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, 2019

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 is a shell company (as defined in Rule 12b-2 of the Exchange Act). YES ☐ NO ☒

The aggregate market value of the registrant's common stock held by non-affiliates of the registrant (without admitting that any person whose shares are not included in such calculation is an affiliate) computed by reference to the price at which the common stock was last sold as of the last business day of the registrant's most recently completed second fiscal quarter was approximately $490 million.

The number of shares of Registrant's Common Stock outstanding as of March 16, 2020 was 32,943,670.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the Proxy Statement for the registrant's 2020 Annual Meeting of Stockholders are incorporated by reference into Part III of this Annual Report on Form 10-K. Except with respect to information specifically incorporated by reference in this Annual Report, the Proxy Statement shall not be deemed to be filed as part hereof.

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PART I

Item 1. Business.

Overview

We are a biotechnology company that is pioneering a new way to treat the underlying causes of severe genetic diseases by precisely upregulating protein expression. We are developing novel antisense oligonucleotide, or ASO, medicines that target ribonucleic acid, or RNA, and modulate precursor-messenger RNA, or pre-mRNA, splicing to upregulate protein expression where needed and with appropriate specificity to near normal levels. We aim to develop the first precision medicine platform to target the underlying cause of a broad spectrum of genetic diseases in which the patient has one healthy copy of a gene and one mutated copy that fails to produce a protein essential to health. These diseases, in which the loss of approximately 50 percent of normal protein expression causes disease, are called autosomal dominant haploinsufficiencies.

We utilize our proprietary technology platform, Targeted Augmentation of Nuclear Gene Output, or TANGO, to design ASOs to upregulate the expression of protein by individual genes in a patient. Our approach is designed to allow us to deliver in a highly precise, durable and controlled manner disease-modifying therapies to a wide range of relevant tissues, including the central nervous system, or CNS, eye, kidney and liver.

Our proprietary technology platform is based on the pioneering work conducted on pre-mRNA splicing and ASOs in the laboratory of one of our co-founders, Adrian R. Krainer, Ph.D., of Cold Spring Harbor Laboratory in New York. Inspired by the clinical success of SPINRAZA, an ASO medicine for the treatment of spinal muscular atrophy that was co-invented by Professor Krainer, our company was founded to develop a general antisense approach to upregulate protein expression. TANGO exploits unique, patented mechanisms for antisense-mediated modulation of splicing to prevent the synthesis of naturally occurring non-productive messenger RNA, or mRNA, and to increase the synthesis of productive mRNA to increase production of functional protein. 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 2,900 monogenic, or single gene, diseases which we believe may be amenable to TANGO. We have an intellectual property estate that includes multi-national allowed and pending claims for the TANGO mechanisms, as well as multi-national pending claims relating to compositions of matter of oligonucleotides designed to target specific TANGO elements in genes for more than 140 genetic diseases that we believe are amenable to upregulation of target protein expression using TANGO.

We are initially focused on applying the transformative potential of our platform to develop precision medicines for autosomal dominant haploinsufficiency diseases. There are more than 660 known monogenic diseases that are categorized as haploinsufficiencies. These diseases are ones in which only one copy, or allele, of the gene needs to be mutated for the disease or trait to develop, and that mutated allele generates a protein that is severely deficient in amount or activity, resulting in approximately 50% of normal protein expression in the patient. We believe TANGO is well-suited to treat haploinsufficiencies by increasing expression of the healthy, or wild-type, allele, thereby restoring the target protein to near normal levels.

We are developing TANGO as potentially the first precision medicine platform for a category of severe genetic diseases known as autosomal dominant haploinsufficiencies. Existing precision medicine platforms, including gene therapy, gene editing, modified mRNA, protein-based drugs, small molecules and oligonucleotides, have fundamental limitations that make them poorly suited to address haploinsufficiencies. Numerous technical challenges preclude effective application of these modalities to haploinsufficiencies, including: (i) the inability to control level and tissue distribution of target protein expression, (ii) potential irreversible on- and off-target effects, (iii) target gene size limitations, (iv) incompatibility with diseases caused by many mutations, (v) drug manufacturing and (vi) delivery hurdles. There is a need for novel therapeutics that can restore protein expression and address the underlying genetic causes of haploinsufficiencies.

Within haploinsufficiency diseases, we are initially prioritizing the development of ASOs for the treatment of genetic epilepsies. According to a 2010 publication in *Nature Reviews Neurology* and a 2018 publication in *JAMA Neurology*, more than 50% of epilepsies are now recognized as having a genetic basis and more than 30% of patients are refractory to existing therapies, especially those with a genetic epilepsy. Our most advanced program is the potentially first disease-modifying therapy for Dravet syndrome, a severe and progressive genetic epilepsy. Dravet syndrome is caused by loss-of-function mutations in one allele of the *SCN1A* gene and is characterized by frequent and prolonged seizures beginning in the first year of life, severe intellectual and developmental disabilities and other serious health problems, including, notably, sudden premature death in approximately 20% of patients with Dravet syndrome. Current treatments for Dravet syndrome only address the occurrence of seizures, not the underlying cause of disease. 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 antiepileptic regimens.

We designed our lead product candidate, STK-001, to treat Dravet syndrome, a severe and progressive genetic epilepsy. With 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 anticipate an efficient clinical program for STK-001.

We submitted an investigational new drug application, or IND, for STK-001 to U.S. Food and Drug Administration, or the FDA, in late 2019. In the first quarter of 2020, we received communication from the FDA confirming that we may proceed with clinical dosing in the planned Phase 1/2a clinical trial called Monarch. The single ascending dose portion of this trial is in two parts, A and B, and is designed to evaluate STK-001 in children and adolescents ages 2 to 18 years of age with Dravet syndrome. Part A allows dosing of two cohorts. We expect to enroll and begin dosing patients in Part A of the study in the second half of 2020.

Part B of the study will evaluate the higher doses of STK-001. The FDA has placed a partial clinical hold for the doses planned in Part B of the study. The partial clinical hold was not due to any identified manufacturing or safety issue, but rather was because additional safety information is needed from preclinical testing to determine the safety profile of doses higher than the current no observed adverse effect level or NOAEL. The NOAEL was determined using data from a pivotal non-human primate study that evaluated intrathecal delivery of single dose levels of STK-001. The highest dose administered in this study was equivalent to a human dose that is higher than what we plan to administer in Part B of our Phase 1/2a clinical study and did not demonstrate effects that were considered adverse. It is the FDA's position that in order to support administration of STK-001 doses above those planned in Part A, additional nonclinical data to identify any potential safety issues of STK-001 at higher doses will need to be provided. We have initiated single-dose toxicology studies to more fully characterize the safety profile at higher doses, in order to facilitate the removal of the partial clinical hold and proceed to Part B of the study. Upon FDA clearance, we will plan to proceed with the higher dosing cohorts planned in Part B of the study.

We are working to minimize any potential delay to continued clinical testing of STK-001. We still anticipate preliminary data from the study in 2021.

We intend to nominate a second candidate for preclinical development in the second half of 2020.

Our business could be adversely impacted by the effects of the coronavirus known as COVID-19, or other epidemics, which may materially or adversely affect development timelines, and our business, financial condition and results of operations, including those described above.

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 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.

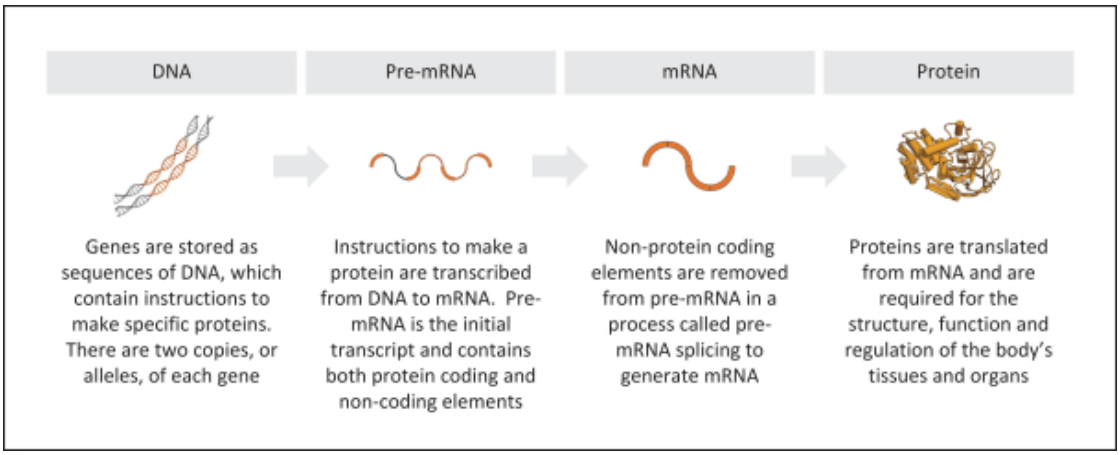
Our strategy

We are using our proprietary TANGO technology platform to create ASOs for the treatment of severe genetic diseases. The critical components of our strategy include:

- *Rapidly advance our lead program, STK-001, to clinical proof-of-concept, approval and commercialization.* We intend to advance our lead product candidate, STK-001, into a Phase 1/2a clinical trial in children and adolescents with Dravet syndrome and to begin dosing patients in the second half of 2020. 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 recently 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 we see evidence of efficacy following clinical data, then we would plan to meet with regulatory authorities to discuss expedited regulatory pathways. If approved, we intend to leverage a lean, targeted internal commercial organization to bring STK-001 to patients.
- *Prioritize genetic epilepsies for near-term development efforts.* We believe that no other haploinsufficiency disease area holds as much clear need or as much promise for near-term medical breakthrough as genetic epilepsies. Leveraging our proprietary database, we have identified over 100 genes that are commonly mutated amongst epilepsy patients and that may be amenable to TANGO. We believe that the learnings from our lead Dravet syndrome program will significantly reduce the developmental risk of subsequent programs in our pipeline, particularly those targeting the CNS.
- *Expand our pipeline into other disease areas to fully exploit the potential of our proprietary platform.* 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 advancing several early programs focused on multiple targets, including haploinsufficiency diseases of the CNS, eye, kidney and liver. Indications beyond genetic epilepsies for which our technology may be applicable include autosomal dominant optic atrophy and autosomal dominant polycystic kidney disease. 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, such as autoimmune diseases, aging and cancer.
- *Maintain broad commercial rights to our product candidates.* We own commercial rights to our technologies and clinical programs, including our lead product candidate, STK-001. We intend to build a fully integrated biotechnology company and independently pursue the development and commercialization of our key product candidates. As we continue to advance our programs, we may 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. We plan to opportunistically evaluate potential collaboration arrangements and may elect to enter into an arrangement with a pharmaceutical or biotechnology company as early as this year.
- *Continue to strengthen and expand our intellectual property portfolio.* We have an intellectual property estate that includes multi-national allowed and pending claims for the TANGO mechanisms, as well as multi-national pending claims relating to compositions of matter of oligonucleotides designed to target specific TANGO elements in genes for more than 140 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.

Genetic diseases and precision medicines

Each person's genetic material, or genome, consists of deoxyribonucleic acid, or DNA, in sequences of genetic code called genes. There are two copies, or alleles, of each gene, which act as instructions to produce specific proteins. When a cell needs to produce a protein, the instructions to make that protein are transcribed from DNA to mRNA for each allele. The initial transcript is called pre-mRNA and contains both protein coding and non-coding elements. During transcription, the non-protein coding elements, such as introns or non-coding exons, are removed in a process called pre-mRNA splicing. Splicing serves to stitch together the coding elements, or exons, to generate mRNA. The mRNA then serves as the instructions to produce protein. Proteins are required for the structure, function, and regulation of the body's tissues and organs. The key steps for protein synthesis are exemplified in the schematic below.



The DNA in the human genome contains approximately three billion nucleotide base pairs, and small changes, or mutations, routinely occur in the base pairs. A mutation in the gene can alter the amount or activity of the protein. Currently, there are estimated to be over 10,000 diseases caused by a genetic abnormality in a single gene. These are also known as monogenic diseases. Monogenic diseases can be categorized as either autosomal recessive or autosomal dominant diseases.

For diseases that are autosomal recessive, both alleles of a gene must be mutated for the disease or trait to develop. The protein that is generated is severely deficient in amount or activity and typically results in less than 10-25% of normal protein expression in the patient. Conversely, autosomal dominant diseases are those in which only one allele of the gene needs to be mutated for the disease or trait to develop. Autosomal dominant diseases can be broken down into two categories: autosomal dominant gain-of-function or dominant negative and autosomal dominant haploinsufficiency, or loss-of-function. In dominant gain-of-function (dominant negative) diseases, the mutant protein possesses a new deleterious or increased function and acts therefore as a toxic protein. In our focus area of haploinsufficiency diseases, the mutated allele generates a protein that is severely deficient in amount or activity and results in approximately 50% of normal protein expression. Haploinsufficiencies include both rare conditions as well as more common disorders. Severe haploinsufficiencies typically arise from spontaneous mutation, and thus the incidence of these diseases is not reduced by pre-conception genetic screening.

Multiple therapeutic modalities, including gene therapy, gene editing, modified mRNA, protein-based drugs, small molecules and oligonucleotides are approved or are being developed to address all types of monogenic diseases. However, most of these therapeutic approaches are focused on autosomal recessive or autosomal dominant gain-of-function (dominant negative) diseases. The nature and fundamental limitations of these modalities make them poorly suited to address the underlying genetic cause of haploinsufficiency diseases. Consequently, there has been little focus on drug development for these diseases despite a significant unmet medical need.

The table below summarizes the major categories of genetic diseases and the various precision medicine approaches that are actively being used or explored to address them.

Category	Autosomal recessive	Autosomal dominant gain-of-function / dominant negative	Autosomal dominant haploinsufficiency
Genetic mutation	Loss-of-function mutations in both gene alleles	Gain-of-function or dominant negative mutation in one gene allele (toxic protein)	Loss-of-function mutation in one gene allele
Result	Less than 10-25% of normal protein expression	Deleterious or increased protein expression	Approximately 50% of normal protein expression
Disease examples	• Phenylketonuria • Lysosomal storage disorders • Beta-thalassemia • Cystic fibrosis	• Huntington's disease • Parkinson's disease • Spinocerebellar ataxia • AD hypocalcemia	• Dravet syndrome • Optic atrophy • Tuberous sclerosis • Polycystic kidney disease
Current and emerging precision medicines	• Gene therapy • Gene editing • Modified mRNA • Protein-based drugs • Small molecules	• Gene therapy • Gene editing • Protein-based drugs • Small molecules • Oligonucleotides	• Our TANGO technology(1) STOKE THERAPEUTICS
Therapeutic goal	Upregulate protein expression to greater than 10-25% of normal	Downregulate protein expression / inhibit protein function	Upregulate protein expression to near normal

(1) We have neither applied for, nor received, FDA approval for any of our product candidates to date.

Current and emerging precision medicines and their limitations

While current and emerging precision medicine approaches have already made and will likely continue to make significant advancements, we believe they currently possess fundamental limitations which must be overcome before they will become a practical approach to treating genetic diseases, especially autosomal dominant haploinsufficiencies.

Gene therapy

Gene therapy is designed to introduce a functional copy of a defective gene or gene sequence into a patient's cell. This therapeutic approach provides the potential to replace the defective genes that lead to disease.

Today, gene therapy is subject to several technical challenges. Single stranded adeno-associated virus (ssAAV) gene therapy approaches are unable to efficiently package more than 4.4 kilobases of coding DNA and the more efficient self-complementary AAV (scAAV) are limited to 2.1 kilobases of coding DNA; thereby restricting their utility to smaller gene targets. In addition, the inability of current approaches to establish tunable control of the level of protein expression and tissue specificity raises concerns of possible unintended DNA changes and unwanted on- and off-target effects. Further, gene therapy vectors are complex delivery systems, which significantly increase the cost of manufacturing and the difficulty of maintaining reliable quality among product lots.

Gene editing

A more recent approach is gene editing, which is the process of replacing, deleting or repairing defective DNA in its native genomic location. The current focus of gene editing is knocking out a diseased gene or correcting an individual mutation within a gene that is frequent within the disease population. The approach faces many similar challenges to gene therapy and has yet to achieve clinical proof-of-concept.

Gene editing currently suffers from numerous limitations, including the inability to control level and duration of protein expression, a potential for irreversible unintended DNA changes and unwanted on- and off-target effects, and a complex delivery and manufacturing process. In addition, gene editing repairs one mutation at a time, and thus is not well-suited for the treatment of diseases caused by many mutations in a single gene, as is the case for many haploinsufficiencies, which typically result from multiple spontaneous mutations.

Modified mRNA

Over the past several years, there has been significant investment and progress in the field of modified mRNA. These therapies are designed to increase mRNA levels by exogenous delivery of modified mRNA.

However, modified mRNA is characterized by significant drug delivery hurdles and its clinical application has largely been limited to novel vaccines. This therapeutic modality also does not permit precise targeting of tissue and requires complex manufacturing processes that are unproven at commercial scale. In addition, modified mRNA requires frequent administration given its short duration and safe repeat dosing has yet to be achieved clinically. Finally, the ability to package large genes is also unproven and may limit utility to smaller gene targets.

Protein-based drugs

Protein-based drugs are manufactured in living cells and can bind with high specificity to a variety of extracellular or cell surface targets or can be used to replace mutated or missing extracellular proteins. Protein-based drugs can also bind to a very narrow spectrum of intracellular proteins (lysosomal storage proteins). Antibodies (and antibody-like proteins) have become the most common type of biologic because of the specificity and long duration of action of this type of molecule. Monoclonal antibody drugs typically act by inhibiting target proteins through competitive binding (antagonists).

Currently, protein-based drugs are unable to address most diseases caused by deficient activity of intracellular or transmembrane proteins, such as ion channels involved in genetic epilepsies. Additionally, complex manufacturing and short duration after administration can prevent maintaining therapeutic levels of the protein in the body.

Small molecules

Small molecules consist predominantly of hydrophobic organic compounds under 500 daltons in molecular weight and are manufactured through chemical synthesis. These drugs typically act by deactivating or inhibiting target proteins through competitive binding (antagonists). In much rarer instances, small molecule agonists can sometimes be identified that increase the activity of a target protein through binding to a regulatory site.

Small molecules are artificial agonists which act through non-natural mechanisms, and therefore do not fully compensate for the loss of a protein that functions in a regulated fashion or as part of a multi-protein complex. Applications for small molecules are also very limited, and proteins that possess small molecule-binding pockets have been estimated to account for only 2-5% of the human proteome. Small molecules also lack selectivity and specificity, creating the potential for off-target toxicity. Finally, these therapeutics typically do not address the underlying cause of genetic diseases and consequently may have limited impact on patient quality of life or life expectancy.

Oligonucleotides

Oligonucleotides are short strands of modified RNA or DNA, usually 12-30 nucleotides in length, that are manufactured by chemical synthesis. Single-stranded oligonucleotides that bind to mRNA are called ASOs, which have been developed primarily to downregulate protein expression by RNase H-mediated cleavage of target mRNA.

Over the past few years, there has been very limited success in developing clinical ASOs to upregulate protein expression due to a focus on indirect and weakly validated mechanisms of action such as targeting microRNAs or long non-coding RNAs that are associated with a gene transcript. The only exceptions are SPINRAZA, which corrects a unique splicing mutation in *SMN2*, and Exondys-51, which generates an internally-truncated form of dystrophin after removing or ‘skipping’ out a mutated exon to restore the reading frame. Neither drug represents a generalizable strategy to upregulate the expression of protein. Similarly, double-stranded oligonucleotides have been developed primarily to downregulate protein expression by RNA interference mediated cleavage of target mRNA. To date, there has been very limited success in developing clinical double-stranded oligonucleotides to upregulate protein expression.

Given these fundamental limitations of existing modalities, most genetic diseases, particularly autosomal dominant haploinsufficiencies, are dramatically underserved by current therapeutic options. Within rare diseases, only 5% of conditions have an approved drug treatment, and most approved drugs only manage symptoms with little impact on outcomes and life expectancy. We believe there is a clear need for our novel ASOs, which precisely upregulate target protein expression and have the potential to provide disease-modifying therapies to treat many diseases beyond the reach of current approaches.

Our precision medicine platform

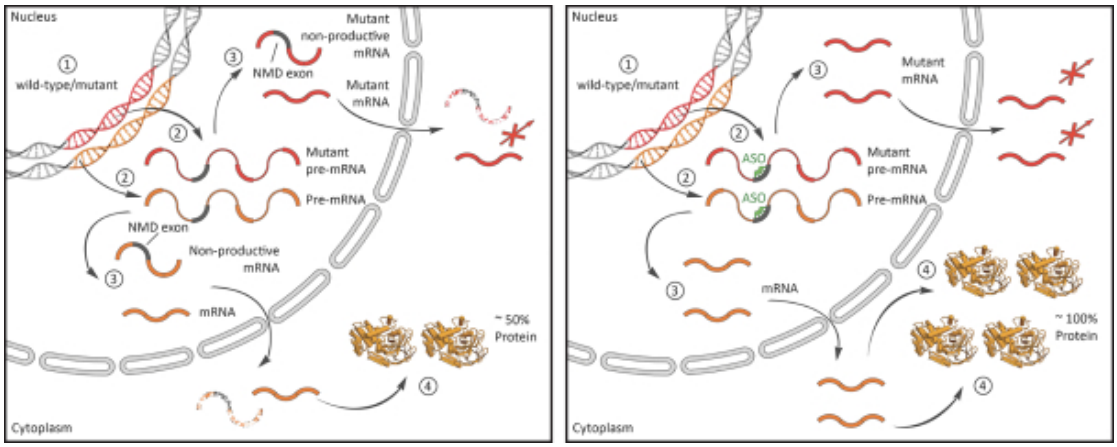
Treatment of autosomal dominant haploinsufficiency diseases with TANGO

We are developing our proprietary technology platform, TANGO, as potentially the first precision medicine platform for a category of severe genetic diseases known as autosomal dominant haploinsufficiencies. We utilize TANGO to design ASOs to increase the expression of protein by individual genes in a patient. 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.

TANGO leverages non-productive mRNA, which is the result of non-productive splicing that leads to either transcript degradation due to non-coding exon inclusion or nuclear retention of transcripts due to intron retention. In some cases, these non-productive splicing events are a part of normal gene regulation, and in all cases the non-productive splicing events are part of the wild-type or normal sequence of the gene. Non-productive mRNA can be produced by both wild-type and mutant alleles and is not translated into protein.

We are initially focused on applying the transformative potential of our platform to developing precision medicines for haploinsufficiencies, or disorders in which only one allele of a gene is mutated, resulting in approximately 50% of normal protein expression. We believe our TANGO technology is well-suited to provide a gene-specific increase in expression of the healthy, or wild-type, allele, thereby restoring the target protein to near normal levels.

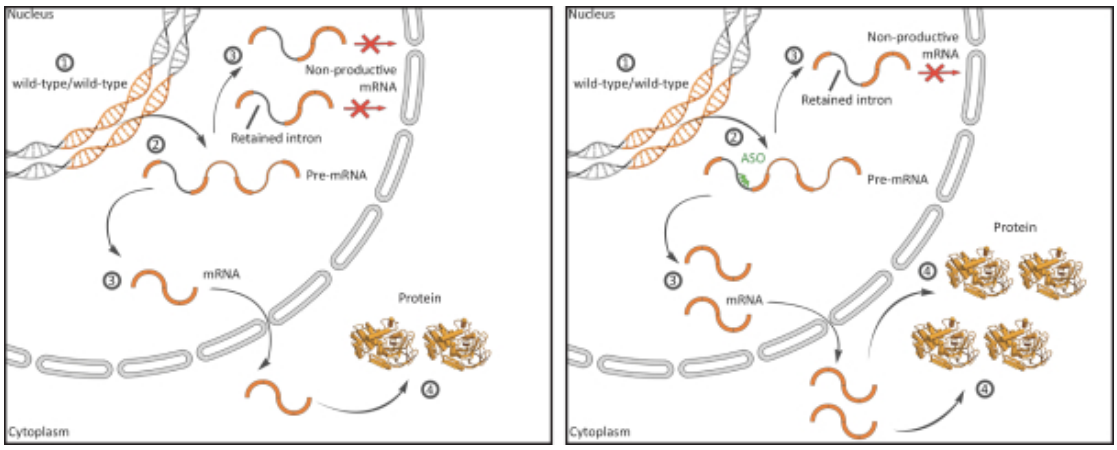
The figures below illustrate the TANGO mechanism for increasing protein synthesis in a prospective patient with a haploinsufficiency. To date, we have demonstrated this TANGO mechanism in preclinical models of haploinsufficiencies. The left panel illustrates the prospective patient with a haploinsufficiency 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. In the right panel, 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.



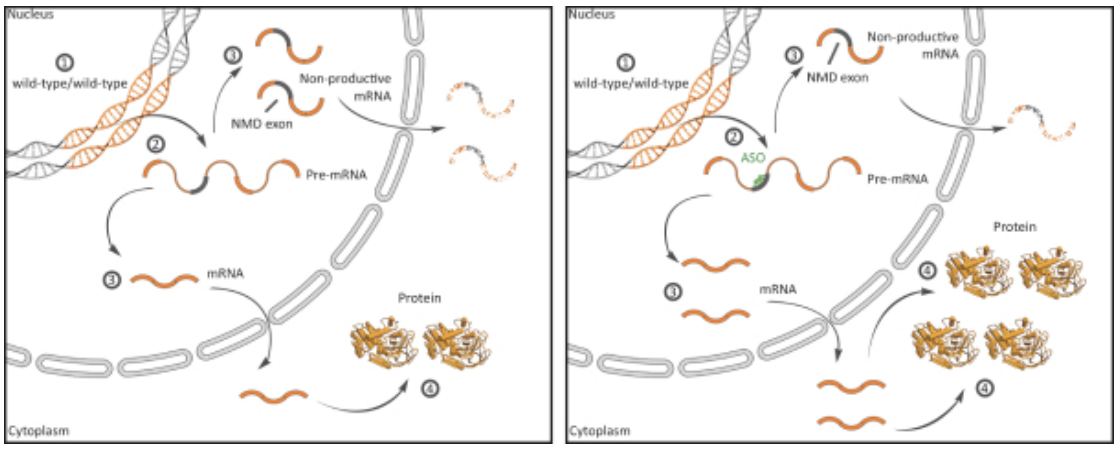
TANGO mechanisms of action

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. The two categories of non-productive splicing events amenable to TANGO are retained introns and nonsense-mediated mRNA decay of the resulting mRNA. While we benefit from leveraging previously-validated ASO chemistries, both of these TANGO mechanisms are novel.

The first category of non-productive splicing events amenable to TANGO is retained introns. Retained introns are found in approximately 60% of gene transcripts and are part of the wild-type sequence of the gene. In some cases, retained introns are part of normal gene regulation. The non-productive mRNA, which contains these retained introns, remain in the nucleus of the cell and are not translated into protein, and offer a reservoir of non-productive mRNA that can be converted into productive mRNA. Our ASOs bind to the pre-mRNA and redirect the splicing machinery to remove the retained intron. This splice-switching decreases non-productive mRNA and increases productive mRNA, which is translated into increased protein expression from the wild-type allele. This is shown in the figures below, with the left panel illustrating non-productive mRNA, which includes retained introns, and the right panel illustrating our ASOs binding to the pre-mRNA and redirecting the splicing machinery.



The second 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 a NMD event is a NMD exon, which is found in over 25% of gene transcripts. Like retained introns, 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. As with retained introns, 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 candidate, STK-001, targets an NMD exon and the general mechanism is shown in the figure 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. Although STK-001 is currently our only current product candidate and is still in preclinical testing, we would expect, based on our preclinical studies, for future product candidates targeting a NMD exon to operate in the same manner.



Advantages of TANGO

We believe TANGO may have several key advantages, including:

- *Ability to address the underlying genetic cause of the disease.* We utilize TANGO to design ASOs to precisely upregulate protein expression, thereby addressing the underlying cause of the disease rather than the symptoms of the disease.
- *Applicability is mutation-independent.* Our ASOs 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.
- *Utility across small and large gene targets encoding intracellular and extracellular proteins.* Our ASOs upregulate protein expression regardless of gene size and are not constrained to smaller gene targets. We believe our therapies also have the flexibility to address genes encoding intracellular as well as extracellular proteins.
- *No observed unwanted off-target effects.* Our ASOs do not create detectable changes at the DNA level and make no detectable irreversible modifications to a patient's genome. 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.
- *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.
- *Utility across wide array of diseases and tissue types.* We believe that ASO delivery to the CNS, eye, kidney and liver is well-established, providing us the potential to address a broad range of genetic diseases. Additionally, although FDA approval for any of our current or future product candidates is not assured, we believe that ASO delivery to the CNS is particularly well-precedented.
- *Fixed dose, rather than weight-based dosing.* We have observed that while the quantity of non-productive mRNA can vary across tissue types for a gene, it remains constant across individuals. As a result, for CNS and eye targets, the dose of our ASOs should not require adjustment between patients to be effective. We believe that a fixed dose across all ages in these targets will lessen reimbursement hurdles associated with a weight-adjusted dose pricing model.
- *Favorable dosing regimen.* We believe our ASOs may require as few as two to three administrations per year for the CNS or the eye and will generally involve relatively low doses, which would translate to simplified use, an improved safety profile from reduced systemic exposure and lower cost of goods.
- *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. To date, we have identified and assembled a proprietary database of approximately 85,000 non-productive events in the human transcriptome. Using this large internal data set, in combination with publicly available genetic disease databases, we have identified approximately 2,900 monogenic disease-associated genes with one or more non-productive events which we believe are amenable to our TANGO technology. 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 tissue that are relevant to the disease, we employ highly-efficient 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. ASO arrays utilize clinically translatable previously-validated ASO chemistries, such as 2' methoxyethyl phosphorothioate and PMO. Hit compounds are evaluated in wild-type animal models 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 treatments 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 are also initially targeting diseases with established clinical and regulatory pathways. As an example, we intend to undertake a Phase 1/2a clinical trial for our lead program in Dravet syndrome with a design and endpoints common to other recently approved antiepileptic drugs.

Commercialization

We intend to retain broad commercial rights and independently bring our therapies to patients through a lean, targeted internal commercial organization. To do this, we are focused on ensuring that we can effectively identify and access those patients who will benefit from our therapies. 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 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 genetic 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 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 believe that no other disease area holds as clear a need or as much promise for near-term medical breakthrough as genetic epilepsies, including Dravet syndrome, and therefore we are prioritizing this disease area for our near-term development efforts.

Genetic epilepsies

Epilepsy is defined as recurrent, unprovoked seizures due to abnormal, asynchronized neuronal firing in the brain. Epilepsy is the fourth most common neurologic disease and affects more than 50 million people worldwide, according to the World Health Organization as of 2019. Epilepsy is the most frequent serious chronic neurologic condition in childhood, and approximately one out of 150 children are diagnosed with epilepsy during the first 10 years of life, with the highest incidence rate observed during infancy, according to a 2017 publication in *Pediatrics*.

More than 30% of patients with epilepsy are refractory to medical treatment, especially those with a genetic epilepsy, despite the availability of approximately 20 antiepileptic drugs. This is largely because existing antiepileptic drugs primarily address the frequency of seizures and lack the capacity to rectify the underlying neuropathological processes or genetic defect. Refractory epilepsy carries the risks of structural damage to the brain and nervous system and increased risk of premature death (e.g. from sudden unexpected death in epilepsy, or SUDEP, suicide, accidents, pneumonia, or vascular disease), as well as psychological, educational, social and vocational consequences. In addition, up to 50% of patients with epilepsy have significant cognitive delay, according to a 2015 review article in *Cold Spring Harbor Perspectives*. Cognitive and behavioral comorbidities are especially common in children with refractory epilepsy. Overall outcomes in patients with epilepsy have not improved significantly over the past two decades, and a novel therapeutic approach is desperately needed to modify the development or progression of the disease and improve long-term outcomes.

A 2010 publication in *Nature Reviews Neurology* estimates that more than 50% of epilepsies are now recognized as having a genetic basis, and many of these are haploinsufficiencies. The genetic bases of both rare and common epilepsies are rapidly being elucidated, and neurologists now routinely include genetic testing for more than 180 disease-associated genes in the diagnostic work-up of epilepsy. Beyond diagnostics, a major goal of genetic testing is to enable individualized treatment choices based on the genetic cause of disease. Today, the application of genetic diagnosis for epilepsy patients is largely limited to medical contraindications, such as avoidance or removal of ion channel blockers for an ion channel deficiency, given that there are no genetically-targeted medicines available for genetic epilepsy patients.

Several hundred epilepsy-related genes have been identified to date, including genes encoding neuronal ion channels and receptors and genes involved in cellular signaling. For example, the number of genes included on the epilepsy panel of Invitae Corporation, a leading genetic information company, has grown from 103 in 2015 to 187 in 2019. Globally, advances in molecular technology are expected to result in discoveries of additional genetic etiologies of epilepsy, implying a greater role than ever before for genetics in the epilepsy clinic.

The table below lists select genes that are commonly mutated amongst patients with epilepsy and we believe are amenable to TANGO, with current estimates of their prevalence. We are continuing to evaluate these CNS targets and expect to nominate a second genetic disease candidate for preclinical development by the second half of 2020.

Gene	Disease	Estimated worldwide prevalence
SCN1A	Dravet Syndrome	5-5.5 in 100,000
TSC2	Tuberous Sclerosis 2	7-8 in 100,000
MECP2	Rett Syndrome	5 in 100,000
TSC1	Tuberous Sclerosis 1	2-3 in 100,000
SCN2A	Epileptic Encephalopathy	1-2 in 100,000
CHD2	CHD2-Myoclonic Epilepsy	1-2 in 100,000
SYNGAP1	Autosomal Dominant Mental Retardation 5	1 in 100,000
SCL6A1	Epileptic Encephalopathy	1 in 100,000
SCN8A	Epileptic Encephalopathy	1 in 100,000
CACNA1A	Episodic Ataxia, Type 2	<1 in 100,000

For some genes, the phenotypic spectrum expands beyond the epilepsies to other neurodevelopmental disorders, including autism and intellectual disability. For example, although most patients with mutations in *STXBP1*, *SYNGAP1* or *CHD2* present with seizures, mutations in these genes have also been identified in individuals with intellectual disability or autism spectrum disorder, but without epilepsy. These neurodevelopmental disorders are not addressed with existing antiepileptic drugs.

Dravet syndrome 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 1,250 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 truncating mutation.

Importantly, patients with Dravet syndrome have an increased risk of premature death, primarily due to SUDEP. 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 60% in North America and 70% in Germany, France and the United Kingdom undergo genetic testing as part of their diagnostic work-up, according to the Health Advances Report. We expect this to increase to approximately 85% in North America, Japan, Germany, France and the United Kingdom by 2024 in the aggregate. 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. By comparison, the prevalence of spinal muscular atrophy is approximately 10,000 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 antiepileptic regimens. As a result, the current treatment strategy involves the use of multiple antiepileptic drugs, including combinations of cannabidiol, stiripentol, 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) and stiripentol (Diacomit) are currently the only FDA-approved antiepileptic drugs for the treatment of Dravet syndrome. Cannabidiol was approved in 2018 for the adjunctive treatment of seizures associated with Lennox-Gastaut syndrome and Dravet syndrome in patients two years of age and older. Diacomit was approved in 2018 for the treatment of seizures associated with Dravet syndrome in patients two years of age and older taking clobazam. There are no clinical data to support the use of Diacomit as monotherapy in Dravet syndrome. These new therapies were approved based on a demonstrated reduction in seizure frequency; however, very few patients had complete control of seizure activity. For patients treated with Epidiolex, only 6.7% reported no convulsive seizures during the treatment period, according to clinical trial data in the drug's prescribing information. Tolerance, or a significant diminishment of efficacy over time, is also observed in approximately 25% of patients, thereby limiting the usefulness of this treatment in the long-term clinical management of patients with Dravet syndrome. These drugs also do not address the significant non-seizure comorbidities. Additionally, cannabinoids as a drug class have been associated with adverse effects on cognitive development in children.

Fenfluramine (Fintepla) is an antiepileptic drug in clinical development for the treatment of Dravet syndrome. Topline efficacy data for seizure frequency were favorable; however, as with Epidiolex and Diacomit, seizure-free rates remain in the low single digits. Moreover, patients are still likely to be affected by non-seizure comorbidities and may develop tolerance to the drug over time.

Many of the antiepileptic drugs that are used to treat Dravet syndrome can carry a substantial adverse event burden. Some of the adverse events can cause deleterious effects on cognition and lead to sedation, somnolence, inattention and fatigue, and potentially lead to death. These adverse effects may exacerbate the underlying cognitive deficits that are part of the natural course of Dravet syndrome. Patients often require regular office visits and laboratory testing to monitor toxicity to vital organ systems, especially the liver, which may be further compounded by polytherapy and associated drug-drug interactions. Despite these risks, the continued use of these medications demonstrates the importance of reducing the frequency of seizures to the patients, caregivers and the prescribing neurologists.

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.

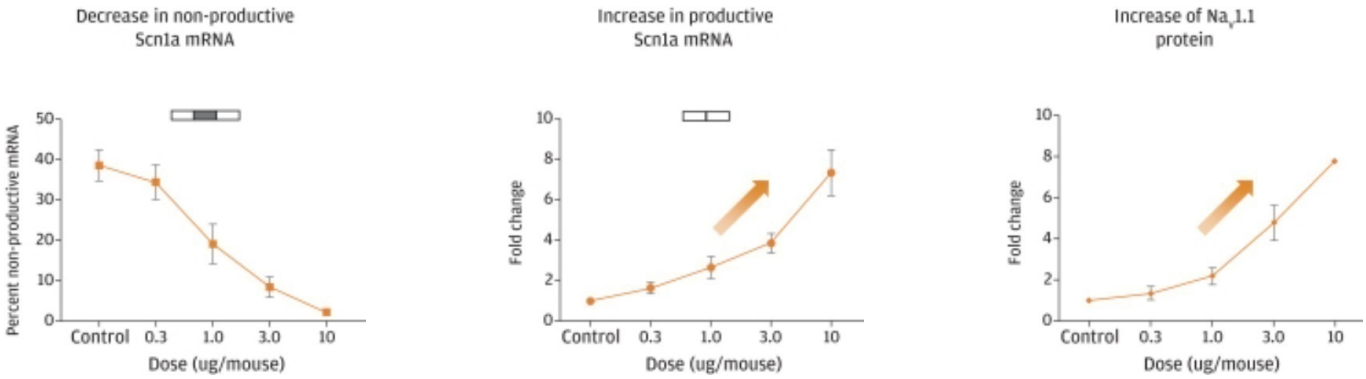
STK-001: Product candidate

We believe that STK-001 has the potential to be the first disease-modifying therapy to address the genetic cause of Dravet syndrome by restoring physiological $Na_V1.1$ levels and reducing both occurrence of seizures and significant non-seizure comorbidities.

STK-001: Preclinical data

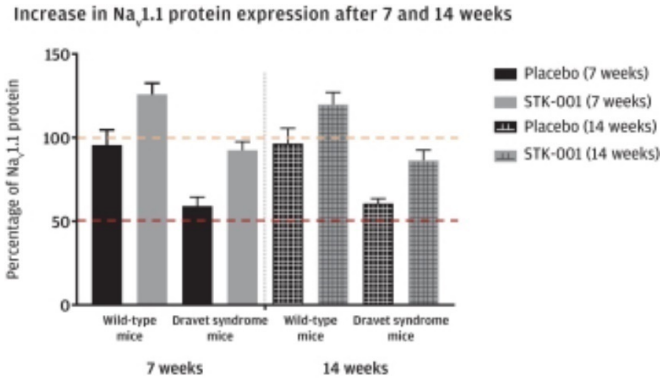
We have generated compelling preclinical data that we believe demonstrates proof-of-mechanism for STK-001. Our initial target engagement, pharmacology and efficacy studies were performed in mice, including both wild-type and a Dravet syndrome mouse model. The Dravet syndrome mouse model replicates many of the symptoms of Dravet syndrome patients, and 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.

In wild-type mice, we characterized target engagement and pharmacology of STK-001. Five groups of neonate (postnatal day two) mice were administered a single injection dose of 0 (n=5), 0.3, (n=5) 1.0. (n=6) 3.0 (n=3) and 10.0 (n=5) µg of STK-001 by intracerebroventricular injection and returned to the home cage for five days. Sections of the brain were processed for RNA and protein. We observed that treatment with STK-001 resulted in a dose-dependent reduction of non-productive mRNA. Furthermore, the reduction of non-productive mRNA was associated with an increase of productive mRNA and an increase in $Na_v1.1$ protein, as denoted in the figures below.

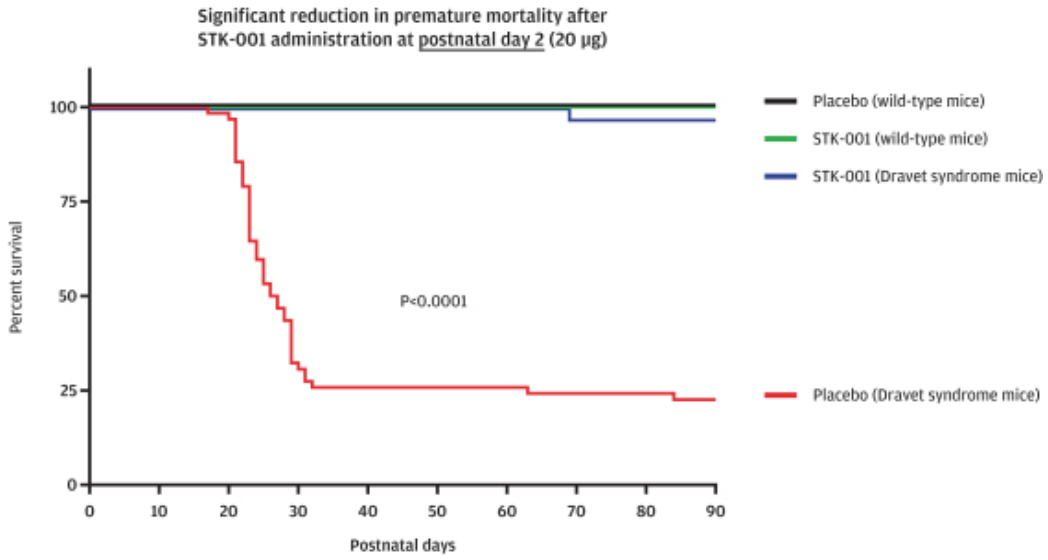


We also evaluated STK-001 pharmacology and efficacy in transgenic mice with a heterozygous deletion of *Scn1a*. This model was created by introducing a targeted deletion in the first coding exon of the *Scn1a* gene; these mice exhibit many aspects of the Dravet syndrome phenotype including seizures and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

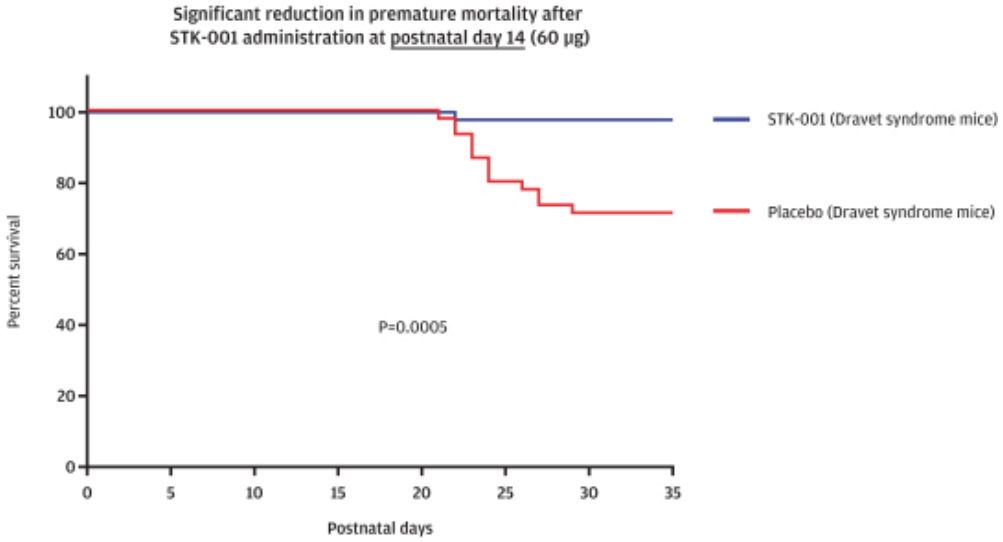
Neonate (postnatal day two) Dravet syndrome mice and wild-type littermate controls were administered a single dose of either placebo (consisting of a phosphate-buffered solution), or 20 µg of STK-001 (n=~50/group) by intracerebroventricular injection. Animals from each group were monitored through day 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. These data demonstrate that STK-001 has an impact on $Na_v1.1$ protein expression and we believe this will translate to a favorable dosing regimen in humans.



In addition to an increase in the Na $_v$1.1 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 the figure below.



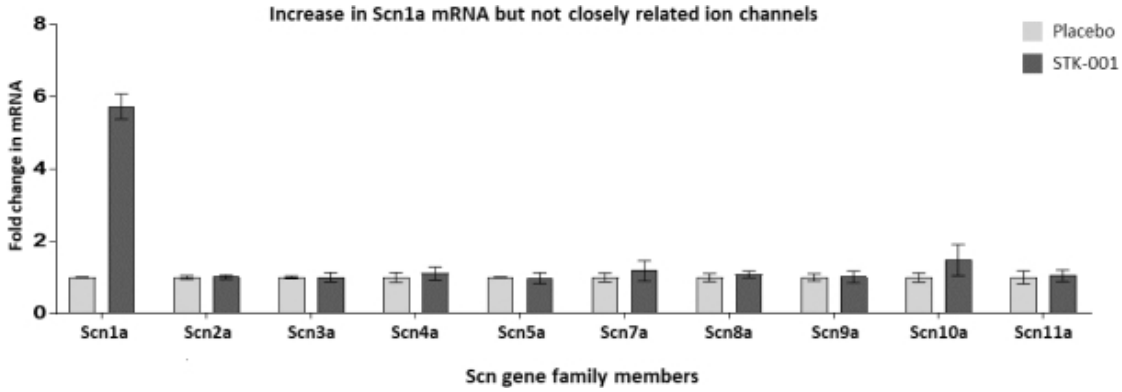
In additional studies, Dravet syndrome mice were treated closer to symptom onset (postnatal day 14). An interim analysis through postnatal day 35 indicated a significant reduction in premature mortality. Treatment with a single dose of 60 µg of STK-001 resulted in 98% survival of Dravet syndrome mice for the 35-day post-natal observation period (survival of 45 out of 46 mice was observed in the STK-001 Dravet syndrome mouse group) compared with 71% survival of placebo mice (survival of 32 out of 45 mice). This is illustrated in the figure below.



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 were presented at the American Epilepsy Society (AES) Annual Meeting in Baltimore in December 2019.

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 was 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. 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.



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, or 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. These data were presented at the American Epilepsy Society (AES) Annual Meeting in Baltimore in December 2019.

Single dose GLP toxicology studies in rats and cynomolgus monkeys, that characterized the pharmacology, exposure and tolerability of STK-001 were included in the IND that was submitted to the FDA in late 2019. These studies provided data to support Part A of the planned initiation of the Phase 1/2a single ascending dose clinical study. We have initiated additional single-dose toxicology studies in order to facilitate the removal of the partial clinical hold and proceed to Part B of the study. Multiple dose GLP toxicology studies are underway to provide data to support the multiple ascending dose part of the Phase 1/2a study.

STK-001: Clinical plan

We expect our Phase 1/2a trial to evaluate STK-001 in children and adolescents with Dravet syndrome. Patients will be eligible for the trial if they are between the ages of 2 to 18, have had four or more convulsive seizures during a four-week pre-dosing observation period, have an established diagnosis of Dravet syndrome and have evidence of a pathogenic genetic mutation in the *SCN1A* gene. Requiring an *SCN1A* mutation (of which more than 1,250 *SCN1A* mutations have been identified) 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 will also have failed at least two epilepsy treatments in the past and currently be taking at least one antiepileptic drug. All medications and interventions will remain unchanged throughout the trial, which will allow for assessment of STK-001 with a variety of antiepileptic therapies.

The single ascending dose Phase 1/2a trial will be conducted in two parts: Part A will evaluate single ascending doses in two cohorts. We plan to begin clinical dosing in Part A at a level that is at least 10-fold below the NOAEL determined in the pivotal GLP toxicology studies. Part B of the study will evaluate higher single ascending doses of STK-001. Phase 1/2a clinical testing will also evaluate multiple ascending doses of STK-001. The primary objectives will be to assess the safety and tolerability of STK-001, as well as to characterize human pharmacokinetics. A secondary objective will be to assess the efficacy as an adjunctive antiepileptic treatment with respect to the percentage change from baseline in convulsive seizure frequency over a 12-week treatment period. We also intend to measure 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), which is ongoing and 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. We expect to enroll approximately 36 children and adolescents in BUTTERFLY.

Importantly, the currently approved antiepileptic drugs for Dravet syndrome, such as Epidiolex, provide a potential regulatory pathway to approval based on defined seizure control endpoints. We will be leveraging an analogous trial design, including a four-week pre-dosing observation period to assess baseline seizure frequency, and serum chemistries, a 12-week treatment period and a 6-month safety follow-up. Dosing by intrathecal injections will be fixed across the patient population given that the quantity of non-productive mRNA remains constant across individuals and that the total cerebral spinal fluid volume is similar between adults and children.

We expect to enroll and begin dosing patients in Part A of the Phase 1/2a study in the second half of 2020. We anticipate preliminary clinical data from Part A of the study in 2021. The FDA has placed a partial clinical hold for the doses planned in Part B of the study. The partial clinical hold was not due to any identified manufacturing or safety issue, but rather was because additional safety information is needed from preclinical testing to determine the safety profile of doses higher than those planned in Part A. We have initiated additional single-dose toxicology studies in order to facilitate the removal of the partial clinical hold and to proceed to Part B of the study after completion of dosing in Part A. Upon FDA clearance, we will plan to proceed with the higher dosing cohorts planned in Part B of the study. At the conclusion of Part B we will evaluate multiple ascending doses of STK-001.

We are working to minimize any potential delay to continued clinical testing of STK-001.

We have not yet discussed with regulatory authorities the evidence necessary for approval of STK-001. However, in addition to requesting Fast Track Designation, if we see evidence of clinical efficacy, then we would plan to meet with regulatory authorities to discuss expedited regulatory pathways, such as Breakthrough Therapy Designation.

Additional product opportunities

Dravet syndrome and genetic epilepsies represent one disease area within a broader spectrum of novel precision medicines for treatment of haploinsufficiency diseases. We intend to nominate a second genetic disease preclinical candidate by the second half of 2020 and will seek to further establish a pipeline of product candidates in the future. Since ASOs have been previously shown to have a very long half-life when injected into the eye and could provide therapeutics with dosing regimens of two to three administrations per year, we are exploring certain ophthalmologic diseases that could be treated through upregulation of protein pathways to reduce inflammation, block neovascularization and reduce retinal degeneration.

We are also advancing several early programs focused on multiple targets, including haploinsufficiency diseases of the CNS, eye, kidney and liver, given the ability of our ASOs to target cells in these organs. These tissues are affected in many severe genetic diseases. Additional non-epilepsy indications for which our technology may be applicable include autosomal dominant optic atrophy and autosomal dominant polycystic kidney disease.

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

Manufacturing

We currently contract with third parties to manufacture our products undergoing late-preclinical testing and anticipate using third parties for all clinical and 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 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

In 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, intraocular, 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 antiepileptic drugs range from cannabidiols, such as GW Pharmaceuticals, plc's Epidiolex, to GABA receptor agonists, such as clobazam, to glutamate blockers, such as topiramate. Companies such as Zogenix, Ovid Therapeutics/Takeda, Xenon Pharmaceuticals, and Encoded Therapeutics are also developing treatments for Dravet syndrome. Many of the currently marketed antiepileptic drugs are available as generics. In addition, numerous compounds are in clinical development for treatment of epilepsy. To our knowledge, the clinical development pipeline includes cannabinoids, 5-HT release stimulants, cholesterol 24-hydroxylase inhibitors, 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.

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 successful 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 government authorities, private health insurers and other organizations. 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 and Cold Spring Harbor Laboratory, which includes issued U.S. patents and pending U.S. and foreign patent applications that cover the TANGO mechanisms. As of December 31, 2019, the issued U.S. 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. As of December 31, 2019, the issued U.S. patent, pending U.S. patent applications and pending foreign patent applications that we have licensed from Cold Spring Harbor Laboratory are anticipated to expire in 2035, absent any patent term adjustments or extensions.

Separately, we have filed patent applications with claims that are intended to cover compositions of matter of oligonucleotides designed to target specific elements in genes for more than 140 genetic diseases that we believe are amenable to upregulation of target protein expression using our TANGO platform. As of December 31, 2019, any patents that may issue from these currently pending patent applications, including PCT international applications, U.S. patent applications, and foreign patent applications, are expected to expire between 2036 and 2040, absent any patent term adjustments or extensions.

With respect to STK-001, as of December 31, 2019, we have exclusively licensed a U.S. patent and a pending U.S. patent application that cover the mechanism of action of STK-001, as well as pending foreign patent applications. The issued patent 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, 2019, we also own pending U.S. patent applications relating to STK-001, and any patents that may issue from these pending patent applications are expected to expire between 2038 and 2040, 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, or 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 2036, 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 2040, 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 may 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 agreements

Cold Spring Harbor Laboratory

In July 2015, we entered into a worldwide license agreement with CSHL, or the CSHL Agreement, with respect to the TANGO patents. Under the CSHL Agreement, we receive an exclusive (except with respect to certain government rights and non-exclusive licenses), worldwide license under certain patents and applications relating to TANGO. As part of the CSHL Agreement, we granted CSHL 164,927 shares of common stock. The CSHL Agreement obligates us to make additional payments that are contingent upon certain milestones being achieved as well as royalties in the low- to mid-single digits on future product sales. These royalty obligations last on a product-by-product and country-by-country basis until the latest of (i) the expiration of the last valid claim of a patent covering a subject product or (ii) the expiration of any regulatory exclusivity for the subject product in a country. In addition, if we sublicense rights under the CSHL Agreement, we are required to pay a maximum of twenty percent of the sublicense revenue to CSHL, which may be reduced upon achievement of certain milestones for the applicable subject product. The maximum aggregate potential milestone payments payable total approximately $900,000. Additionally, certain licenses under the CSHL Agreement require us 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, 2019 and 2018.

University of Southampton

In April 2016, we entered into an exclusive, worldwide license agreement with the University of Southampton, or the Southampton Agreement, whereby we acquired rights to foundational technologies related to our TANGO technology. Under the Southampton Agreement, we receive an exclusive, worldwide license under certain licensed patents and applications relating to TANGO. As part of the Southampton Agreement, we paid 55,000 pounds sterling (approximately $73,000 as of the date thereof) as an up-front license fee. Under the Southampton Agreement, we may be obligated to make additional payments that are contingent upon certain milestones being achieved, as well as royalties in the low- to mid-single digits 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 we sublicense our rights under the Southampton Agreement, we are required to pay a mid-single digit percentage of the sublicense revenue to the University of Southampton. The maximum aggregate potential milestone payments payable by us total approximately 400,000 pounds sterling (approximately $530,000 as of December 31, 2019). As of December 31, 2019, we have recorded no liabilities under the Southampton Agreement.

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 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 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 good laboratory practices. 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. If FDA has neither commented on nor questioned the IND within this 30-day period, the clinical trial proposed in the IND may begin.

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, or 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 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 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. The study protocol and informed consent information for patients in clinical trials must also be submitted to an institutional review board, or 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, such as 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.

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 exceeding $2,580,000 for fiscal year 2019, and the manufacturer and sponsor under an approved NDA are also subject to annual program fees, currently exceeding $300,000 for each prescription 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. 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; most applications for priority review drugs are reviewed in six to eight months. Priority review can be applied to drugs that FDA determines offer major advances in treatment 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 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 is manufactured. FDA will not approve the product unless compliance with current good manufacturing practices, or 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. 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, or 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, or 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. Moreover, product approval may require substantial post-approval testing and surveillance to monitor the drug's safety or efficacy. Once granted, product approvals may be withdrawn if compliance with regulatory standards is not maintained or problems are identified following initial marketing.

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, Priority Review and Accelerated Approval Pathway

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 designation. The programs are intended to help ensure that therapies for serious conditions are approved and available to patients as soon as it can be concluded that the therapies "benefits justify their risks".

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; however, FDA recognizes that the data cannot be expected to be definitive at the time of designation. Breakthrough therapy designation facilitates Intensive Guidance from the FDA on an "Efficient Drug Development Program, Beginning as Early as Phase 1".

Under the FDA's Accelerated Approval regulations, 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.

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 application 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 ($2,457,140 in fiscal year 2019). FDA must take action on an NDA or BLA under priority review within six months of receipt of the NDA or BLA.

The Rare Pediatric Disease Priority Review Voucher program was reauthorized in the 21st Century Cures Act, allowing a product that is designated as a product for a rare pediatric disease prior to October 1, 2020 to be eligible to receive a rare pediatric disease priority review voucher upon approval of a qualifying application prior to October 1, 2022.

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, risk evaluation and mitigation strategies, or 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, or 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, PREA does not apply to any drug for an indication for which orphan designation has been granted.

The Best Pharmaceuticals for Children Act, or 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 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, or 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. Certain changes to a drug, such as the addition of a new indication to the package insert, are associated with a three-year period of exclusivity during which FDA cannot approval an ANDA for a generic drug that includes the change. 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.

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.

Foreign regulation

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. Whether or not we obtain FDA approval for a product, we must obtain approval of a product by regulatory authorities of foreign countries before we can commence clinical trials or marketing of the product in those countries. The approval process varies from country to country and the time may be longer or shorter than that required for FDA approval. The requirements governing the conduct of clinical trials, 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.

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, or 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, or 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.

Further, pursuant to the ACA, the Centers for Medicare & Medicaid Services, or CMS, has issued a final rule that requires manufacturers of prescription drugs to collect and report information on certain payments or transfers of value to physicians and teaching hospitals, as well as investment interests held by physicians and their immediate family members. The first reports were due in 2014 and must be submitted on an annual basis. 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. Effective January 1, 2022, reporting on transfers of value to physician assistants, nurse practitioners or clinical nurse specialists, certified registered nurse anesthetists, and certified nurse-midwives will also be required.

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. Some states require the reporting of certain pricing information, including information pertaining to and justifying price increases, or prohibit prescription drug price gouging. In addition, states such as California, Connecticut, Nevada, and Massachusetts require pharmaceutical companies to implement compliance programs and/or marketing codes. Several additional states are considering similar proposals. 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.

U.S. healthcare reform

In the United States there have been, and continue to be, proposals by the federal government, state governments, regulators and third-party payors to control or manage the increased costs of health care and, more generally, to reform the U.S. healthcare system. The pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major legislative initiatives For example, in March 2010, the ACA was enacted, which 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 the healthcare and health insurance industries, impose new taxes and fees on the health industry and impose additional health policy reforms, substantially changed the way healthcare is financed by both governmental and private insurers, and significantly impacts the U.S. pharmaceutical industry. The ACA, among other things, (i) subjected therapeutic biologics to potential competition by lower-cost biosimilars by creating a licensure framework for follow-on biologic products, (ii) proscribed a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs and therapeutic biologics that are inhaled, infused, instilled, implanted or injected, (iii) increased the minimum Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program and extended the rebate program to individuals enrolled in Medicaid managed care organizations, (iv) established annual nondeductible fees and taxes on manufacturers of certain branded prescription drugs and therapeutic biologics, apportioned among these entities according to their market share in certain government healthcare programs (v) established a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer what are now 70% point of-sale discounts off negotiated prices of applicable brand drugs and therapeutic biologics to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs and therapeutic biologics to be covered under Medicare Part D, (vi) expanded eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to additional individuals and by adding new mandatory eligibility categories for individuals with income at or below 133% of the federal poverty level, thereby potentially increasing manufacturers' Medicaid rebate liability, (vii) expanded the entities eligible for discounts under the Public Health program (viii) created a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research, and (ix) established a Center for Medicare Innovation at CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending.

The current U.S. presidential administration and Congress have, and we expect they will continue to, seek to modify, repeal, or otherwise invalidate all, or certain provisions of, the ACA. Since January 2017, the current U.S. presidential administration has issued two executive orders and other directives designed to delay the implementation of certain provisions of the ACA or otherwise circumvent some of the requirements for health insurance mandated by the ACA. For example, on October 12, 2017, the current U.S. presidential administration issued an executive order that expands the use of association health plans and allows anyone to purchase short-term health plans that provide temporary, limited insurance. This executive order also calls for the halt of federal payments to health insurers for cost-sharing reductions previously available to lower-income Americans to afford coverage. There is still uncertainty with respect to the impact this executive order could have on coverage and reimbursement for healthcare items and services covered by plans that were authorized by

the ACA. Concurrently, Congress has considered legislation that would repeal or repeal and replace all or part of the ACA. While Congress has not passed comprehensive repeal legislation, two bills affecting the implementation of certain taxes under the ACA have been signed into law. The TCJA, among other things, included a provision repealing, effective January 1, 2019, the tax-based shared responsibility payment imposed by the ACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate". Additionally, on January 22, 2018, the current U.S. presidential administration signed a continuing resolution on appropriations for fiscal year 2018 that delayed the implementation of certain ACA-mandated fees, including the so-called "Cadillac" tax on certain high cost employer-sponsored insurance plans, the annual fee imposed on certain health insurance providers based on market share, and the medical device excise tax on non-exempt medical devices. Further, the Bipartisan Budget Act of 2018, or the BBA, among other things, amended the ACA, effective January 1, 2019, to increase from 50% to 70% the point-of-sale discount that is owed by pharmaceutical manufacturers who participate in Medicare Part D and to close the coverage gap in most Medicare drug plans, commonly referred to as the "donut hole". More recently, in July 2018, CMS published a final rule permitting further collections and payments to and from certain ACA qualified health plans and health insurance issuers under the ACA risk adjustment program in response to the outcome of federal district court litigation regarding the method CMS uses to determine this risk adjustment. There is still uncertainty with respect to the impact the current U.S. presidential administration and the Congress may have, if any, and any changes will likely take time to unfold, and could have an impact on coverage and reimbursement for healthcare items and services covered by plans that were authorized by the ACA. However, we cannot predict the ultimate content, timing or effect of any healthcare reform legislation or the impact of potential legislation on us.

In addition, other legislative changes have been proposed and adopted in the United States since the ACA was enacted to reduce healthcare expenditures. United States federal government agencies also currently face potentially significant spending reductions, which may further impact healthcare expenditures. On August 2, 2011, the Budget Control Act of 2011 among other things, created measures for spending reductions by Congress. A joint select committee on deficit reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. This includes aggregate reductions of Medicare payments to providers of 2% per fiscal year. These reductions went into effect on April 1, 2013 and, due to subsequent legislative amendments to the statute, including the BBA, will remain in effect through 2027 unless additional Congressional action is taken. Moreover, on January 2, 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, further reduced Medicare payments to several types of providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. If federal spending is further reduced, anticipated budgetary shortfalls may also impact the ability of relevant agencies, such as the FDA or the National Institutes of Health to continue to function at current levels. Amounts allocated to federal grants and contracts may be reduced or eliminated. These reductions may also impact the ability of relevant agencies to timely review and approve research and development, manufacturing, and marketing activities, which may delay our ability to develop, market and sell any products we may develop.

Moreover, payment methodologies may be subject to changes in healthcare legislation and regulatory initiatives. For example, the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, or MMA, changed the way Medicare covers and pays for pharmaceutical products. The legislation expanded Medicare coverage for drug purchases by the elderly and introduced a new reimbursement methodology based on average sales prices for physician-administered drugs. In addition, this legislation provided authority for limiting the number of drugs that will be covered in any therapeutic class. While the MMA only applies to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policy and payment limitations in setting their own reimbursement rates. Therefore, any reduction in reimbursement that results from the MMA may result in a similar reduction in payments from private payors.

Recently there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drug products. At the federal level, the current U.S. presidential administration's budget proposal for fiscal year 2019 contains further drug price control measures that could be enacted during the 2019 budget process or in other future legislation, including, for example, measures to permit Medicare Part D plans to negotiate the price of certain drugs under Medicare Part B, to allow some states to negotiate drug prices under Medicaid, and to eliminate cost sharing for generic drugs for low-income patients. Additionally, on May 11, 2018, the current U.S. presidential administration laid out the administration's "Blueprint" to reduce the cost of prescription medications while preserving innovation and cures. While the Department of Health and Human Services, or HHS, is soliciting feedback on some of these measures, other actions may be immediately implemented by HHS under existing authority. Although a number of these, and other potential, proposals will require authorization through additional legislation to become effective, Congress and the current U.S. presidential administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs. At the state level, legislatures are increasingly passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing.

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 I 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.

Employees

As of December 31, 2019, we had 56 employees. We have not experienced any work stoppages. We consider our relationship with our employees to be good.

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.

A description of the risks and uncertainties associated with our business is set forth below. You should carefully consider the risks described below, together with the other information contained in this quarterly 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.

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 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 TANGO and our current lead product candidate, STK-001 for the treatment of Dravet syndrome. We submitted an investigational new drug application, or IND, for STK-001 in late 2019. 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 and our future product candidates must be authorized for marketing by the U.S. Food and Drug Administration, or the FDA, or certain other foreign regulatory agencies, such as the European Medicines Agency, or the EMA, before we may commercialize any of our product candidates.

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

- effective INDs and Clinical Trial Authorizations, or CTAs, that allow commencement of our planned clinical trials or future clinical trials for our product candidates in relevant territories;
- successful completion of preclinical studies, including those compliant with Good Laboratory Practices, or GLP, or GLP toxicology studies, biodistribution studies and minimum effective dose studies in animals, and successful enrollment and completion of clinical trials compliant with current Good Clinical Practices, or GCPs;
- positive results from our clinical programs that are supportive of 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, or 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.

We have not tested any of our product candidates in clinical trials. Success in early preclinical studies or clinical trials may not be indicative of results obtained in later preclinical studies and clinical trials.

Though ASOs have been evaluated by others in clinical trials, STK-001 has not been 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. 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. 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. Even if our clinical trials demonstrate acceptable safety and efficacy of STK-001, 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, 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.

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 and our future product candidates must be approved by the FDA pursuant to a new drug application, or 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 or any of our 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 and our 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 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; and
- 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.

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 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 Risk Evaluation and Mitigation Strategies. 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.

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 or our future product candidates are approved.

Genetically defined diseases generally, and especially those for which our lead product candidate is targeted, have low incidence and prevalence. We estimate that the incidence of Dravet syndrome is approximately 1 in 15,625 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.

Our 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, as well as the people with this disease who have the potential to benefit from treatment with our product candidate, 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 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, our per-patient therapy pricing of STK-001, 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.

Although we intend to nominate a second genetic disease candidate for preclinical development in the second half of 2020, we are primarily focused on our lead product candidate, 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, or cGMPs, 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 drugs and biologics 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. Violations of the Federal Food, Drug, and Cosmetic Act 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 and our future product candidates in other jurisdictions, we must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. The approval procedure varies among countries and can involve additional testing. The time required to obtain approval may differ substantially from that required to obtain FDA approval. 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 pending exit from the European Union, or the EU, which is referred to as "Brexit," continues to create political and economic uncertainty, particularly in the United Kingdom and the EU. Since a significant proportion of the regulatory framework in the United Kingdom is derived from EU directives and regulations, the withdrawal of the United Kingdom from the EU 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 and 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 and our future product candidates and drugs in the antisense oligonucleotide class.

In addition to side effects caused by our product candidates, the intrathecal 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 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 Risk Evaluation and Mitigation Strategy 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 on the label;
- 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 Fast Track Designation by the FDA, even if granted for STK-001 or any of our future product candidates, may not lead to a faster development or regulatory review or approval process, and does not increase the likelihood that our product candidates will receive marketing approval.

We may seek Fast Track Designation for STK-001 or our future product candidates. 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, 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 product candidates that have obtained Fast Track Designation. 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. 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 some cases, the FDA may require that the trial be designed and/or initiated prior to approval. 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 for STK-001 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 candidate will receive marketing approval.

We may seek a Breakthrough Therapy Designation for STK-001 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 lose any marketing approval that we may have obtained and we may not achieve or sustain profitability.

For example, in March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively the Affordable Care Act, or the ACA, was enacted 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. As implementation of the ACA is ongoing, the law appears likely to continue the downward pressure on pharmaceutical pricing, especially under the Medicare program, and may also increase our regulatory burdens and operating costs. The current U.S. presidential administration and U.S. Congress have sought, and we expect they will continue to, seek to modify, repeal, or otherwise invalidate all, or certain provisions of, the ACA. Since January 2017, the current U.S. presidential administration has issued two executive orders and other directives designed to delay the implementation of certain provisions of the ACA or otherwise circumvent some of the requirements for health insurance mandated by the ACA. For example, on October 12, 2017, the current U.S. presidential administration issued an executive order that expands the use of association health plans and allows anyone to purchase short-term health plans that provide temporary, limited insurance. This executive order also calls for the halt of federal payments to health insurers for cost-sharing reductions previously available to lower-income Americans to afford coverage. There is uncertainty with respect to which legislation, if any, will be enacted and the impact the current U.S. presidential administration may have, if any, and any changes likely will take time to unfold, and could have an impact on coverage and reimbursement for healthcare items and services covered by plans that were authorized by the ACA. However, we cannot predict the ultimate content, timing or effect of any healthcare reform legislation or the impact of potential legislation on us. In addition, other legislative changes have been proposed and adopted since the ACA was enacted. These changes included aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, effective April 1, 2013, which, due to subsequent legislative amendments, will stay in effect through 2027 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 I 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.

We expect that the ACA, 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.

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 or our future product candidates.

As part of our business strategy, we applied for and, in August 2019, received Orphan Drug Designation for STK-001 in the United States, and we may seek such designation in Europe and other countries. However, Orphan Drug Designation does not guarantee future orphan drug marketing exclusivity.

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.

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 or any of 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 BLA, or NDA. We may seek Rare Pediatric Disease designations for STK-001. If a product candidate is designated before October 1, 2020, it is eligible to receive a voucher if it is approved before October 1, 2022. However, there is no expectation that STK-001 or any of our future product candidates will be approved by that date, or at all, and, therefore, we may not be in a position to obtain priority review vouchers prior to expiration of the program, unless Congress further reauthorizes the program. 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.

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

The ability of the FDA to review and approve new products can be affected by a variety of factors, including budget and funding levels, 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 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. Currently, the FDA Commissioner position is vacant, pending the appointment of a new Commissioner by the new presidential administration. The confirmation process for a new commissioner may not occur efficiently. Delays in filling or replacing key positions could significantly impact the ability of the FDA 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 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 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 federal healthcare programs such as Medicare and Medicaid;
- 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 or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government;

- the federal Health Insurance Portability and Accountability Act of 1996, or 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, or 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 payments and other transfers of value to physicians and teaching hospitals, as well as 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 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 or marketing expenditures. 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, 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 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, including acceptance of 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 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 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, 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, 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 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 Centers for Medicare & Medicaid Services, or CMS, since CMS 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, or the AMA, 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, or any future clinical trials, 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 contract research organizations, or CROs, contract manufacturing organizations, or 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.

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. 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 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 ASO treatments in various indications as well as several companies addressing other methods for modifying genes and regulating protein expression. We may also 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 cannabidiols, such as GW Pharmaceuticals, plc's Epidiolex, GABA receptor agonists, such as clobazam, and glutamate blockers, such as 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, and sodium channel antagonists 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, modified mRNA therapies or other ASO approaches.

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 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 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, 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 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 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 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 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 $32.3 million and $12.5 million, for the years ended December 31, 2019 and 2018, respectively. As of December 31, 2019, we had an accumulated deficit of $58.0 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 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 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 restricted cash of $222.7 million as of December 31, 2019, will enable us to fund our operating expenses and capital expenditure requirements into 2023. 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 an early-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 and preclinical studies 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 and do not expect to become profitable in the near future and we may never achieve profitability. As of December 31, 2019, we had federal and state net operating loss carryforwards, or NOLs, of approximately $54.5 million and $56.3 million, respectively, which expire at various dates beginning in 2034, for those net operating loss carryforwards generated prior to 2018. Net operating losses generated in 2018 and beyond have no expiration. To the extent that we continue to generate taxable losses, unused losses will carry forward to offset future taxable income, if any, until such unused losses expire. Under Sections 382 and 383 of the Internal Revenue Code of 1986, 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. We may have experienced one or more ownership changes in prior years, and we may experience ownership changes in the future as a result of subsequent shifts in our stock ownership. As a result, if we earn net taxable income, our ability to use our pre-change NOLs to offset U.S. federal taxable income may be subject to limitations, which could potentially result in increased future tax liability to us. 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, or 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.

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.

In addition, new legislation or regulation which could affect our tax burden could be enacted by any governmental authority. We cannot predict the timing or extent of such tax-related developments which could have a negative impact on our financial results. Additionally, we use our best judgment in attempting to quantify and reserve for these tax obligations. However, a challenge by a taxing authority, our ability to utilize tax benefits such as carryforwards or tax credits, or a deviation from other tax-related assumptions could have a material adverse effect on our business, results of operations, or financial condition.

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 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 license agreements with Cold Spring Harbor Laboratory and the University of Southampton, pursuant to which we in-license key patent and patent applications for our TANGO platform, STK-001 and future product candidates. For more information regarding these agreements, please see “Business—License agreements.” These agreements impose various diligence, milestone payment, royalty, insurance and other obligations on us. If we fail to comply with these obligations, our licensors may have the right to terminate our license, in which event we would not be able to develop or market our TANGO platform or STK-001 or any other technology or product candidates covered by the intellectual property licensed under these agreements. In addition, we may need to obtain additional licenses from our existing licensors 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 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 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 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 in-licensed patents and patent applications were made using U.S. government funding or other non-governmental funding. We rely on our 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 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 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, or STK-001, 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.

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 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 and our STK-001 product candidate and our future product candidates or result in any competitive advantage.

We have in-licensed an issued U.S. patent and patent applications that cover the mechanism of action of STK-001. As of the date of this Annual Report on Form 10K, we have applied for patent applications intended to specifically cover STK-001 and its use, but do not currently own or in-license any issued U.S. patents that specifically cover STK-001 or its use. We cannot be certain that any of these patent applications will issue as patents, and if they do, that such patents will cover or adequately protect STK-001 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, or 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, or 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 2040, 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 Cold Spring Harbor Laboratory and 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 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, or 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, 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.

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, or 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.

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 and data exclusivity 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, or 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. The GDPR governs the collection, use, disclosure, transfer or other processing of personal data of European persons. Among other things, the GDPR imposes new requirements regarding the security of personal data and notification of data processing obligations to the competent national data processing authorities, changes the lawful bases on which personal data can be processed, expands the definition of personal data and requires changes to informed consent practices, as well as more detailed notices for clinical trial subjects and investigators. In addition, the GDPR increases the scrutiny of transfers of personal data from clinical trial sites located in the EEA to the United States and other jurisdictions that the European Commission does not recognize as having “adequate” data protection laws, and imposes substantial fines for breaches and violations (up to the

greater of €20 million or 4% of our consolidated annual worldwide gross revenue). The GDPR also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies and obtain compensation for damages resulting from violations of the GDPR. Moreover, the UK implemented a Data Protection Act, effective in May 2018 and statutorily amended in 2019, that substantially implements the GDPR. Brexit has created uncertainty with regard to the requirements for data transfers between the UK and the EU and other jurisdictions. 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 and our future product candidates. In particular, we believe that our future success is highly dependent upon the contributions of our senior management, particularly our Chief Executive Officer, our Chief Financial Officer, our Chief Operating Officer and Chief Business Officer, our Chief Medical Officer, our Chief Legal Officer, our Executive Vice President of Research and Development, and our Co-Founder and Vice President, Head of Biology, as well as our senior scientists and other members of our senior management team. The loss of services of any 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 caused extreme volatility and disruptions in the capital and credit markets. A severe or prolonged economic downturn, such as the 2008 global financial crisis, could result in a variety of risks to our business, including, weakened demand for our product candidates and our ability to raise additional capital when needed on acceptable terms, if at all. As another example, our financial results may be negatively impacted by the recent COVID-19 outbreak. The extent and duration of such impacts remain largely uncertain and dependent on future developments that cannot be accurately predicted at this time, such as the severity and transmission rate of COVID-19, the extent and effectiveness of containment actions taken and the impact of these and other factors on our operations and the global economy in general. 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. 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 our third party service providers, face risks related to health epidemics and other outbreaks, which could significantly disrupt our operations.

Our business could be adversely impacted by the effects of COVID-19 or other epidemics. A public health epidemic, including COVID-19, poses the risk that we or our employees, contractors, suppliers, and other partners may be prevented from conducting business activities for an indefinite period of time, including due to shutdowns that may be requested or mandated by governmental authorities. We currently rely, and may continue to rely, on third-party service providers that are located in locals significantly impacted by COVID-19 and/or who source raw materials, samples, components, or other materials and reports from countries significantly impacted by COVID-19. Consequently, supply of research materials and early research activities are susceptible to factors adversely affecting one or more of our third-party service providers who are located in and/or who source from locations significantly impacted by COVID-19. We may also experience impacts to certain of our suppliers as a result of COVID-19 or other health epidemic or outbreak occurring in one or more of these locations, which may materially and adversely affect our business, financial condition and results of operations. In addition, hospitals or other clinical trial sites could also become overwhelmed by COVID-19 and shift resources or attention away from our clinical trials, which may cause delays in our trials or negatively affect enrollment. COVID-19 and mitigation measures may also have an adverse impact on global economic conditions which could have an adverse effect on our business and financial condition. The extent to which COVID-19 impacts our results will depend on future developments that are highly uncertain and cannot be predicted, including new information that may emerge concerning the severity of the virus and the actions to contain its impact.

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.

We may be unable to adequately protect our information systems from cyberattacks, which could result in the disclosure of confidential information, damage our reputation, and subject us to significant financial and legal exposure.

Cyberattacks are increasing in their frequency, sophistication and intensity, and have become increasingly difficult to detect. Cyberattacks 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 cyberattack 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 cyberattacks 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.

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 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 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;
- natural disasters and other calamities; and
- general economic, industry and market conditions.

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

Based on the beneficial ownership of our common stock as of December 31, 2019, our executive officers, directors and affiliates beneficially owned approximately 51.8% of our outstanding voting stock. As a result, these stockholders, if acting together, will continue to have significant 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 these stockholders may not be the same as or may even conflict with your interests. For example, these stockholders could 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. The significant concentration of stock ownership may adversely affect the trading price of our common stock due to investors' perception that conflicts of interest may exist or arise.

We are a "controlled company" within the meaning of the Nasdaq listing rules and qualify for exemptions from certain corporate governance requirements. While we do not intend to rely on these exemptions, we may change our decision in the future.

An entity affiliated with Apple Tree Partners beneficially owns a majority of the voting power of all outstanding shares of our common stock. As a result, we are a "controlled company" within the meaning of the corporate governance standards of Nasdaq. Under these rules, a "controlled company" may elect not to comply with certain corporate governance requirements, including:

- the requirement that a majority of our board of directors consists of independent directors;
- the requirement that we have a nominating and corporate governance committee that is composed entirely of independent directors with a written charter addressing the committee's purpose and responsibilities;
- the requirement that we have a compensation committee that is composed entirely of independent directors with a written charter addressing the committee's purpose and responsibilities; and
- the requirement for an annual performance evaluation of the nominating and corporate governance and compensation committees.

Although we have not taken advantage of these exemptions to date, we could change our decision in the future. In such event, you would not have the same protections afforded to shareholders of companies that are subject to all of the Nasdaq corporate governance requirements.

A future sale and issuance of our common stock or debt securities convertible into equity will dilute our share capital and may cause the price of our common stock to decline.

Sales of a substantial number of shares of our common stock in the public market could occur at any time. If our stockholders sell, or the market perceives that our stockholders intend to sell, substantial amounts of our common stock in the public market, the market price of our common stock could decline significantly.

We cannot predict what effect, if any, sales of our shares in the public market or the availability of shares for sale will have on the market price of our common stock. However, future sales of substantial amounts of our common stock in the public market, including shares issued upon exercise of outstanding options, or the perception that such sales may occur, could adversely affect the market price of our common stock. To the extent that additional capital is raised through the sale and issuance of shares or other securities convertible into shares, our stockholders will be diluted. No prediction can be made as to the effect, if any, that future sales of common stock or the availability of common stock for future sales will have on the trading price of our common stock.

We also expect that significant additional capital may be needed in the future to continue our planned operations. To raise capital, we may sell common stock, convertible securities or other equity securities in one or more transactions at prices and in a manner we determine from time to time. These sales, or the perception in the market that the holders of a large number of shares intend to sell shares, could reduce the market price of our common stock.

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, or 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, or the Sarbanes-Oxley Act, (ii) reduced disclosure obligations regarding executive compensation in this Annual Report on Form 10K and 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. In addition, as an emerging growth company, we are only required to provide two years of audited financial statements and two years of selected financial data in this Annual Report on Form 10K.

We will remain an emerging growth company until the earlier of (i) the last day of the fiscal year (a) following the fifth anniversary of the closing of our initial public offering, (b) in which we have total annual gross revenue of at least $1.07 billion or (c) in which we are deemed to be a large accelerated filer, which requires the market value of our common stock that is held by non-affiliates to exceed $700 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 during the prior three-year period.

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 million and our annual revenue was less than $100 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 million or (ii) our annual revenue is less than $100 million during the most recently completed fiscal year and the market value of our stock held by non-affiliates is less than $700 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.

In addition, 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, or 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.

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, or 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 are not currently required to comply with the SEC's, rules that implement Section 404 of the Sarbanes-Oxley Act, and are therefore not required to make a formal assessment of the effectiveness of our internal control over financial reporting for that purpose. Pursuant to Section 404, we will be required to furnish a report by our management on our internal control over financial reporting. However, while we remain an emerging growth company, we will not be required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. To achieve compliance with Section 404 within the prescribed period, we will be 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 2. Properties.

We currently occupy approximately 23,000 square feet of office and laboratory space in Bedford, Massachusetts, under a lease that expires in 2021. We have also signed a lease for an additional 2,485 square feet of office space in Cambridge, Massachusetts that expires in 2022, and we occupied this space in May 2019. 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 involved in legal proceedings arising in the ordinary course of our business. We are not presently a party to any legal proceedings that, in the opinion of management, would have a material adverse effect on our business. Regardless of outcome, litigation can have an adverse impact on us due to defense and settlement costs, diversion of management resources, negative publicity and reputation harm, and other factors.

Item 4. Mine Safety Disclosures.

Not Applicable.

PART II

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

Recent Sales of Unregistered Securities

Not applicable.

Holders of Record

As of December 31, 2019, there were 21 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 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 10K. Some of the information contained in this discussion and analysis or set forth elsewhere in this Annual Report on Form 10K, 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 section entitled "Risk factors" to gain an understanding of the important factors that could cause actual results to differ materially from our forward-looking statements.

Overview

We are pioneering a new way to treat the underlying causes of severe genetic diseases by precisely upregulating protein expression. We are developing novel antisense oligonucleotide, or ASO, medicines that target ribonucleic acid, or RNA, and modulate precursor-messenger RNA, or pre-mRNA, splicing to upregulate protein expression where needed and with appropriate specificity to near normal levels. We utilize our proprietary technology platform, Targeted Augmentation of Nuclear Gene Output, or TANGO, to design ASOs to upregulate the expression of protein by individual genes in a patient. Our approach is designed to allow us to deliver in a highly precise, durable and controlled manner disease-modifying therapies to a wide range of relevant tissues, including the central nervous system, or CNS, eye, kidney and liver.

We designed our lead product candidate, STK-001, to treat Dravet syndrome, a severe and progressive genetic epilepsy. With 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 anticipate an efficient clinical program for STK-001.

We submitted an investigational new drug application, or IND, for STK-001 to U.S. Food and Drug Administration, or the FDA, in late 2019. In the first quarter of 2020, we received communication from the FDA confirming that we may proceed with clinical dosing in the planned Phase 1/2a clinical trial called Monarch. The single ascending dose portion of this trial is in two parts, A and B, and is designed to evaluate STK-001 in children and adolescents ages 2 to 18 years of age with Dravet syndrome. Part A allows dosing of two cohorts. We expect to enroll and begin dosing patients in Part A of the study in the second half of 2020.

Part B of the study will evaluate the higher doses of STK-001. The FDA has placed a partial clinical hold for the doses planned in Part B of the study. The partial clinical hold was not due to any identified manufacturing or safety issue, but rather was because additional safety information is needed from preclinical testing to determine the safety profile of doses higher than the current no observed adverse effect level or NOAEL. The NOAEL was determined using data from a pivotal non-human primate study that evaluated intrathecal delivery of single dose levels of STK-001. The highest dose administered in this study was equivalent to a human dose that is higher than what we plan to administer in Part B of our Phase 1/2a clinical study and did not demonstrate effects that were considered adverse. It is the FDA's position that in order to support administration of STK-001 doses above those planned in Part A, additional nonclinical data to identify any potential safety issues of STK-001 at higher doses will need to be provided. We have initiated single-dose toxicology studies to more fully characterize the safety profile at higher doses, in order to facilitate the removal of the partial clinical hold and proceed to Part B of the study. Upon FDA clearance, we will plan to proceed with the higher dosing cohorts planned in Part B of the study.

We are working to minimize any potential delay to continued clinical testing of STK-001. We still anticipate preliminary data from the study in 2021.

We intend to nominate a second candidate for preclinical development in the second half of 2020.

We were incorporated in June 2014. In July 2015 and April 2016, we entered into worldwide license agreements with Cold Spring Harbor Laboratory, or CSHL, and the University of Southampton, respectively, with respect to certain licensed patents and applications relating to TANGO. TANGO exploits non-productive splicing events to effect targeted enhancement of protein expression. Since our inception through December 31, 2019, our operations have been financed by net proceeds of $280.4 million from the sale of convertible notes payable and our convertible preferred stock as well as our IPO. As of December 31, 2019, we had $222.7 million in cash, cash equivalents and restricted cash.

On June 21, 2019, we completed an initial public offering ("IPO") of our common stock and issued and sold 9,074,776 shares of common stock at a public offering price of $18.00 per share, which included 1,183,666 shares sold upon full exercise of the underwriters' option to purchase additional shares of common stock resulting in net proceeds of $151.9 million after deducting underwriting discounts and commissions but before deducting offering costs of approximately $2.5 million.

Since inception, we have had operating losses, the majority of which are attributable to research and development activities. Our net losses were $32.3 million and $12.5 million for the years ended December 31, 2019 and 2018, respectively, and as of December 31, 2019, we had an accumulated deficit of $58.0 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 existing cash, cash equivalents and restricted cash as of December 31, 2019, will enable us to fund our operating expenses and capital expenditure requirements into 2023. 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 agreements

Cold Spring Harbor Laboratory

In July 2015, we entered into a worldwide license agreement with CSHL, or the CSHL Agreement, with respect to the TANGO patents. Under the CSHL Agreement, we receive an exclusive (except with respect to certain government rights and non-exclusive licenses), worldwide license under certain patents and applications relating to TANGO. As part of the CSHL Agreement, we granted CSHL 164,927 shares of common stock. The CSHL Agreement obligates us to make additional payments that are contingent upon certain milestones being achieved as well as royalties on future product sales. These royalty obligations last on a product-by-product and country-by-country basis until the latest of (i) the expiration of the last valid claim of a patent covering a subject product or (ii) the expiration of any regulatory exclusivity for the subject product in a country. In addition, if we sublicense rights under the CSHL Agreement, we are required to pay a percentage of the sublicense revenue to CSHL, which may be reduced upon achievement of certain milestones for the applicable subject product. The maximum aggregate potential milestone payments payable total approximately $900,000. Additionally, certain licenses under the CSHL Agreement require us 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, 2019 and 2018. For more information, please see "Business—License agreements."

University of Southampton

In April 2016, we entered into an exclusive, worldwide license agreement with the University of Southampton, or the Southampton Agreement, whereby we acquired rights to foundational technologies related to our TANGO technology. Under the Southampton Agreement, we receive an exclusive, worldwide license under certain licensed patents and applications relating to TANGO. As part of the Southampton Agreement, we paid 55,000 pounds sterling (approximately $73,000 as of the date thereof) as an up-front license fee. Under the Southampton Agreement, we 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 we sublicense our rights under the Southampton Agreement, we are required to pay a percentage of the sublicense revenue to the University of Southampton. The maximum aggregate potential milestone payments payable by us total approximately 400,000 pounds sterling (approximately $530,000 as of December 31, 2019). As of December 31, 2019, and 2018, we have recorded no liabilities under the Southampton Agreement. For more information, please see "Business—License agreements."

Financial operations overview

Revenue

We currently do not have any products approved for sale and have not generated any revenue since inception. 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.

Operating expenses

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 equipment and 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,	
	2019	2018
	(in thousands)	
STK-001	$ 10,724	$ 1,960
Non-program specific and unallocated research and development expenses	13,040	6,411
Total research and development expenses	$ 23,764	$ 8,371

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.

Interest Income

Interest income consists primarily of interest received on our invested funds.

Other income (expense)

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

Results of operations for the years ended December 31, 2019 and 2018

The following table sets forth our results of operations:

	Year ended December 31,	
	2019	2018
	(in thousands)	
Consolidated statements of operations and comprehensive loss:		
Revenue	$ —	$ —
Operating expenses:		
Research and development	23,764	8,371
General and administrative	11,914	4,410
Total operating expenses	35,678	12,781
Loss from operations	(35,678)	(12,781)
Other income (expense):		
Interest income	3,351	270
Other income, net	2	(10)
Total other income (expense)	3,353	260
Net loss	$ (32,325)	$ (12,521)

Research and development expenses

Research and development expenses were $23.8 million for the year ended December 31, 2019 as compared to $8.4 million for the year ended December 31, 2018, an increase of $15.4 million. The table below summarizes our research and development expenses:

	Year Ended December 31,	
	2019	2018
STK-001	$ 10,724	$ 1,960
Personnel-related expenses	7,064	3,825
Third-party services	1,019	1,680
Scientific consulting	839	161
Facilities and other research and development expenses	4,118	745
Total research and development expenses	$ 23,764	$ 8,371

The increases in research and development expenses were primarily attributable to an increase of $8.8 million on our STK-001 program, comprised primarily of third-party services and scientific consulting fees, an increase of $3.2 million in personnel costs resulting from an increase in headcount, and an increase of $3.4 million in facilities and other costs resulting from the growth in our research and development personnel.

General and administrative expenses

General and administrative expenses were $11.9 million for the year ended December 31, 2019 as compared to $4.4 million for the year ended December 31, 2018, an increase of $7.5 million.

The increases in general and administrative expenses were primarily attributable to an increase of $1.8 million in personnel costs resulting from an increase in headcount, an increase of $1.6 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 and an increase of $4.1 million in facilities and other costs resulting from the growth in our general and administrative personnel.

Other income (expense)

The change in our other income (expense) for the year ended December 31, 2019 as compared to the year ended December 31, 2018 principally reflects returns on higher levels of cash reserves.

Liquidity and capital resources

Since our inception through December 31, 2019, our operations have been financed by net proceeds of $280.4 million from the sale of convertible notes payable and our convertible preferred stock as well as our IPO. As of December 31, 2019, we had $222.7 million in cash, cash equivalents and restricted cash. 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, 2019, we had an accumulated deficit of $58.0 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.

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 existing cash, cash equivalents and restricted cash as of December 31, 2019, will enable us to fund our operating expenses and capital expenditure requirements into 2023. 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,	
	2019	2018
	(in thousands)	
Net cash (used in) provided by:		
Operating activities	$ (31,055)	$ (10,964)
Investing activities	(1,634)	(925)
Financing activities	149,762	115,639
Net increase in cash, cash equivalents and restricted cash	$ 117,073	$ 103,750

Operating activities

During the year ended December 31, 2019, cash used in operating activities was $31.1 million and was attributable to a net loss of $32.3 million, a net change of $1.1 million in our operating assets and liabilities, partially offset by non-cash charges of $2.3 million for share-based compensation and depreciation.

During the year ended December 31, 2018, cash used in operating activities was $11.0 million and was attributable to a net loss of $12.5 million, partially offset by non-cash charges of $0.5 million and a net change of $1.0 million in our net operating assets and liabilities.

Investing activities

Our investing activities during the years ended December 31, 2019 and 2018 have consisted principally of purchases of property and equipment.

Financing activities

Our financing activities during the year ended December 31, 2019 included primarily net proceeds of $149.4 million from our Initial Public Offering in June 2019.

Our financing activities during the year ended December 31, 2018 included net proceeds of $115.6 million from closings on our Series A-2 convertible preferred stock financing in January and September 2018 and the sale of Series B convertible preferred stock in October 2018.

Contractual obligations and commitments

The following table summarizes our contractual obligations as of December 31, 2019 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	$ 2,332	$ 1,149	$ 1,183	$ —	$ —
Total	$ 2,332	$ 1,149	$ 1,183	$ —	$ —

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 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.

Commitments

Our commitments primarily consist of obligations under our agreements with CSHL and the University of Southampton. As of December 31, 2019, 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 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.

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

We recognize compensation costs related to share-based awards granted to employees and directors, including stock options and vesting restricted stock, based on the estimated fair value of the awards on the date of grant. 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-based awards. These assumptions include:

- *Fair value of common stock*—Historically, for all periods prior to our initial public offering, the fair value of the shares of common stock underlying our share-based awards was estimated on each grant date by our board of directors. To determine the fair value of our common stock underlying option grants, our board of directors considered, among other things, valuations of our common stock prepared by an unrelated third-party valuation firm in accordance with the guidance provided by the American Institute of Certified Public Accountants Practice Guide, *Valuation of Privately-Held-Company Equity Securities Issued as Compensation*, or the *Practice Aid*. Since becoming a public company we have used our stock price to determine fair value of our common stock.
- *Expected term*—The expected term represents the period that stock-based awards are expected to be outstanding. The expected term for option grants 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-based awards.

- *Expected volatility*—As a privately held company we did not have any trading history for our common stock; accordingly the expected volatility was estimated based on the average volatility for comparable publicly traded biotechnology companies over a period equal to the expected term of the stock option grants. The comparable companies were chosen based on their similar size, stage in the life cycle or area of specialty. As a public company we have computed the historical volatility of our own stock price and will continue to use the historical volatility data of our common stock.
- *Risk-free interest rate*—The risk-free interest rate is based on the U.S. Treasury zero coupon issues in effect at the time of grant for periods corresponding with the expected term of option.
- *Expected dividend*—We have never paid dividends on our common stock and have no plans to pay dividends on our common stock. Therefore, we used an expected dividend yield of zero.

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

	Year ended December 31,	
	2019	2018
Risk-free interest rate	1.42-2.81%	2.67-2.84%
Expected dividend yield	0%	0%
Expected life	5.5-6.375 years	6.25-6.375 years
Expected volatility	60-68%	57-60%

We will continue to use judgment in evaluating the assumptions utilized for our share-based compensation expense calculations on a prospective basis. In addition to the assumptions used in the Black-Scholes option-pricing model, the amount of stock-based compensation expense we recognize in our consolidated financial statements includes actual stock option forfeitures.

Other Information

Net Operating Loss Carryforwards

As of December 31, 2019 and 2018, we had federal net operating loss carryforwards of $54.5 million and $24.4 million, respectively, which may be available to reduce future taxable income, and expire at various dates beginning in 2034, for those net operating loss carryforwards generated prior to 2018. Net operating losses generated in 2018 and beyond have no expiration. As of December 31, 2019 and 2018, we had state net operating loss carry forwards of $56.3 million and $24.0 million, respectively, which may be available to reduce future taxable income and expire at various dates beginning in 2034. In addition, at December 31, 2019 and 2018, we had federal research and development tax credit carryforwards of $1.5 million and $0.4 million, respectively, and state research and development tax credit carry forwards of $0.8 million and $0.4 million, respectively. Both federal and state research and development tax credit carry forwards may be available to reduce future tax liabilities and expire at various dates beginning in 2030.

In accordance with Statement of Accounting Standards Codification (ASC) 740, *Accounting for Income Taxes*, our management has evaluated the positive and negative evidence bearing upon the realizability of its deferred tax assets, which are comprised principally of net operating loss carryforwards. Management has determined that it is more likely than not that we will not recognize the benefits of federal and state deferred tax assets and, as a result, a full valuation allowance of $17.9 million and $7.6 million was established at December 31, 2019 and 2018, respectively. The change in the valuation allowance was an increase of $10.3 million and $3.5 million in 2019 and 2018, respectively.

Utilization of the net operating loss carryforwards and research and development tax credit carryforwards may be subject to a substantial annual limitation under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended, or the Code due to ownership changes that have occurred previously or that could occur in the future. These ownership changes may limit the amount of carryforwards that can be utilized annually to offset future taxable income. We have not conducted a formal study to assess whether a change of control has occurred or whether there have been multiple changes of control since inception due to the significant complexity and cost associated with such a study. If we have experienced a change of control, as defined for purposes of Section 382 and 383 of the Code, at any time since inception, utilization of the net operating loss carryforwards or research and development tax credit carryforwards may be subject to an annual limitation under Section 382 and 383 of the Code, which is determined by first multiplying the value of our stock at the time of the ownership change by the applicable long-term tax-exempt rate, and then could be subject to additional adjustments, as required. Any limitation may result in expiration of a portion of the net operating loss carryforwards or research and development tax credit carryforwards before utilization.

We apply ASC 740 related to accounting for uncertainty in income taxes. Our reserves related to income taxes are based on a determination of whether, and how much of, a tax benefit taken by us in our 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, 2019, and 2018 we 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.

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 $1.07 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 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 are also a "smaller reporting company," meaning that the market value of our stock held by non-affiliates plus the proposed aggregate amount of gross proceeds to us as a result of our IPO was less than $700 million and our annual revenue is less than $100 million during the most recently completed fiscal year. We may continue to be a smaller reporting company after our IPO if either (i) the market value of our stock held by non-affiliates is less than $250 million or (ii) our annual revenue is less than $100 million during the most recently completed fiscal year and the market value of our stock held by non-affiliates is less than $700 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 February 2016, the Financial Accounting Standards Board (FASB) issued Accounting Standards Updates (ASU) No. 2016-02, Leases (Topic 842). This standard established a right-of-use model that requires all lessees to recognize right-of-use assets and lease liabilities on their balance sheet that arise from leases as well as provide disclosures with respect to certain qualitative and quantitative information related to a company's leasing arrangements. For Income Statement purposes, a dual model was retained requiring leases to be classified as either operating or finance. Operating leases result in straight line expense while finance leases results in a front-loaded expense pattern. In July 2018, the FASB issues ASU 2018-11, which provided for an alternative transition method by allowing entities to apply Topic 842 as of the adoption date. We adopted Topic 842 on January 1, 2020 using the modified retrospective approach and elected to apply the transition method that allows companies to continue applying guidance under the lease standard in effect at that time in the comparative period financial statements and recognize a cumulative-effect adjustment to retained earnings (accumulated deficit) on the date of adoption. We have also elected the package of practical expedients to not reassess our prior conclusions about lease identification, lease classification and indirect costs and to not separate lease and non-lease components

Upon adoption of Topic 842 on January 1, 2020, we recorded right-of-use assets of $2.2 million, operating lease liabilities of $2.2 million and the elimination of deferred rent of $0.03 million. Adoption of the standard did not result in us recording a cumulative effect adjustment to retained earnings (accumulated deficit).

In July 2017, the FASB issued ASU 2017-11, Earnings Per Share (Topic 260), Distinguishing Liabilities from Equity (Topic 480) and Derivatives and Hedging (Topic 815): I. Accounting for Certain Financial Instruments with Down Round Features; II. Replacement of the Indefinite Deferral for Mandatorily Redeemable Financial Instruments of Certain Nonpublic Entities and Certain Mandatorily Redeemable Noncontrolling Interests with a Scope Exception. Part I of this update addresses the complexity of accounting for certain financial instruments with down round features. Down round features are features of certain equity-linked instruments (or embedded features) that result in the strike price being reduced on the basis of the pricing of future equity offerings. Current accounting guidance creates cost and complexity for entities that issue financial instruments (such as warrants and convertible instruments) with down round features that require fair value measurement of the entire instrument or conversion option. Part II of this update addresses the difficulty of navigating Topic 480, Distinguishing Liabilities from Equity, because of the existence of extensive pending content in the FASB Accounting Standards Codification. This pending content is the result of the indefinite deferral of accounting requirements about mandatorily redeemable financial instruments of certain nonpublic entities and certain mandatorily redeemable noncontrolling interests. The amendments in Part II of this update do not have an accounting effect. For public business entities, the amendments in Part I of ASU-2017-11 are effective for fiscal years and interim periods within those years beginning after December 15, 2018. For all other entities, the amendments in Part I of this update are effective for fiscal years beginning after December 15, 2019, and interim periods within fiscal years beginning after December 15, 2020. We intend to adopt Part I of this update on January 1, 2020. Early adoption is permitted for all entities, including adoption in an interim period. We are currently assessing the potential impact of adopting ASU 2017-11 on its consolidated financial statements and financial statement disclosures and do not expect that the adoption of this update will have a material impact on our consolidated financial statements.

In August 2018, the FASB issued ASU 2018-13, “Fair Value Measurement (Topic 820), Disclosure Framework—Changes to the Disclosure Requirements for Fair Value Measurement”. This ASU removed the following disclosure requirements: (1) the amount of and reasons for transfers between Level 1 and Level 2 of the fair value hierarchy; (2) the policy for timing of transfers between levels; and (3) the valuation processes for Level 3 fair value measurements. Additionally, this update added the following disclosure requirements: (1) the changes in unrealized gains and losses for the period included in other comprehensive income and loss for recurring Level 3 fair value measurements held at the end of the reporting period; (2) the range and weighted average of significant unobservable inputs used to develop Level 3 fair value measurements. For certain unobservable inputs, an entity may disclose other quantitative information (such as the median or arithmetic average) in lieu of the weighted average if the entity determines that other quantitative information would be a more reasonable and rational method to reflect the distribution of unobservable inputs used to develop Level 3 fair value measurements. ASU 2018-13 will be effective for all entities, for fiscal years beginning after December 15, 2019 with early adoption permitted. We intend to adopt this standard on January 1, 2020 and we do not expect that the adoption of this update will have a material impact on our consolidated financial statements.

Quantitative and Qualitative disclosures about market risk

Interest rate risk

We are exposed to market risks in the ordinary course of our business. These risks primarily include interest rate sensitivities. We held cash, cash equivalents and restricted cash of $222.7 million and $105.6 million as of December 31, 2019 and 2018 respectively. We generally hold our cash in interest-bearing money market accounts. Our primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of U.S. interest rates. An immediate 100 basis point change in interest would affect the fair market value of our cash equivalents by approximately $2.2 million.

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.

Conclusion Regarding the Effectiveness 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, 2019. 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.

This Annual Report on Form 10-K does not include a report of management’s assessment regarding internal control over financial reporting or 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, 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 the period covered by this report that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information.

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 2020 Annual Meeting of Stockholders and is incorporated herein by reference.

Item 11. Executive Compensation.

The information required by this Item 11 will be included in our Definitive Proxy Statement to be filed with the SEC with respect to our 2020 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 2020 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 2020 Annual Meeting of Stockholders and is incorporated herein by reference.

Item 14. Principal Accounting 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 2020 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.	10-Q	001-38938	August 14, 2019	3.1	
3.2	Restated Bylaws	10-Q	001-38938	August 14, 2019	3.2	
4.1	Form of Common Stock Certificate	S-1	333-231700	June 7, 2019	4.1	
4.2	Amended and Restated Investors' Rights Agreement, dated October 22, 2018, by and among the Registrant and certain of its stockholders.	S-1	333-231700	May 23, 2019	4.2	
4.3	Description of Common Stock Registered Under Section 12 of the Securities Exchange Act of 1934.					X
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, to become effective on the date immediately prior to the date the registration statement is declared effective, and forms of award agreements.	S-1	333-231700	June 7, 2019	10.4	
10.4*	2019 Employee Stock Purchase Plan, to become effective on the date the registration statement is declared effective, and forms of award agreements.	S-1	333-231700	June 7, 2019	10.5	
10.5	Lease Agreement, dated August 20, 2018, by and between Homology Medicines, Inc., and the Registrant.	S-1	333-231700	May 23, 2019	10.5	
10.6	Lease Agreement dated January 2, 2019, by and between MIT 139 Main Street Leasehold LLC., and the Registrant.	S-1	333-231700	May 23, 2019	10.6	
10.7†	License Agreement, dated July 31, 2015, by and between Cold Spring Harbor Laboratory and the Registrant.	S-1	333-231700	June 12, 2019	10.8	
10.8†	License Agreement, dated April 18, 2016, by and between the University of Southampton and the Registrant.	S-1	333-231700	June 12, 2019	10.9	
10.9*	Employment Agreement, dated October 5, 2017, by and between the Registrant and Edward M. Kaye, as amended.	S-1	333-231700	May 23, 2019	10.9	

Exhibit Number	Description	Form	File No.	Exhibit Filing Date	Exhibit No.	Filed/Furnished Herewith
10.10*	Employment Agreement, dated November 20, 2015, by and between the Registrant and Huw M. Nash.	S-1	333-231700	May 23, 2019	10.10	
10.11*	Employment Agreement, dated September 8, 2017, by and between the Registrant and Barry J. Ticho, as amended.	S-1	333-231700	May 23, 2019	10.11	
10.12*	Employment Agreement, dated January 7, 2018, by and between the Registrant and Gene Liau.	S-1	333-231700	May 23, 2019	10.12	
10.13*	Employment Agreement, dated February 12, 2019, by and between the Registrant and Stephen J. Tulipano.	S-1	333-231700	May 23, 2019	10.13	
10.14*	Consulting Agreement, dated October 24, 2014, by and between the Registrant and Adrian R. Krainer.	S-1	333-231700	May 23, 2019	10.14	
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 Financial Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.					X
32.1*	Certification of Principal Executive Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.					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
101.INS	XBRL Instance Document.					X
101.SCH	XBRL Taxonomy Extension Schema Document.					X
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document.					X
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document.					X
101.LAB	XBRL Taxonomy Extension Label Linkbase Document.					X
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document.					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.*

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 Report to be signed on its behalf by the undersigned, thereunto duly authorized**.**

STOKE THERAPEUTICS, INC.

Date: March 23, 2020

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

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

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

Name	Title	Date
/s/ Edward M. Kaye Edward M. Kaye, M.D.	Chief Executive Officer and Director (Principal Executive Officer)	March 23, 2020
/s/ Stephen J. Tulipano Stephen J. Tulipano	Chief Financial Officer (Principal Financial and Accounting Officer)	March 23, 2020
/s/ Samuel W. Hall Samuel W. Hall, Ph.D.	Director	March 23, 2020
/s/ Seth L. Harrison Seth L. Harrison, M.D.	Director	March 23, 2020
/s/ Adrian R. Krainer Adrian R. Krainer, Ph.D.	Director	March 23, 2020
s/ Arthur A. Levin Arthur A. Levin, Ph.D.	Director	March 23, 2020
/s/ Arthur O. Tzianabos Arthur O. Tzianabos, Ph.D.	Director	March 23, 2020
/s/ Jennifer C. Burstein Jennifer C. Burstein	Director	March 23, 2020

STOKE THERAPEUTICS, INC.

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

Report of independent registered public accounting firm

To the Stockholders and 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, 2019 and 2018, the related consolidated statements of operations and comprehensive loss, stockholders' equity (deficit), and cash flows for each of the years in the two year period ended, December 31, 2019 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, 2019 and 2018, and the results of its operations and its cash flows for each of the years in the two year period ended December 31, 2019, 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. 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 23, 2020

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

	As of December 31,	
	2019	2018
Assets		
Current assets:		
Cash and cash equivalents	$ 222,471	$ 105,399
Prepaid expenses and other current assets	3,281	548
Interest receivable	281	196
Total current assets	226,033	106,143
Restricted cash	205	204
Property and equipment, net	2,512	1,192
Total assets	$ 228,750	$ 107,539
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 751	$ 1,071
Accrued and other current liabilities	3,350	1,396
Total current liabilities	4,101	2,467
Long term liabilities	221	4
Total liabilities	4,322	2,471
Commitments and contingencies (Note 7)		
Stockholders' equity		
Preferred Stock, par value of $0.0001 per share; 10,000,000 shares authorized, none issued and outstanding as of December 31, 2019; and no shares authorized, issued or outstanding as of December 31, 2018	—	—
Convertible Preferred Stock, par value of $0.0001 per share; no shares authorized, issued or outstanding at December 31, 2019; 225,584,874 shares authorized, 22,677,585 shares issued and outstanding as of December 31, 2018, aggregate liquidation preference of $130,850 at December 31, 2018	—	2
Common stock, par value of $0.0001 per share; 300,000,000 and 278,527,249 shares authorized, 32,861,842 and 727,413 shares issued and outstanding as of December 31, 2019 and 2018, respectively	3	—
Additional paid-in capital	282,460	130,776
Accumulated deficit	(58,035)	(25,710)
Total stockholders' equity	224,428	105,068
Total liabilities and stockholders' equity	$ 228,750	$ 107,539

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

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

	Year Ended December 31,	
	2019	2018
Revenue	$ —	$ —
Operating expenses:		
Research and development	23,764	8,371
General and administrative	11,914	4,410
Total operating expenses	35,678	12,781
Loss from operations	(35,678)	(12,781)
Other income (expense):		
Interest income	3,351	270
Other income, net	2	(10)
Total other income (expense)	3,353	260
Net loss and comprehensive loss	(32,325)	(12,521)
Net loss per share attributable to common stockholders—basic and diluted	$ (1.80)	$ (17.65)
Weighted average common shares outstanding—basic and diluted	17,971,443	709,336

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

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

	Convertible Preferred Stock		Common Stock		Additional paid-in capital	Accumulated deficit	Stockholders' equity (Deficit)
	Shares	Amount	Shares	Amount			
Balance as of December 31, 2017	4,980,168	$ —	670,090	$ —	$ 11,897	$ (13,189)	$ (1,292)
Stock-based compensation	—	—	—	—	240	—	240
Issuance of common stock upon exercise of stock options	—	—	57,323	—	19	—	19
Issuance of convertible Preferred Stock, net of issuance costs of $378	17,697,417	2	—	—	118,620	—	118,622
Net loss	—	—	—	—	—	(12,521)	(12,521)
Balance as of December 31, 2018	22,677,585	2	727,413	—	130,776	(25,710)	105,068
Stock-based compensation	—	—	—	—	1,922	—	1,922
Issuance of common stock upon exercise of stock options	—	—	382,068	—	314	—	314
Issuance of common stock upon initial public offering, net of underwriting discounts, commissions, and offering costs	—	—	9,074,776	1	149,448	—	149,449
Conversion of preferred stock to common stock	(22,677,585)	(2)	22,677,585	2	—	—	—
Net loss	—	—	—	—	—	(32,325)	(32,325)
Balance as of December 31, 2019	—	$ —	32,861,842	$ 3	$ 282,460	$ (58,035)	$ 224,428

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

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

	Year Ended December 31,	
	2019	2018
Cash flows from operating activities:		
Net loss	$ (32,325)	$ (12,521)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation	450	214
Stock-based compensation	1,922	240
Loss on disposal of property and equipment	3	10
Changes in assets and liabilities:		
Prepaid expenses and other current assets	(2,024)	(632)
Accounts payable and accrued liabilities	891	1,735
Deferred rent	28	(10)
Net cash used in operating activities	(31,055)	(10,964)
Cash flows from investing activities:		
Purchases of property and equipment	(1,635)	(935)
Proceeds from sale of property and equipment	1	10
Net cash used in investing activities	(1,634)	(925)
Cash flows from financing activities:		
Proceeds from issuance of convertible Preferred Stock	—	116,000
Preferred Stock Issuance Cost	—	(378)
Proceeds from issuance of common stock upon initial public offering	151,912	—
Payments of initial public offering costs	(2,463)	—
Proceeds from exercise of stock options	315	19
Other	(2)	(2)
Net cash provided by financing activities	149,762	115,639
Net increase in cash, cash equivalents and restricted cash	117,073	103,750
Cash, cash equivalents and restricted cash—beginning of year	105,603	1,853
Cash, cash equivalents and restricted cash—end of year	$ 222,676	$ 105,603
Supplemental disclosure of non-cash investing and financing activities:		
Property and equipment included in accrued expenses and accounts payable	$ 140	$ 19
Issuance of convertible Preferred Stock in exchange for simple agreement for future equity	$ —	$ 3,000

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.

Initial public offering

On June 21, 2019, the Company completed an initial public offering ("IPO") of its common stock and issued and sold 9,074,776 shares of common stock at a public offering price of $18.00 per share, which included 1,183,666 shares sold upon full exercise of the underwriters' option to purchase additional shares, resulting in net proceeds of approximately $149.4 million after deducting underwriting discounts, commissions and offering costs of $13.9 million. Upon closing of the IPO, the Company's outstanding convertible preferred stock automatically converted into shares of common stock (see Note 8). Upon conversion of the convertible preferred stock, the Company reclassified the carrying value of the convertible preferred stock to common stock and additional paid-in capital.

On June 6, 2019, the Company effected a one-for-9.95 reverse split of the Company's issued and outstanding common and convertible preferred stock. Upon the effectiveness of the reverse stock split, (i) all shares of outstanding common stock and convertible preferred stock were adjusted; (ii) the number of shares of common stock for which each outstanding option to purchase common stock is exercisable were adjusted; and (iii) the exercise price of each outstanding option to purchase common stock were adjusted. All of the outstanding common stock share numbers (including shares of common stock subject to the Company's options and as converted for the outstanding convertible preferred stock shares), share prices, exercise prices and per share amounts contained in the consolidated financial statements have been retroactively adjusted in the consolidated financial statements to reflect this reverse stock split for all periods presented. The par value per share and the authorized number of shares of common stock and convertible preferred stock were not adjusted as a result of the reverse stock split.

On June 21, 2019, the Company filed an amended and restate certificate of incorporation with the Secretary of State of the State of Delaware to authorize the issuance of up to 300 million shares of common stock. $0.0001 par value, and 10 million shares of undesignated preferred stock, $0.0001 par value per share.

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 its consolidated financial statements for the year ended December 31, 2019, the Company expects that its cash and cash equivalents will be sufficient to fund its operating expenses and capital expenditure requirements through at least twelve months from the issuance date of its consolidated financial statements.

The Company plans to seek additional funding through public or private equity offerings, debt financings, other collaborations, strategic alliances and licensing arrangements. The Company may not be able to obtain financing on acceptable terms, or at all, and the Company may not be able to enter into strategic alliances or other arrangements on favorable terms, or at all. The terms of any financing may adversely affect the holdings or the rights of the Company's stockholders. If the Company is unable to obtain funding, the Company could be required to delay, reduce or eliminate research and development programs, product portfolio expansion or future commercialization efforts, which could adversely affect its business prospects.

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, 2019, 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 sheet to the statement of cash flows:

	As of December 31,	
	2019	2018
Cash and cash equivalents	$ 222,471	$ 105,399
Restricted cash	205	204
	$ 222,676	$ 105,603

Concentration of credit risk

Financial instruments that potentially expose the Company to concentrations of credit risk primarily consist of cash and cash equivalents. The Company maintains its cash and cash equivalents at an accredited financial institution 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.

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 (deficit) as a reduction of additional paid-in capital generated as a result of the offering. Should the in-process equity financing be abandoned, the deferred offering costs will be expensed immediately as a charge to operating expenses in the consolidated statements of operations and comprehensive loss.

Property and equipment

Property and equipment are initially 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 and without interest expense) 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, 2019 and 2018.

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 made 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 options

The Company measures its stock-based awards granted based on the estimated fair values of the awards and recognizes the compensation for employees and nonemployees over the requisite service period. The Company uses the Black-Scholes option-pricing model to estimate the fair value of its stock-based awards. 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.

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.

Rent expense

The Company's real estate operating leases provide for scheduled annual rent increases throughout the lease term. The Company recognizes the effects of the scheduled rent increases on a straight-line basis over the full term of the leases. Tenant improvement allowances, if any, provided by a landlord are recorded as deferred rent and amortized as reduction to rent expense over the lease term.

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, 2019 and 2018, 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.

The Tax Cuts and Jobs Act (the TCJA) was enacted on December 22, 2017. The TCJA reduced the U.S. federal corporate tax rate from a top rate of 35% to a flat rate of 21%. The Company continues to monitor for legislative developments, issuance of regulations and technical memorandum to provide further clarification and/or interpretations of the TCJA and will adjust its consolidated financial statements as needed.

Net loss per share

The Company calculates basic and diluted net loss per share attributable to common stockholders in conformity with the two-class method required for participating securities. The Company considers its convertible preferred stock (Preferred Stock) to be participating securities as in the event a dividend is paid on common stock, the holders of Preferred Stock would be entitled to receive dividends on a basis consistent with the common stockholders. Under the two-class method, the net loss attributable to common stockholders is not allocated to the Preferred Stock as the holders of the Preferred Stock do not have a contractual obligation to share in losses.

Under the two-class method, basic net loss per share attributable to common stockholders is computed by dividing the net loss attributable to common stockholders by the weighted average number of shares of common stock.

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 Company's first fiscal year (a) following the fifth anniversary of the completion of our IPO, (b) in which the Company has total annual gross revenues of at least $1.07 billion, or (c) when 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 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 million and its annual revenue is less than $100 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 million or (ii) its annual revenue is less than $100 million during the most recently completed fiscal year and the market value of its stock held by non-affiliates is less than $700 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 adopted Accounting Pronouncements

In May 2017, the FASB issued ASU 2017-09, *Compensation – Stock Compensation* (Topic 718): *Scope of Modification Accounting*, which provides guidance about which changes to the terms or conditions of a share-based payment award require an entity to apply modification accounting in Topic 718. The amendments in this ASU should be applied prospectively to an award modified on or after the adoption date. The Company adopted ASU 2017-09 effective January 1, 2018, and the adoption of ASU 2017-09 did not impact the Company's consolidated financial statements or financial statement disclosures.

Recently issued accounting pronouncements

In February 2016, the FASB issued ASU No. 2016-02, *Leases* (Topic 842). This standard established a right-of-use model that requires all lessees to recognize right-of-use assets and lease liabilities on their balance sheet that arise from leases as well as provide disclosures with respect to certain qualitative and quantitative information related to a company's leasing arrangements. For Income Statement purposes, a dual model was retained requiring leases to be classified as either operating or finance. Operating leases result in straight line expense while finance leases results in a front-loaded expense pattern. In July 2018, the FASB issues ASU 2018-11, which provided for an alternative transfer method by allowing entities to apply Topic 842 as of the adoption date. The Company adopted Topic 842 on January 1, 2020 using the modified retrospective approach and elected to apply the transition method that allows companies to continue applying guidance under the lease standard in effect at that time in the comparative period financial statements and recognize a cumulative-effect adjustment to the balance sheet on the date of adoption. The Company has also elected the package of practical expedients to not reassess our prior conclusions about lease identification, lease classification and indirect costs and to not separate lease and non-lease components.

Upon adoption of Topic 842 on January 1, 2020, the Company recorded right-of-use assets of $2.2 million and operating lease liabilities of $2.2 million and the elimination of deferred rent of $0.03 million. Adoption of the standard did not result in the Company recording a cumulative effect adjustment to retained earnings.

In July 2017, the FASB issued ASU 2017-11, *Earnings Per Share* (Topic 260), Distinguishing Liabilities from Equity (Topic 480) and Derivatives and Hedging (Topic 815): *I. Accounting for Certain Financial Instruments with Down Round Features; II. Replacement of the Indefinite Deferral for Mandatorily Redeemable Financial Instruments of Certain Nonpublic Entities and Certain Mandatorily Redeemable Noncontrolling Interests with a Scope Exception*. Part I of this update addresses the complexity of accounting for certain financial instruments with down round features. Down round features are features of certain equity-linked instruments (or embedded features) that result in the strike price being reduced on the basis of the pricing of future equity offerings. Current accounting guidance creates cost and complexity for entities that issue financial instruments (such as warrants and convertible instruments) with down round features that require fair value measurement of the entire instrument or conversion option. Part II of this update addresses the difficulty of navigating Topic 480, Distinguishing Liabilities from Equity, because of the existence of extensive pending content in the FASB Accounting Standards Codification. This pending content is the result of the indefinite deferral of accounting requirements about mandatorily redeemable financial instruments of certain nonpublic entities and certain mandatorily redeemable noncontrolling interests. The amendments in Part II of this update do not have an accounting effect. For public business entities, the amendments in Part I of ASU-2017-11 are effective for fiscal years and interim periods within those years beginning after December 15, 2018. For all other entities, the amendments in Part I of this update are effective for fiscal years beginning after December 15, 2019, and interim periods within fiscal years beginning after December 15, 2020. The Company intends to adopt Part I of this update on January 1, 2020. Early adoption is permitted for all entities, including adoption in an interim period. The Company is currently assessing the potential impact of adopting ASU 2017-11 on its consolidated financial statements and financial statement disclosures and does not expect that the adoption of this update will have a material impact on its consolidated financial statements.

In August 2018, the FASB issued ASU 2018-13, *"Fair Value Measurement (Topic 820), Disclosure Framework—Changes to the Disclosure Requirements for Fair Value Measurement"*. This ASU removed the following disclosure requirements: (1) the amount of and reasons for transfers between Level 1 and Level 2 of the fair value hierarchy; (2) the policy for timing of transfers between levels; and (3) the valuation processes for Level 3 fair value measurements. Additionally, this update added the following disclosure requirements: (1) the changes in unrealized gains and losses for the period included in other comprehensive income and loss for recurring Level 3 fair value measurements held at the end of the reporting period; (2) the range and weighted average of significant unobservable inputs used to develop Level 3 fair value measurements. For certain unobservable inputs, an entity may disclose other quantitative information (such as the median or arithmetic average) in lieu of the weighted average if the entity determines that other quantitative information would be a more reasonable and rational method to reflect the distribution of unobservable inputs used to develop Level 3 fair value measurements. ASU 2018-13 will be effective for all entities, for fiscal years beginning after December 15, 2019 with early adoption permitted. The Company intends to adopt this standard on January 1, 2020 and does not expect that the adoption of this update will have a material impact on its consolidated financial statements.

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, 2019			
	Level 1	Level 2	Level 3	Total
Cash equivalents:				
Money market funds	$ 222,471	$ —	$ —	$ 222,471
Total	$ 222,471	$ —	$ —	$ 222,471

	Fair value measurements as of December 31, 2018			
	Level 1	Level 2	Level 3	Total
Cash equivalents:				
Money market funds	$ 105,399	$ —	$ —	$ 105,399
Total	$ 105,399	$ —	$ —	$ 105,399

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, 2019 and 2018.

The following table presents a roll-forward of the fair value of the Simple Agreement for Future Equity (SAFE) for which fair value is determined by Level 3 inputs:

Balance as of January 1, 2018	$ 3,000
Fair value adjustment	—
Conversion into Preferred Stock, January 2018	(3,000)
Balance as of December 31, 2018	$ —

Fair value of the SAFE on issuance was determined to be equal to the proceeds received. Fair value of the SAFE on conversion into Preferred Stock (see Notes 6 and 8) was determined to be equal to the fair value of the 788,042 Preferred Stock received ($3.0 million).

There were no transfers among Level 1, Level 2, or Level 3 categories in the periods presented.

The carrying value of cash, cash equivalents, accounts payable and accrued expenses that are reported on the consolidated balance sheets approximate their fair value due to the short-term nature of these assets and liabilities.

4. Property and equipment, net

Property and equipment, net consisted of the following:

	As of December 31,	
	2019	2018
Laboratory equipment	$ 2,489	$ 1,485
Furniture and fixtures	108	—
Leasehold improvements	40	—
Office equipment	79	70
Construction in progress	611	16
	3,327	1,571
Less accumulated depreciation	(815)	(379)
	$ 2,512	$ 1,192

Depreciation expense was $0.5 million and $0.2 million for the years ended December 31, 2019 and 2018, respectively.

5. Accrued and other current liabilities

Accrued and other current liabilities consisted of the following:

	As of December 31,	
	2019	2018
Accrued employee compensation costs	$ 2,053	901
Accrued professional	228	200
Accrued research and development costs	959	234
Accrued other	56	61
Other current liabilities	54	-
	$ 3,350	$ 1,396

6. Simple agreement for future equity

In October 2017, the Company entered into the SAFE with an investor, receiving $3.0 million in exchange for the investor's right to participate in a future equity financing. The SAFE contained a number of conversion and redemption provisions, including settlement upon liquidity or dissolution events. The Company elected the fair value option of accounting for the SAFE (see Note 3). In January 2018, the investor exercised its rights to convert the SAFE in connection with the Company's equity financing (See Note 8) and exchanged the SAFE for 788,042 shares of Series A-2 convertible Preferred Stock (Series A-2 Preferred).

7. Commitments and contingencies

Operating lease

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 three percent annual base rent increases plus operating expenses, real estate taxes, utilities and janitorial fees. The lease commencement date was December 10, 2018.

In December 2018, the Company 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 annum, with 2.5 percent annual base rent increases plus operating expenses, real estate taxes, utilities and janitorial fees. The lease commencement date was May 1, 2019.

As of December 31, 2019, the future minimum payments for operating leases are as follows:

2020	1,149
2021	1,102
2022	81
2023	—
Thereafter	—
	$ 2,332

Rent expense incurred under operating leases was approximately $1.1 million and $0.3 million for the years ended December 31, 2019 and 2018, respectively.

Consulting Agreement

In October 2014, we entered into a consulting agreement with a member of our board of directors, who is also an employee of Cold Spring Harbor Laboratory (CSHL), to provide consulting services related to scientific research related to the development of antisense-based drugs, therapies, diagnostic and research tools, products, services and intellectual property. We recognized expense of $0.1 million in each of the years ended December 31, 2019 and 2018, respectively, for such consulting services. The initial term of this agreement was five years and has been extended by the mutual consent of the Company and the board member.

License and research agreements

In July 2015, the Company entered into a worldwide license agreement, or the CSHL Agreement, with CSHL, with respect to Targeted Augmentation of Nuclear Gene Output (TANGO) patents. Under the CSHL Agreement, the Company receives an exclusive (except with respect to certain government rights and non-exclusive licenses), worldwide license under certain patents and applications relating to TANGO. As part of the CSHL Agreement, the Company granted CSHL 164,927 shares of common stock valued based on an independent appraisal at approximately $0.07 million. The CSHL Agreement obligates the Company to make additional payments that are contingent upon certain milestones being achieved. The Company is 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 apply 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 sublicenses the rights under the CSHL Agreement, the Company is required to pay a maximum of twenty percent of the sublicense revenue to CSHL, which may be 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 is 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 total approximately $0.9 million. Additionally, certain licenses under the CSHL Agreement require 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, 2019 and 2018.

In April 2016, the Company entered into an exclusive, worldwide license agreement with the University of Southampton, or 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. As part of the Southampton Agreement, the Company paid 0.06 million pounds sterling (approximately $0.07 million as of the date thereof) as an up-front license fee. 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. The maximum aggregate potential milestone payments payable by the Company total approximately 0.4 million pounds sterling (approximately $0.5 million as of December 31, 2019). As of December 31, 2019, and 2018, the Company has recorded no liabilities under the Southampton Agreement.

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, 2019, the Company had no legal proceedings to which it was a party or to which its property was subject.

8. Convertible preferred stock

As of December 31, 2018, the Company's amended and restated certificate of incorporation authorized the Company to issue 22,677,585 shares of $0.0001 par value convertible preferred stock, 4,980,168 are designated Series A convertible preferred stock (Series A Preferred), 7,617,746 are designated Series A-2 Preferred and 10,079,671 are designated Series B convertible preferred stock (Series B Preferred) (collectively, the Preferred Stock). Upon closing of the IPO, the Company's outstanding convertible preferred stock automatically converted into shares of common stock. Upon conversion of the convertible preferred stock, the Company reclassified their carrying value of the convertible preferred stock to common stock and additional paid-in capital.

The following table summarizes the Company's issued and outstanding Preferred Stock:

	Series A Preferred		Series A-2 Preferred		Series B Preferred		Total convertible Preferred	
	Shares	Amount	Shares	Amount	Shares	Amount	Shares	Amount
Balance, December 31, 2017	4,980,168	11,725	—	—	—	—	4,980,168	11,725
Issuance upon conversion of SAFE	—	—	788,042	3,000	—	—	788,042	3,000
Issuance, net of issuance costs of $120	—	—	6,829,704	25,880	—	—	6,829,704	25,880
Issuance, net of issuance costs of $258	—	—	—	—	10,079,671	89,742	10,079,671	89,742
Balance, December 31, 2018	4,980,168	$ 11,725	7,617,746	$ 28,880	10,079,671	$ 89,742	22,677,585	$ 130,347
Conversion to Common Stock upon initial public offering	(4,980,168)	(11,725)	(7,617,746)	(28,880)	(10,079,671)	(89,742)	(22,677,585)	(130,347)
Balance, December 31, 2019	—	—	—	—	—	—	—	—

The Company's Preferred Stock has the following rights and preferences, privileges and restrictions:

Voting rights

On any matter presented to the stockholders of the Company for their action or consideration at any meeting of stockholders of the Company, each holder of outstanding shares of Preferred Stock shall be entitled to cast the number of votes equal to the number of whole shares of Common Stock into which the shares of Preferred Stock held by such holder are convertible as of the record date for determining stockholders entitled to vote on such matter. Except as provided by law or by the other provisions of the certificate of incorporation of the Company, holders of Preferred Stock shall vote together with the holders of Common Stock as a single class.

For so long as any shares of Preferred Stock remain outstanding, the holders of record of the shares of Preferred Stock, exclusively and as a separate class, shall be entitled to elect two directors of the Company.

Dividends

The holders of shares of Preferred Stock shall be entitled to receive non-cumulative dividends at the rate of eight percent of the original issue price (see below) of such series of such Preferred Stock per annum on such shares of Preferred Stock (subject to appropriate adjustment in the event of any stock dividend, stock split, combination or other similar recapitalization with respect to the Preferred Stock) when, as, and if declared by the Board of Directors (the Preferred Dividend).

The Company shall not declare, pay or set aside any dividends on shares of any other class or series of capital stock of the Company (other than dividends on shares of Common Stock payable in shares of Common Stock) unless the holders of the Preferred Stock then outstanding shall first receive, or simultaneously receive, a dividend on each outstanding share of Preferred Stock in an amount at least equal to the sum of (i) the amount of the Preferred Dividend then accrued on such share of Preferred Stock for the calendar year in which such dividends are being paid hereunder and not previously paid and (ii) (A) in the case of a dividend on common stock or any class or series that is convertible into common stock, that dividend per share of Preferred Stock as would equal the product of (l) the dividend payable on each share of such class or series determined, if applicable, as if all shares of such class or series had been converted into common stock and (2) the number of shares of common stock issuable upon conversion of a share of such Preferred Stock, in each case calculated on the record date for determination of holders entitled to receive such dividend or (B) in the case of a dividend on any class or series that is not convertible into common stock, at a rate per share of Preferred Stock determined by (1) dividing the amount of the dividend payable on each share of such class or series of capital stock by the original issuance price of such class or series of capital stock (subject to appropriate adjustment in the event of any stock dividend, stock split, combination or other similar recapitalization with respect to such class or series) and (2) multiplying such fraction by an amount equal to the original issue price (see below) of such Preferred Stock; provided that, if the Company declares, pays or sets aside, on the same date, a dividend on shares of more than one class or series of capital stock of the Company, the dividend payable to the holders of a series of Preferred Stock shall be calculated based upon the dividend on the class or series of capital stock that would result in the highest dividend to such series of Preferred Stock.

The original issue price shall mean $8.9289 per share of Series B Preferred, subject to appropriate adjustment in the event of any stock dividend, stock split, combination or other similar recapitalization with respect to the Series B Preferred, $2.3794 per share of Series A Preferred, subject to appropriate adjustment in the event of any stock dividend, stock split, combination or other similar recapitalization with respect to the Series A Preferred, and $3.8069 per share of Series A-2 Preferred, subject to appropriate adjustment in the event of any stock dividend, stock split, combination or other similar recapitalization with respect to the Series A-2 Preferred.

Optional conversion rights

Each share of Preferred Stock shall be convertible, at the option of the holder thereof, at any time and from time to time, and without the payment of additional consideration by the holder thereof, into such number of fully paid and non-assessable shares of common stock as is determined by dividing the original issue price of such share of Preferred Stock by the conversion price (as described below) of such share of Preferred Stock in effect at the time of conversion. The conversion price for each share of Preferred Stock shall initially be equal to the original issue price of such share of Preferred Stock. Such initial conversion price, and the rate at which shares of Preferred Stock may be converted into shares of common stock, is subject to adjustment.

Mandatory conversion rights

Upon either (a) an initial public offering valuing the company at least $275,000 and for total offering proceeds not less than $75,000 or (b) the date and time, or the occurrence of an event, specified by vote or written consent of (i) a majority of the then-outstanding shares of Series A Preferred and Series A-2 Preferred, voting as a single class and (b) a majority of the outstanding Series B Preferred Stock voting together as a single class, then all outstanding shares of Preferred Stock shall automatically be converted into shares of common stock, at the then effective conversion rate.

Liquidation

In the event of (i) any voluntary or involuntary liquidation, dissolution or winding up of the Company or (ii) the merger or consolidation of the Company or a subsidiary relinquishing a majority of the voting power of the capital stock, or the sale, lease, transfer, exclusive license or other disposition of all or substantially all assets of the Company (Deemed Liquidation Event), the holders of shares of Preferred Stock then outstanding shall be entitled to be paid out of the assets of the Company available for distribution to its stockholders before any payment shall be made to the holders of common stock by reason of their ownership thereof, an amount per share equal to the original issue price of such share of Preferred Stock, plus any dividends declared but unpaid thereon. If upon any such liquidation, dissolution or winding up of the Company or Deemed Liquidation Event, the assets of the Company available for distribution to its stockholders shall be insufficient to pay the holders of shares of Preferred Stock the full amount to which they shall be entitled, the holders of shares of Preferred Stock shall share ratably and on a *pari passu* basis in any distribution of the assets available for distribution in proportion to the respective amounts which would otherwise be payable in respect of the shares held by them upon such distribution if all amounts payable on or with respect to such shares were paid in full.

In the event of any voluntary or involuntary liquidation, dissolution or winding up of the Company or Deemed Liquidation Event, after the payment of all preferential amounts required to be paid to the holders of shares of Preferred Stock the remaining assets of the Company available for distribution to its stockholders shall be distributed among the holders of the shares of Preferred Stock and common stock, pro rata based on the number of shares held by each such holder, treating for this purpose all such securities as if they had been converted to common stock pursuant to the terms of the certificate of incorporation of the Company immediately prior to such liquidation, dissolution or winding up of the Company.

Anti-Dilution

Holders of convertible Preferred Stock are afforded certain anti-dilution protection with respect to corporate events such as stock splits and recapitalizations.

Redemption

The Company’s convertible Preferred Stock is not redeemable except in the event of any voluntary or involuntary liquidation, dissolution or winding up of the Company or a Deemed Liquidation Event, and only if elected by a majority of the Company’s Board of Directors.

9. Common stock

In June 2014, the Company issued 502,638 shares of common stock to its two founders. The shares vest at a rate of 1/3 on the first anniversary date and in 36 equal monthly installments thereafter. These shares were fully vested as of December 31, 2018. In July 2015, the Company issued 164,927 shares of common stock to CSHL in exchange for an exclusive license to a patent (Note 7).

10. Share-Based Compensation

In June 2014, the Company's board of directors and stockholders approved the 2014 Equity Incentive Plan (the 2014 Plan) under which it may grant incentive stock options, non-qualified stock options, restricted stock awards, unrestricted stock awards, or restricted stock units to purchase up to 679,222 shares of common stock to employees, officers, directors and consultants of the Company. In January 2018, the Company increased the number of shares of common stock reserved for issuance under the 2014 Plan to 4,652,098 shares.

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.

As of December 31, 2019, there were no shares available for future issuance under the 2014 Plan and 2,180,010 shares were available under the 2019 Plan.

During the year ended December 31, 2019, the Company granted options to purchase 1,234,569 shares of common stock to certain of its employees, and directors, respectively. The options vest over four years except for certain options granted to members of our board of directors which vest over one or three years and are exercisable at a per share price equal to the fair value of the common stock on the grant date.

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 January 1, 2018	585,441	$ 0.40	8.0	$ —
Granted	2,969,181	1.34		
Exercised	(57,324)	0.44		
Forfeited or expired	(12,670)	0.40		
Outstanding as of December 31, 2018	3,484,628	1.20	8.9	3,436
Granted	1,234,569	10.39		
Exercised	(382,068)	0.91		
Forfeited or expired	(94,772)	1.24		
Outstanding as of December 31, 2019	4,242,357	$ 3.91	8.8	$ 106,138
Exercisable as of December 31, 2019	1,583,859	$ 1.03	8.0	$ 43,223

(1) The aggregate intrinsic value is calculated as the difference between the exercise price of the underlying options and the estimated fair value of the common stock for the options that were in the money at December 31, 2019 and 2018.

The weighted average grant date fair value per share of stock options granted during the years ended December 31, 2019 and 2018 was $6.06 and $0.79, respectively. The aggregate grant date fair value of stock options granted during the years ended December 31, 2019 and 2018 was approximately $7.5 million and $2.3 million, respectively. The aggregate intrinsic value of stock options exercised during the year ended December 31, 2019 and 2018 was approximately $10.5 million and $0.1 million, respectively.

Stock-based compensation

The Company recorded stock-based compensation expense of $1.9 million and $0.2 million during the years ended December 31, 2019 and 2018, respectively. As of December 31, 2019, there was $7.5 million of unrecognized compensation cost related to unvested stock-based compensation arrangements granted under the 2014 and the 2019 Plans. The compensation is expected to be recognized over a weighted average period of 4 years as of December 31, 2019.

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

	Year ended December 31,	
	2019	2018
Research and development	$ 499	$ 117
General and administrative	1,423	123
	$ 1,922	$ 240

The Company uses the Black-Scholes option pricing model to calculate the grant-date fair value of an award. The fair values of the options granted to employees and directors were calculated using the following assumptions for the years ended December 31, 2019 and 2018:

	Year ended December 31,	
	2019	2018
Risk-free interest rate	1.42-2.81%	2.67%—2.84%
Expected dividend yield	0%	0%
Expected life	5.5-6.375 years	6.25—6.375 years
Expected volatility	60-68%	57%—60%

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. 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.

11. Net loss per share attributable to common stockholders

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

	Year ended December 31,	
	2019	2018
Numerator:		
Net loss	$ (32,325)	$ (12,521)
Denominator:		
Weighted-average number of common shares, basic and diluted	17,971,443	709,336
Net loss per common share attributable to common stockholders, basic and diluted	$ (1.80)	$ (17.65)

The Company's potential dilutive securities, which include Preferred Stock and common stock options, 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 attributable to common stockholders 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 attributable to common stockholders for the period indicated because including them would have had an anti-dilutive effect:

	December 31,	
	2019	2018
Preferred Stock	—	22,677,585
Outstanding options to purchase common stock	4,242,357	3,484,628
	4,242,357	26,162,213

12. Income taxes

A reconciliation of the expected income tax expense (benefit) computed using the federal statutory income tax rate to the Company's effective income tax rate is as follows:

	Year ended December 31,	
	2019	2018
Expected income tax benefit at the federal statutory rate	21.0	21.0
State income taxes, net of federal benefit	6.7	6.2
Non-deductible items	(0.4)	(0.3)
Research and development credit, net	4.3	0.9
Other	0.3	0.1
Change in valuation allowance	(31.9)	(27.9)
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,	
	2019	2018
Deferred tax assets:		
Federal and state net operating loss carryforwards	$ 14,999	$ 6,637
Research and development tax credits	2,171	778
Other	761	210
Gross deferred tax assets	$ 17,931	7,625
Less: valuation allowance	(17,931)	(7,625)
Net deferred tax assets	$ —	$ —

As of December 31, 2019 and 2018, the Company had federal net operating loss carryforwards of $54.5 million and $24.4 million, respectively, which may be available to reduce future taxable income, and expire at various dates beginning in 2034, for those net operating loss carryforwards generated prior to 2018. Net operating losses generated in 2018 and beyond have no expiration. As of December 31, 2019 and 2018, the Company had state net operating loss carry forwards of $56.3 million and $24.0 million, respectively, which may be available to reduce future taxable income and expire at various dates beginning in 2034. In addition, at December 31, 2019 and 2018, the Company had federal research and development tax credit carryforwards of $1.5 million and $0.4 million, respectively, and state research and development tax credit carry forwards of $0.8 million and $0.4 million, respectively. Both federal and state research and development tax credit carry forwards may be available to reduce future tax liabilities and expire at various dates beginning in 2030. In accordance with Statement of 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, which are comprised principally of net operating loss carryforwards. Management has determined that it is more likely than not that the Company will not recognize the benefits of federal and state deferred tax assets and, as a result, a full valuation allowance of $17.9 million and $7.6 million was established at December 31, 2019 and 2018, respectively. The change in the valuation allowance was an increase of $10.3 million and $3.5 million in 2019 and 2018, respectively.

Utilization of the net operating loss carryforwards and research and development tax credit carryforwards may be subject to a substantial annual limitation under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended (the Code) due to ownership changes that have occurred previously or that could occur in the future. These ownership changes may limit the amount of carryforwards that can be utilized annually to offset future taxable income. The Company has not conducted a formal study to assess whether a change of control has occurred or whether there have been multiple changes of control since inception due to the significant complexity and cost associated with such a study. If the Company has experienced a change of control, as defined for purposes of Section 382 and 383 of the Code, at any time since inception, utilization of the net operating loss carryforwards or research and development tax credit carryforwards may be subject to an annual limitation under Section 382 and 383 of the Code, which is determined by first multiplying the value of the Company's stock at the time of the ownership change by the applicable long-term tax-exempt rate, and then could be subject to additional adjustments, as required. Any limitation may result in expiration of a portion of the net operating loss carryforwards or research and development tax credit carryforwards before utilization.

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, 2019, and 2018 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.

13. 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 is not required to make and has not made any contributions to the 401(k) Plan for the years ended December 31, 2019 and 2018.

14. Selected Quarterly Financial Information (Unaudited)

Selected quarterly results from operations for the years ended December 31, 2019 and 2018 are as follows:

(in thousands, except for per share data)

	2019 Quarter End			
	March 31	June 30	September 30	December 31
Revenue	-	-	-	-
Operating expenses	$ 6,322	$ 8,445	$ 9,842	$ 11,069
Loss from operations	(6,322)	(8,445)	(9,842)	(11,069)
Net loss	(5,742)	(7,819)	(8,604)	(10,160)
Net loss per share attributable to common stockholders, basic and diluted	$ (6.89)	$ (1.54)	$ (0.26)	$ (0.31)

	2018 Quarter End			
	March 31	June 30	September 30	December 31
Revenue	-	-	-	-
Operating expenses	$ 1,912	$ 3,010	$ 3,317	$ 4,542
Loss from operations	(1,912)	(3,010)	(3,317)	(4,542)
Net loss	(1,912)	(3,010)	(3,317)	(4,282)
Net loss per share attributable to common stockholders, basic and diluted	$ (2.78)	$ (4.36)	$ (4.75)	$ (6.05)

15. Subsequent events

The Company has evaluated subsequent events through the issuance date of these consolidated financial statements. The Company has concluded that no events or transactions have occurred that require disclosure in the accompanying consolidated financial statements.

Exhibit 4.3

Description of the Registrant's Securities Registered Pursuant to Section 12 of the Securities Exchange Act of 1934

As of December 31, 2019, Stoke Therapeutics, Inc. (the "Company," "we," or "our") had one class of securities registered under Section 12 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"): our common stock.

The following description summarizes the most important terms of our capital stock and certain provisions of our restated certificate of incorporation and restated bylaws. Because it is only a summary, it does not contain all of the information that may be important to you. For a complete description, you should refer to our restated certificate of incorporation and restated bylaws, which are incorporated by reference as an exhibit to the Annual Report on Form 10-K of which this Exhibit 4.3 is a part, and to the provisions of applicable Delaware law.

Authorized Capital Stock

Our authorized capital stock consists of 300,000,000 shares of common stock, $0.0001 par value per share, and 10,000,000 shares of undesignated preferred stock, $0.0001 par value per share.

Common stock

Dividend rights

Subject to preferences that may apply to any shares of preferred stock outstanding at the time, the holders of our common stock are entitled to receive dividends out of funds legally available if our board of directors, in its discretion, determines to issue dividends and then only at the times and in the amounts that our board of directors may determine.

Voting rights

Holders of our common stock are entitled to one vote for each share held on all matters submitted to a vote of stockholders. We have not provided for cumulative voting for the election of directors in our restated certificate of incorporation, which means that holders of a majority of the shares of our common stock are able to elect all of our directors. Our restated certificate of incorporation established a classified board of directors, divided into three classes with staggered three-year terms. Only one class of directors is elected at each annual meeting of our stockholders, with the other classes continuing for the remainder of their respective three-year terms.

No preemptive or similar rights

Our common stock is not entitled to preemptive rights, and is not subject to conversion, redemption or sinking fund provisions.

Right to receive liquidation distributions

Upon our liquidation, dissolution or winding-up, the assets legally available for distribution to our stockholders would be distributable ratably among the holders of our common stock and any participating preferred stock outstanding at that time, subject to prior satisfaction of all outstanding debt and liabilities and the preferential rights of and the payment of liquidation preferences, if any, on any outstanding shares of preferred stock.

Preferred stock

Our board of directors is authorized, subject to limitations prescribed by Delaware law, to issue up to 10,000,000 shares of preferred stock in one or more series, to establish from time to time the number of shares to be included in each series and to fix the designation, powers, preferences and rights of the shares of each series and any of their qualifications, limitations or restrictions, in each case without further vote or action by our stockholders. Our board of directors is also able to increase or decrease the number of shares of any series of preferred stock, but not below the number of shares of that series then outstanding, without any further vote or action by our stockholders. Our board of directors may authorize the issuance of preferred stock with voting or conversion rights that could adversely affect the voting power or other rights of the holders of our common stock. The issuance of preferred stock, while providing flexibility in connection with possible acquisitions and other corporate purposes, could, among other things, have the effect of delaying, deferring or preventing a change in control of our company and might adversely affect the market price of our common stock and the voting and other rights of the holders of our common stock. We have no current plan to issue any shares of preferred stock.

Anti-takeover provisions

Certain provisions of Delaware General Corporation Law, or DGCL, our restated certificate of incorporation and our restated bylaws could have the effect of delaying, deferring or discouraging another person from acquiring control of our company. These provisions, which are summarized below, may have the effect of discouraging takeover bids. They are also designed, in part, to encourage persons seeking to acquire control of us to negotiate first with our board of directors.

Delaware law

We are subject to the provisions of Section 203 of the DGCL regulating corporate takeovers. In general, Section 203 prohibits a publicly held Delaware corporation from engaging in a “business combination” with an “interested stockholder” for a period of three years following the date on which the person became an interested stockholder unless:

- prior to the date of the transaction, the board of directors of the corporation approved either the business combination or the transaction which resulted in the stockholder becoming an interested stockholder;

- the interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced, excluding for purposes of determining the voting stock outstanding, but not the outstanding voting stock owned by the interested stockholder, (i) shares owned by persons who are directors and also officers and (ii) shares owned by employee stock plans in which employee participants do not have the right to determine confidentially whether shares held subject to the plan will be tendered in a tender or exchange offer; or

- at or subsequent to the date of the transaction, the business combination is approved by the board of directors of the corporation and authorized at an annual or special meeting of stockholders, and not by written consent, by the affirmative vote of at least 66.67% of the outstanding voting stock that is not owned by the interested stockholder.

Generally, a business combination includes a merger, asset or stock sale, or other transaction or series of transactions together resulting in a financial benefit to the interested stockholder. An interested stockholder is a person who, together with affiliates and associates, owns or, within three years prior to the determination of interested stockholder status, did own 15% or more of a corporation’s outstanding voting stock.

Restated certificate of incorporation and restated bylaw provisions

Our restated certificate of incorporation and our restated bylaws include a number of provisions that could deter hostile takeovers or delay or prevent changes in control of our company, including the following:

- *Board of directors vacancies.* Our restated certificate of incorporation and restated bylaws authorize only our board of directors to fill vacant directorships, including newly created seats. In addition, the number of directors constituting our board of directors is permitted to be set only by a resolution adopted by a majority vote of our entire board of directors. These provisions would prevent a stockholder from increasing the size of our board of directors and then gaining control of our board of directors by filling the resulting vacancies with its own nominees. This makes it more difficult to change the composition of our board of directors but promotes continuity of management.

- *Classified board.* Our restated certificate of incorporation and restated bylaws provide that our board of directors is classified into three classes of directors, each with staggered three-year terms. A third party may be discouraged from making a tender offer or otherwise attempting to obtain control of us as it is more difficult and time consuming for stockholders to replace a majority of the directors on a classified board of directors.

- *Stockholder action; special meetings of stockholders.* Our restated certificate of incorporation provides that our stockholders may not take action by written consent, but may only take action at annual or special meetings of our stockholders. As a result, a holder controlling a majority of our capital stock would not be able to amend our restated bylaws or remove directors without holding a meeting of our stockholders called in accordance with our restated bylaws. Further, our restated bylaws provide that special meetings of our stockholders may be called only by a majority of our board of directors, the chairman of our board of directors, our Chief Executive Officer or our President, thus prohibiting a stockholder from calling a special meeting. These provisions might delay the ability of our stockholders to force consideration of a proposal or for stockholders controlling a majority of our capital stock to take any action, including the removal of directors.

- *Advance notice requirements for stockholder proposals and director nominations.* Our restated bylaws provide advance notice procedures for stockholders seeking to bring business before our annual meeting of stockholders or to nominate candidates for election as directors at our annual meeting of stockholders. Our restated bylaws also specify certain requirements regarding the form and content of a stockholder's notice. These provisions might preclude our stockholders from bringing matters before our annual meeting of stockholders or from making nominations for directors at our annual meeting of stockholders if the proper procedures are not followed. We expect that these provisions might also discourage or deter a potential acquirer from conducting a solicitation of proxies to elect the acquirer's own slate of directors or otherwise attempting to obtain control of our company.

- *No cumulative voting.* The DGCL provides that stockholders are not entitled to the right to cumulate votes in the election of directors unless a corporation's certificate of incorporation provides otherwise. Our restated certificate of incorporation and restated bylaws do not provide for cumulative voting.

- *Directors removed only for cause.* Our restated certificate of incorporation provides that stockholders may remove directors only for cause and only by the affirmative vote of the holders of at least two-thirds of our outstanding common stock.

- *Amendment of charter provisions.* Any amendment of the above expected provisions in our restated certificate of incorporation requires approval by holders of at least two-thirds of our outstanding common stock.

- *Issuance of undesignated preferred stock.* Our board of directors has the authority, without further action by the stockholders, to issue up to 10,000,000 shares of undesignated preferred stock with rights and preferences, including voting rights, designated from time to time by our board of directors. The existence of authorized but unissued shares of preferred stock would enable our board of directors to render more difficult or to discourage an attempt to obtain control of us by merger, tender offer, proxy contest or other means.

- *Choice of forum.* Our restated certificate of incorporation provides that, to the fullest extent permitted by law, the Court of Chancery of the State of Delaware will be 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 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. The enforceability of similar choice of forum provisions in other companies' certificates of incorporation has been challenged in legal proceedings, and it is possible that a court could find these types of provisions to be inapplicable or unenforceable. 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 of 1933, as amended (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 rules 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.

Transfer agent and registrar

The transfer agent and registrar for our common stock is American Stock Transfer & Trust Company, LLC.

Nasdaq Global Select Market listing

Our common stock is traded on the Nasdaq Global Select Market under the symbol "STOK."

Exhibit 23.1

Consent of Independent Registered Public Accounting Firm

The Board of Directors
Stoke Therapeutics, Inc.:

We consent to the incorporation by reference in the registration statement (No. 333-232191) on Form S-8 of Stoke Therapeutics, Inc., of our report dated March 23, 2020, with respect to the consolidated balance sheets of Stoke Therapeutics, Inc. as of December 31, 2019 and 2018, the related consolidated statements of operations and comprehensive loss, stockholders' equity (deficit), and cash flows for each of the years in the two-year period ended December 31, 2019, and the related notes (collectively, the consolidated financial statements), which report appears in the December 31, 2019 annual report on Form 10-K of Stoke Therapeutics, Inc.

/s/ KPMG LLP

Boston, Massachusetts
March 23, 2020

Exhibit 31.1

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

I, Edward M. Kaye, certify that:

1. I have reviewed this Form 10-K of Stoke Therapeutics, Inc.;

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

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

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

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

   (b) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (c) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 23, 2020

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

Edward M. Kaye, M.D.
Chief Executive Officer
(Principal Executive Officer)

Exhibit 31.2

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

I, Stephen J. Tulipano, certify that:

1. I have reviewed this Form 10-K of Stoke Therapeutics, Inc.;

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

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

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

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

   (b) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (c) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 23, 2020

By: /s/ Stephen J. Tulipano

Stephen J. Tulipano
Chief Financial Officer
(Principal Financial Officer and Principal Accounting Officer)

Exhibit 32.1

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

In connection with the Annual Report of Stoke Therapeutics, Inc. (the "Company") on Form 10-K for the period ending December 31, 2019 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I certify, pursuant to 18 U.S.C. § 1350, as adopted pursuant to § 906 of the Sarbanes-Oxley Act of 2002, that:

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

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

Date: March 23, 2020

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

Edward M. Kaye, M.D.
Chief Executive Officer
(Principal Executive Officer)

Exhibit 32.2

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

In connection with the Annual Report of Stoke Therapeutics, Inc. (the "Company") on Form 10-K for the period ending December 31, 2019 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I certify, pursuant to 18 U.S.C. § 1350, as adopted pursuant to § 906 of the Sarbanes-Oxley Act of 2002, that:

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

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

Date: March 23, 2020

By: /s/ Stephen J. Tulipano

Stephen J. Tulipano
Chief Financial Officer
(Principal Financial Officer and Principal Accounting Officer)