act. Management assessed the effectiveness of our internal control over financial reporting as of December 31, 2023. In making this assessment, management used the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission (COSO) in *Internal Control—Integrated Framework* issued in 2013. Based upon the assessments, management has concluded that as of December 31, 2023 our internal control over financial reporting was effective to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements in accordance with GAAP.

This Annual Report on Form 10-K does not include an attestation report from our independent registered public accounting firm due to a transition period established by the rules of the Securities and Exchange Commission for newly public companies. Additionally, for so long as we remain an "emerging growth company" under the JOBS Act or a "smaller reporting company," our independent registered public accounting firm is not required to attest to the effectiveness of our internal control over financial reporting.

Changes in Internal Control over Financial Reporting

There has been no change in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) of the Exchange Act) during three months ended December 31, 2023 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Inherent Limitations on Effectiveness of Controls

Internal control over financial reporting may not prevent or detect all errors and all fraud. Any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving the desired control objective and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures.

Item 9B. Other Information.

Trading Arrangements

During the three months ended December 31, 2023, none of our directors or officers, as defined in Rule 16a-1(f), informed us of the adoption, modification or termination of a "Rule 10b5-1 trading arrangement" or "non-Rule 10b5-1 trading arrangement," as those terms are defined in Regulation S-K, Item 408, except as described in the table below:

Name	Title	Action	Date	Rule 10b5-1*	Non Rule 10b5-1**	Total Shares to be Sold	Expiration Date[1]
Jonathan Allan	General Counsel and Corporate Secretary	Termination(2)	12/6/2023	X		43,896	3/20/2024
Jonathan Allan	General Counsel and Corporate Secretary	Adoption	12/15/2023	X		16,065	12/15/2024
Edward Kaye	Chief Executive Officer	Adoption	12/26/2023	X		45,000	3/20/2025
Huw Nash	Chief Operating Officer & Chief Business Officer	Termination(3)	12/29/2023	X		631,450	6/1/2024
Huw Nash	Chief Operating Officer & Chief Business Officer	Adoption	12/29/2023	X		670,338	4/1/2025

* Intended to satisfy the affirmative defense of Rule 10b5-1(c) Act.

** Not intended to satisfy the affirmative defense of Rule 10b5-1(c) Act.

(1) Except as indicated by footnote, each trading arrangement permitted or permits transactions through and including the earlier to occur of (a) the completion of all purchases or sales or (b) the date listed in the table.

(2) On December 6, 2023, Jonathan Allan, General Counsel and Corporate Secretary, terminated a trading arrangement that was intended to satisfy the affirmative defense of Rule 10b5-1 (the "Allan 10b5-1 Plan"). The Allan 10b5-1 Plan was entered into on March 22, 2023, with an expiration date of March 20, 2024.

(3) On December 29, 2023, Huw Nash, COO and CBO, terminated a trading arrangement that was intended to satisfy the affirmative defense of Rule 10b5-1 (the "Nash 10b5-1 Plan"). The Nash 10b5-1 Plan was entered into on March 28, 2022, with an expiration date of June 1, 2024.

Each new Rule 10b5-1 Plan that was adopted in the above table includes a representation from Messrs. Allan, Kaye and Nash, respectively, to the broker administering the plan that he was not in possession of any material nonpublic information regarding the Company or the securities subject to the Rule 10b5-1 Plan at the time the Rule 10b5-1 Plan was entered into. A similar representation was made to us in connection with the adoption of the Rule 10b5-1 Plan under our insider trading policy. Those representations were made as of the Adoption Date set forth above, and speak only as of that date. In making those representations, there is no assurance with respect to any material nonpublic information of which the

directors and officers was unaware, or with respect to any material nonpublic information acquired by the above directors and officers or passage after the date of the representation.

Once executed, transactions under a Rule 10b5-1 Plan adopted during the period described above will be disclosed publicly through Form 4 and/or Form 144 filings with the SEC in accordance with applicable securities laws, rules, and regulations. Except as may be required by law, we do not undertake any obligation to update or report any modification, termination, or other activity under current or future Rule 10b5-1 plans that may be adopted by Messrs. Allan, Kaye or Nash, respectively, or other officers or directors of the Company.

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

None.

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 2024 Annual Meeting of Stockholders and is incorporated herein by reference.

We have adopted a Code of Conduct that applies to all of our officers, directors, and employees, including our principal executive officer, principal financial officer, principal accounting officer, and controller, or persons performing similar functions, which is posted on our website. Our Code of Conduct is a "code of ethics," as defined in Item 406(b) of Regulation S-K. We will make any legally required disclosures regarding amendments to, or waivers of, provisions of our Code of Conduct on our website. The information contained on, or accessible from, our website is not part of this Annual Report on Form 10-K by reference or otherwise.

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 2024 Annual Meeting of Stockholders and 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 2024 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 2024 Annual Meeting of Stockholders and is incorporated herein by reference.

Item 14. Principal Accountant Fees and Services.

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 2024 Annual Meeting of Stockholders and is incorporated herein by reference.

PART IV

Item 15. Exhibits, Financial Statement Schedules.

(a) The following documents are filed as a part of this Form 10-K:

Financial Statements

Our consolidated financial statements are listed in the "Index to Consolidated Financial Statements" under Part II, Item 8 of this Form 10-K.

Financial Statement Schedules

Financial statement schedules not listed have been omitted because they are not applicable, or the required information is shown in the consolidated financial statements or notes thereto.

Exhibits

Exhibit Number	Description	Form	File No.	Exhibit Filing Date	Exhibit No.	Filed/Furnished Herewith
3.1	Restated Certificate of Incorporation, as amended.					X
3.2	Restated Bylaws, as amended.	8-K	001-38938	February 3, 2023	3.1	
4.1	Form of Common Stock Certificate.	S-1	333-231700	June 7, 2019	4.1	
4.2	Description of Common Stock Registered Under Section 12 of the Securities Exchange Act of 1934.					X
4.3#	Registration Rights Agreement, by and among the Registrant, Blue Horizon Enterprise Ltd. and Ezbon International Limited, dated May 3, 2023.	10Q	001-38938	May 4, 2023	4.1	
10.1*	Form of Indemnification Agreement with directors and officers.	S-1	333-231700	June 7, 2019	10.1	
10.2*	2014 Equity Incentive Plan, as amended, and forms of award agreements.	S-1	333-231700	May 23, 2019	10.2	
10.3*	2019 Equity Incentive Plan, and forms of award agreements.	10-K	001-38938	March 6, 2023	10.3	
10.4*	2019 Employee Stock Purchase Plan, and forms of award agreements.	S-1	333-231700	June 7, 2019	10.5	
10.5*	2023 Inducement Plan, and forms of award agreements.	S-8	333-271273	April 13, 2023	99.1	
10.6*	Amended and Restated Executive Employment Agreement, by and between the Registrant and Edward M. Kaye, effective as of October 21, 2020.	10-Q	001-38938	November 12, 2020	10.1	
10.7*	Amended and Restated Executive Employment Agreement, by and between the Registrant and Stephen J. Tulipano, effective as of October 21, 2020.	10-Q	001-38938	November 12, 2020	10.2	
10.8*	Amended and Restated Executive Employment Agreement, by and between the Registrant and Barry Ticho, effective as of October 21, 2020.	10-K	001-38938	March 9, 2021	10.7	

Exhibit Number	Description	Form	File No.	Exhibit Filing Date	Exhibit No.	Filed/Furnished Herewith
10.9*	Change of Control and Severance Agreement, by and between the Registrant and Edward M. Kaye, effective as of October 21, 2020.	10-Q	001-38938	November 12, 2020	10.4	
10.10*	Change of Control and Severance Agreement, by and between the Registrant and Stephen J. Tulipano, effective as of October 21, 2020.	10-Q	001-38938	November 12, 2020	10.5	
10.11*	Change of Control and Severance Agreement, by and between the Registrant and Barry Ticho, effective as of October 21, 2020.	10-K	001-38938	March 9, 2021	10.10	
10.12	Lease Agreement, dated as of September 8, 2021, by and between ARE-MA Region No. 24, LLC and the Registrant, as amended to date.					X
10.13	Lease Agreement, by and between MIT 139 Main Street Leasehold LLC, and the Registrant., as amended to date.	10-Q	001-38938	August 10, 2021	10.1	
10.14	Scientific Advisory Board Agreement by and between the Registrant and Adrian Krainer, Ph.D., dated June 1, 2022.	10-Q	001-38938	August 8, 2022	10.1	
10.15†	License and Collaboration Agreement, dated as of January 9, 2022, by and between Acadia Pharmaceuticals Inc. and the Registrant.	10-Q	001-38938	May 10, 2022	10.1	
10.16	Controlled Equity Offering Sales Agreement, dated as of May 20, 2022, between the Registrant and Cantor Fitzgerald & Co..	S-3	333-265107	May 20, 2022	1.2	
21.1	Subsidiary of the Registrant.	S-1	333-231700	May 23, 2019	21.1	
23.1	Consent of independent registered public accounting firm.					X
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.					X
31.2	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.					X
32.1**	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.					X
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.					X
97	Compensation Recovery Policy					X
101.INS	Inline XBRL Instance Document.					X
101.SCH	Inline XBRL Taxonomy Extension Schema Document.					X

Exhibit Number	Description	Form	File No.	Exhibit Filing Date	Exhibit No.	Filed/Furnished Herewith
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document.					X
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document.					X
101.LAB	Inline XBRL Taxonomy Extension Label Linkbase Document.					X
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document.					X
104	Inline Cover Page Interactive Data File (formatted as inline XBRL and contained in Exhibit 101).					X

† Registrant has omitted certain portions of the exhibit pursuant to Item 601(b)(10) of Regulation S-K.
* Indicates a management contract or compensatory plan or arrangement in which directors or executive officers are eligible to participate.
*** The certifications furnished in Exhibits 32.1 and 32.2 hereto are deemed to accompany this Form 10-K and are not deemed "filed" for purposes of Section 18 of the Exchange Act, or otherwise subject to the liability of that section, nor shall they be deemed incorporated by reference into any filing under the Securities Act or the Exchange Act.*
 # Registrant has omitted schedules and exhibits pursuant to Item 601(a)(5) of Regulation S-K. The Registrant agrees to furnish supplementally a copy of the omitted schedules and exhibits to the SEC upon request.

Item 16. Form 10-K Summary

None.

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 Annual Report on Form 10-K to be signed on its behalf by the undersigned, thereunto duly authorized**.**

STOKE THERAPEUTICS, INC.

Date: March 25, 2024

By: /s/ Edward M. Kaye, M.D.

Edward M. Kaye, M.D.
Chief Executive Officer

POWER OF ATTORNEY

Each person whose individual signature appears below hereby authorizes and appoints Edward M. Kaye and Stephen J. Tulipano, and each of them, with full power of substitution and re-substitution 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 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 Annual Report on Form 10-K 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/ Edward M. Kaye Edward M. Kaye, M.D.	Chief Executive Officer and Director (Principal Executive Officer)	March 25, 2024
/s/ Stephen J. Tulipano Stephen J. Tulipano	Chief Financial Officer (Principal Financial and Accounting Officer)	March 25, 2024
/s/ Julie A. Smith Julie A. Smith	Director	March 25, 2024
/s/ Seth L. Harrison Seth L. Harrison, M.D.	Director	March 25, 2024
/s/ Adrian R. Krainer Adrian R. Krainer, Ph.D.	Director	March 25, 2024
/s/ Arthur A. Levin Arthur A. Levin, Ph.D.	Director	March 25, 2024
/s/ Arthur O. Tzianabos Arthur O. Tzianabos, Ph.D.	Director	March 25, 2024
/s/ Jennifer C. Burstein Jennifer C. Burstein	Director	March 25, 2024
/s/ Garry E. Menzel Garry E. Menzel	Director	March 25, 2024
/s/ Ian F. Smith Ian F. Smith	Director	March 25, 2024

STOKE THERAPEUTICS, INC.

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

Report of independent registered public accounting firm

To the Stockholders and the Board of Directors
Stoke Therapeutics, Inc.:

Opinion on the Consolidated Financial Statements

We have audited the accompanying consolidated balance sheets of Stoke Therapeutics, Inc. and subsidiary (the Company) as of December 31, 2023 and 2022, the related consolidated statements of operations and comprehensive loss, stockholders' equity, and cash flows for the years then ended, and the related notes (collectively, 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, 2023 and 2022, and the results of its operations and its cash flows for the years then ended, in conformity with U.S. generally accepted accounting principles.

Basis for Opinion

These consolidated financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these 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 in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit 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/ KPMG LLP

We have served as the Company's auditor since 2019.

Boston, Massachusetts
March 25, 2024

Stoke Therapeutics, Inc. and subsidiary
Consolidated balance sheets
(in thousands, except share and per share amounts)

	As of December 31,	
	2023	2022
Assets		
Current assets:		
Cash and cash equivalents	$ 191,442	$ 113,556
Marketable securities	9,952	116,039
Prepaid expenses	11,320	10,932
Other current assets	2,561	2,955
Interest receivable	64	588
Total current assets	$ 215,339	$ 244,070
Restricted cash	569	569
Operating lease right-of-use assets	6,611	4,753
Property and equipment, net	5,823	6,675
Total assets	$ 228,342	$ 256,067
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 1,695	$ 766
Accrued and other current liabilities	13,815	15,748
Deferred revenue - current portion	15,309	14,880
Total current liabilities	$ 30,819	$ 31,394
Deferred revenue - net of current portion	33,074	36,856
Other long term liabilities	4,884	2,968
Total long term liabilities	$ 37,958	$ 39,824
Total liabilities	$ 68,777	$ 71,218
Commitments and contingencies (Note 7)		
Stockholders' equity		
Common stock, par value of $0.0001 per share; 300,000,000 shares authorized, 45,918,233 and 39,439,575 shares issued and outstanding as of December 31, 2023 and 2022, respectively	5	4
Additional paid-in capital	561,433	483,170
Accumulated other comprehensive loss	(24)	(1,175)
Accumulated deficit	(401,849)	(297,150)
Total stockholders' equity	$ 159,565	$ 184,849
Total liabilities and stockholders' equity	$ 228,342	$ 256,067

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

Stoke Therapeutics, Inc. and subsidiary
Consolidated statements of operations and comprehensive loss
(in thousands, except share and per share amounts)

	Year Ended December 31,	
	2023	2022
Revenue	$ 8,780	$ 12,405
Operating expenses:		
Research and development	82,231	77,837
General and administrative	41,322	38,924
Total operating expenses	123,553	116,761
Loss from operations	(114,773)	(104,356)
Other income (expense):		
Interest income (expense), net	9,908	3,122
Other income (expense), net	166	167
Total other income (expense)	10,074	3,289
Net loss	$ (104,699)	$ (101,067)
Net loss per share—basic and diluted	$ (2.38)	$ (2.60)
Weighted average common shares outstanding—basic and diluted	43,994,862	38,897,442
Comprehensive loss:		
Net loss	$ (104,699)	$ (101,067)
Other comprehensive loss:		
Unrealized gain (loss) on marketable securities	1,151	(1,007)
Total other comprehensive gain (loss)	$ 1,151	$ (1,007)
Comprehensive loss	$ (103,548)	$ (102,074)

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

Stoke Therapeutics, Inc. and subsidiary
Consolidated statements of stockholders' equity
(in thousands, except share and per share amounts)

	Common Stock		Additional paid-in	Accumulated Other Comprehensive	Accumulated	Total Stockholders'
	Shares	Amount	capital	Gain (Loss)	deficit	equity
Balance as of December 31, 2021	36,902,499	$ 4	$ 414,024	$ (168)	$ (196,083)	$ 217,777
Unrealized loss on marketable securities	—	—	—	(1,007)	—	(1,007)
Stock-based compensation	—	—	22,854	—	—	22,854
Issuance of common stock upon exercise of stock options	269,288	—	494	—	—	494
Issuance of common stock related to employee stock purchase plan	44,002	—	570	—	—	570
Shares sold as part of controlled equity offering sales agreement	2,223,786	—	45,228	—	—	45,228
Net loss	—	—	—	—	(101,067)	(101,067)
Balance as of December 31, 2022	39,439,575	$ 4	$ 483,170	$ (1,175)	$ (297,150)	$ 184,849
Unrealized gain on marketable securities	—	—	—	1,151	—	1,151
Stock-based compensation	—	—	25,257	—	—	25,257
Issuance of common stock upon exercise of stock options	148,211	—	371	—	—	371
Issuance of common stock related to employee stock purchase plan	71,471	—	555	—	—	555
Shares sold as part of controlled equity offering sales agreement	6,258,976	1	52,080	—	—	52,081
Net loss	—	—	—	—	(104,699)	(104,699)
Balance as of December 31, 2023	45,918,233	$ 5	$ 561,433	$ (24)	$ (401,849)	$ 159,565

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

Stoke Therapeutics, Inc. and subsidiary
Consolidated statements of cash flows
(in thousands)

	Year Ended December 31,	
	2023	2022
Cash flows from operating activities:		
Net loss	$ (104,699)	$ (101,067)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation	2,469	1,546
Amortization and accretion of marketable securities	(325)	(211)
Stock-based compensation	25,257	22,854
Loss on disposal of property and equipment	1	—
Reduction in the carrying amount of right of use assets	2,260	1,989
Changes in assets and liabilities:		
Prepaid expenses and other current assets	529	(5,183)
Accounts payable, accrued liabilities, and operating leases	(3,208)	(3,530)
Deferred revenue	(3,351)	51,736
Net cash used in operating activities	(81,067)	(31,866)
Cash flows from investing activities:		
Purchases of property and equipment	(1,616)	(3,962)
Purchases of marketable securities	—	(201,320)
Sales of marketable securities	107,562	159,400
Net cash provided by (used in) investing activities	105,946	(45,882)
Cash flows from financing activities:		
Proceeds from issuance of common stock upon exercise of stock options	371	494
Proceeds from Employee Stock Purchase Plan	555	570
Proceeds from controlled equity offering sales agreement	52,081	45,344
Other	—	1
Net cash provided by financing activities	53,007	46,409
Net increase (decrease) in cash, cash equivalents and restricted cash	77,886	(31,339)
Cash, cash equivalents and restricted cash—beginning of year	114,125	145,464
Cash, cash equivalents and restricted cash—end of year	$ 192,011	$ 114,125
Supplemental Disclosure of Non-Cash Investing and Financing Activities:		
Right-of-use assets recognized in exchange for operating leases	$ 4,118	$ 1,802
Property and equipment included in accrued expense and accounts payable	$ —	$ 121

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

Stoke Therapeutics, Inc. and subsidiary

Notes to consolidated financial statements

(in thousands, except share and per share amounts)

1. Nature of the business and basis of presentation

Organization

Stoke Therapeutics, Inc. (the Company) was founded in June 2014 and was incorporated under the laws of the State of Delaware. The Company is an early-stage biopharmaceutical company pioneering a new way to treat the underlying causes of severe genetic diseases by precisely upregulating protein expression.

Shelf Registration

In May 2022, the Company filed a universal Shelf Registration statement on Form S-3 (the "Registration Statement") with the SEC. The Registration Statement was declared effective by the SEC on May 31, 2022, and contains two prospectuses: a base prospectus, which covers the offering, issuance and sale by the Company of up to a maximum aggregate offering price of $400.0 million of its common stock, preferred stock, debt securities, warrants to purchase common stock, preferred stock or debt securities, subscription rights to purchase common stock, preferred stock or debt securities and/or units consisting of some or all of these securities; and a sales agreement prospectus covering the offering, issuance and sale by the Company of up to a maximum aggregate offering price of $150.0 million of its common stock that may be issued and sold under a Controlled Equity Offering Sales Agreement ("Sales Agreement"). The specific terms of any securities to be offered pursuant to the base prospectus will be specified in a prospectus supplement to the base prospectus. The $150.0 million of common stock that may be offered, issued and sold under the sales agreement prospectus is included in the $400.0 million of securities that may be offered, issued and sold by the Company under the base prospectus. As of December 31, 2023, the Company had issued approximately 6.3 million shares of common stock pursuant to the Sales Agreement for net proceeds of $52.1 million. Since December 31, 2023, through the date of the issuance of these consolidated financial statements, the Company sold approximately 0.2 million shares of common stock and received $1.3 million after deducting commissions related to the Sales Agreement. The Company may terminate this at-the-market program at any time, pursuant to its terms.

Uncertainties

The Company is subject to risks and uncertainties common to early-stage companies in the biotechnology industry including, but not limited to, development by competitors of new technological innovations, dependence on key personnel, protection of proprietary technology, compliance with government regulations and ability to secure additional capital to fund operations. Product candidates currently under development will require significant additional research and development efforts, including extensive preclinical and clinical testing and regulatory approval prior to commercialization. These efforts require significant amounts of additional capital, adequate personnel and infrastructure and extensive compliance-reporting capabilities. Even if the Company's product development efforts are successful, it is uncertain when, if ever, the Company will realize significant revenue from product sales.

Liquidity

The Company expects that its operating losses and negative cash flows will continue for the foreseeable future. As of the issuance date of these consolidated financial statements, the Company expects that its cash, cash equivalents, marketable securities and restricted cash will be sufficient to fund its operating expenses and capital expenditure requirements through at least twelve months from the issuance date of these consolidated financial statements.

2. Summary of significant accounting policies and recent accounting pronouncements

Basis of presentation and consolidation

The accompanying consolidated financial statements have been prepared in accordance with U.S. generally accepted accounting principles (GAAP), and include the accounts of Stoke Therapeutics, Inc. and its wholly-owned subsidiary. Any reference in these notes to applicable guidance is meant to refer to GAAP as found in the Accounting Standards Codification ("ASC") and Accounting Standards Update ("ASU") of the Financial Accounting Standards Board ("FASB"). All intercompany transactions between and among the Company and its consolidated subsidiary have been eliminated.

Use of estimates

The preparation of consolidated financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the reported amounts of assets, liabilities, equity, expenses and disclosure of contingent assets and liabilities. Estimates are periodically reviewed in light of changes in circumstances, facts and experience. Actual results could differ from those estimates.

Cash and cash equivalents

The Company considers all highly liquid investments with an original maturity of three months or less at the date of purchase to be cash equivalents. The Company deposits its cash in checking, sweep and money market accounts.

Restricted cash

At December 31, 2023, restricted cash consisted of money market accounts collateralizing letters of credit issued as security deposits in connection with the Company's leases of its corporate facilities.

The following table reconciles cash and cash equivalents and restricted cash per the consolidated balance sheets to the statements of cash flows:

	As of December 31,	
	2023	2022
Cash and cash equivalents	$ 191,442	$ 113,556
Restricted cash	569	569
	$ 192,011	$ 114,125

Marketable Securities

Marketable securities consist of government securities and obligations, corporate bonds and commercial paper with original maturities of more than 90 days at the purchase date. Investments are classified as available-for-sale and are recorded on the balance sheet at fair value with unrealized gains or losses reported as a separate component of other comprehensive income/(loss). Management determines the appropriate classification of its investments at the time of purchase and reevaluates such determination at each balance sheet date.

Concentration of credit risk

Financial instruments that potentially expose the Company to concentrations of credit risk primarily consist of cash, cash equivalents and marketable securities. The Company maintains its cash, cash equivalents and marketable securities at accredited financial institutions in amounts that exceed federally insured limits. The Company does not believe that it is subject to unusual credit risk beyond the normal credit risk associated with commercial banking relationships.

Fair value of financial instruments

ASC Topic 820, Fair Value Measurement (ASC 820), establishes a fair value hierarchy for instruments measured at fair value that distinguishes between assumptions based on market data (observable inputs) and the Company's own assumptions (unobservable inputs). Observable inputs are those that market participants would use in pricing the asset or liability based on market data obtained from sources independent of the Company. Unobservable inputs are inputs that reflect the Company's assumptions about the inputs that market participants would use in pricing the asset or liability and are developed based on the best information available in the circumstances. ASC 820 identifies fair value as the exchange price, or exit price, representing the amount that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants. As a basis for considering market participant assumptions in fair value measurements, ASC 820 establishes a three-tier value hierarchy that distinguishes between the following:

Level 1—Quoted market prices in active markets for identical assets or liabilities.

Level 2—Inputs other than Level 1 inputs that are either directly or indirectly observable, such as quoted market prices, interest rates and yield curves.

Level 3—Unobservable inputs developed using estimates of assumptions developed by the Company, which reflect those that a market participant would use.

To the extent the valuation is based on models or inputs that are less observable or unobservable in the market, the determination of fair values requires more judgment. Accordingly, the degree of judgment exercised by the Company in determining fair value is greatest for instruments categorized as Level 3. A financial instrument's level within the fair value hierarchy is based on the lowest level of any input that is significant to the fair value measurement.

Revenue recognition

The Company recognizes revenue in accordance with ASC Topic 606, *Revenue from Contracts with Customers* ("ASC 606"). This standard applies to all contracts with customers, except for contracts that are within the scope of other standards. Under ASC 606, an entity recognizes revenue when its customer obtains control of promised goods or services, in an amount that reflects the consideration which the entity expects to receive in exchange for those goods or services.

In January 2022, the Company entered into a license and collaboration agreement with Acadia Pharmaceuticals, Inc. ("Acadia") which is within the scope of ASC 606 (see Note 8). In determining the appropriate amount of revenue to be recognized as it fulfills its obligations under this agreement, the Company performs the following steps: (i) identification of the promised goods or services in the contract; (ii) determination of whether the promised goods or services are performance obligations including whether they are distinct in the context of the contract; (iii) measurement of the transaction price, including the constraint on variable consideration; (iv) allocation of the transaction price to the performance obligations; and (v) recognition of revenue when (or as) the Company satisfies each performance obligation. As part of the accounting for this agreement, the Company must use its judgment to determine: (a) the number of performance obligations based on the determination under step (ii) above; (b) the transaction price under step (iii) above; (c) the stand-alone selling price for each performance obligation identified in the contract for the allocation of transaction price in step (iv) above; and (d) the contract term and pattern of satisfaction of the performance obligations under step (v) above. The Company uses judgment to determine whether milestones or other variable consideration, except for royalties, should be included in the transaction price. The transaction price is allocated to each performance obligation on a relative stand-alone selling price basis, for which the Company recognizes revenue as or when the performance obligations under the contract are satisfied.

Amounts due to the Company for satisfying the revenue recognition criteria or that are contractually due based upon the terms of the collaboration agreement are recorded as accounts receivable in the Company's consolidated balance sheets. Amounts received prior to satisfying the revenue recognition criteria are recorded as deferred revenue in the Company's consolidated balance sheets. Amounts expected to be recognized as revenue within the 12 months following the balance sheet date are classified as current deferred revenue. Amounts not expected to be recognized as revenue within the 12 months following the balance sheet date are classified as deferred revenue, net of current portion.

Upfront license fees

The licenses of the Company's intellectual property granted to Acadia was not determined to be distinct from the other promises or performance obligations identified in the agreement. Accordingly, such licenses are therefore combined with other promises in the agreement. The Company exercises judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress for purposes of recognizing revenue. The Company evaluates the measure of progress each reporting period and, if necessary, adjusts the measure of performance and related revenue recognition.

Customer options

If an arrangement is determined to contain customer options that allow the customer to acquire additional goods or services, the goods and services underlying the customer options are not considered to be performance obligations at the outset of the arrangement, as they are contingent upon option exercise. The Company evaluates the customer options for material rights or options to acquire additional goods or services for free or at a discount. If the customer options are determined to represent a material right, the material right is recognized as a separate performance obligation at the outset of the arrangement. No such material rights were identified in the arrangement with Acadia. If such material rights were identified, then the Company would allocate the transaction price to material rights based on the relative standalone selling price, which is determined based on the identified discount and the probability that the customer will exercise the option. Amounts allocated to a material right are not recognized or begin to be recognized as revenue until, at the earliest, the option is exercised.

Research and development services

The promises under the Company's collaboration agreement with Acadia includes research and development services to be performed by the Company for or on behalf of the customer. Payments or reimbursements resulting from the Company's research and development efforts are recognized as the services are performed and presented on a gross basis because the Company is the principal for such efforts.

Milestone payments

At the inception of the Acadia arrangement that includes development milestone payments, the Company evaluates whether the milestones are considered probable of being achieved and estimates the amount to be included in the transaction price using the most likely amount method. If it is probable that a significant revenue reversal would not occur, the associated milestone value is included in the transaction price. Milestone payments that are not within the control of the Company or the licensee, such as regulatory approvals, are not considered probable of being achieved until those approvals are received. The Company evaluates factors such as the scientific, clinical, regulatory, commercial and other risks that must be overcome to achieve the particular milestone in making this assessment. There is judgment involved in determining whether it is probable that a significant revenue reversal would not occur. At the end of each reporting period, the Company reevaluates the probability of achievement of all milestones subject to constraint and, if necessary, adjusts its estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis, which would affect revenues and earnings in the period of adjustment. The development milestones in the Acadia arrangement were not considered probable of achievement at the outset of the arrangement and as of December 31, 2023.

Deferred offering costs

The Company capitalizes certain legal, professional 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 in the consolidated statement of stockholders' equity as a reduction of additional paid-in capital.

Property and equipment

Property and equipment are recorded at cost less accumulated depreciation. Cost includes the acquisition costs and all costs necessary to bring the asset to the location and working condition necessary for its intended use. Depreciation expense is recognized using the straight-line method over the estimated useful life of each asset. 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 the accompanying consolidated statements of operations and comprehensive loss. Expenditures for normal, recurring or periodic repairs and maintenance related to property and equipment are charged to expense as incurred. The cost for planned major maintenance activities, including the related acquisition or construction of assets, is capitalized if it will result in future economic benefits.

Estimated useful lives for property and equipment are as follows:

Property and equipment	Estimated useful life
Computer and office equipment	3-5 years
Laboratory equipment and Furniture and fixtures	5-7 years
Leasehold improvements	Lesser of estimated useful life or remaining lease term

Impairment of long-lived assets

The Company reviews the recoverability of its long-lived assets when events or changes in circumstances occur that indicate that the carrying value of the assets may not be recoverable. The assessment of possible impairment is based on the ability to recover the carrying value of the assets from the expected future cash flows (undiscounted) of the related operations. If these cash flows are less than the carrying value of such assets, an impairment loss for the difference between the estimated fair value and carrying value is recorded. There were no impairment losses recognized during the years ended December 31, 2023 and 2022.

Research and development costs

Research and development costs are expensed as incurred. Research and development expenses are comprised of costs incurred in performing research and development activities, including salaries and benefits, facilities costs, depreciation, third-party license fees, and costs related to third parties engaged to conduct preclinical research development activities.

The Company has entered into various research and development contracts with research institutions and other companies to conduct research on its behalf. These agreements are generally cancellable. The Company records accruals for estimated ongoing research costs. When evaluating the adequacy of the accrued liabilities, the Company analyzes progress of the studies, including the phase or completion of events, invoices received and contracted costs. Significant judgments and estimates may be required in determining the accrued balances at the end of any reporting period. Actual results could differ from the Company's estimates. The Company's historical accrual estimates have not been materially different from the actual costs.

Stock-based compensation

The Company measures its stock-based awards granted based on the estimated fair values of the awards and recognizes the compensation expense for employees and nonemployees over the requisite service period.

Stock options

The Company uses the Black-Scholes option-pricing model to estimate the fair value of its stock options.

The Company has elected the practical expedient to use the midpoint between vesting date and the contractual term as the expected term for certain awards with service or performance conditions. Stock-based compensation is recognized using the straight-line method. Forfeitures of unvested stock-based awards are accounted for when they occur.

Restricted stock units ("RSUs")

For RSUs issued to employees, the Company recognizes the grant date fair value of the RSUs on a straight-line basis over the requisite service period, which is generally the vesting period of the respective awards. RSUs granted typically vest annually over a four-year period but may be granted with different vesting terms.

Patent costs

All patent-related costs 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 are classified as general and administrative expenses in the accompanying consolidated statements of operations and comprehensive loss.

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 estimated future tax consequences attributable to temporary differences between the consolidated financial statement carrying amounts of existing assets and liabilities and their respective tax base. Deferred tax assets and liabilities are determined on the basis of the differences between the consolidated financial statements and tax basis of assets and liabilities using enacted tax rates in effect for the year in which the temporary differences are expected to be settled or recovered. 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 taxable profits expected and considering prudent and feasible tax planning strategies. At December 31, 2023 and 2022, the Company has recorded a full valuation allowance.

Reserves are provided for tax benefits for which realization is uncertain. Such benefits are only recognized when the underlying tax position is considered more-likely-than-not to be sustained on examination by a taxing authority, assuming they possess full knowledge of the position and facts. Interest and penalties related to uncertain tax positions are recognized in the provision of income taxes; however, the Company currently has no interest or penalties related to uncertain income tax benefits.

Segment and geographic information

Operating segments are defined as components of an entity about which separate discrete information is available for evaluation by the chief operating decision maker, or decision-making group, in deciding how to allocate resources and in assessing performance. The Company operates in one segment in the United States. The Company's chief executive officer, as the chief operating decision-maker, manages and allocates resources to the operations of the Company on a total company basis using consolidated financial information.

Emerging growth company and smaller reporting company status

The Company is an emerging growth company, as defined in the Jumpstart Our Business Startups Act of 2012 (the JOBS Act). Under the JOBS Act, emerging growth companies can delay adopting new or revised accounting standards issued subsequent to the enactment of the JOBS Act, until such time as those standards apply to private companies.

The Company has elected to use this extended transition period for complying with new or revised accounting standards that have different effective dates for public and private companies until the earlier of the date that it is (i) no longer an emerging growth company or (ii) affirmatively and irrevocably opt out of the extended transition period provided in the JOBS Act. As a result, the Company's consolidated financial statements may not be comparable to companies that comply with the new or revised accounting pronouncements as of public company effective dates.

The Company will remain an emerging growth company until the earliest of (i) the last day of the first fiscal year (a) following the fifth anniversary of the completion of our IPO, (b) in which the Company has total annual gross revenue of at least $1.235 billion or (c) in which the Company is deemed to be a large accelerated filer, which means the market value of the Company's common stock that is held by non-affiliates exceeds $700.0 million as of the prior June 30th, and (ii) the date on which the Company has issued more than $1.0 billion in non-convertible debt securities during the prior three--year period. The Company anticipates ceasing to be an emerging growth company as of December 31, 2024, which is the last day of our fiscal year following the fifth anniversary of the completion of our IPO.

The Company is also a "smaller reporting company," meaning that in the event of an initial public offering the market value of its stock held by non-affiliates plus the proposed aggregate amount of gross proceeds to the Company as a result of such offering is less than $700.0 million and its annual revenue is less than $100.0 million during the most recently completed fiscal year. The Company may continue to be a smaller reporting company as long as either (i) the market value of its stock held by non-affiliates is less than $250.0 million or (ii) its annual revenue is less than $100.0 million during the most recently completed fiscal year and the market value of its stock held by non-affiliates is less than $700.0 million. If the Company is a smaller reporting company at the time it ceases to be an emerging growth company, the Company may continue to rely on exemptions from certain disclosure requirements that are available to smaller reporting companies. Specifically, as a smaller reporting company, the Company may choose to present only the two most recent fiscal years of audited financial statements in its Annual Report on Form 10-K and, similar to emerging growth companies, smaller reporting companies have reduced disclosure obligations regarding executive compensation.

Recently issued accounting pronouncements

In November 2023, the FASB issued ASU 2023-07, "*Segment Reporting (Topic 280): Improvements to Reportable Segment Disclosures*" ("ASU 2023-07"), which expands disclosures about a public entity's reportable segments and requires more enhanced information about a reportable segment's expenses, interim segment profit or loss, and how a public entity's chief operating decision maker uses reported segment profit or loss information in assessing segment performance and allocating resources. The standard is effective for annual reporting periods beginning after December 15, 2023, and interim periods within years beginning after December 15, 2024, with early adoption permitted. The Company is currently assessing the impact that the adoption will have on its consolidated financial statements.

In December 2023, the FASB issued ASU 2023-09, "*Income Taxes (Topic 740): Improvements to Income Tax Disclosures*" ("ASU 2023-09"). ASU 2023-09 requires that an entity disclose specific categories in the effective tax rate reconciliation as well as provide additional information for reconciling items that meet a quantitative threshold and certain disclosures of state versus federal income tax expenses and taxes paid. ASC 2023-09 is effective for fiscal years beginning after December 15, 2024. The Company does not expect the adoption of ASU 2023-09 to have a material impact on its consolidated financial statements and will adopt the standard effective January 1, 2025.

3. Fair value measurements

The following tables present information about the Company's financial assets measured at fair value on a recurring basis and indicate the level of the fair value hierarchy utilized to determine such fair values:

	Fair value measurements as of December 31, 2023			
	Level 1	Level 2	Level 3	Total
Cash equivalents:				
Money market funds	$ 186,186	$ —	$ —	$ 186,186
Total	$ 186,186	$ —	$ —	$ 186,186
Marketable Securities:				
US Government debt securities	$ —	$ 9,952	$ —	$ 9,952
Total	$ —	$ 9,952	$ —	$ 9,952

	Fair value measurements as of December 31, 2022			
	Level 1	Level 2	Level 3	Total
Cash equivalents:				
Money market funds	$ 111,927	$ —	$ —	$ 111,927
Total	$ 111,927	$ —	$ —	$ 111,927
Marketable Securities:				
Corporate bonds	$ —	$ 34,527	$ —	$ 34,527
Commercial paper	—	7,978	—	7,978
US Government debt securities	—	73,534	—	73,534
Total	$ —	$ 116,039	$ —	$ 116,039

The Company's cash equivalents and marketable securities are carried at fair value, determined according to the fair value hierarchy described above and in Note 2. The carrying value of the Company's accounts payable and accrued expenses approximate their fair values due to the short-term nature of these liabilities.

The Company's assets with fair value categorized as Level 1 within the fair value hierarchy include money market funds. Money market funds are publicly traded mutual funds and are presented as cash equivalents on the consolidated balance sheets as of December 31, 2023 and 2022.

The Company measures its marketable securities at fair value on a recurring basis and classifies those instruments within Level 2 of the fair value hierarchy. Marketable securities are valued using models or other valuation methodologies that use Level 2 inputs. These models are primarily industry-standard models that consider various assumptions, including time value, yield curve, volatility factors, default rates, current market and contractual prices for the underlying financial instruments, as well as other economic measures. Substantially all of these assumptions are observable in the marketplace, can be derived from observable data or are supported by observable levels at which transactions are executed in the marketplace.

There were no transfers to Level 3 in the periods presented.

4. Marketable Securities

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

	As of December 31, 2023			
	Amortized Cost	Unrealized Gains	Unrealized Loss	Fair Value
Marketable securities:				
US Government debt securities	$ 9,976	$ —	$ (24)	9,952
Total	$ 9,976	$ —	$ (24)	$ 9,952

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

	As of December 31, 2022			
	Amortized Cost	Unrealized Gains	Unrealized Loss	Fair Value
Marketable securities:				
Corporate bonds	$ 34,662	$ —	$ (135)	$ 34,527
Commercial paper	8,019	—	(41)	7,978
US Government debt securities	74,533	—	(999)	73,534
Total	$ 117,214	$ —	$ (1,175)	$ 116,039

The weighted average maturity of the Company's marketable securities as of December 31, 2023 ranges from approximately 0.09 years to 0.16 years.

The Company did not record an allowance for credit losses as of December 31, 2023 related to our marketable securities. Further, given the lack of significant change in the credit risk of these investments, the Company did not recognize any other-than-temporary impairment losses.

5. Property and equipment, net

Property and equipment, net consisted of the following:

	As of December 31,	
	2023	2022
Laboratory equipment	$ 9,383	$ 7,903
Furniture and fixtures	312	312
Leasehold improvements	2,294	1,867
Office equipment	440	353
Construction in progress	65	447
	12,494	10,882
Less accumulated depreciation	(6,671)	(4,207)
	$ 5,823	$ 6,675

Depreciation expense was $2.5 million and $1.5 million for the years ended December 31, 2023 and 2022, respectively.

6. Accrued and other current liabilities

Accrued and other current liabilities consisted of the following:

	As of December 31,	
	2023	2022
Accrued employee compensation costs	$ 5,611	$ 5,754
Accrued professional	651	525
Accrued research and development costs	4,634	6,601
Current portion of operating lease liabilities	2,062	2,359
Other current liabilities	857	509
	$ 13,815	$ 15,748

7. Commitments and contingencies

Operating leases

The Company determines whether an arrangement is a lease at inception. The Company accounts for a lease when it has the right to control the leased asset for a period of time while obtaining substantially all of the assets' economic benefits. Operating lease right-of-use assets and operating lease liabilities are recognized based on the present value of the future minimum lease payments over the lease term at the lease commencement date. The discount rate used to determine the present value of the lease payments is the Company's incremental borrowing rate based on the information available at lease inception, as the Company did not have information to determine the rate implicit in the leases. Lease expense for operating

leases is recognized on a straight-line basis over the reasonably assured lease term based on the total lease payments (which include initial direct costs and lease incentives). Lease expense is included in operating expenses in the consolidated statements of operations and comprehensive loss. The Company's lease agreements also contain variable payments, primarily maintenance-related costs, which are expensed as incurred and not included in the measurement of the right-of-use assets and lease liabilities.

In August 2018, the Company entered into an agreement to lease approximately 23,000 square feet of space for a term of three years. Lease terms are triple net lease commencing at $0.9 million per year, then with 3% annual base rent increases plus operating expenses, real estate taxes, utilities and janitorial fees. The lease commencement date was December 10, 2018.

In September 2021, the Company entered into an agreement to extend the initial term of the 23,000 square foot lease for a period of three years commencing on December 15, 2021 and ending December 31, 2024. In addition, this lease provides for the lease of an additional 15,000 square feet of rentable space beginning on April 1, 2022 and ending on December 31, 2024. In December 2021, the Company recognized a right-of-use asset and operating lease liability of $3.5 million for the 23,000 square feet. On April 1, 2022, the Company recognized a right-of-use asset and operating lease liability of $1.8 million for the 15,000 square feet.

In December 2023, the Company entered into an agreement to extend the term of the 38,000 square foot lease for a period of two years commencing on January 1, 2025 and ending on December 31, 2026. In December 2023, the Company recognized a right-of-use asset and operating lease liability of $4.1 million.

In December 2018, the Company entered into an agreement to lease 2,485 square feet of space for an initial term of three years. The lease includes one renewal option for an additional two years, however, any time after the initial term the landlord may relocate the Company from the premises to a space reasonably comparable in size and utility. As the Company does not have the right to control the use of the identified asset after the initial term, the renewal option was excluded from the lease liability calculation. Lease terms commence at $0.2 million per annum, with 2.5% annual base rent increases plus operating expenses, real estate taxes, utilities and janitorial fees. The lease commencement date was May 1, 2019.

In June 2021, the Company amended the agreement to extend the initial term of the 2,485 square foot lease for a period of three years commencing May 1, 2022 and ending April 30, 2025. In addition, the amendment provided for the lease of an additional 2,357 square feet of rentable space beginning on July 6, 2021 and ending on April 30, 2025. The amended lease provides the Company with the option to extend the term of the lease for an additional two years. In 2021, the Company recognized a right-of-use asset and operating lease liabilities of $0.7 million for the extension of the lease to April 30, 2025 and a right-of-use asset and operating lease liabilities of $0.8 million for the additional 2,357 square feet of rentable space.

Future minimum lease payments under non-cancellable leases as of December 31, 2023, are as follows (in thousands):

2024	$ 2,608
2025	2,661
2026	2,564
Total lease payments	7,833
Less imputed interest	(998)
Present value of lease liabilities	$ 6,835

Lease balances as of December 31, 2023 and December 31, 2022 are as follows (in thousands):

	As of December 31,	
	2023	2022
Operating right-of-use assets	$ 6,611	$ 4,753
Current portion of operating lease liabilities	$ 2,062	$ 2,359
Non-current portion of operating lease liabilities	4,773	2,717
Total operating lease liabilities	$ 6,835	$ 5,076

The weighted average remaining lease term and weighted average discount rate of our operating leases as of December 31, 2023 are as follows:

Weighted average remaining lease term in years	2.9
Weighted average discount rate	9.92%

In accordance with Topic 842, lease expense incurred under operating leases was $2.4 million for the year ended December 31, 2023, and $2.2 million for the year ended December 31, 2022.

Scientific Advisory Board Agreement

In June 2020, the Company entered into a scientific advisory board agreement with a member of the Company's board of directors, who is also an employee of Cold Spring Harbor Laboratory ("CSHL"), to provide scientific advisory services related to the Company's Targeted Augmentation of Nuclear Gene Output ("TANGO") antisense oligonucleotide technology and other antisense oligonucleotide technologies, as well as current and future therapeutic targets and programs. Following the expiration of the initial scientific agreement in June 2021 and a renewal agreement in June 2022, the parties entered into subsequent scientific board agreements on substantially the same terms. The Company did not recognize any expense in the year ending December 31, 2023 compared to expense of $0.02 million for the year ended December 31, 2022. The agreement has expired with no renewal put in place.

License and research agreements

In July 2015, the Company entered into a worldwide license agreement with CSHL (the "CSHL Agreement"), with respect to TANGO patents. Under the CSHL Agreement, the Company received an exclusive (except with respect to certain government rights and non-exclusive licenses), worldwide license under certain patents and applications relating to TANGO. The CSHL Agreement obligated the Company to make payments that are contingent upon certain milestones being achieved. The Company was also required to pay royalties, tiered based on the scope of patent coverage for each licensed product, ranging from a low-single digit percentage to a mid-single digit percentage on annual net sales. These royalty obligations applied on a licensed product-by-licensed product and country-by-country basis until the latest of (i) the expiration of the last valid claim of a CSHL patent covering the applicable licensed product or (ii) the expiration of any regulatory exclusivity for the applicable licensed product. In addition, if the Company sublicensed the rights under the CSHL Agreement, it was required to pay a maximum of twenty percent of the sublicense revenue to CSHL, which may have been reduced to a mid-teens or a mid-single digit percentage upon achievement of certain clinical milestones for the applicable licensed product. Finally, the Company was required to pay an annual license maintenance fee of $0.01 million, which amount is creditable against any owed royalty or milestone payments. The maximum aggregate potential milestone payments payable totaled approximately $0.90 million. Additionally, certain licenses under the CSHL Agreement required the Company to reimburse CSHL for certain past and ongoing patent related expenses, however there were no expenses related to these reimbursable patent costs during the years ended December 31, 2023 and 2022. After the completion of a 90-day waiting period, in May 2023 the Company terminated the CSHL Agreement. The Company does not expect the termination of the CSHL Agreement to have a significant impact on the intellectual property underlying any of its current product candidates, including STK-001 and STK-002, or its continued development of the TANGO platform.

In April 2016, the Company entered into an exclusive, worldwide license agreement with the University of Southampton (the "Southampton Agreement"), whereby the Company acquired rights to foundational technologies related to the Company's TANGO technology. Under the Southampton Agreement, the Company receives an exclusive, worldwide license under certain licensed patents and applications relating to TANGO. Under the Southampton Agreement, the Company may be obligated to make additional payments that are contingent upon certain milestones being achieved, as well as royalties on future product sales. These royalty obligations survive until the latest of (i) the expiration of the last valid claim of a licensed patent covering a subject product or (ii) the expiration of any regulatory exclusivity for the subject product in a country. In addition, if the Company sublicenses its rights under the Southampton Agreement, the Company is required to pay a mid-single digit percentage of the sublicense revenue to the University of Southampton. As of December 31, 2023, the Company had paid $0.7 million under the Southampton Agreement as a result of entering into the Acadia Pharmaceuticals Inc. license and collaboration agreement in January 2022 (see Note 8). Additionally, certain licenses under the Southampton Agreement require the Company to reimburse the University of Southampton for certain past and ongoing patent related expenses. For the year ended December 31, 2023 these expenses were $0.2 million compared to $0.02 million for the year ended December 31, 2022.

Litigation

The Company may periodically become subject to legal proceedings and claims arising in connection with ongoing business activities, including claims or disputes related to patents that have been issued or that are pending in the field of research on which it is focused. As of December 31, 2023, the Company had no legal proceedings to which it was a party or to which its property was subject that, in the opinion of management, would have a material adverse effect on its business.

8. License and Collaboration Agreement with Acadia Pharmaceuticals Inc.

In January 2022, the Company entered into a license and collaboration agreement with Acadia Pharmaceuticals Inc. for the discovery, development and commercialization of novel RNA-based medicines for the treatment of severe and rare genetic neurodevelopmental diseases of the central nervous system. The agreement focuses on the targets SYNGAP1, MECP2 (Rett syndrome), and an undisclosed neurodevelopmental target of mutual interest. In connection with each target, the Company will collaborate with Acadia to identify potential treatments for further development and commercialization as licensed products. With respect to SYNGAP1, the Company has agreed with Acadia to co-develop and co-commercialize licensed products for such target globally, and in connection therewith the Company granted to Acadia worldwide, co-exclusive (with Stoke) licenses for such licensed products. With respect to MECP2 and the neurodevelopmental target, the Company granted to Acadia worldwide, exclusive licenses to develop and commercialize licensed products for such targets.

Pursuant to the terms of the agreement, the Company received an upfront payment of $60.0 million from Acadia. Acadia agreed to fund the research to identify potential licensed products for MECP2 and the neurodevelopmental target, and the Company will equally fund with Acadia the research to identify potential licensed products for SYNGAP1. The Company is eligible to receive up to $907.5 million in potential total milestone payments based upon the achievement of certain development, regulatory, first commercial sales and sales milestone events across the programs for the three targets, assuming each milestone were achieved at least once. With respect to licensed products for MECP2 and the neurodevelopmental target, the Company is also eligible to receive tiered royalties at percentages ranging from the mid-single digits to the mid-teens on future net sales by Acadia of licensed products worldwide. Royalties payable under the agreement are subject to standard royalty reductions. For SYNGAP1 licensed products that the Company is co-developing and co-commercializing, the Company will be responsible for 50% of the development and commercialization costs and will receive 50% of the profits from global commercialization. The Company is provided with a co-development and co-commercialization opt out option relating to the SYNGAP1 target indication at the Company's discretion. Such opt-out would reduce development and commercialization milestones but would provide the Company with royalties on an escalating basis attributable to net sales milestones.

Acadia Agreement Accounting

At the commencement of the Acadia agreement the Company identified three performance obligations consisting of pre-clinical research activities for each of the three targets, SYNGAP1, MECP2, and the undisclosed neurodevelopmental target. The exclusive or co-exclusive licenses granted to Acadia to conduct pre-clinical research activities on each of the three targets, and participation on each of the respective joint research committees were identified as promised services. However, the licenses granted to Acadia and the research activities were determined to be not distinct from each other, and therefore are considered a combined performance obligation for each of the three targets. Participation on each of the joint research committees was determined to be quantitatively and qualitatively immaterial in the context of the arrangement with Acadia.

The Company is recognizing the transaction price for the pre-clinical research activities for each of the three targets over time as the research services are provided. The transfer of control to Acadia occurs over this time period, and in management's judgment, is the best measure of progress towards satisfying the performance obligation. An input method is used that measures the cost incurred to date in satisfying each of the three research activities in relation to the estimated total projected cost of each of the research activities to fulfill the respective obligations. The cumulative effect of revisions to estimated costs and/or the transaction price to complete the research performance obligations will be recorded in the period in which changes are identified and amounts can be reasonably estimated. Payments or reimbursements resulting from the Company's research and development efforts were recognized as the services are performed.

Milestone payments that are not within the control of the Company, such as regulatory approvals, are not considered probable of being achieved until those approvals are received. For other milestones, the Company evaluated factors such as the scientific, clinical, regulatory, commercial, and other risks that must be overcome to achieve the particular milestone in making this assessment. Milestones that are outside of the Company's or Acadia's control will not be recognized until such milestones are achieved. As to the other milestones, to date, no milestone payments have been included in the transaction price due the uncertainty as to whether these milestones will be achieved. The Company will at the end of each reporting period reevaluate the probability of achievement of all milestones subject to constraint and, if necessary, adjust its estimate of

the overall transaction price for each of the research activities on the three targets. Any such adjustments will be recorded on a cumulative catch-up basis.

As of December 31, 2023, the Company had $48.4 million in upfront consideration associated with the Acadia agreement relating to performance obligations that are unsatisfied or partially unsatisfied.

9. Stock-Based Compensation

In June 2019, the Company's board of directors and stockholders approved the 2019 Equity Incentive Plan (the "2019 Plan") which became effective on June 17, 2019 and replaced the Company's 2014 Equity Incentive Plan (the "2014 Plan"). In addition to the shares of common stock reserved for future issuance under the 2014 Plan that were added to the 2019 Plan upon its effective date, the Company initially reserved 2,200,000 shares of common stock for issuance under the 2019 Plan. The number of shares reserved for issuance under the Company's 2019 Plan will increase automatically on January 1 of each of 2020 through 2029 by the number of shares equal to 4% of the aggregate number of outstanding shares of the Company's common stock as of the immediately preceding December 31, or a lesser number as may be determined by the Company's board of directors.

In April 2023, the Company's board of directors adopted the Stoke Therapeutics, Inc. 2023 Inducement Plan (the "2023 Plan"). As permitted by Nasdaq stock market rules, the Company's stockholders were not required to approve the Inducement Plan. The Inducement Plan provides for up to 1,000,000 shares of the Company's common stock under awards granted to newly hired employees. An "award" is any right to receive common stock of the Company through nonstatutory stock options or restricted stock units.

As of December 31, 2023 there were no shares available for future issuance under the 2014 Plan, 2,767,209 shares were available for future issuance under the 2019 Plan and 940,300 shares were available under the 2023 Plan.

During the years ended December 31, 2023 and 2022, the Company granted options to purchase 1,599,227 and 3,459,500 shares of common stock to certain of its employees, and directors, respectively. The options vest over a period of up to four years. During the year ended December 31, 2023, the Company granted 1,538,302 restricted stock units to its employees. The restricted stock units vest over a period of up to four years.

In December 2023, the Company offered employees with outstanding option grants that had an exercise price of greater than $14.00 per share the opportunity to exchange those options for a number of restricted stock units with a fair value equal to the then fair value of the options surrendered. As a result, there was no material incremental compensation expense associated with those RSUs issued in exchange for options. The RSUs vest annually over a period of one to two years. In the aggregate, 2,907,127 options were exchanged for 730,602 RSUs.

A summary of stock option activity for awards is presented below:

	Number of shares	Weighted average exercise price	Weighted average remaining contractual life (years)	Aggregate intrinsic value[1]
Outstanding as of December 31, 2022	8,274,647	$ 18.28	7.6	$ 20,598
Granted	1,599,227	9.32		
Exercised	(145,877)	2.55		
Forfeitures[2]	(1,449,164)	28.00		
Expired[2]	(1,800,770)	34.88		
Outstanding as of December 31, 2023	6,478,063	$ 9.64	6.9	$ 8,435
Exercisable as of December 31, 2023	4,034,517	$ 8.88	5.7	$ 8,439

(1) The aggregate intrinsic value is calculated as the difference between the exercise price of the underlying options and the fair value of the common stock for the options that were in the money at December 31, 2023 and 2022.

(2) Options exchanged are classified as either forfeitures or expired based on vesting status at the time of Exchange Offer.

The weighted average grant date fair value for stock options granted during the years ended December 31, 2023 and 2022 was $6.13 and $10.32, respectively. The aggregate grant date fair value of stock options granted during the years ended

December 31, 2023 and 2022 was $9.8 million and $35.7 million, respectively. The aggregate intrinsic value of stock options exercised during the year ended December 31, 2023 and 2022 was $0.9 million and $3.5 million, respectively.

A summary of restricted stock unit activity is presented below:

	Number of shares	Aggregate intrinsic value	Weighted average grant date fair value
Outstanding as of December 31, 2022	—	$ —	$ —
Awarded	807,700		9.04
RSUs in exchange for options as part of option exchange	730,602		3.95
Vested	—		—
Forfeitures	(25,200)		9.15
Outstanding as of December 31, 2023	1,513,102	$ 7,959	$ 6.58
Vested or expected to vest as of December 31, 2023	1,513,102	$ 7,959	$ 6.58

For the year ended December 31, 2023, there were no vested RSUs.

Stock-based compensation

The Company recorded stock-based compensation expense of $25.3 million and $22.9 million during the years ended December 31, 2023 and 2022, respectively. Of the total stock-based compensation recorded during the year ending December 31, 2023, $2.3 million is related to restricted stock units. There were no grants of restricted stock units prior to 2023.

As of December 31, 2023, there was $16.1 million of unrecognized compensation cost related to unvested stock options granted under the 2019 and the 2023 Plans. Compensation expense is expected to be recognized over a weighted average period of 2.6 years as of December 31, 2023. As of December 31, 2023, there was $26.5 million of unrecognized stock-based compensation related to restricted stock units and it is expected to be recognized over a weighted average period of 2.5 years.

Stock-based compensation expense recorded as research and development and general and administrative expenses in the accompanying consolidated statements of operations and comprehensive loss is as follows:

	Year ended December 31,	
	2023	2022
Research and development	$ 9,925	$ 8,901
General and administrative	15,332	13,953
	$ 25,257	$ 22,854

The Company uses the Black-Scholes option pricing model to calculate the grant-date fair value of stock options. The fair values of the options granted to employees and directors were calculated using the following assumptions for the years ended December 31, 2023 and 2022:

	Year ended December 31,	
	2023	2022
Risk-free interest rate	3.57-3.94%	1.82-4.15%
Expected dividend yield	0%	0%
Expected life	5.5-6.25 years	5.5-6.25 years
Expected volatility	70-73%	70-71%

2019 Employee stock purchase plan

In June 2019, the Company adopted the 2019 Employee Stock Purchase Plan (“ESPP”), which became effective on June 18, 2019. The Company initially reserved 315,000 shares of common stock for sale under the ESPP. At December 31, 2023, the Company had 1,704,168 shares available for issuance under the plan. The average grant date fair value per share under the plan was $9.88 for 2023. The total ESPP stock-based compensation expense for the year ended December 31, 2023 was $0.3 million and for the year ended December 31, 2022 was $0.3 million. The number of shares reserved for issuance under the ESPP will increase automatically on January 1st of each of the first ten calendar years following the first offering

date by the number of shares equal to the lesser of 1% of the total outstanding shares of the Company's common stock as of the immediately preceding December 31 or a lower amount determined by the Company's board of directors. The aggregate number of shares issued over the term of the ESPP will not exceed 3,150,000 shares of the Company's common stock.

10. Net loss per share

The following table summarizes the computation of basic and diluted net loss per share of the Company:

	Year ended December 31,	
	2023	2022
Numerator:		
Net loss	$ (104,699)	$ (101,067)
Denominator:		
Weighted-average number of common shares, basic and diluted	43,994,862	38,897,442
Net loss per share, basic and diluted	$ (2.38)	$ (2.60)

The Company's potential dilutive securities, which include common stock, RSUs, and ESPP purchase rights, have been excluded from the computation of diluted net loss per share as the effect would be anti-dilutive. Therefore, the weighted average number of common shares outstanding used to calculate both basic and diluted net loss per share is the same.

The Company excluded the following potential common shares, presented based on amounts outstanding at period end, from the computation of diluted net loss per share for the periods indicated because including them would have had an anti-dilutive effect:

	As of December 31,	
	2023	2022
Outstanding options to purchase common stock	6,478,063	8,274,647
Restricted stock units	1,513,102	—
Total	7,991,165	8,274,647

11. Income taxes

A reconciliation of the expected income tax expense (benefit) computed using the federal statutory income tax rate the Company's effective income tax rate is as follows:

	Year ended December 31,	
	2023	2022
Expected income tax benefit at the federal statutory rate	21.0 %	21.0 %
State income taxes, net of federal benefit	7.7	7.4
Non-deductible items	(1.1)	(0.9)
Research and development credit, net	3.5	3.9
Other	2.4	0.1
Change in valuation allowance	(33.5)	(31.5)
Total	0.0 %	0.0 %

The principal components of the Company's deferred tax assets and liabilities consist of the following:

	As of December 31,	
	2023	2022
Deferred tax assets:		
Federal and state net operating loss carryforwards	$ 52,643	$ 57,746
Research and development tax credits	17,444	12,613
Research and development capitalized expenses	32,290	17,148
Accrued compensation and stock-based compensation	17,912	10,274
Deferred revenue/other	13,017	142
Gross deferred tax assets	133,306	97,923
Less: valuation allowance	(133,306)	(97,923)
Net deferred tax assets	$ —	$ —

From inception through December 31, 2022, the Company has incurred net operating losses ("NOL"). During 2023, for income tax purposes, the Company was required to fully recognize any unamortized advanced payments from the Acadia Collaboration Agreement as income, which in addition to capitalizing Section 174 research expenses resulted in taxable income that was fully offset by the use of existing net operating losses and tax credits. The Company does not expect future taxable income and should incur substantial future losses.

In accordance with ASC 740, Accounting for Income Taxes, management of the Company has evaluated the positive and negative evidence bearing upon the realizability of its deferred tax assets and has determined that it is more likely than not that the Company will not recognize the net benefits of federal and state deferred tax assets. A full valuation allowance of $133.3 million and $97.9 million was established at December 31, 2023 and 2022, respectively. The change in the valuation allowance was an increase of $35.4 million and $31.8 million in 2023 and 2022, respectively.

As of December 31, 2023, and 2022, the Company had federal NOL carryforwards of $189.5 million and $210.9 million, respectively, which may be available to reduce future taxable income. Federal NOLs generated prior to December 31, 2018 expire at various dates beginning in 2035 and NOLs generated after December 31, 2018 carryforward indefinitely. As of December 31, 2023, and 2022, the Company had state NOLs of $199.4 million and $212.8 million, respectively, which may be available to reduce future taxable income. The state NOLs expire at various dates beginning in 2035.

As of December 31, 2023 and 2022, the Company had federal research and development tax credit ("R&D Credit") carryforwards of $12.8 million and $9.2 million, respectively, and state R&D Credit carryforwards of $5.9 million and $4.3 million, respectively. Both federal and state R&D Credit carryforwards may be available to reduce future tax liabilities and expire at various dates beginning in 2034.

The Internal Revenue Code of 1986, as amended ("IRC"), provides for a limitation of the annual use of NOLs, R&D Credits, and other tax attributes following certain ownership changes that could limit our ability to utilize NOL and R&D Credit carryforwards. Under IRC Sections 382 and 383 an ownership change is generally defined as a greater than 50% change (by value) in its equity ownership over a three-year period. The Company has experienced ownership changes in the past and based on the existing Section 382 limitations, $0.9 million and $0.02 million of existing Federal NOLs and R&D credits, respectively, will not be utilizable. The Company may experience additional ownership changes in the future because of subsequent shifts in its stock ownership. As a result, the Company's ability to use its pre-change NOLs to offset taxable income, if any, is subject to limitations, which could potentially result in increased future tax liability. In addition, at the state level, there may be periods during which the use of NOLs is suspended or otherwise limited, which could accelerate or permanently increase state taxes owed.

The Company applies ASC 740 related to accounting for uncertainty in income taxes. The Company's reserves related to income taxes are based on a determination of whether, and how much of, a tax benefit taken by the Company in its tax filings or positions is more likely than not to be realized following resolution of any potential contingencies present related to the tax benefit. At December 31, 2023, and 2022 the Company had no unrecognized tax benefits. Interest and penalty charges, if any, related to unrecognized tax benefits would be classified as income tax expense in the accompanying consolidated statements of operations and comprehensive loss.

12. Employee benefits

In 2016, the Company established a defined-contribution savings plan under Section 401(k) of the Internal Revenue Code (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 pretax basis. The Company matches contributions up to 4% of annual salary for those employees who are participating in the 401(k) Plan. For the year ended December 31, 2023, the Company made matching contributions of $0.7 million and for the year ended December 31, 2022, the Company made matching contributions of $0.6 million.

13. Subsequent events

Since December 31, 2023, through the date of the issuance of these consolidated financial statements, the Company sold 0.2 million shares of our common stock and received $1.3 million after deducting commissions related to the Sales Agreement.