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As Filed with the
Securities and Exchange Commission on , 2019.

Registration No. 333-

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM S-1
REGISTRATION STATEMENT
UNDER
THE SECURITIES ACT OF 1933

STOKE THERAPEUTICS, INC.
(Exact name of registrant as specified in its charter)

Delaware	2834	47-1144582
(State or other jurisdiction of incorporation or organization)	(Primary Standard Industrial Classification Code Number)	(I.R.S. Employer Identification Number)

45 Wiggins Avenue
Bedford, MA 01730
(781)-430-8200
(Address, including zip code, and telephone number, including area code, of registrant's principal executive offices)

Edward M. Kaye, M.D.
Chief Executive Officer
Stoke Therapeutics, Inc.
45 Wiggins Avenue
Bedford, MA 01730
(781)-430-8200
(Name, address, including zip code, and telephone number, including area code, of agent for service)

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Approximate date of commencement of proposed sale to the public: As soon as practicable after the effective date of this registration statement.

If any of the securities being registered on this form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933 check the following box. ☐

If this form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ☐

If this form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ☐

If this form is a post-effective amendment filed pursuant to Rule 462(d) under the Securities Act, check the following box and list the Securities Act registration number of the earlier effective registration statement for the same offering. ☐

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company, or and "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 to Section 7(a)(2)(B) of the Securities Act. ☐

Calculation of registration fee

Title of each class of securities to be registered	Proposed maximum aggregate offering price(1)(2)	Amount of registration fee
Common Stock, par value $0.0001 per share	$	$

(1) The proposed maximum aggregate offering price includes the offering price of additional shares that the underwriters have the option to purchase.

(2) Estimated solely for purposes of calculating the registration fee in accordance with Rule 457(o) under the Securities Act of 1933, as amended.

The Registrant hereby amends this Registration Statement on such date or dates as may be necessary to delay its effective date until the Registrant shall file a further amendment which specifically states that this Registration Statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933, as amended, or until the Registration Statement shall become effective on such date as the Securities and Exchange Commission, acting pursuant to said Section 8(a), may determine.

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The information in this prospectus is not complete and may be changed. We may not sell these securities until the registration statement filed with the Securities and Exchange Commission is effective. This prospectus is not an offer to sell these securities, and we are not soliciting offers to buy these securities in any jurisdiction where the offer or sale is not permitted.

Subject to completion, dated April 30, 2019

Prospectus

shares

STOKE THERAPEUTICS

Common stock

This is the initial public offering of shares of our common stock. We are offering shares of our common stock. The initial public offering price is expected to be between $ and $ per share.

Prior to this offering, there has been no market for our common stock. We intend to apply to list our common stock on the Nasdaq Global Market under the symbol "STOK."

We are an "emerging growth company" and a "smaller reporting company" as defined under the federal securities laws and, as such, may elect to comply with certain reduced public company reporting requirements for future filings. Investing in our common stock involves a high degree of risk. Please see the section entitled "Risk Factors" starting on page 11 to read about risks you should consider carefully before buying shares of our common stock.

	Per share	Total
Initial public offering price	$	$
Underwriting discounts and commissions(1)	$	$
Proceeds to Stoke Therapeutics, Inc., before expenses	$	$

(1) We have agreed to reimburse the underwriters for certain FINRA-related expenses. See "Underwriting" for additional information regarding the compensation payable to the underwriters.

We have granted the underwriters an option for a period of 30 days to purchase up to additional shares of common stock from us at the public offering price, less underwriting discounts and commissions.

Neither the Securities and Exchange Commission nor any other regulatory body has approved or disapproved of these securities or passed on the adequacy or accuracy of this prospectus. Any representation to the contrary is a criminal offense.

The underwriters expect to deliver the shares of common stock to purchasers on , 2019.

J.P. Morgan **Cowen** **Credit Suisse**

Canaccord Genuity

Prospectus dated , 2019

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Through and including , 2019 (the 25th day after the date of this prospectus), all dealers effecting transactions in these securities, whether or not participating in this offering, may be required to deliver a prospectus. This delivery is in addition to a dealer's obligation to deliver a prospectus when acting as an underwriter and with respect to an unsold allotment or subscription.

Neither we nor the underwriters have authorized anyone to provide any information or to make any representations other than those contained in this prospectus or in any free writing prospectuses we have prepared. We and the underwriters take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. This prospectus is an offer to sell only the shares offered hereby, but only under circumstances and in jurisdictions where it is lawful to do so. The information contained in this prospectus is accurate only as of the date of this prospectus, regardless of the time of delivery of this prospectus or of any sale of the common stock.

Persons who come into possession of this prospectus and any applicable free writing prospectus in jurisdictions outside the United States are required to inform themselves about and to observe any restrictions as to this

offering and the distribution of this prospectus and any such free writing prospectus applicable to that jurisdiction.

Trademarks and tradenames

The mark “Stoke Therapeutics” is our registered trademark. The Stoke logo and all product names are our common law trademarks. All other service marks, trademarks and tradenames appearing in this prospectus are the property of their respective owners. Solely for convenience, the trademarks and tradenames referred to in this prospectus appear without the ® and ™ symbols, but those references are not intended to indicate, in any way, that we will not assert, to the fullest extent under applicable law, our rights, or the right of the applicable licensor to these trademarks and tradenames.

Market and industry data

This prospectus contains estimates and other statistical data made by independent parties, as well as by Health Advances LLC in a report that we commissioned, and by us relating to our industry and the markets in which we operate, including our general expectations and market position, market opportunity, the incidence of certain medical conditions and other industry data. These data, to the extent they contain estimates or projections, involve a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates or projections. Although we have not independently verified the accuracy or completeness of the data contained in these industry publications and reports, based on our industry experience we believe that the publications are reliable, the conclusions contained in the publications and reports are reasonable and the third-party information included in this prospectus and in our estimates is accurate and complete. While we are not aware of any misstatements regarding the industry, survey or research data provided herein, our estimates involve risks and uncertainties and are subject to change based upon various factors, including those discussed under the sections titled “Risk factors” and “Special note regarding forward-looking statements.” These and other factors could cause results to differ materially from those expressed in these publications and reports.

Prospectus summary

This summary highlights selected information contained elsewhere in this prospectus and does not contain all of the information that you should consider in making your investment decision. Before investing in our common stock, you should carefully read this entire prospectus, including our consolidated financial statements and the related notes thereto and the information set forth under the sections entitled "Risk factors," "Selected consolidated financial data" and "Management's discussion and analysis of financial condition and results of operations," in each case included in this prospectus. Some of the statements in this prospectus constitute forward-looking statements that involve risks and uncertainties. See the section entitled "Special note regarding forward-looking statements." Unless the context otherwise requires, we use the terms "Stoke," "company," "we," "us" and "our" in this prospectus to refer to Stoke Therapeutics, Inc.

Company 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 broad 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 recently approved drugs 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 plan to submit an investigational new drug application, or IND, for STK-001 by early 2020 and expect to initiate a Phase 1/2 clinical trial in the first half of 2020. We intend to nominate a second candidate to treat an additional genetic disease for preclinical development by the first half of 2020.

We are developing TANGO as potentially the first precision medicine platform for treating a category of severe genetic diseases known as autosomal dominant haploinsufficiencies, or diseases in which only one copy, or allele, of the gene needs to be mutated for the disease or trait to develop, and in which 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. Our novel ASOs are designed to address this protein deficiency by precisely upregulating target protein expression and have the potential to provide disease-modifying therapies to treat many diseases beyond the reach of current approaches. Within haploinsufficiencies, we are initially prioritizing the development of ASOs for the treatment of genetic epilepsies, and specifically Dravet syndrome. Current treatments for Dravet syndrome only address the occurrence of seizures. 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 believe we have the first genetic medicine designed to target the underlying cause of Dravet syndrome with the potential to significantly reduce the occurrence of seizures, and also potentially address, for the first time, the severe intellectual and developmental disabilities of the disease.

Today, 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 diseases, and existing precision medicine platforms have fundamental

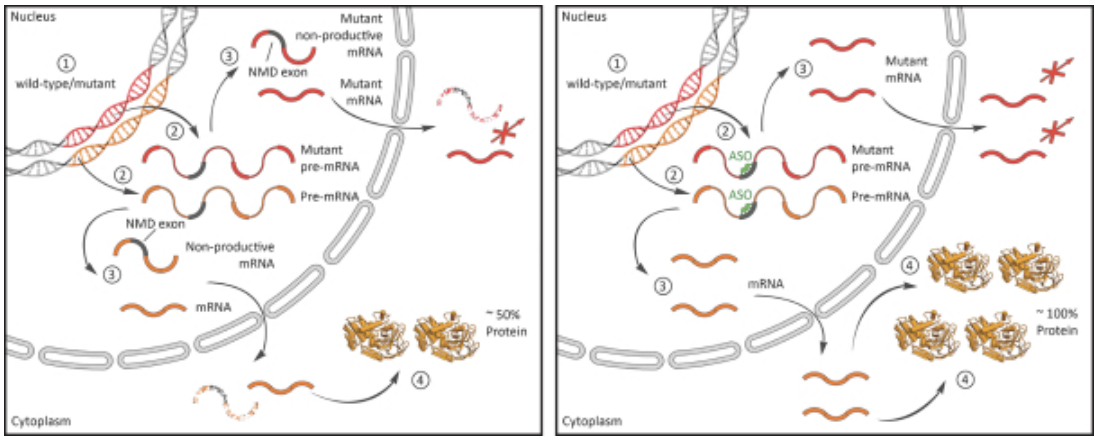
limitations that make them poorly suited to address haploinsufficiencies. Numerous technical challenges preclude effective application of these modalities, including the inability to control level and tissue distribution of target protein expression, potential irreversible on- and off-target effects, target gene size limitations and incompatibility with diseases caused by many mutations. As a result, there is a need for novel therapeutics that can restore protein expression and address the underlying genetic causes of haploinsufficiencies.

Our precision medicine platform

Treatment of autosomal dominant haploinsufficiency diseases with TANGO

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. TANGO is designed to address multiple forms of non-productive splicing events and is amenable to most loss-of-function mutations, thereby potentially providing a single-drug approach for diseases that are caused by a large number of mutations in a single gene. We have assembled a proprietary database of non-productive events in the human transcriptome and have identified approximately 2,900 monogenic, or single gene, diseases which we believe are 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.

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 haploinsufficiency. 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.



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.
- *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.
- *No observed unwanted off-target effects.* 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 a 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, we believe ASO delivery to the CNS is particularly well-precedented.
- *Fixed dose, rather than weight-based dosing*. 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 programs

Dravet syndrome—STK-001

Our most advanced program is a potentially disease-modifying treatment for Dravet syndrome, a severe and progressive genetic epilepsy. We have generated preclinical data demonstrating proof-of-mechanism for STK-001 and intend to submit an IND by early 2020. We are leveraging similar ASO chemistry as the approved drug, SPINRAZA, which minimizes potential safety and biodistribution risks in the CNS. We plan to apply for Orphan Drug Designation from the FDA in the first half of 2019, expect to initiate a Phase 1/2 clinical trial in children and adolescents with Dravet syndrome in the first half of 2020 and anticipate clinical data, including preliminary efficacy data, in 2021. If we see evidence of efficacy following clinical data, then we would plan to meet with regulatory authorities to discuss expedited regulatory pathways, in addition to requesting Fast Track Designation and Breakthrough Therapy Designation. To date, the FDA has given no indication regarding whether our product candidate will receive Orphan Drug Designation or be permitted to use any such expedited pathway.

Additional product opportunities

We intend to nominate a second genetic disease preclinical candidate by the first half of 2020. We are also advancing several other early programs focused on multiple targets, including haploinsufficiency diseases of the CNS, eye, kidney and liver, given the potential of our ASOs to target cells in these organs, and will seek to further establish a pipeline of product candidates in the future. Additional non-epilepsy indications for which our technology may be applicable include autosomal dominant optic atrophy and autosomal dominant polycystic kidney disease.

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.
- Prioritize genetic epilepsies for near-term development efforts.
- Expand our pipeline into other disease areas to fully exploit the potential of our proprietary platform.
- Maintain broad commercial rights to our product candidates.
- Continue to strengthen and expand our intellectual property portfolio.

Our team

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 Chief Executive Officer, Edward M. Kaye, M.D., our Chief Operating Officer and Chief Business Officer, Huw M. Nash, Ph.D., and our Chief Medical Officer, Barry S. Ticho, M.D., Ph.D., FACC, bring extensive biotechnology and pharmaceutical industry experience to our team. In addition, our co-founders, Adrian R. Krainer, Ph.D. (who serves on our board of directors) and Isabel Aznarez, Ph.D. (who serves as our Vice President of Biology), offer extensive academic and research experience, including Professor Krainer's experience which led to the invention and development of SPINRAZA. Finally, 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.

Our funding

As of December 31, 2018, we have raised over $130 million in funding from two financing rounds, including investments from Apple Tree Partners, RTW Investments, RA Capital Management, Cormorant Asset Management, Perceptive Advisors and funds managed by Janus Henderson Investors, Redmile Group, Sphera Funds Management and Alexandria Venture Investments.

Risks affecting us

Our business is subject to a number of risks and uncertainties, including those highlighted in the section entitled "Risk factors" immediately following this prospectus summary. These risks include, among others, the following:

- 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 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.
- Even if we complete the necessary preclinical studies and clinical trials, we cannot predict when, or if, we will obtain regulatory approval to commercialize a product candidate and the approval may be for a narrower indication than we seek.
- Certain of the diseases we seek to treat have low prevalence, and it may be difficult to identify patients with these diseases, which may lead to delays in enrollment for our trials or slower commercial revenue growth if STK-001 or our future product candidates are approved.
- We may not be successful in our efforts to use TANGO to expand our pipeline of product candidates and develop marketable products.
- Any product candidate for which we obtain marketing approval will be subject to extensive post-marketing regulatory requirements and could be subject to post-marketing restrictions or withdrawal from the market, and we may be subject to penalties if we fail to comply with regulatory requirements or if we experience unanticipated problems with our product candidates, when and if any of them are approved.
- Our 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.
- We depend on intellectual property licensed from third parties, and disputes regarding or termination of these licenses could result in loss of significant rights, which would harm our business.
- We have a limited operating history, a history of operating losses and may never achieve or sustain profitability.
- Even if we complete this offering, we will need substantial additional funds to advance development of STK-001 and our future product candidates, and failure to obtain timely funding may force us to delay, limit or terminate our product development programs, commercialization efforts or other operations.

Corporate information

We were incorporated under the laws of the State of Delaware in June 2014 under the name ASOthera Pharmaceuticals, Inc. We subsequently changed our name to Stoke Therapeutics, Inc. on May 18, 2016. Our principal executive office is located at 45 Wiggins Avenue, 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 prospectus. Investors should not rely on any such information in deciding whether to purchase our common stock.

Implications of being an emerging growth company and smaller reporting company

As a company with less than $1.07 billion in revenue during our last fiscal year, we qualify as an “emerging growth company” as defined in the Jumpstart Our Business Startups Act of 2012, or JOBS Act. An emerging growth company may take advantage of reduced reporting requirements that are otherwise applicable to public companies. These provisions include, but are not limited to:

- being permitted to present only two years of audited financial statements and only two years of related Management’s discussion and analysis of financial condition and results of operations in this prospectus;

- not being required to comply with the auditor attestation requirements on the effectiveness of our internal controls over financial reporting;
- not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements;
- reduced disclosure obligations regarding executive compensation arrangements; and
- exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved.

We may use these provisions until the last day of our fiscal year following the fifth anniversary of the completion of this offering. However, if certain events occur prior to the end of such five-year period, including if we become a "large accelerated filer," our annual gross revenues exceed $1.07 billion or we issue more than $1.0 billion of non-convertible debt in the prior three-year period, we will cease to be an emerging growth company prior to the end of such five-year period.

We have elected to take advantage of certain of the reduced disclosure obligations in the registration statement of which this prospectus is a part and may elect to take advantage of other reduced reporting requirements in future filings. As a result, the information that we provide to our stockholders may be different than you might receive from other public reporting companies in which you hold equity interests.

The JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards, until those standards apply to private companies. We have elected to take advantage of the benefits of this extended transition period and, therefore, we will not be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies. 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 of 1933, as amended, 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 plus the proposed aggregate amount of gross proceeds to us as a result of this offering is 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 this offering 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.

The offering

Common stock offered by us	shares
Common stock to be outstanding immediately after this offering	shares (or shares if the underwriters exercise their option to purchase additional shares in full).
Option to purchase additional shares	We have granted the underwriters an option, exercisable for 30 days after the date of this prospectus, to purchase up to an additional shares from us.
Use of proceeds	We estimate that the net proceeds from this offering will be approximately $ million (or approximately $ million if the underwriters exercise their option to purchase additional shares in full), based upon the assumed initial public offering price of $ per share, which is the midpoint of the estimated price range set forth on the cover of this prospectus, after deducting the estimated underwriting discounts and commissions and estimated offering expenses. We intend to use the net proceeds that we receive in this offering to advance our lead product candidate, STK-001, through initiation of a Phase 3 clinical trial, to nominate, conduct preclinical studies for and demonstrate clinical proof of concept for additional product candidates and for general corporate purposes. See the section entitled “Use of proceeds.”
Risk factors	You should read the section entitled “Risk factors” in this prospectus for a discussion of factors to consider carefully before deciding to invest in shares of our common stock.
Proposed Nasdaq Global Market symbol	“STOK”

The number of shares of our common stock to be outstanding after this offering is based on (i) 7,236,019 shares of our common stock outstanding as of December 31, 2018 and (ii) the automatic conversion of all outstanding shares of our convertible preferred stock as of December 31, 2018 into an aggregate of shares of common stock immediately prior to the completion of this offering and excludes:

- 34,663,530 shares of common stock issuable upon the exercise of options outstanding as of December 31, 2018 under our 2014 Equity Incentive Plan, or the 2014 Plan, with a weighted-average exercise price of $0.12 per share;
- 7,110,806 shares of common stock issuable upon the exercise of options granted after December 31, 2018 under the 2014 Plan, with a weighted-average exercise price of $0.35 per share; and
- shares of common stock reserved for future issuance under our stock-based compensation plans, consisting of (i) 11,042,826 shares of common stock reserved for future issuance under our 2014 Plan as of

December 31, 2018 and (ii) shares of common stock reserved for future issuance under our 2019 Equity Incentive Plan, which will become effective on the date immediately prior to the date of the effectiveness of the registration statement of which this prospectus forms a part. Upon completion of this offering, any remaining shares available for issuance under our 2014 Plan will be added to the shares reserved under our 2019 Equity Incentive Plan and we will cease granting awards under our 2014 Plan. Our 2019 Equity Incentive Plan also provides for automatic annual increases in the number of shares reserved under the plans each year, as more fully described in "Executive compensation—Equity compensation plans and other benefit plans."

Except as otherwise indicated, all information in this prospectus assumes or gives effect to:

- the automatic conversion of all outstanding shares of our convertible preferred stock into an aggregate of 225,584,874 shares of common stock immediately prior to the completion of this offering;
- a -for- reverse stock split to be effected on , 2019;
- the effectiveness of our restated certificate of incorporation and restated bylaws in connection with the completion of this offering;
- no exercise of outstanding options after December 31, 2018; and
- no exercise of the underwriters' option to purchase additional shares of our common stock.

Summary consolidated financial data

The following tables set forth our summary consolidated statements of operations and consolidated balance sheet data. The summary consolidated statements of operations data presented below for the years ended December 31, 2018 and 2017 are derived from our audited consolidated financial statements included elsewhere in this prospectus. The following summary consolidated financial data should be read in conjunction with "Selected consolidated financial data," "Management's discussion and analysis of financial condition and results of operations" and our consolidated financial statements and related notes included elsewhere in this prospectus. Our historical results are not necessarily indicative of the results that may be expected in any future period. The summary consolidated financial data in this section are not intended to replace the consolidated financial statements and are qualified in their entirety by the consolidated financial statements and related notes included elsewhere in this prospectus.

	Year ended December 31,	
	2018	2017
	(In thousands, except share and per share amounts)	
Consolidated statements of operations data:		
Revenue	$ —	$ —
Operating expenses:		
Research and development	8,371	3,598
General and administrative	4,410	1,956
Total operating expenses	12,781	5,554
Loss from operations	(12,781)	(5,554)
Other income (expense):		
Interest income	270	—
Other expense, net	(10)	(4)
Total other income (expense)	260	(4)
Net loss	$ (12,521)	$ (5,558)
Net loss per share attributable to common stockholders, basic and diluted[1]	$ (1.77)	$ (0.83)
Weighted-average common shares outstanding, basic and diluted[1]	7,056,159	6,665,733
Pro forma net loss per share, basic and diluted[1]	$ (0.10)	
Weighted-average shares used in computing pro forma net loss per share, basic and diluted[1]	127,659,034	

(1) See Notes 2 and 11 to our consolidated financial statements included elsewhere in this prospectus for a description of how we compute basic and diluted net loss per share and basic and diluted pro forma net loss per share, and the weighted-average number of shares used in the computation of these per share amounts.

	As of December 31, 2018	
	Actual	Pro forma[1][2]
		(unaudited) (in thousands)
Consolidated balance sheet data:		
Cash, cash equivalents and restricted cash	$ 105,603	$
Total assets	107,539	
Working capital[3]	103,676	
Total liabilities	2,471	
Accumulated deficit	(25,710)	
Total stockholders' equity	105,068	

(1) The pro forma balance sheet data gives effect to (i) the automatic conversion of all outstanding shares of our convertible preferred stock as of December 31, 2018 into an aggregate of 225,584,874 shares of common stock immediately prior to the completion of this offering and (ii) the receipt of $ million in net proceeds from the sale of shares of common stock in this offering, based upon an assumed initial public offering price of $ per share, which is the midpoint of the estimated price range set forth on the cover of this prospectus, after deducting the estimated underwriting discounts and commissions and estimated offering expenses.

(2) Each $1.00 increase (decrease) in the assumed initial public offering price of $ per share, which is the midpoint of the estimated price range set forth on the cover of this prospectus, would increase (decrease) each of our pro forma cash, cash equivalents and restricted cash, working capital, total assets and total stockholders' equity by approximately $ million, assuming that the number of shares offered, as set forth on the cover of this prospectus, remains the same and after deducting the estimated underwriting discounts and commissions. Similarly, each increase (decrease) of 1,000,000 shares in the number of shares of common stock offered would increase (decrease) each of our pro forma cash, cash equivalents and restricted cash, working capital, total assets and total stockholders' equity by approximately $ million, assuming the assumed initial public offering price per share as set forth on the cover of this prospectus remains the same and after deducting the estimated underwriting discounts and commissions. The pro forma information is illustrative only, and we will adjust this information based on the actual initial public offering price and other terms of this offering determined at pricing.

(3) We define working capital as current assets less current liabilities. See our consolidated financial statements and related notes included elsewhere in this prospectus for further details regarding our current assets and current liabilities.

Risk factors

Investing in our common stock involves a high degree of risk. Before making your decision to invest in shares of our common stock, you should carefully consider the risks described below, together with the other information contained in this prospectus, including our consolidated financial statements and the related notes appearing at the end of this prospectus. 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 plan to submit an investigational new drug application, or IND, for STK-001 by early 2020. 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 first 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.

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.

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

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.

Although few companies focus treatments on Dravet syndrome, 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 a net loss of $12.5 million and $5.6 million for the years ended December 31, 2018 and 2017, respectively. As of December 31, 2018, we had an

accumulated deficit of $25.7 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 the net proceeds from this offering, together with our existing cash, cash equivalents and restricted cash as of December 31, 2018, will enable us to fund our operating expenses and capital expenditure requirements through the end of 2022. 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 operations have consumed significant amounts of cash since inception. As of December 31, 2018, our cash, cash equivalents and restricted cash were $105.6 million.

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, 2018, we had federal and state net operating loss carryforwards, or NOLs, of approximately $24.4 million and $24.0 million, respectively, which expire on 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 prospectus, 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. 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, Edward M. Kaye, M.D., our Chief Operating Officer and Chief Business Officer, Huw M. Nash, Ph.D., our Chief Medical Officer, Barry S. Ticho, M.D., Ph.D., FACC, and our Co-Founder and Vice President, Head of Biology, Isabel Aznarez, 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. In addition, certain members of our senior management team, including our Chief Financial Officer, who joined us in March 2019, have worked together for only a relatively short period of time and it may be difficult to evaluate their effectiveness, on an individual or collective basis, and ability to address future challenges to our business.

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. 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 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 our common stock and this offering

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 following this offering is likely to be highly volatile and subject to wide fluctuations in response to various factors, some of which we cannot control. As a result of this volatility, investors may not be able to sell their common stock at or above the initial public offering price. The market price for our common stock may be influenced by many factors, including the other risks described in this section of the prospectus entitled “Risk factors” 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.

You will experience immediate and substantial dilution as a result of this offering and may experience additional dilution in the future.

If you purchase common stock in this offering, assuming an initial public offering price of $ per share, the midpoint of the estimated price range set forth on the cover of this prospectus, you will incur immediate and substantial dilution of $ per share, representing the difference between the assumed initial public offering price of $ share and our pro forma net tangible book value per share as of December 31, 2018 after giving effect to this offering and the conversion of all outstanding shares of our redeemable convertible preferred stock upon the completion of this offering.

Moreover, we issued options in the past to acquire common stock at prices below the assumed initial public offering price. As of December 31, 2018, there were 34,663,530 shares of common stock subject to outstanding options under our 2014 Equity Incentive Plan. To the extent that these outstanding options and options granted in the future are ultimately exercised, you will incur further dilution.

An active and liquid trading market for our common stock may not develop and you may not be able to resell your shares of common stock at or above the public offering price.

Prior to this offering, no market for shares of our common stock existed and an active trading market for our shares may never develop or be sustained following this offering. The initial public offering price for our common stock will be determined through negotiations with the underwriters and the negotiated price may not be indicative of the market price of our common stock after this offering. The market value of our common stock may decrease from the initial public offering price. As a result of these and other factors, you may be

unable to resell your shares of our common stock at or above the initial public offering price. The lack of an active market may impair your ability to sell your shares at the time you wish to sell them or at a price that you consider reasonable. The lack of an active market may also reduce the fair market value of your shares. Furthermore, an inactive market may also impair our ability to raise capital by selling shares of our common stock and may impair our ability to enter into strategic collaborations or acquire companies or products by using our shares of common stock as consideration. Further, Apple Tree Partners IV, L.P, together with its affiliates, or Apple Tree, owned approximately 66% of our outstanding capital stock as of December 31, 2018, and the sales of stock by Apple Tree, or the lack thereof, may have a material adverse effect on our stock price and trading volume.

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, 2018, prior to this, our executive officers, directors and affiliates beneficially owned approximately % of our voting stock and, upon the completion of this offering, that same group will hold approximately % of our outstanding voting stock (assuming no exercise of the underwriters' option to purchase additional shares, no exercise of outstanding options or warrants and no purchases of shares in this offering by any of this group), in each case assuming the conversion of all outstanding shares of our redeemable convertible preferred stock into shares of our common stock and the net exercise of warrants outstanding that would otherwise expire upon the completion of this offering. 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.

A sale of a substantial number of shares of our common stock may cause the price of our common stock to decline.

Based on shares outstanding as of December 31, 2018, upon completion of this offering, we will have outstanding a total of shares of common stock. Of these shares, only shares of common stock sold in this offering, or shares if the underwriters exercise their option to purchase additional shares in full, will be freely tradable, without restriction, in the public market immediately after this offering. Each of our officers, directors and substantially all of our stockholders have entered or will enter into lock-up agreements with the underwriters that restrict their ability to sell or transfer their shares. The lock-up agreements pertaining to this offering will expire 180 days from the date of this prospectus. However, our underwriters may, in their sole discretion, permit our officers, directors and other current stockholders who are subject to the contractual lock-up to sell shares prior to the expiration of the lock-up agreements. After the lock-up agreements expire, based on shares outstanding as of December 31, 2018, up to an additional shares of common stock will be eligible for sale in the public market, approximately of which are held by our officers, directors and their affiliated entities, and will be subject to volume limitations under Rule 144 under the Securities Act. In addition, 34,663,530 shares of our common stock that are subject to outstanding options as of December 31, 2018 will become eligible for sale in the public market to the extent permitted by the provisions of various vesting agreements, the lock-up agreements and Rules 144 and 701 under the Securities Act.

After this offering, the holders of an aggregate of 225,584,874 shares of our outstanding common stock as of December 31, 2018 will have rights, subject to some conditions, to require us to file registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or our stockholders. We also intend to register shares of common stock that we may issue under our equity incentive plans. Once we register these shares, they will be able to be sold freely in the public market upon issuance, subject to the 180-day lock-up period under the lock-up agreements described above and in the section entitled “Underwriting.”

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 warrants, or the perception that such sales may occur, could adversely affect the market 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.

We will have broad discretion in the use of the net proceeds from this offering and may not use them effectively.

Our management will have broad discretion in the application of the net proceeds from this offering, and you will be relying on the judgment of our management regarding the application of these proceeds. You will not have the opportunity, as part of your investment decision, to assess whether we are using the proceeds appropriately. Our management might not apply our net proceeds in ways that ultimately increase the value of your investment. If we do not invest or apply the net proceeds from this offering in ways that enhance stockholder value, we may fail to achieve expected financial results, which could cause our stock price to decline.

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 currently have and may never obtain research coverage by securities and industry analysts. If no or few securities or industry analysts commence coverage of us, the trading price for our common stock could be impacted negatively. In the event we obtain securities or industry analyst coverage, 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.

The future sale and issuance of equity or of debt securities that are convertible into equity will dilute our share capital.

We may choose to raise additional capital in the future, depending on market conditions, strategic considerations and operational requirements. 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. Future issuances of our common stock or other equity securities, or the perception that such sales may occur, could adversely affect the trading price of our common stock and impair our ability to raise capital through future

offerings of shares or equity securities. 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 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 prospectus 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 prospectus.

We could be an emerging growth company for up to five years following the completion of this offering, although circumstances could cause us to lose that status earlier, including if we are deemed to be a "large accelerated filer," which occurs when the market value of our common stock that is held by non-affiliates exceeds $700 million as of the prior June 30, or if we have total annual gross revenue of $1.07 billion or more during any fiscal year before that time, in which cases we would no longer be an emerging growth company as of the following December 31, or if we issue more than $1.0 billion in non-convertible debt during the prior three-year period before that time, in which case we would no longer be an emerging growth company immediately. Even after we no longer qualify as an emerging growth company, we may still qualify as a "smaller reporting company," as such term is defined in Rule 12b-2 under the Securities Exchange Act of 1934, as amended, which would allow us to take advantage of many of the same exemptions from disclosure requirements, including not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act and reduced disclosure obligations regarding executive compensation in this prospectus and in our periodic reports and proxy statements. We cannot predict if investors will find our common stock less attractive because we may rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our share price may be more volatile.

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 plus the proposed aggregate amount of gross proceeds to us as a result of this offering is 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 this offering 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.

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 that will be in effect upon completion of this offering 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, will provide that 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 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 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 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. For example, we expect that these rules and regulations may make it more difficult and more expensive for us to obtain director and officer liability insurance and we may be required to incur substantial costs to maintain sufficient coverage. 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 Securities and Exchange Commission's, or 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.

Special note regarding forward-looking statements

This prospectus, including the sections entitled “Prospectus summary,” “Risk factors,” “Use of proceeds,” “Management’s discussion and analysis of financial condition and results of operations,” and “Business” contains forward-looking statements. The words “believe,” “may,” “will,” “potentially,” “estimate,” “continue,” “anticipate,” “intend,” “could,” “would,” “project,” “plan,” “expect” and similar expressions that convey uncertainty of future events or outcomes are intended to identify forward-looking statements. These forward-looking statements are subject to a number of risks, uncertainties and assumptions, including those described in “Risk factors” and elsewhere in this prospectus. Moreover, we operate in a competitive and rapidly changing environment, and new risks emerge from time to time. It is not possible for our management to predict all risks, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in any forward-looking statements we may make. In light of these risks, uncertainties and assumptions, the forward-looking events and circumstances discussed in this prospectus may not occur and actual results could differ materially and adversely from those anticipated or implied in the forward-looking statements. Forward-looking statements include statements about:

- our ability to develop, obtain regulatory approval for and commercialize STK-001 and our future product candidates;
- our success in early preclinical studies or clinical trials, which may not be indicative of results obtained in later studies or trials;
- our ability to obtain regulatory approval to commercialize STK-001 or any other future product candidate;
- our ability to identify patients with the diseases treated by STK-001 or our future product candidates, and to enroll patients in trials;
- the success of our efforts to use TANGO to expand our pipeline of product candidates and develop marketable products;
- our ability to obtain, maintain and protect our intellectual property;
- our reliance upon intellectual property licensed from third parties;
- our ability to identify, recruit and retain key personnel;
- our use of proceeds from this offering;
- our financial performance; and
- developments or projections relating to our competitors or our industry.

You should not rely upon forward-looking statements as predictions of future events. Although we believe that the expectations reflected in the forward-looking statements are reasonable, we cannot guarantee that the future results, levels of activity, performance or events and circumstances reflected in the forward-looking statements will be achieved or occur. We undertake no obligation to update publicly any forward-looking statements for any reason after the date of this prospectus to conform these statements to actual results or to changes in our expectations, except as required by law.

You should read this prospectus and the documents that we reference in this prospectus and have filed with the SEC as exhibits to the registration statement of which this prospectus is a part with the understanding that our actual future results, levels of activity, performance and events and circumstances may be materially different from what we expect.

Use of proceeds

We estimate that the net proceeds from our sale of shares of common stock in this offering at an assumed initial public offering price of $ per share, which is the midpoint of the estimated price range set forth on the cover of this prospectus, after deducting the estimated underwriting discounts and commissions and estimated offering expenses, will be approximately $ million. If the underwriters exercise their option to purchase additional shares in full, then the net proceeds will be approximately $ million.

Each $1.00 increase (decrease) in the assumed initial public offering price of $ per share, which is the midpoint of the estimated price range set forth on the cover of this prospectus, would increase (decrease) the net proceeds to us from this offering by $ million, assuming the number of shares offered, as set forth on the cover of this prospectus, remains the same, and after deducting the estimated underwriting discounts and commissions. Similarly, each increase (decrease) of 1,000,000 shares in the number of shares of common stock offered would increase (decrease) the net proceeds that we receive from this offering by $ million, assuming that the assumed initial public offering price remains the same and after deducting the estimated underwriting discounts and commissions.

We currently intend to use the net proceeds we receive from this offering as follows:

- approximately $ million to $ million to advance our lead product candidate, STK-001, through initiation of a Phase 3 clinical trial;
- approximately $ million to $ million to nominate, conduct preclinical studies for and demonstrate clinical proof of concept for additional product candidates; and
- any remaining amounts to fund working capital and general corporate purposes.

Based on our planned use of the net proceeds, we estimate such funds, together with our existing cash, cash equivalents and restricted cash, will be sufficient for us to fund our operating expenses and capital expenditure requirements through the end of 2022.

The expected use of the net proceeds from the offering represents our intentions based upon our current plans and business conditions. The amounts we actually expend in these areas, and the timing thereof, may vary significantly from our current intentions and will depend on a number of factors, including the success of research and product development efforts, cash generated from future operations and actual expenses to operate our business. We may use a portion of the net proceeds for the acquisition of, or investment in, businesses that complement our business, although we have no present commitments or agreements.

The amounts and timing of our clinical expenditures and the extent of clinical development may vary significantly depending on numerous factors, including the status, results and timing of our current preclinical studies and those clinical trials which we may commence in the future, the product approval process with the FDA and other regulatory agencies, our current collaborations and any new collaborations we may enter into with third parties and any unforeseen cash needs. As a result, we cannot predict with any certainty all of the particular uses for the net proceeds or the amounts that we will actually spend on the uses set forth above. Accordingly, our management will have broad discretion in the application of the net proceeds, and investors will be relying on the judgment of our management regarding the application of the net proceeds of this offering.

The expected net proceeds of this offering will not be sufficient for us to fund any of our product candidates through regulatory approval, and we will need to raise substantial additional capital to complete the development and commercialization of our product candidates.

Pending the uses described above, we intend to invest the net proceeds from this offering in short term, investment-grade interest-bearing securities such as money market accounts, certificates of deposit, commercial paper and guaranteed obligations of the U.S. government.

Dividend policy

We have never declared or paid cash dividends on our common stock. We currently intend to retain all available funds and any future earnings for use in the operation of our business and do not anticipate paying any cash dividends on our common stock in the foreseeable future. Any future determination to declare dividends will be made at the discretion of our board of directors and will depend on our financial condition, operating results, capital requirements, general business conditions and other factors that our board of directors may deem relevant.

Capitalization

The following table sets forth our cash, cash equivalents and restricted cash and capitalization as of December 31, 2018 on:

- an actual basis;
- a pro forma basis, giving effect to (i) the automatic conversion of 225,584,874 outstanding shares of our convertible preferred stock as of December 31, 2018 into an aggregate of 225,584,874 shares of common stock immediately prior to the completion of this offering and (ii) the effectiveness of our restated certificate of incorporation in connection with the completion of this offering; and
- a pro forma as adjusted basis, giving effect to (i) the pro forma adjustments described above and (ii) the sale of shares of common stock in this offering, based upon an assumed initial public offering price of $ per share, which is the midpoint of the estimated price range set forth on the cover of this prospectus, after deducting the estimated underwriting discounts and commissions and estimated offering expenses.

The pro forma as adjusted information set forth in the table below is illustrative only and will be adjusted based on the actual initial public offering price and other terms of this offering as determined at pricing.

You should read this table together with “Management’s discussion and analysis of financial condition and results of operations,” “Selected consolidated financial data” and our audited consolidated financial statements and related notes, each included elsewhere in this prospectus.

	As of December 31, 2018		
	Actual	Pro forma	Pro forma as adjusted[1]
	(Unaudited) (in thousands, except share and per share amounts)		
Cash, cash equivalents and restricted cash	$105,603	$	$
Convertible preferred stock, par value of $0.0001 per share; 225,584,874 shares authorized, 225,584,874 shares issued and outstanding as of December 31, 2018; aggregate liquidation preference of $130,850 at December 31, 2018	23		
Preferred stock, $0.0001 par value: no shares authorized, issued or outstanding, actual; shares authorized, no shares issued or outstanding pro forma and pro forma as adjusted	—		
Common stock, $0.0001 par value: 278,527,249 shares authorized; 7,236,019 shares issued and outstanding, actual; shares authorized, shares issued and outstanding, pro forma shares issued and outstanding, pro forma as adjusted	1		
Additional paid-in-capital	130,754		
Accumulated deficit	(25,710)		
Total stockholders’ equity	105,068		
Total capitalization	$105,068	$	$

(1) Each $1.00 increase (decrease) in the assumed initial public offering price of $ per share, which is the midpoint of the estimated price range set forth on the cover of this prospectus, would increase (decrease) each of our pro forma as adjusted cash, cash equivalents and restricted cash, additional paid-in-capital, total stockholders’ equity and total capitalization by approximately $ million, assuming that the number of shares offered remains the same and after deducting the estimated underwriting discounts and commissions. Similarly, each increase (decrease) of 1,000,000 shares in the number of shares of common stock offered would increase (decrease) each of our pro forma as adjusted cash, cash equivalents and restricted cash, additional paid-in-capital, total stockholders’ equity and total capitalization by approximately $ million, assuming the assumed initial public offering price remains the same and after deducting the estimated underwriting discounts and commissions.

The table above excludes the following shares:

- 34,663,530 shares of common stock issuable upon the exercise of options outstanding as of December 31, 2018 under our 2014 Equity Incentive Plan, or the 2014 Plan, with a weighted-average exercise price of $0.12 per share;
- 7,110,806 shares of common stock issuable upon the exercise of options granted after December 31, 2018 under the 2014 Plan, with a weighted-average exercise price of $0.35 per share; and
- shares of common stock reserved for future issuance under our stock-based compensation plans, consisting of (i) 11,042,826 shares of common stock reserved for future issuance under our 2014 Plan as of December 31, 2018 and (ii) shares of common stock reserved for future issuance under our 2019 Equity Incentive Plan, which will become effective on the date immediately prior to the date of the effectiveness of the registration statement of which this prospectus forms a part. Upon completion of this offering, any remaining shares available for issuance under our 2014 Plan will be added to the shares reserved under our 2019 Equity Incentive Plan and we will cease granting awards under our 2014 Plan. Our 2019 Equity Incentive Plan also provides for automatic annual increases in the number of shares reserved under the plans each year, as more fully described in “Executive compensation—Equity compensation plans and other benefit plans.”

Dilution

If you invest in our common stock in this offering, your ownership interest will be immediately diluted to the extent of the difference between the amount per share paid by purchasers of shares of common stock in this offering and the pro forma as adjusted net tangible book value per share of common stock immediately after this offering.

Net tangible book value (deficit) per share is determined by dividing our total tangible assets (which excludes deferred offering costs) less our total liabilities and convertible preferred stock by the number of shares of common stock outstanding. Our historical net tangible book value (deficit) as of December 31, 2018 was $(25.3) million, or $(3.49) per share, based on 7,236,019 shares of common stock outstanding as of December 31, 2018. Our pro forma net tangible book value as of December 31, 2018 was approximately $ million, or $ per share of common stock. Our pro forma net tangible book value per share represents the amount of our total tangible assets (which excludes deferred offering costs) reduced by the amount of our total liabilities and divided by the total number of shares of our common stock outstanding as of December 31, 2018, after giving effect to the automatic conversion of 225,584,874 outstanding shares of our convertible preferred stock as of December 31, 2018 into an aggregate of 225,584,874 shares of common stock immediately prior to the completion of this offering.

Net tangible book value dilution per share to new investors in this offering represents the difference between the amount per share paid by purchasers of shares of common stock in this offering and the pro forma as adjusted net tangible book value per share of common stock immediately after completion of this offering. After giving effect to (i) the pro forma adjustments set forth above and (ii) our sale in this offering of shares of our common stock at an assumed initial public offering price of $ per share, which is the midpoint of the estimated price range set forth on the cover of this prospectus, and after deducting the estimated underwriting discounts and commissions and estimated offering expenses, our pro forma as adjusted net tangible book value as of December 31, 2018 would have been approximately $ million, or $ per share of our common stock. This represents an immediate increase in pro forma net tangible book value of $ per share to our existing stockholders and an immediate dilution of $ per share to investors in this offering, as illustrated in the following table:

Assumed initial public offering price, per share		$
Pro forma net tangible book value per share as of December 31, 2018	$	
Increase in pro forma net tangible book value per share attributable to new investors in this offering		
Pro forma as adjusted net tangible book value per share after this offering		
Dilution per share to new investors in this offering		$

Each $1.00 increase (decrease) in the assumed initial public offering price of $ per share, which is the midpoint of the estimated price range set forth on the cover of this prospectus, would increase (decrease) our pro forma as adjusted net tangible book value by $ million, or $ per share and the dilution in pro forma as adjusted net tangible book value per share to new investors in this offering by $ per share, assuming the number of shares offered, as set forth on the cover of this prospectus, remains the same, and after deducting the estimated underwriting discounts and commissions. Similarly, each increase of 1,000,000 shares in the number of shares of common stock offered in this offering would increase our pro forma as adjusted net tangible book value by approximately $ million, or approximately $ per share, and would increase dilution per share to new investors in this offering by approximately $ per share and each decrease of 1,000,000 shares in the number of shares of common stock offered in this offering would decrease our pro

forma as adjusted net tangible book value by approximately $ million, or approximately $ per share, and would decrease dilution per share to new investors in this offering by approximately $ per share, assuming the assumed initial public offering price per share remains the same and after deducting the estimated underwriting discounts and commissions. The pro forma as adjusted information is illustrative only, and we will adjust this information based on the actual initial public offering price and other terms of this offering determined at pricing.

If the underwriters exercise their option in full to purchase additional shares, the pro forma as adjusted net tangible book value per share after this offering would be $ per share, the increase in pro forma as adjusted net tangible book value per share to existing stockholders would be $ per share and the dilution to new investors in this offering would be $ per share.

The following table shows, as of December 31, 2018, on a pro forma as adjusted basis described above, the differences between the existing stockholders and the purchasers of shares in this offering with respect to the number of shares purchased from us, the total consideration paid, which includes net proceeds received from the issuance of common and convertible preferred stock, cash received from the exercise of stock options, and the value of any stock issued for services and the average price paid per share (in thousands, except per share amounts and percentages):

	Shares purchased		Total consideration		Average price per share
	Number	Percent	Amount	Percent	
Existing stockholders		%	$	%	$
New public investors					$
Total		100.0%	$	100.0%	

Each $1.00 increase (decrease) in the assumed initial public offering price of $ per share, which is the midpoint of the estimated price range set forth on the cover of this prospectus, would increase (decrease) total consideration paid by new investors and total consideration paid by all stockholders by approximately $ million, assuming that the number of shares offered, as set forth on the cover of this prospectus, remains the same, and after deducting the estimated underwriting discounts and commissions. Similarly, each increase (decrease) of 1,000,000 shares in the number of shares of common stock offered in this offering would increase (decrease) total consideration paid by new investors and total consideration paid by all stockholders by approximately $ million, assuming the assumed initial public offering price remains the same and after deducting the estimated underwriting discounts and commissions. In addition, to the extent that any outstanding options are exercised, investors in this offering will experience further dilution.

Except as otherwise indicated, the above discussion and tables assume no exercise of the underwriters' option to purchase additional shares. If the underwriters exercise their option to purchase additional shares in full, our existing stockholders would own % and our new investors would own % of the total number of shares of our common stock outstanding upon the completion of this offering.

The number of shares of common stock outstanding as of December 31, 2018 excludes:

- 34,663,530 shares of common stock issuable upon the exercise of options outstanding as of December 31, 2018 under our 2014 Equity Incentive Plan, or the 2014 Plan, with a weighted-average exercise price of $0.12 per share;
- 7,110,806 shares of common stock issuable upon the exercise of options granted after December 31, 2018 under the 2014 Plan, with a weighted-average exercise price of $0.35 per share; and

- shares of common stock reserved for future issuance under our stock-based compensation plans, consisting of (i) 11,042,826 shares of common stock reserved for future issuance under our 2014 Plan as of December 31, 2018 and (ii) shares of common stock reserved for future issuance under our 2019 Equity Incentive Plan, which will become effective on the date immediately prior to the date of the effectiveness of the registration statement of which this prospectus forms a part. Upon completion of this offering, any remaining shares available for issuance under our 2014 Plan will be added to the shares reserved under our 2019 Equity Incentive Plan and we will cease granting awards under our 2014 Plan. Our 2019 Equity Incentive Plan also provides for automatic annual increases in the number of shares reserved under the plans each year, as more fully described in "Executive compensation—Equity compensation plans and other benefit plans."

Selected consolidated financial data

The following tables set forth our selected consolidated financial data as of, and for the periods ended on, the dates indicated. The selected consolidated statements of operations data presented below for the years ended December 31, 2018 and 2017 and the selected consolidated balance sheet data as of December 31, 2018 and 2017 are derived from our audited consolidated financial statements included elsewhere in this prospectus. The selected consolidated financial data included in this section are not intended to replace the consolidated financial statements and related notes included elsewhere in this prospectus. You should read the selected consolidated financial data together with the section entitled “Management’s discussion and analysis of financial condition and results of operations” and our consolidated financial statements and related notes included elsewhere in this prospectus. Our historical results are not necessarily indicative of the results to be expected for any other period in the future.

	Year ended December 31,	
	2018	2017
	(In thousands, except share and per share amounts)	
Consolidated statements of operations data:		
Revenue	$ —	$ —
Operating expenses:		
Research and development	8,371	3,598
General and administrative	4,410	1,956
Total operating expenses	12,781	5,554
Loss from operations	(12,781)	(5,554)
Other income (expense):		
Interest income	270	—
Other expense, net	(10)	(4)
Total other income (expense)	260	(4)
Net loss	$ (12,521)	$ (5,558)
Net loss per share attributable to common stockholders, basic and diluted[1]	$ (1.77)	$ (0.83)
Weighted-average common shares outstanding, basic and diluted[1]	7,056,159	6,665,733
Pro forma net loss per share, basic and diluted[1]	$ (0.10)	
Weighted-average shares used in computing pro forma net loss per share, basic and diluted[1]	127,659,034	

(1) See Notes 2 and 11 to our consolidated financial statements included elsewhere in this prospectus for a description of how we compute basic and diluted net loss per share and basic and diluted pro forma net loss per share, and the weighted-average number of shares used in the computation of these per share amounts.

	As of December 31,	
	2018	2017
		(In thousands)
Consolidated balance sheet data:		
Cash, cash equivalents and restricted cash	$105,603	$ 1,797
Total assets	107,539	2,439
Working capital[1]	103,676	(1,805)
Total liabilities	2,471	3,731
Accumulated deficit	(25,710)	(13,189)
Total stockholders' equity (deficit)	105,068	(1,292)

(1) We define working capital as current assets less current liabilities. See our consolidated financial statements and related notes included elsewhere in this prospectus for further details regarding our current assets and current liabilities.

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 the section entitled "Selected financial data" and our consolidated financial statements and related notes appearing elsewhere in this prospectus. Some of the information contained in this discussion and analysis or set forth elsewhere in this prospectus, 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 recently approved drugs for the treatment of Dravet syndrome to inform the clinical and regulatory pathways, we anticipate an efficient clinical program for STK-001. We plan to submit an investigational new drug application for STK-001 by early 2020 and expect to initiate a Phase 1/2 clinical trial in the first half of 2020. We intend to nominate a second candidate to treat an additional genetic disease for preclinical development by the first 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, 2018, our operations have been financed by net proceeds of $130.8 million primarily from the sale of convertible notes payable and our convertible preferred stock. As of December 31, 2018, we had $105.6 million in cash, cash equivalents and restricted cash.

Since inception, we have had operating losses, the majority of which are attributable to research and development activities. Our net losses were $12.5 million and $5.6 million for the years ended December 31, 2018 and 2017, respectively, and as of December 31, 2018, we had an accumulated deficit of $25.7 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 the net proceeds from this offering, together with our existing cash, cash equivalents and restricted cash as of December 31, 2018, will enable us to fund our operating expenses and capital expenditure requirements through the end of 2022. 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 1,640,608 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, 2018 and 2017. 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 $72,000 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 $508,000 as of December 31, 2018). As of December 31, 2018, and 2017, 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 consist 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,	
	2018	2017
	(in thousands)	
STK-001	$1,960	$ —
Non-program specific and unallocated research and development expenses	6,411	3,598
Total research and development expenses	$8,371	$3,598

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

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

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

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

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

General and administrative expenses

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

Other income (expense)

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

Results of operations for the years ended December 31, 2018 and 2017

The following table sets forth our results of operations:

	Year ended December 31,	
	2018	2017
	(in thousands)	
Consolidated statements of operations:		
Revenue	$ —	$ —
Operating expenses:		
Research and development	8,371	3,598
General and administrative	4,410	1,956
Total operating expenses	12,781	5,554
Loss from operations	(12,781)	(5,554)
Other income (expense):		
Interest income	270	—
Other expense, net	(10)	(4)
Total other income (expense)	260	(4)
Net loss	$(12,521)	$(5,558)

Research and development expenses

Research and development expenses were $8.4 million for the year ended December 31, 2018 as compared to $3.6 million for the year ended December 31, 2017, an increase of $4.8 million. The table below summarizes our research and development expenses:

	Year Ended December 31,	
	2018	**2017**
STK-001	$1,960	$ —
Personnel-related expenses	3,825	1,823
Third-party services	1,680	1,199
Scientific consulting	161	160
Facilities and other research and development expenses	745	416
Total research and development expenses	$8,371	$3,598

The increases in research and development expenses were primarily attributable to an increase of $2.0 million on our STK-001 program, comprised of third-party services and scientific consulting fees, an increase of $2.0 million in personnel costs resulting from an increase in headcount, an increase of $0.5 million in third-party services, materials and other costs as we advance our discovery and preclinical activities, and an increase of $0.3 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 $4.4 million for the year ended December 31, 2018 as compared to $2.0 million for the year ended December 31, 2017, an increase of $2.4 million.

The increases in general and administrative expenses were primarily attributable to an increase of $0.8 million in personnel costs resulting from an increase in headcount, an increase of $0.5 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, an increase of $0.7 million related to cost of maintaining and filing of our intellectual property and an increase of $0.4 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) the year ended December 31, 2018 as compared to the year ended December 31, 2017 principally reflects returns on higher levels of cash reserves.

Liquidity and capital resources

Since our inception through December 31, 2018, our operations have been financed by net proceeds of $130.8 million primarily from the sale of convertible notes and our convertible preferred stock. As of December 31, 2018, we had $105.6 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, 2018, we had an accumulated deficit of $25.7 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 the net proceeds from this offering, together with our existing cash, cash equivalents and restricted cash as of December 31, 2018 will enable us to fund our operating expenses and capital expenditure requirements through at least the end of 2022. 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, including investors in this offering, 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,	
	2018	**2017**
	(in thousands)	
Net cash (used in) provided by:		
Operating activities	$ (10,964)	$(5,384)
Investing activities	(925)	(113)
Financing activities	115,639	5,974
Net increase in cash, cash equivalents and restricted cash	$103,750	$ 477

Operating activities

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 for share-based compensation and depreciation, and a net change of $1.0 million in our net operating assets and liabilities.

During the year ended December 31, 2017, cash used in operating activities was $5.4 million and was attributable to a net loss of $5.6 million, partially offset by non-cash charges of $0.1 million and a net change of $0.1 million in our net operating assets and liabilities.

Investing activities

Our investing activities during the years ended December 31, 2018 and 2017 have consisted principally of purchases of property and equipment.

Financing activities

Our financing activities during the year ended December 31, 2018 included closings on our Series A-2 convertible preferred stock financing in January and September 2018 aggregating gross proceeds of $26.0 million, and the sale of Series B convertible preferred stock in October 2018 raising gross proceeds of $90.0 million.

Our financing activities during the year ended December 31, 2017 included a second extension on our Series A convertible preferred stock financing in February 2017 with gross proceeds of $3.0 million and proceeds on a $3.0 million simple agreement for future equity, or SAFE, in October 2017 which was converted in the initial closing of our Series A-2 convertible preferred stock financing in January 2018.

Contractual obligations and commitments

The following table summarizes our contractual obligations as of December 31, 2018 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	$3,373	$ 1,051	$2,251	$ 71	$ —
Total	$3,373	$ 1,051	$2,251	$ 71	$ —

In August 2018, we entered into an agreement to sublease 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 expect to occupy this space in the first half of 2019.

Commitments

Our commitments primarily consist of obligations under our agreements with CSHL and the University of Southampton. As of December 31, 2018, 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 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.

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 this 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*.
- *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*—Since we have been a privately held company and do not have any trading history for our common stock, the expected volatility is 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. We will continue to apply this process until a sufficient amount of historical information regarding the volatility of our own stock price becomes available.
- *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,	
	2018	**2017**
Risk-free interest rate	2.67-2.84%	2.27%
Expected dividend yield	0%	0%
Expected life	6.25-6.375 years	6.25-6.375 years
Expected volatility	57-60%	65%

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.

Determination of the fair value of common stock

Historically, for all periods prior to this offering, the fair values of the shares of common stock underlying our share-based awards were estimated on each grant date by our board of directors. In order to determine the fair value of our common stock our board of directors considered, among other things, contemporaneous valuations of our common stock prepared by an independent third-party valuation specialist in accordance with the guidance provide by the Practice Aid.

Given the absence of a public trading market for our common stock, our board of directors exercised their judgment and considered a number of objective and subjective factors to determine the best estimate of the fair value of our common stock, including contemporaneous valuations performed by an independent third party, our stage of development, important developments in our operations, the prices at which we sold shares of our preferred stock, the rights, preferences and privileges of our preferred stock relative to those of our common stock, actual operating results and financial performance, the conditions in the biotechnology industry and the economy in general, the stock price performance and volatility of comparable public companies, and the lack of liquidity of our common stock, among other factors. After the closing of this offering, our board of directors will determine the fair value of each share of underlying common stock based on the closing price of our common stock as reported on the date of the grant. Our board of directors intended all options granted to be exercisable at a price per share not less than the per share fair value of our common stock underlying those options on the grant date.

We performed common stock valuations, with the assistance of an independent third-party valuation specialist, as of August 2016, January 2018, October 2018 and February 2019 which resulted in a valuation of our common stock of $0.04, $0.06, $0.22 and $0.45, respectively. In conducting the valuations, the independent third-party valuation specialist considered all objective and subjective factors that it believed to be relevant for each valuation conducted in accordance with the Practice Aid, including our best estimate of our business condition, prospects and operating performance at each valuation date. Other significant factors included:

- the prices of our preferred stock sold to outside investors in arm's length transactions, and the rights, preferences and privileges of our preferred stock as compared to those of our common stock, including the liquidation preferences of our preferred stock;
- our stage of development and business strategy and the material risks related to our business and industry;
- the valuation of publicly traded companies in the life sciences and biotechnology sectors, as well as recently completed mergers and acquisitions of guideline companies;
- our results of operations and financial position;
- the composition of, and changes to, our management team and board of directors;
- the lack of liquidity of our common stock;
- any external market conditions affecting the life sciences and biotechnology industry sectors;
- the likelihood of achieving a liquidity event for the holders of our common stock and stock options, such as an initial public offering, or IPO, or a sale of our company, given prevailing market conditions; and
- the state of the IPO market for similarly situated privately held life sciences companies.

For the August 2016 valuation, we employed an option pricing method, or OPM, framework and utilized a guideline transactions market approach for inferring the equity value implied by a selection of guideline transactions. This method was selected as there was no recent arm's-length financing transaction and, as of the

valuation date, we were at an early stage of development and future liquidity events were difficult to forecast. Application of OPM involves making assumptions for the expected time to liquidity, volatility and risk-free rate and then solving for the value of equity such that value for the most recent financing equals the amount paid. For the August 2016 valuation we assumed a weighted average cost of capital of 40% and a 3.25-year term to a liquidity event to estimate total equity value and, for purposes of the OPM allocation of total equity value, a 65% volatility rate and a 1.38-year estimated term. We then reflected a probability weighted average discount for lack of marketability of 35% to arrive at a $0.04 per share valuation of our common stock.

For the January 2018 valuation, we employed an OPM framework and utilized the back-solve method for inferring and allocating the equity value predicated on the capital raise that transpired just prior to the valuation date. This method was selected as management concluded that the recent financing transaction was an arm's-length transaction. Furthermore, as of the valuation date we were at an early stage of development and future liquidity events were difficult to forecast. Application of the OPM back-solve method involves making assumptions for the expected time to liquidity, volatility and risk-free rate and then solving for the value of equity such that value for the most recent financing equals the amount paid. For the January 2018 valuation and for purposes of the OPM allocation of total equity value determined with reference to a recent financing transaction, we assumed a 57% volatility rate and a 1.5-year estimated term. We then reflected a probability weighted average discount for lack of marketability of 35% to arrive at a $0.06 per share valuation of our common stock.

For the October 2018 valuation, the independent third-party valuation specialist used a hybrid method of two potential liquidity outcomes: a trade-sale scenario predicated on the arm's length capital raise that transpired just prior to the valuation date and an IPO scenario with reference to recent IPO transactions in the biotechnology and pharmaceutical industry and considering our preclinical stage of development. Under the hybrid method, the per share value calculated under the two scenarios are weighted based on expected exit outcomes and the quality of the information specific to each allocation methodology to arrive at a final estimated fair value per share value of the common stock before a discount for lack of marketability is applied. For the October 2018 valuation we (i) assigned a 90% probability of occurrence to the trade-sale scenario, with a 73% volatility rate and a 1.13-year estimated term applied within the OPM, then reflected a probability weighted average discount for lack of marketability of 35%; and (ii) we assigned a 10% probability of occurrence to the IPO scenario, with a 30% weighted average cost of capital and a 0.88-year estimated term to an IPO event, then reflected a probability weighted average discount for lack of marketability of 18%.

For the February 2019 valuation, the independent third-party valuation specialist used a hybrid method of two potential liquidity outcomes: a trade-sale scenario predicated on the arm's length capital raise that transpired prior to the valuation date and an IPO scenario with reference to recent IPO transactions in the biotechnology and pharmaceutical industry and considering our preclinical stage of development. Under the hybrid method, the per share values calculated under the two scenarios are weighted based on expected exit outcomes and the quality of the information specific to each allocation methodology to arrive at a final estimated fair value per share value of the common stock before a discount for lack of marketability is applied. For the February 2019 valuation, we (i) assigned a 65% probability of occurrence to the trade-sale scenario, with a 61% volatility rate and a 1.75-year estimated term applied within the OPM, then reflected a probability weighted average discount for lack of marketability of 30%; and (ii) we assigned a 35% probability of occurrence to the IPO scenario, with a 25% weighted average cost of capital and a 0.38-year estimated term to an IPO event, then reflected a probability weighted average discount for lack of marketability of 12.5%.

The estimates of fair value of our common stock are highly complex and subjective. There are significant judgments and estimates inherent in the determination of the fair value of our common stock. These judgments and estimates include assumptions regarding our future operating performance, the time to completing an IPO or other liquidity event, the related valuations associated with these events, and the determinations of the

appropriate valuation methods at each valuation date. The assumptions underlying these valuations represent management's best estimates, which involve inherent uncertainties and the application of management judgment. If we had made different assumptions, our stock-based compensation expense, net loss and net loss per share applicable to common stockholders could have been materially different.

For valuations after the completion of this offering, our board of directors will determine the fair value of each share of underlying common stock based on the closing price of our common stock as reported on the date of grant.

Determination of estimated offering price

We and our underwriters determined the estimated price range set forth on the cover of this preliminary prospectus, which is $ to $ per share. In comparison, our estimate of the fair value of our common stock was $ per share at , 2019, which was determined by our board of directors with the assistance of an independent third-party valuation of our common shares.

We note that, as is typical in initial public offerings, the estimated price range for this offering was not derived using a formal determination of fair value but was determined based upon discussions between us and the underwriters. Among the factors considered in setting the estimated range were prevailing market conditions, estimates of our business potential, progress in our clinical trials and developments in our business, the general condition of the securities market and the market prices of, and demand for, publicly-traded common stock of generally comparable companies.

The intrinsic value of all outstanding options as of December 31, 2018 was $ million based on an assumed initial public offering price of $ per share, the midpoint of the price range set forth on the cover of this prospectus.

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 this offering, (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 this offering is 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 this offering 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 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. We adopted ASU 2017-09 effective January 1, 2018, and the adoption of ASU 2017-09 did not impact our consolidated financial statements or financial statement disclosures.

Recently issued accounting pronouncements

In February 2016, the FASB issued ASU 2016-02, *Leases* (Topic 842), with guidance regarding the accounting for and disclosure of leases. The update requires lessees to recognize all leases, including operating leases, with a term greater than 12 months on the balance sheet. This update also requires lessees and lessors to disclose key information about their leasing transactions. This guidance will be effective for public companies for annual and interim periods beginning after December 15, 2018. For all other companies, this standard is effective for annual reporting periods beginning after December 15, 2019, and interim periods within annual periods beginning after December 15, 2020. We will adopt this standard on January 1, 2020. While we expect the implementation of ASU 2016-02 to result in the recognition of right-of-use assets and lease liabilities for leased facilities, we are still evaluating the impact that the adoption of ASU 2016-02 will have on our consolidated financial statements.

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 our consolidated financial statements and financial statement disclosures.

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: (i) the amount of and reasons for transfers between Level 1 and Level 2 of the fair value hierarchy; (ii) the policy for timing of transfers between levels; and (i) the valuation processes for Level 3 fair value measurements. Additionally, this update added the following disclosure requirements: (i) 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; and (ii) 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 does not expect that the adoption of the 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 $105.6 million as of December 31, 2018. 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 rates would affect the fair market value of our cash equivalents by approximately $1.1 million.

Business

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 recently approved drugs 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 plan to submit an investigational new drug application, or IND, for STK-001 by early 2020 and expect to initiate a Phase 1/2 clinical trial in the first half of 2020. We intend to nominate a second candidate to treat an additional genetic disease for preclinical development by the first half of 2020.

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 are 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 have generated preclinical data demonstrating proof-of-mechanism for STK-001 and intend to submit an IND application by early 2020. With 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, we anticipate an efficient clinical program for STK-001. We are leveraging similar ASO chemistry as the approved drug SPINRAZA, which minimizes potential safety and biodistribution risks in the CNS. We expect to initiate a Phase 1/2 clinical trial in children and adolescents with Dravet syndrome in the first half of 2020 and anticipate clinical data, including preliminary efficacy data, in 2021. Beyond STK-001, we are building a pipeline of novel precision medicines for genetic epilepsies and other haploinsufficiencies, and we intend to nominate our second candidate to treat an additional genetic disease for preclinical development by the first half of 2020.

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. As of December 31, 2018, we have raised over $130 million in funding from two financing rounds, including investments from Apple Tree Partners, RTW Investments, RA Capital Management, Cormorant Asset Management, Perceptive Advisors and funds managed by Janus Henderson Investors, Redmile Group, Sphera Funds Management and Alexandria Venture Investments.

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 1/2 clinical trial in children and adolescents with Dravet syndrome in the first 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

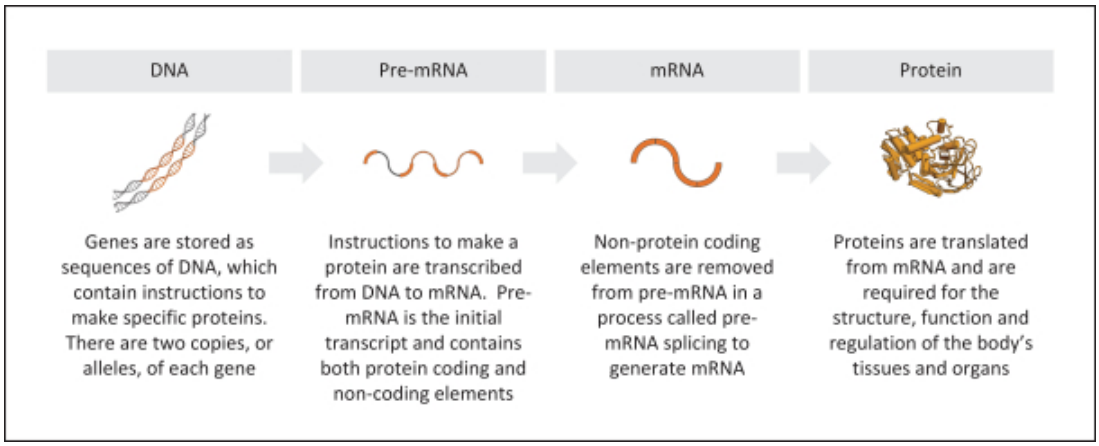
treatment of Dravet syndrome to inform the clinical and regulatory pathways for STK-001 and minimize potential safety concerns and development risk. We believe STK-001 has the potential to significantly reduce both the occurrence of seizures and significant non-seizure comorbidities. If we see evidence 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 globally.

- *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 global 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 disease areas with higher inherent biology risk, larger clinical trial sizes and longer or more complex clinical and regulatory 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

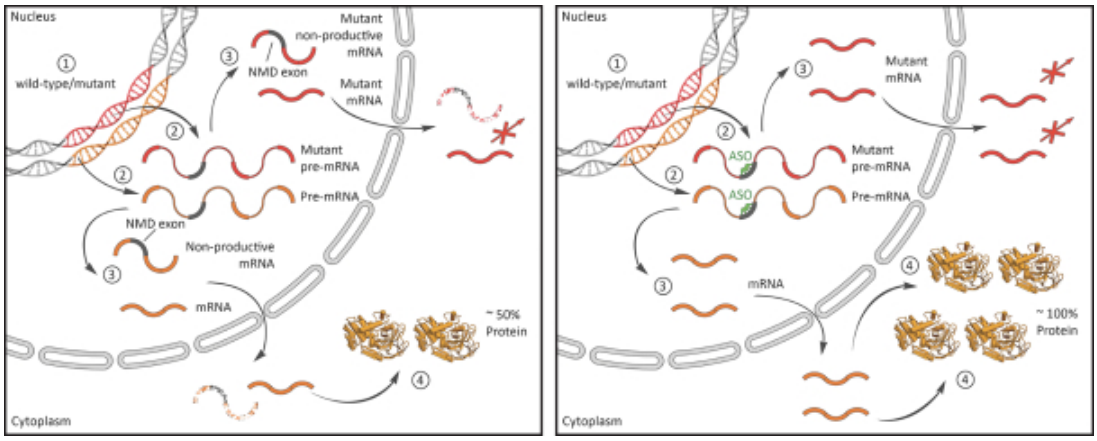
We are developing our proprietary technology platform, TANGO, as potentially the first precision medicine platform for a category of severe genetic diseases known as autosomal dominant haploinsufficiencies. We utilize TANGO to design ASOs to increase the expression of protein by individual genes in a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

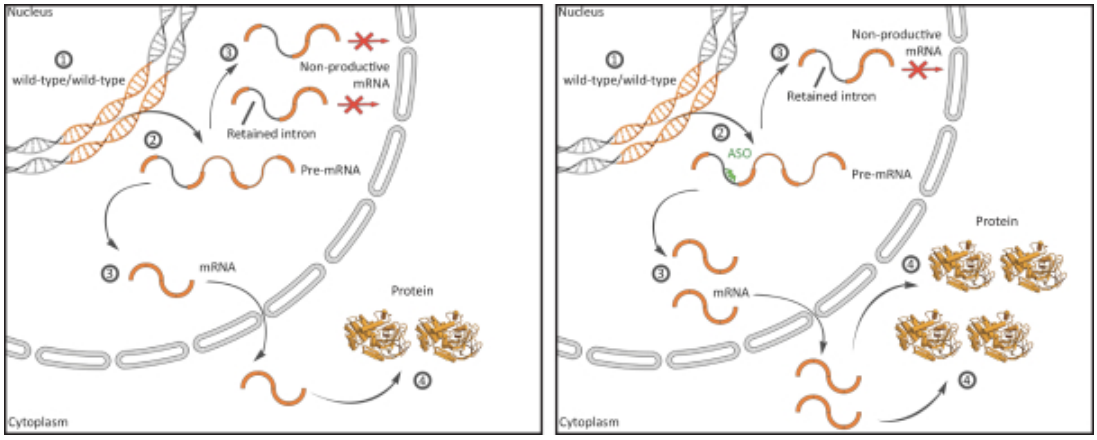
approximately 50% of normal protein expression. In the right panel, treatment with our ASO would prevent the synthesis of naturally occurring non-productive mRNA and would increase the synthesis of productive mRNA, thereby restoring the target protein to near normal levels. Our preclinical studies show that any increase in mutant mRNA would have no effect on the net protein level.



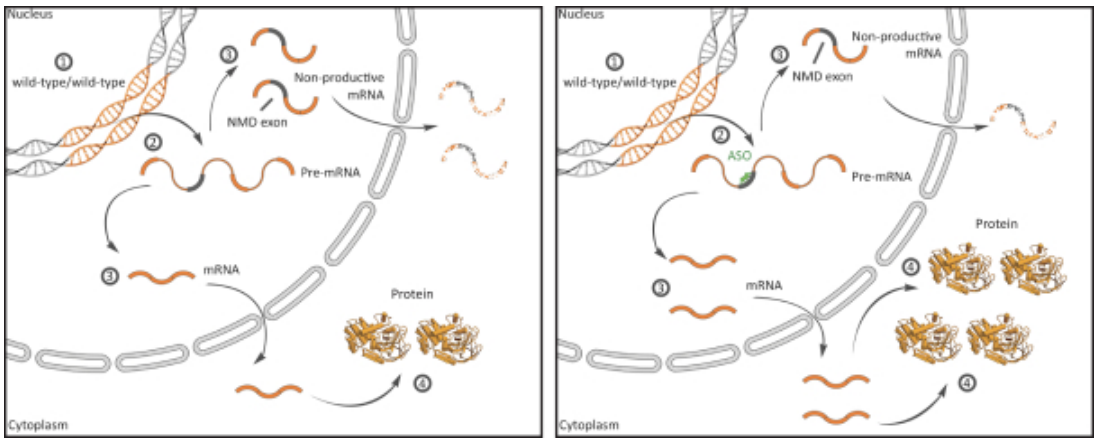
TANGO mechanisms of action

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 are typically 25-50 compounds per non-productive event and 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 1/2 clinical trial for our lead program in Dravet syndrome with a design and endpoints common to other recently approved antiepileptic drugs. Additionally, we plan to begin clinical dosing in patients at a dose anticipated to have biological effect to allow for early insight into the therapeutic potential of a product candidate and the possibility for rapid clinical development and expedited regulatory pathways, in addition to Fast Track Designation and Breakthrough Therapy Designation.

Commercialization

We intend to retain broad commercial rights and independently bring our therapies to patients around the world 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 first 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—STK-001

Our most advanced program is a potentially disease-modifying treatment for Dravet syndrome, a severe and progressive genetic epilepsy. STK-001 is a proprietary ASO and utilizes an established delivery mechanism of intrathecal delivery to target the CNS. We plan to apply for Orphan Drug Designation from the FDA in the first half of 2019, and intend to submit an IND by early 2020. We expect to initiate a Phase 1/2 clinical trial in children and adolescents with Dravet syndrome in the first half of 2020 and anticipate clinical data, including preliminary efficacy data, in 2021. If we see evidence of efficacy following clinical data, then we would plan to meet with regulatory authorities to discuss expedited regulatory pathways, in addition to requesting Fast Track Designation and Breakthrough Therapy Designation. To date, the FDA has given no indication to whether our product candidate will receive Orphan Drug Designation or be permitted to use any such expedited pathway.

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.

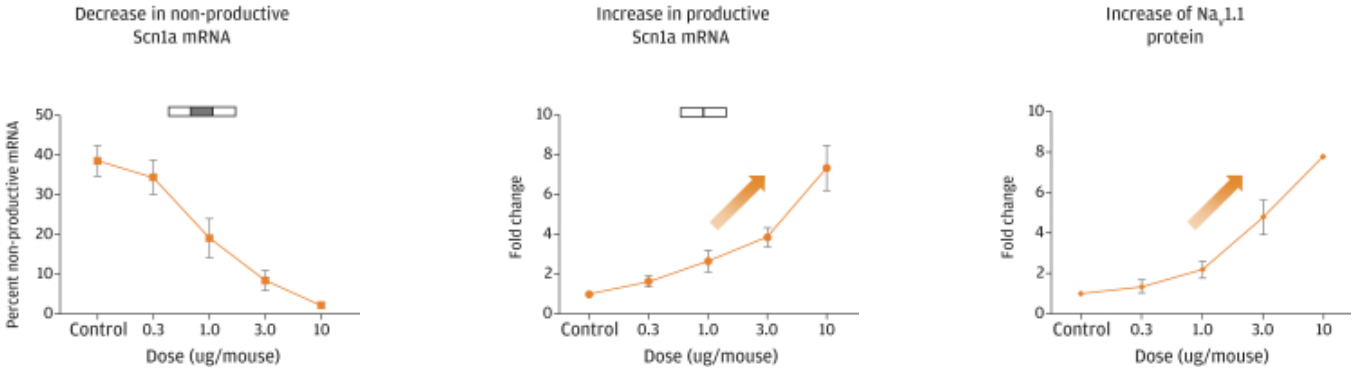
STK-001: Product candidate

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

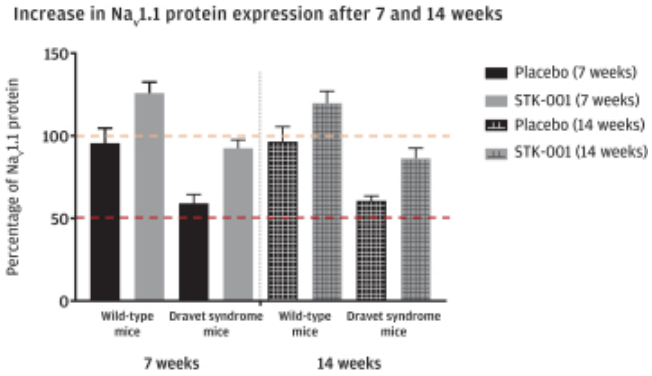
We have generated compelling preclinical data that we believe demonstrates proof-of-mechanism for STK-001. Our initial target engagement, pharmacology and efficacy studies were performed in mice, including both wild-type and a Dravet syndrome mouse model. The Dravet syndrome mouse model replicates many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

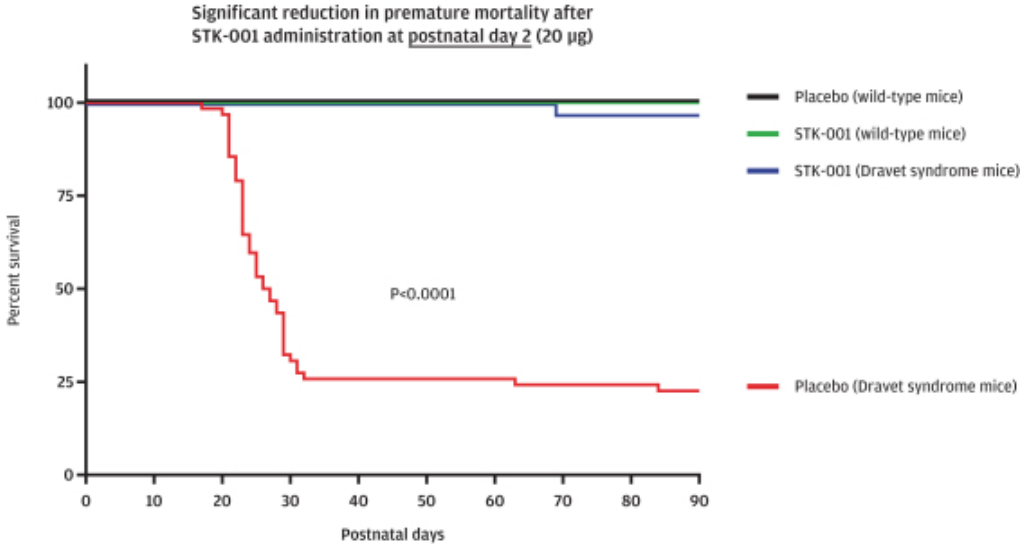


We also evaluated STK-001 pharmacology and efficacy in transgenic mice with a heterozygous deletion of *Scn1a*. This model was created by introducing a targeted deletion in the first coding exon of the *Scn1a* gene; these mice exhibit many aspects of the Dravet syndrome phenotype including seizures and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

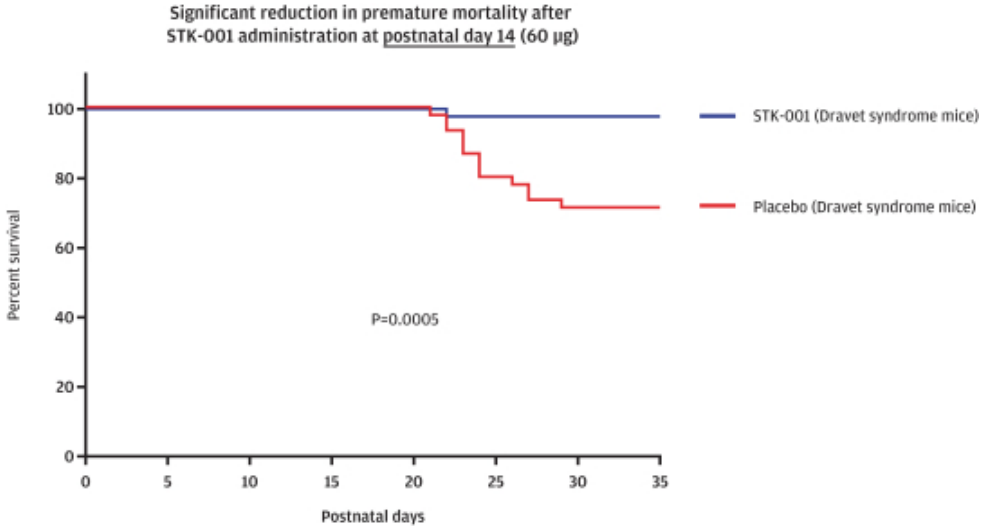
Neonate (postnatal day two) Dravet syndrome mice and wild-type littermate controls were administered a single dose of either placebo (consisting of a phosphate-buffered solution), or 20 µg of STK-001 (n=~50/group) by intracerebroventricular injection. Animals from each group were monitored through day 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 $Na_v1.1$ protein, the administration of a single dose of 20 µg of STK-001 in neonate Dravet syndrome mice (postnatal day two) resulted in a significant reduction in premature mortality. Treatment with STK-001 resulted in 97% survival of Dravet syndrome mice for the 90-day post-natal observation period (survival of 33 out of 34 mice was observed in the STK-001 Dravet syndrome mouse group) compared with 23% survival of placebo-treated mice (survival of 14 out of 62 mice). This is illustrated in the figure below.

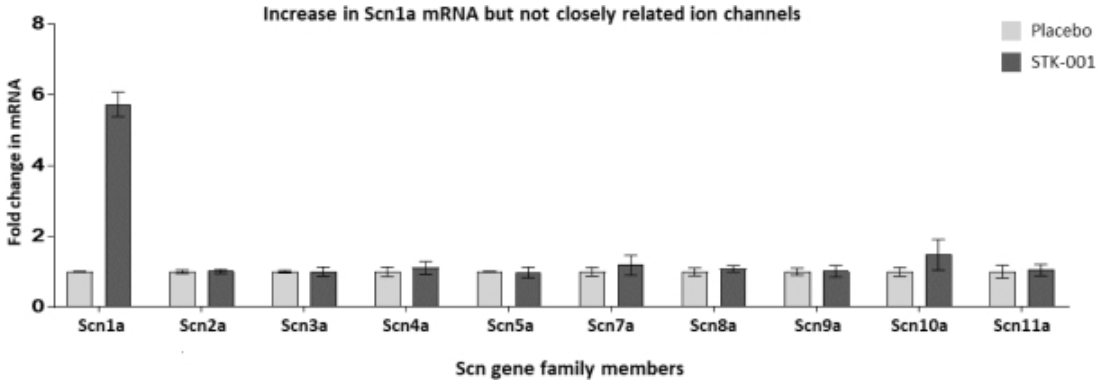


In additional studies, Dravet syndrome mice were treated closer to symptom onset (postnatal day 14). An interim analysis through postnatal day 35 indicated a significant reduction in premature mortality. Treatment with a single dose of 60 µg of STK-001 resulted in 98% survival of Dravet syndrome mice 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).



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) or control solution (n=2/group) 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.

While the non-GLP study described above will be included in our IND application, further studies in rats and cynomolgus monkeys, including GLP single and multiple dose toxicology studies, are planned to further characterize the pharmacology, exposure and tolerability of STK-001 and will be necessary to support an IND.

STK-001: Clinical plan

We expect our Phase 1/2 trial to be a two-part study 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 trial will be conducted in two parts: single ascending dose and multiple ascending dose. 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 12-week treatment period. We also intend to measure non-seizure aspects of the disease, such as cognitive function, behavior, sleep or quality of life as exploratory endpoints. These exploratory endpoints will be informed based on our planned observational study, which is designed to evaluate the course of neurodevelopmental status and adaptive status, quality of life, gait and ambulation in patients with Dravet syndrome over a timespan of two years. To help identify patients eligible for our studies, we have an ongoing partnership with Invitae Corporation to offer epilepsy panel testing at no cost to any child up to 60 months who has had an unprovoked seizure. Patients enrolled in our observational study will be eligible for enrollment in our Phase 1/2 clinical trial.

Importantly, recently approved antiepileptic drugs for Dravet syndrome, such as Epidiolex, provide a potential regulatory pathway to approval 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, cognitive function and serum chemistries, a 12-week treatment period and a 6-month safety follow-up. We plan to begin clinical dosing at the minimum anticipated biological effect level given the limited treatment options for this patient population, known pharmacology and mechanism of action of STK-001, and reasonable confidence in the predictive value of the preclinical data generated in non-human primates. 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 plan to submit an IND for STK-001 by early 2020. We expect to initiate the Phase 1/2 trial in the first half of 2020 and we anticipate preliminary clinical data for the primary and secondary endpoints of our single ascending dose phase in 2021. While we have not yet discussed with regulatory authorities the evidence necessary for approval of STK-001, if we see evidence of efficacy following clinical data, then we would plan to meet with regulatory authorities to discuss expedited regulatory pathways, in addition to Fast Track Designation and 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 first 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 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 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. 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 these small molecule drugs 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 March 15, 2019, there are approximately three issued U.S. patents, approximately two pending U.S. patent applications and approximately 23 pending foreign patent applications that we have licensed from the University of Southampton, which are anticipated to expire between 2035 and 2036, absent any patent term adjustments or extensions. As of March 15, 2019, there is one issued U.S. patent, one pending U.S. patent application and approximately ten pending foreign patent applications that we have licensed from Cold Spring Harbor Laboratory, which 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 March 15, 2019, these filed patent applications include approximately two PCT international applications, approximately seven such U.S. patent applications, and approximately 34 such foreign patent applications. Any patents that may issue from these currently pending patent applications are expected to expire between 2036 and 2040, absent any patent term adjustments or extensions.

With respect to STK-001, as of March 15, 2019, we have exclusively licensed one issued U.S. patent and one pending U.S. patent application that cover the mechanism of action of STK-001, as well as approximately 12 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 March 15, 2019, we also own one pending PCT international application and approximately three 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 intend to file applications for trademark registrations in connection with our product candidates in various jurisdictions, including the United States. We have filed for trademark protection of the Stoke Therapeutics mark with the United States Patent and Trademark Office and foreign patent and trademark organizations. The Stoke Therapeutics mark was registered by the United States Patent and Trademark Office in 2017, in the European Union in 2016, in Japan in 2016, in China in 2017, in India in 2016, and in Singapore in 2016. We have chosen to not file for trademark protection of the TANGO mark.

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 1,640,608 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 low double-digit 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, 2018 and 2017.

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 $72,000 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 $508,000 as of December 31, 2018). As of December 31, 2018, and 2017, 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. requirements 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 tests, the submission to FDA of an IND which must become effective before clinical testing may commence, and adequate and well-controlled clinical trials to establish 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 tests include laboratory evaluation of product chemistry, formulation and toxicity, as well as 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 meant to protect the rights and health of patients and to define the roles 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 FDA as part of the IND.

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 for a particular 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 outside 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 and accelerated approval

FDA is required to facilitate the development, and expedite the review, of drugs that are intended for the treatment of a serious or life-threatening disease or condition for which there is no effective treatment and which demonstrate the potential to address unmet medical needs for the condition. 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.

Under the Fast Track program and 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 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.

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 application is complete. This rolling review is available if the applicant provides, and FDA approves, a schedule for the submission of the remaining information and

the applicant pays applicable user fees. However, FDA's time period goal for reviewing an application does not begin until the last section of the NDA is submitted. Additionally, Fast Track Designation may be withdrawn by FDA if FDA believes that the designation is no longer supported by data emerging in the clinical trial process.

Breakthrough Therapy Designation

FDA is also required to expedite the development and review of the application for approval of drugs that are intended to treat a serious or life-threatening disease or condition where preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints. Under the Breakthrough Therapy program, the sponsor of a new drug candidate may request that FDA designate the drug candidate for a specific indication as a breakthrough therapy concurrent with, or after, the filing of the IND for the drug candidate. FDA must determine if the drug candidate qualifies for Breakthrough Therapy designation within 60 days of receipt of the sponsor's request.

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 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, known as Phase 4 testing, 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 offerer 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 April 26, 2019, we had 42 full-time employees and five part-time contract employees. Of these employees, 21 have an M.D. or Ph.D. None of our employees are represented by a labor union or covered by collective bargaining agreements, and we believe our relationship with our employees is good.

Facilities

We currently occupy approximately 23,000 square feet of office and laboratory space in Bedford, Massachusetts, under a lease that expires in 2021. The Bedford facility can accommodate at least 75 full-time employees. 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 expect to occupy this space in the first half of 2019. The Cambridge office can accommodate at least 14 full-time employees. 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.

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.

Management

Executive officers, key employees and directors

The following table provides information regarding our executive officers, key employees and directors as of April 26, 2019:

Name	Age	Position
Executive officers:		
Edward M. Kaye, M.D.	70	Chief Executive Officer and Director
Huw M. Nash, Ph.D.	52	Chief Operating Officer and Chief Business Officer
Stephen J. Tulipano, CPA	60	Chief Financial Officer
Barry S. Ticho, M.D., Ph.D., FACC	59	Chief Medical Officer
Gene Liau, Ph.D.	64	Executive Vice President, Head of Research and Preclinical Development
Key employees:		
Isabel Aznarez, Ph.D.	47	Vice President of Biology
Charles R. Allerson, Ph.D.	51	Vice President of Chemistry
Dawn Kalmar	42	Vice President, Head of Corporate Affairs
Meena, Ph.D.	46	Vice President of Bioanalytical, DMPK and Biomarker Development
Shamim Ruff	59	Senior Vice President of Regulatory Affairs and Quality
Nancy M. Wyant	47	Vice President and Head of Clinical Operations
Non-employee directors:		
Adrian R. Krainer, Ph.D.	60	Director
Arthur A. Levin, Ph.D.	65	Director
Seth L. Harrison, M.D.	58	Director
Samuel W. Hall, Ph.D.	37	Director
Arthur O. Tzianabos, Ph.D.	56	Director

(1) Member of the Audit Committee.

(2) Member of the Compensation Committee.

(3) Member of the Nominating and Governance Committee.

Executive officers

Edward M. Kaye, M.D., has served as our Chief Executive Officer and a member of our board of directors since October 2017. Dr. Kaye joined us from Sarepta Therapeutics, Inc., a medical research and drug development company, where he served as President and Chief Executive Officer from September 2016 to July 2017, Interim Chief Executive Officer from April 2015 to September 2016 and Chief Medical Officer from June 2011 to March 2017. From 2001 to 2007, Dr. Kaye served in various positions at Genzyme Corporation, a biotechnology company, including most recently as Group Vice President of Clinical Development. Previously, Dr. Kaye served as Chief of Biochemical Genetics at Children's Hospital of Philadelphia, Chief of Neurology at St. Christopher's

Hospital for Children, and as a member of the research staff at Massachusetts General Hospital and Tufts University Medical Center. Dr. Kaye currently serves as a Neurological Consultant at the Children's Hospital of Boston. Dr. Kaye is also a member of the boards of directors of Cytokinetics, Inc., a public biopharmaceutical company, and the Massachusetts Biotechnology Council, a private non-profit life sciences industry organization. Dr. Kaye holds a B.S. in Biology/Chemistry from Loyola University and a M.D. from the Loyola University Stritch School of Medicine. We believe that Dr. Kaye is qualified to serve on our board of directors because of his extensive leadership and clinical experience in the medical and biotechnology fields.

Huw M. Nash, Ph.D., has served as our Chief Operating Officer and Chief Business Officer since October 2017, and served as our Chief Executive Officer from October 2014 to October 2017. Dr. Nash also serves as an Entrepreneur-in-Residence at Apple Tree Partners, a venture capital firm. While at Apple Tree Partners, Dr. Nash was part of the founding group of entrepreneurs who worked on the original platform technology for Aileron Therapeutics, Inc., a biopharmaceutical company. Dr. Nash also served as Vice President of Corporate Development at Aileron Therapeutics, Inc. from 2005 to 2013. Prior to joining Aileron Therapeutics, Inc., Dr. Nash was a founding scientist of NeoGenesis Pharmaceuticals, Inc., a drug discovery company, where he served as Vice President of External Collaborations from 1997 to 2005 until its acquisition by Schering-Plough Corp. Dr. Nash holds a B.A. in Biochemical Sciences from Harvard College and a Ph.D. in Organic Chemistry from Harvard University.

Stephen J. Tulipano, CPA, has served as our Chief Financial Officer since March 2019. From June 2014 to July 2018, Mr. Tulipano served as Chief Financial Officer and Treasurer of Aldeyra Therapeutics, Inc., a biotechnology company. From January 2011 to June 2014, Mr. Tulipano served in an accounting and management advisory role at Three Tulips, Inc. Previously, Mr. Tulipano was Chief Financial Officer and Secretary of Javelin Pharmaceuticals, Inc. Mr. Tulipano holds a B.S. from Salem State College and an M.B.A. from Suffolk University. He is a Certified Public Accountant.

Barry S. Ticho, M.D., Ph.D., FACC, has served as our Chief Medical Officer since October 2017. From February 2016 to September 2017, Dr. Ticho served as Head of Cardiovascular and Metabolic Diseases at Moderna, Inc., a biotechnology company. From October 2013 to February 2016, Dr. Ticho served as Head of External Research and Development Innovation for the Cardiovascular and Metabolic Disease Research Unit at Pfizer, Inc., a pharmaceutical company. Previously, Dr. Ticho served as the Vice President of Clinical Development at Biogen Inc., a biopharmaceutical company. Dr. Ticho holds a B.A. in Biology from Haverford College and an M.D. and a Ph.D. in Biochemistry and Molecular Biology from the University of Chicago.

Gene Liau, *Ph.D.*, has served as our Executive Vice President, Head of Research and Preclinical Development since January 2018. From September 2015 to August 2017, Dr. Liau served as Senior Vice President and Head of Gene Therapy Research and Development at Precision Biosciences, Inc., a biotechnology company. From July 2011 to June 2015, Dr. Liau served in various roles at Pfizer, Inc., a pharmaceutical company, most recently as Executive Director and Head of External Research and Development Rare Diseases and Hematology. Dr. Liau holds a B.S. in Biology from the University of North Carolina at Chapel Hill and a Ph.D. in Biochemistry from Vanderbilt University.

Key employees

Isabel Aznarez, Ph.D., co-founded Stoke Therapeutics, Inc. and has served as our Vice President of Biology since October 2014. Prior to co-founding Stoke Therapeutics, Inc., Dr. Aznarez served as a Postdoctoral Fellow, then Research Investigator, at Cold Spring Harbor Laboratory, a biological research institution, from January 2008 to November 2015. Dr. Aznarez also serves on the board of directors of the Oligonucleotide Therapeutics Society. Dr. Aznarez holds a B.S. in Biology and Human Genetics from the University of Uruguay and a Ph.D. in Molecular Genetics from the University of Toronto.

Charles R. Allerson, Ph.D., has served as our Vice President of Chemistry since December 2017. Prior to joining us, Dr. Allerson served as Associate Director and then Director of Chemistry at Regulus Therapeutics Inc., a microRNA-focused biopharmaceutical company, from August 2010 to December 2017, and also as a Senior Scientist and Principal Scientist at Ionis Pharmaceuticals Inc., a RNA-focused biopharmaceutical company, from August 2002 to August 2010. Dr. Allerson holds a B.S. in Chemistry from Lafayette College and a Ph.D. in Chemistry from Harvard University.

Dawn Kalmar has served as our Vice President, Head of Corporate Affairs since April 2019. From May 2014 to January 2018, Ms. Kalmar served as Vice President, Corporate Communications at Vertex Pharmaceuticals, Inc., a biopharmaceutical company. From September 2010 to May 2014, Ms. Kalmar served in various roles at Vertex Pharmaceuticals, Inc., including leading Internal Communications and Employee Engagement from October 2012 to May 2014 and, prior to that, leading Product Communications from September 2010 to October 2012. From April 2003 to August 2010, Ms. Kalmar held roles of increasing responsibility for Internal and External Communications and Patient Advocacy for Genentech, Inc., a biotechnology company. Ms. Kalmar holds a B.S. in Journalism from California Polytechnic State University, San Luis Obispo, California.

Meena, Ph.D., has served as our Vice President of Bioanalytical, DMPK and Biomarker Development since April 2018. Prior to joining us, Ms. Meena served at Wave Life Sciences Ltd., a biopharmaceutical company, from March 2010 to March 2018, where most recently she was Senior Director of Bioanalytical, Pharmacology, and Biomarker Development. From July 2006 to January 2010, Ms. Meena served at Alnylam Pharmaceuticals, Inc., a biopharmaceutical company, as a scientist supporting drug discovery. Ms. Meena holds a B.S. from S.R. Govt. College for Women, B.Ed. from the D.A.V. College of Education for Women, Amritsar, an M.S. in Chemistry from Khalsa College, Amritsar, and a Ph.D. in Chemistry from the National Chemical Laboratory, Pune, India.

Shamim Ruff, has served as our Senior Vice President of Regulatory Affairs and Quality since December 2018. Prior to joining us, Ms. Ruff led the Regulatory Affairs and Quality teams at Sarepta Therapeutics, Inc., a medical research and drug development company, where she was Chief Regulatory Affairs Officer and Senior Vice President of Quality from December 2015 to May 2018 and Vice President of Regulatory Affairs and Quality from January 2013 to November 2015. Prior to joining Sarepta Therapeutics, Inc., Ms. Ruff served as Vice President, Head of Global Regulatory Affairs Oncology at Sanofi Genzyme, a biotechnology company, and held senior positions at Amgen Inc., Abbott Laboratories Inc., and AstraZeneca PLC, where she oversaw the development and filings of multiple successful regulatory approvals across the world. Ms. Ruff holds a B.S. in Chemistry and Biology from the University of Leicester, UK and an MSc. in Analytical Chemistry from the University of Loughborough, UK.

Nancy M. Wyant has served as our Vice President and Head of Clinical Operations since December 2018. Prior to this appointment, Ms. Wyant served as an independent clinical program management and operations consultant for us from February 2018 to December 2018. From January 2017 to January 2018, Ms. Wyant served as Vice President of Global Clinical Operations at BeiGene USA, Inc., a biopharmaceutical company. Prior to joining BeiGene USA, Inc., Ms. Wyant served as Vice President of Clinical Operations at Idera Pharmaceuticals, Inc., a biotechnology company, from May 2014 to June 2016, and as Head of Clinical Operations at Sarepta Therapeutics, Inc., a medical research and drug development company, from January 2013 to May 2014. Ms. Wyant holds a B.A. in Psychology from Hartwick College.

Non-employee directors

Adrian R. Krainer, Ph.D., co-founded Stoke Therapeutics, Inc. and has served as a member of our board of directors since June 2014. Professor Krainer is the St. Giles Professor at Cold Spring Harbor Laboratory, a biological research institution, where he has served since 1986 and where his work led directly to the invention and development of SPINRAZA. Professor Krainer holds a B.A. in Biochemistry from Columbia University and a

Ph.D. in Biochemistry from Harvard University. We believe that Professor Krainer is qualified to serve on our board of directors because of his extensive experience in biopharmaceutical research and development and experience in RNA splicing and antisense therapies.

Arthur A. Levin, Ph.D., has served as a member of our board of directors since September 2015. Since January 2014, Dr. Levin has served as Executive Vice President of Research and Development at Avidity Biosciences LLC, a biotechnology company. From April 2012 to January 2014, Dr. Levin served as Executive Vice President at miRagen Therapeutics, Inc., an RNA-focused therapeutics company. Prior to joining miRagen Therapeutics, Inc., Dr. Levin served in various senior management positions at Santaris Pharma A/S Corp., a biopharmaceutical company, and Ionis Pharmaceuticals, Inc., a public, RNA-focused biopharmaceutical company. Dr. Levin holds a B.S. in Biology from Muhlenberg College and a Ph.D. in Toxicology from the University of Rochester. We believe that Dr. Levin is qualified to serve on our board of directors because of his industry experience, including his expertise in nucleic-acid-based therapeutics.

Seth L. Harrison, *M.D.*, has served as the chairman of our board of directors since July 2015. Dr. Harrison serves as Managing Partner at Apple Tree Partners, a venture capital firm, which he founded in 1999. Prior to founding Apple Tree Partners, Dr. Harrison served as a General Partner at Oak Investment Partners, a venture capital and private equity firm, and as a Venture Partner at Sevin Rosen Funds, a technology-focused venture capital firm. Dr. Harrison currently serves as the chairman of the boards of directors of Braeburn Pharmaceuticals, Inc., a pharmaceutical company, Elstar Therapeutics, Inc., an immunotherapy company, and Limelight Bio, Inc., a gene therapy company, as well as several private companies. Dr. Harrison holds an A.B. from Princeton University and an M.D. and M.B.A. from Columbia University. We believe that Dr. Harrison is qualified to serve on our board of directors because of his experience in the life sciences industry, his experience as a venture capitalist, as well as his service on the boards of directors of numerous biopharmaceutical companies.

Samuel W. Hall, Ph.D., has served as a member of our board of directors since July 2015. Dr. Hall serves as a Partner at Apple Tree Partners, a venture capital firm. From October 2008 until joining Apple Tree Partners in April 2013, Dr. Hall served as a researcher at the University of Cambridge. Previously, Dr. Hall served on the investment team at Symphony Capital, a private equity firm dedicated to investments in biopharmaceutical development, and a member of the healthcare investment banking team at Citigroup Inc., a multinational investment bank. Dr. Hall currently serves on the boards of directors of Elstar Therapeutics, Inc., an immunotherapy company, Limelight Bio, Inc., a gene therapy company, Chinook Therapeutics, Inc., a biotechnology company, and the Burke Neurological Institute, a non-profit research institute. Dr. Hall previously served on the board of directors of Syntimmune, Inc., a biotechnology company, prior to its acquisition by Alexion Pharmaceuticals, Inc. in November 2018. Dr. Hall holds an A.B. in Molecular Biology from Princeton University and an M.Phil. and Ph.D. from the University of Cambridge. We believe that Dr. Hall is qualified to serve on our board of directors because of his experience working with and serving on the boards of directors of various life sciences companies and his experience as a venture capitalist.

Arthur O. Tzianabos, Ph.D., has served as a member of our board of directors since September 2018. Since April 2016, Dr. Tzianabos has served as President and Chief Executive Officer at Homology Medicines, Inc., a genetic medicines company. Prior to joining Homology Medicines, Inc., Dr. Tzianabos served as President and Chief Scientific Officer at OvaScience, Inc., a biotechnology company, from September 2013 to March 2016. Previously, Dr. Tzianabos served in various senior management positions at Shire Plc, a pharmaceutical company, and as a professor at Harvard Medical School. Dr. Tzianabos serves on the board of directors of Akouos, Inc., a private biotechnology company. Dr. Tzianabos holds a B.S. in Biology from Boston College and a Ph.D. in Microbiology from the University of New Hampshire. We believe that Dr. Tzianabos is qualified to serve on our board of directors because of his executive and clinical experience, as well as his extensive involvement in the biotechnology industry.

Election of officers

Our executive officers are appointed by, and serve at the discretion of, our board of directors. There are no family relationships among any of our directors or executive officers.

Board composition

Our board of directors currently consists of six members. Four of our directors are independent within the meaning of the independent director guidelines of Nasdaq. Pursuant to our current voting agreement and certificate of incorporation, Adrian R. Krainer, Seth L. Harrison, Samuel W. Hall, Arthur A. Levin, Arthur O. Tzianabos, and Edward M. Kaye have been designated to serve as members of our board of directors. Adrian R. Krainer and Edward M. Kaye were elected by the holders of our common stock. Seth L. Harrison and Samuel W. Hall were elected by the holders of our Series A convertible preferred stock. Arthur A. Levin was elected by the holders of our common stock and the Series A convertible preferred stock, voting together as a single class on an as-converted basis. Arthur O. Tzianabos was elected by the holders of our common stock and convertible preferred stock, voting together as a single class on an as-converted basis.

The voting agreement and the provisions of our current certificate of incorporation that govern the election and designation of our directors will terminate in connection with this offering, after which no contractual obligations will concern the election of our directors. Each of our current directors will continue to serve until the election and qualification of his or her successor, or until his or her earlier death, resignation or removal.

Classified board of directors

Upon the completion of this offering, our board of directors will be divided into three staggered classes of directors. At each annual meeting of stockholders, a class of directors will be subject to re-election for a three-year term. As a result, only one class of directors will be elected at each annual meeting of our stockholders, with the other classes continuing for the remainder of their respective three-year terms. Our directors will be divided among the three classes as follows:

- the Class I directors will be and and their terms will expire at the first annual meeting of stockholders held following the completion of the offering;
- the Class II directors will be and and their terms will expire at the second annual meeting of stockholders held following the completion of the offering; and
- the Class III directors will be and and their terms will expire at the third annual meeting of stockholders held following the completion of the offering.

Each director's term continues until the election and qualification of his or her successor, or his or her earlier death, resignation or removal. Our restated certificate of incorporation and restated bylaws that will be in effect upon the completion of this offering authorize only our board of directors to fill vacancies on our board of directors. Any increase or decrease in the number of directors will be distributed among the three classes so that, as nearly as possible, each class will consist of one-third of the directors. This classification of our board of directors may have the effect of delaying or preventing changes in control of our company. See the section entitled "Description of capital stock—Anti-takeover provisions—Restated certificate of incorporation and restated bylaw provisions."

Director independence

In connection with this offering, we intend to apply to list our common stock on Nasdaq. Under the rules of Nasdaq, independent directors must comprise a majority of a listed company's board of directors within a specified period following the completion of this offering. In addition, the rules of Nasdaq require that, subject

to specified exceptions, each member of a listed company's audit, compensation and nominating and governance committees be independent. Under the rules of Nasdaq, a director will only qualify as an "independent director" if, in the opinion of that company's board of directors, that person does not have a relationship that would interfere with the exercise of independent judgment in carrying out the responsibilities of a director.

Audit committee members must also satisfy the independence criteria set forth in Rule 10A-3 under the Securities Exchange Act of 1934, as amended, or the Exchange Act. In order to be considered independent for purposes of Rule 10A-3, a member of an audit committee of a listed company may not, other than in his or her capacity as a member of the audit committee, the board of directors or any other board committee: (i) accept, directly or indirectly, any consulting, advisory or other compensatory fee from the listed company or any of its subsidiaries; or (ii) be an affiliated person of the listed company or any of its subsidiaries. We intend to satisfy the audit committee independence requirements of Rule 10A-3 as of the completion of this offering. Additionally, compensation committee members must not have a relationship with us that is material to the director's ability to be independent from management in connection with the duties of a compensation committee member.

Our board of directors has undertaken a review of the independence of each director and considered whether each director has a material relationship with us that could compromise his or her ability to exercise independent judgment in carrying out his or her responsibilities. As a result of this review, our board of directors determined that all of our directors, except for Edward M. Kaye, M.D. and Adrian R. Krainer, Ph.D. are "independent directors" as defined under the applicable rules and regulations of the SEC and the listing requirements and rules of Nasdaq. In making these determinations, our board of directors reviewed and discussed information provided by the directors and us with regard to each director's business and personal activities and relationships as the may relate to us and our management, including the beneficial ownership of our capital stock by each non-employee director and then transactions involving them described in the section entitled "Certain relationships and related party transactions."

Committees of the board of directors

Our board of directors has an audit committee, a compensation committee and a nominating and governance committee, each of which will have the composition and responsibilities described below as of the completion of this offering. Each of the below committees has a written charter approved by our board of directors. Upon completion of this offering, copies of each charter will be posted on the investor relations section of our website. Members serve on these committees will serve until their resignation or until otherwise determined by our board of directors.

Audit committee

Our audit committee is comprised of , and , with serving as the chairman of our audit committee. The composition of our audit committee meets the requirements for independence under the current Nasdaq listing standards and SEC rules and regulations. Each member of our audit committee is financially literate. In addition, our board of directors has determined that is an "audit committee financial expert" as defined in Item 407(d)(5)(ii) of Regulation S-K promulgated under the Securities Act of 1933, as amended. This designation does not impose on him or her any duties, obligations or liabilities that are greater than are generally imposed on members of our audit committee and our board of directors. Our audit committee is directly responsible for, among other things:

- selecting and hiring our independent registered public accounting firm;
- the qualifications, independence and performance of our independent auditors;

- the preparation of the audit committee report to be included in our annual proxy statement;
- our compliance with legal and regulatory requirements;
- our accounting and financial reporting processes, including our consolidated financial statement audits and the integrity of our consolidated financial statements; and
- reviewing and approving related-person transactions.

Compensation committee

Our compensation committee is comprised of , and , with serving as the chairman of our compensation committee. Each member of our compensation committee is a non-employee director, as defined by Rule 16b-3 promulgated under the Exchange Act and meets the requirements for independence under the current Nasdaq listing standards and SEC rules and regulations. Our compensation committee is responsible for, among other things:

- evaluating, recommending, approving and reviewing executive officer compensation arrangements, plans, policies and programs;
- evaluating and recommending non-employee director compensation arrangements for determination by our board of directors;
- administering our cash-based and equity-based compensation plans; and
- overseeing our compliance with regulatory requirements associated with the compensation of directors, officers and employees.

Nominating and governance committee

Our nominating and governance committee is comprised of , and , with serving as the chairman of our nominating and governance committee. Each member of our nominating and governance committee meets the requirements for independence under the current Nasdaq listing standards. Our nominating and governance committee is responsible for, among other things:

- identifying, considering and recommending candidates for membership on our board of directors;
- overseeing the process of evaluating the performance of our board of directors; and
- advising our board of directors on other corporate governance matters.

Compensation committee interlocks and insider participation

None of the members of our compensation committee has at any time been one of our officers or employees, and none of our executive officers has served as a member of the board of directors, or as a member of the compensation or similar committee, of any entity that has one or more executive officers who served on our board of directors or compensation committee during the year ended December 31, 2018. Prior to establishing the compensation committee, our full board of directors made decisions relating to the compensation of our officers.

Code of business conduct and ethics

Prior to the completion of this offering, our board of directors will adopt a code of business conduct and ethics that applies to all of our employees, officers and directors, including our Chief Executive Officer, Chief Financial Officer and other executive and senior officers. The full text of our code of business conduct and ethics will be

posted on the investor relations section of our website. The reference to our website address in this prospectus does not include or incorporate by reference the information on or accessible through our website into this prospectus. We intend to disclose future amendments to certain provisions of our code of business conduct and ethics, or waivers of these provisions, on our website or in public filings to the extent required by the applicable rules.

Non-employee director compensation

The following table presents the total compensation earned by each of our non-employee directors in the year ended December 31, 2018. Our Chief Executive Officer, Dr. Kaye, receives no compensation for his service as a director. Other than as described below, none of our non-employee directors received any fees or reimbursement of any expenses (other than customary expenses in connection with the attendance of meetings of our board of directors) or any equity or non-equity awards in the year ended December 31, 2018.

Name	Fees earned or paid in cash ($)	Option awards ($)(1)(2)	All other compensation ($)	Total ($)
Adrian R. Krainer, Ph.D.	—	88,734	100,000(3)	188,734
Arthur A. Levin, Ph.D.	30,000	36,536	—	66,536
Seth L. Harrison, M.D.	—	—	—	—
Samuel W. Hall, Ph.D.	—	—	—	—
Arthur O. Tzianabos, Ph.D.	7,500	79,206	—	86,706

(1) The amounts reported in this column represent the aggregate grant date fair value of the awards granted under our 2014 Plan to our directors during the year ended December 31, 2018 as computed in accordance with FASB ASC Topic 718. The assumptions used in calculating the grant date fair value of the awards reported in the Option Awards column are set forth in Note 10 to our consolidated financial statements included elsewhere in this prospectus. Note that the amounts reported in this column reflect the aggregate accounting cost for these awards, and do not necessarily correspond to the actual economic value that may be received by the director from the awards.

(2) The following table sets forth the aggregate number of shares of our common stock subject to outstanding options held by our non-employee directors as of December 31, 2018:

Director name	Number of shares underlying options held as of December 31, 2018(1)
Adrian R. Krainer, Ph.D.(2)	2,165,682
Arthur A. Levin, Ph.D.(3)	435,269
Seth L. Harrison, M.D.	—
Samuel W. Hall, Ph.D.	—
Arthur O. Tzianabos, Ph.D.(4)	614,149

(1) All of the outstanding equity awards were granted under our 2014 Plan.

(2) This amount reflects (i) options to purchase 1,483,294 shares, all of which are fully vested and (ii) options to purchase 682,388 shares, 1/48th of which vest monthly following the October 22, 2018 vesting commencement date.

(3) This amount reflects (i) options to purchase 27,605 shares, 1/48th of which vest monthly following the October 6, 2015 vesting commencement date, (ii) options to purchase 18,322 shares, 1/48th of which vest monthly following the August 1, 2016 vesting commencement date, (iii) options to purchase 165,585 shares, 1/48th of which vest monthly following the January 31, 2018 vesting commencement date and (iv) options to purchase 223,757 shares, 1/48th of which vest monthly following the October 22, 2018 vesting commencement date.

(4) This amount reflects options to purchase 614,149 shares, 1/48th of which vest monthly following the September 4, 2018 vesting commencement date.

(3) Represents fees paid to Professor Krainer pursuant to Professor Krainer's consulting agreement. See "Certain relationships and related party transactions—Consulting agreement."

Prior to this offering, we did not have a formal policy to provide any cash or equity compensation to our non-employee directors for their service on our board of directors or committees of our board of directors. In connection with this offering, our board of directors expects to approve annual non-employee director compensation, which will take effect following the completion of this offering.

Executive compensation

The following tables and accompanying narrative disclosure set forth information about the compensation earned by our named executive officers during the year ended December 31, 2018. Our named executive officers, who are our principal executive officer and the two most highly-compensated executive officers (other than our principal executive officer) serving as executive officers as of December 31, 2018, were:

- Edward M. Kaye, M.D., Chief Executive Officer and Director;
- Huw M. Nash, Ph.D., Chief Operating Officer and Chief Business Officer; and
- Barry S. Ticho, M.D., Ph.D., FACC, Chief Medical Officer.

Summary compensation table

The following table presents summary information regarding the total compensation for services rendered in all capacities that was awarded to and earned by our named executive officers during the year ended December 31, 2018:

Name and principal position	Salary($)	Non-equity incentive plan compensation ($)	Option awards ($)(1)	Total ($)
Edward M. Kaye, M.D. *Chief Executive Officer*	463,500	185,400	837,748	1,486,648
Huw M. Nash, Ph.D. *Chief Operating Officer and Chief Business Officer*	318,270	111,395	440,190	869,855
Barry S. Ticho, M.D., Ph.D., FACC *Chief Medical Officer*	360,500	140,650	239,940	741,090

(1) Represents the grant date fair value of options awarded during the year ended December 31, 2018 as computed in accordance with FASB ASC Topic 718. The assumptions used in calculating the grant date fair value of the stock options reported in the Options Award column are set forth in Note 10 to our consolidated financial statements included elsewhere in this prospectus. Note that the amounts reported in this column reflect the aggregate accounting cost for these awards, and do not necessarily correspond to the actual economic value that may be received by each named executive officer from the options.

Outstanding equity awards at 2018 fiscal year-end table

	Option awards					
Name	Grant date(1)	Vesting commencement date	Number of securities underlying unexercised options exercisable	Number of securities underlying unexercised options unexercisable	Option exercise price ($)	Option expiration date
Edward M. Kaye	4/2/2018(2)	10/17/2017	2,024,563	4,916,798	0.06	4/2/2028
	12/12/2018(3)	10/22/2018	194,134	4,465,089	0.22	12/12/2028
Huw M. Nash	2/11/2016(4)	12/1/2015	1,515,240	—	0.04	2/11/2026
	2/2/2017(3)	8/1/2016	292,591	208,994	0.04	2/2/2027
	4/2/2018(3)	1/31/2018	590,327	1,985,648	0.06	4/2/2028
	12/12/2018(3)	10/22/2018	113,400	2,608,203	0.22	12/12/2028
Barry S. Ticho	4/2/2018(2)	10/2/2017	629,864	1,529,671	0.06	4/2/2028
	12/12/2018(3)	10/22/2018	53,320	1,226,377	0.22	12/12/2028

(1) All of the outstanding equity awards were granted under the 2014 Plan. In the event of a merger or a change in control (as defined in the 2014 Plan), each outstanding option shall be assumed or an equivalent option substituted by the successor corporation or a parent or subsidiary of the successor corporation. In the event that the successor corporation in a merger or change in control refuses to assume or substitute for the option, then the optionee shall fully vest in and have the right to exercise the option as to all of the optioned stock, including shares as to which it would not otherwise be vested or exercisable.

(2) 1/4th of the option vested on the one-year anniversary of the vesting commencement date and an additional 1/48th vests monthly thereafter, subject to the executive's continued service to us.

(3) 1/48th of the option vests on each one-month anniversary of the vesting commencement date, subject to the executive's continued service to us.

(4) The option is 100% vested.

Employment agreements

We have entered into employment agreements with each of our named executive officers that provide for "at-will" employment and include each named executive officer's base salary, target discretionary annual incentive bonus opportunity, and initial option grant, or Initial Option Grant. These agreements also provide for severance benefits upon certain involuntary terminations of employment, as described below.

Pursuant to the employment agreements, upon a termination of each named executive officer's employment without "cause' or for "good reason" (each as defined in the applicable executive's employment agreement and as described below), subject to the executive's execution and non-revocation of a release of claims in favor of the company, the executive will be entitled to continued salary payments and COBRA reimbursement for 12 months following termination of employment, in the case of Drs. Nash and Kaye, and six months following termination of employment, in the case of Dr. Ticho.

Each named executive officer is also entitled to his earned but unpaid bonus upon a termination for any reason other than for cause.

Additionally, upon a termination without cause or for good reason within the 90-day period prior to the execution of a definitive agreement providing for the consummation of a "change in control" (as defined in the employment agreement) or the one-year period following a change in control, Drs. Kaye and Ticho will be entitled to full acceleration of the Initial Option Grant.

Pursuant to the employment agreements, each named executive officer is also subject to a post-termination non-competition covenant that extends for 12 months following termination of employment, in the case of Drs. Kaye and Nash, and six months following termination of employment, in the case of Dr. Ticho. In the event the named executive officer breaches his non-competition covenant, such executive will forfeit any unpaid severance benefits.

We have also entered into employee invention assignment and confidentiality agreements with each of our named executive officers, which agreements include a 12-month post-termination non-solicitation covenant.

For purposes of the employment agreements "cause" generally means:

- the executive willfully engages in conduct that is in bad faith and materially injurious to us, including but not limited to, misappropriation of trade secrets, fraud or embezzlement;
- the executive commits a material breach of any written agreement between the executive and us that causes harm to the company, which breach is not timely cured;
- the executive willfully refuses to implement or follow a directive by the board of directors, directly related to the executive's duties, which breach is not timely cured; or
- the executive engages in material misfeasance or malfeasance demonstrated by a continued pattern of material failure to perform the essential job duties associated with executive's position, which breach is not timely cured.

For purposes of the employment agreements "good reason" generally means:

- a material reduction in the executive's duties or responsibilities that is inconsistent with the executive's position;

- the requirement that the executive change his principal office to a facility that increases his commute by more than 40 miles from his commute to the location at which he was employed prior to such change, or
- a material reduction in the executive's base salary or a material reduction in the executive's employee benefits.

Equity compensation plans and other benefit plans

2014 equity incentive plan

In 2014, we adopted the 2014 Equity Incentive Plan, or the 2014 Plan, as most recently amended on October 15, 2018. The purposes of the 2014 Plan are to attract and retain the best available personnel for positions of substantial responsibility, to provide additional incentive to employees, directors and consultants and to promote the success of our business. The material terms of the 2014 Plan are summarized below:

Share reserve. As of December 31, 2018, we had 46,276,642 shares of our common stock reserved for issuance pursuant to grants under our 2014 Plan of which 11,042,826 shares remained available for grant. As of December 31, 2018, options to purchase 570,286 shares had been exercised and options to purchase 34,663,530 of shares remained outstanding, with a weighted-average exercise price of $0.12 per share. As of December 31, 2018, no shares of restricted stock, no restricted stock units and no stock appreciation rights were granted under the 2014 Plan. No new awards will be granted under the 2014 Plan after the offering.

Administration. Our 2014 Plan is administered by our board of directors or a committee appointed by our board of directors, referred to herein as the "administrator". Subject to the terms of the 2014 Plan, the administrator has the authority to, among other things, select the persons to whom awards will be granted, construe and interpret our 2014 Plan as well as to prescribe, amend and rescind rules and regulations relating to the 2014 Plan and awards granted thereunder. The administrator may modify awards subject to the terms of the 2014 Plan.

Eligibility. Pursuant to the 2014 Plan, we may grant incentive stock options only to our employees (including officers and directors who are also employees). We may grant non-statutory stock options and stock purchase rights to our employees (including officers and directors who are also employees), non-employee directors and consultants.

Options. The 2014 Plan provides for the grant of both (i) incentive stock options, which are intended to qualify for tax treatment as set forth under Section 422 of the Code, as amended, or the Code, and (ii) non-statutory stock options to purchase shares of our common stock, each at a stated exercise price. The exercise price of each option must be at least equal to the fair market value of our common stock on the date of grant (unless otherwise determined by the administrator). However, the exercise price of any incentive stock option granted to an individual who owns more than ten percent of the total combined voting power of all classes of our capital stock must be at least equal to 110% of the fair market value of our common stock on the date of grant.

The administrator will determine the vesting schedule applicable to each option. The maximum permitted term of options granted under our 2014 Plan is ten years from the date of grant, except that the maximum permitted term of incentive stock options granted to an individual who owns more than ten percent of the total combined voting power of all classes of our capital stock is five years from the date of grant.

Restricted stock, restricted stock units, stock appreciation rights. In addition, the 2014 Plan allows for the grant of restricted stock awards, restricted stock units and stock appreciation rights, with terms as generally determined by the administrator (in accordance with the 2014 Plan) and to be set forth in an award agreement. We have not granted any shares of restricted stock, any restricted stock units or any stock appreciation rights under the 2014 Plan.

Limited transferability. Unless otherwise determined by the Administrator, awards under the 2014 Plan generally may not be sold, pledged, assigned, hypothecated, transferred or disposed of in any manner other than by will, the laws of descent and distribution or qualified domestic relations orders.

Change of control. In the event that we are subject to an "acquisition" or "other combination" (as defined in the 2014 Plan and generally meaning, collectively, a merger, a sale or transfer of more than 50% of the voting power of all of our outstanding securities, or a sale of all or substantially all of the assets of ours), the 2014 Plan provides that awards will be subject to the agreement evidencing such acquisition or other combination, which agreement need not treat all awards in a similar manner. Such agreement may, without the participant's consent, provide for the continuation of outstanding awards, the assumption or substitution of awards, the acceleration of vesting of awards, the settlement of awards (whether or not vested) in cash, securities or other consideration, or the cancellation of such awards for no consideration.

Adjustments. In the event of a dividend or other distribution, recapitalization, stock split, reverse stock split, reorganization, merger, consolidation, split-up, spin-off, combination, repurchase or exchange of any of our securities, or other change in our corporate structure affecting the shares of common stock issued under the 2014 Plan, the number and class of shares that may be delivered under 2014 Plan and/or the number, class and price of shares covered by each outstanding award will (to the extent appropriate) be appropriately adjusted (subject to required action by the board), in order to prevent diminution or enlargement of benefits or potential benefits intended to be made available under the 2014 Plan or otherwise as required by applicable law.

Exchange, repricing and buyout of awards. The administrator may, with the consent of the respective participants, issue new awards in exchange for the surrender and cancelation of any or all outstanding awards. The administrator may also reduce the exercise price of options or stock appreciation rights or buy an award previously granted with payment in cash, shares or other consideration, in each case, subject to the terms of the 2014 Plan.

Amendment/termination. The Board may amend or terminate the 2014 Plan at any time and may terminate any and all outstanding options or stock appreciation rights upon a dissolution or liquidation of us, provided that certain amendments will require shareholder approval. We expect to terminate the 2014 Plan and will cease issuing awards thereunder upon the effective date of our 2019 Equity Incentive Plan (described below), which is the date immediately prior to the date of the effectiveness of the registration statement of which this prospectus forms a part. Any outstanding awards granted under the 2014 Plan will remain outstanding following the offering, subject to the terms of our 2014 Plan and applicable award agreements, until such awards are exercised or until they terminate or expire by their terms.

2019 equity incentive plan

We intend to adopt our 2019 Equity Incentive Plan, or the 2019 Plan, that will become effective on the date immediately prior to the date of the effectiveness of the registration of which this prospectus forms a part and will serve as the successor to our 2014 Plan. Our 2019 Plan authorizes the award of stock options, restricted stock awards, or RSAs, stock appreciation rights, or SARs, restricted stock units, or RSUs, performance awards and stock bonus awards. We have initially reserved shares of our common stock, plus any reserved shares not issued or subject to outstanding grants under the 2014 Plan on the effective date of the 2019 Plan, for issuance pursuant to awards granted under our 2019 Plan. The number of shares reserved for issuance under our 2019 Plan will increase automatically on January 1 of each of 2020 through 2029 by the number of shares equal to % of the aggregate number of outstanding shares of our common stock as of the immediately preceding December 31, or a lesser number as may be determined by our board of directors.

In addition, the following shares will again be available for issuance pursuant to awards granted under our 2019 Plan:

- shares subject to options or SARs granted under our 2019 Plan that cease to be subject to the option or SAR for any reason other than exercise of the option or SAR;
- shares subject to awards granted under our 2019 Plan that are subsequently forfeited or repurchased by us at the original issue price;
- shares subject to awards granted under our 2019 Plan that otherwise terminate without such shares being issued;
- shares subject to awards granted under our 2019 Plan that are surrendered, cancelled or exchanged for cash or a different award (or combination thereof);
- shares issuable upon the exercise of options or subject to other awards granted under our 2014 Plan that cease to be subject to such options or other awards, by forfeiture or otherwise, after the termination of the 2014 Plan;
- shares subject to awards granted under our 2014 Plan that are forfeited or repurchased by us at the original price after the termination of the 2014 Plan; and
- shares subject to awards under our 2014 Plan or our 2019 Plan that are used to pay the exercise price of an option or withheld to satisfy the tax withholding obligations related to any award.

Administration. Our 2019 Plan is expected to be administered by our compensation committee, or by our board of directors acting in place of our compensation committee. Subject to the terms and conditions of the 2019 Plan, the compensation committee will have the authority, among other things, to select the persons to whom awards may be granted, construe and interpret our 2019 Plan as well as to determine the terms of such awards and prescribe, amend and rescind the rules and regulations relating to the plan or any award granted thereunder. The 2019 Plan provides that the board or compensation committee may delegate its authority, including the authority to grant awards, to one or more executive officers to the extent permitted by applicable law, provided that awards granted to non-employee directors may only be determined by our board of directors.

Eligibility. Our 2019 Plan provides for the grant of awards to our employees, directors, consultants, independent contractors and advisors. No non-employee director may receive awards under our 2019 Plan that exceed $ in a calendar year or $ in the calendar year of his or her initial services as a non-employee director with us.

Options. The 2019 Plan provides for the grant of both incentive stock options intended to qualify under Section 422 of the Code, and non-statutory stock options to purchase shares of our common stock at a stated exercise price. Incentive stock options may only be granted to employees, including officers and directors who are also employees. The exercise price of stock options granted under the 2019 Plan must be at least equal to the fair market value of our common stock on the date of grant. Incentive stock options granted to an individual who holds, directly or by attribution, more than ten percent of the total combined voting power of all classes of our capital stock must have an exercise price of at least 110% the fair market value of our common stock on the date of grant. Subject to stock splits, dividends, recapitalizations or similar events, no more than shares may be issued pursuant to the exercise of incentive stock options granted under the 2019 Plan.

Options may vest based on service or achievement of performance conditions. Our compensation committee may provide for options to be exercised only as they vest or to be immediately exercisable, with any shares

issued on exercise being subject to our right of repurchase that lapses as the shares vest. The maximum term of options granted under our 2019 Plan is ten years from the date of grant, except that the maximum permitted term of incentive stock options granted to an individual who holds, directly or by attribution, more than ten percent of the total combined voting power of all classes of our capital stock is five years from the date of grant.

Restricted stock awards. An RSA is an offer by us to sell shares of our common stock subject to restrictions, which may lapse based on the satisfaction of service or achievement of performance conditions. The price, if any, of an RSA will be determined by the compensation committee. Holders of RSAs, unlike holders of options, will have the right to vote and any dividends or stock distributions paid pursuant to RSAs will be accrued and paid when the restrictions on such shares lapse. Unless otherwise determined by the compensation committee at the time of award, vesting will cease on the date the participant no longer provides services to us and unvested shares may be forfeited to or repurchased by us.

Stock appreciation rights. A SAR provides for a payment, in cash or shares of our common stock (up to a specified maximum of shares, if determined by our compensation committee), to the holder based upon the difference between the fair market value of our common stock on the date of exercise and a predetermined exercise price, multiplied by the number of shares. The exercise price of a SAR must be at least the fair market value of a share of our common stock on the date of grant. SARs may vest based on service or achievement of performance conditions, and may not have a term that is longer than ten years from the date of grant.

Restricted stock units. RSUs represent the right to receive shares of our common stock at a specified date in the future, and may be subject to vesting based on service or achievement of performance conditions. Payment of earned RSUs will be made as soon as practicable on a date determined at the time of grant, and may be settled in cash, shares of our common stock or a combination of both. No RSU may have a term that is longer than ten years from the date of grant.

Performance awards. Performance awards granted to pursuant to the 2019 Plan may be in the form of a cash bonus, or an award of performance shares or performance units denominated in shares of our common stock that may be settled in cash, property or by issuance of those shares subject to the satisfaction or achievement of specified performance conditions.

Stock bonus awards. A stock bonus award provides for payment in the form of cash, shares of our common stock or a combination thereof, based on the fair market value of shares subject to such award as determined by our compensation committee. The awards may be granted as consideration for services already rendered, or at the discretion of the compensation committee, may be subject to vesting restrictions based on continued service or performance conditions.

Dividend equivalents rights. Dividend equivalent rights may be granted at the discretion of our compensation committee, and represent the right to receive the value of dividends, if any, paid by us in respect of the number of shares of our common stock underlying an award. Dividend equivalent rights will be subject to the same vesting or performance conditions as the underlying award and will be paid only at such time as the underlying award has become fully vested. Dividend equivalent rights may be settled in cash, shares or other property, or a combination of thereof as determined by the compensation committee.

Change of control. Our 2019 Plan provides that, in the event of a change of control (as defined in the 2019 Plan), outstanding awards under our 2019 Plan shall be subject to the agreement evidencing the change of control, which need not treat all outstanding awards in an identical manner, and may include one or more of the following: (i) the continuation of the outstanding awards; (ii) the assumption of the outstanding awards by the surviving corporation or its parent; (iii) the substitution by the surviving corporation or its parent of new options or equity awards for the outstanding awards; (iv) the full or partial acceleration of exercisability or

vesting or lapse of Company's right to repurchase or forfeiture rights and accelerated expiration of the award; or (v) the settlement of the full value of the outstanding awards (whether or not then vested or exercisable) in cash, cash equivalents, or securities of the successor entity with a fair market value equal to the required amount, as determined in accordance with the 2019 Plan and which payments may be deferred until the date or dates the award would have become exercisable or vested. However, in the event a successor or acquiring corporation refuses to assume, substitute or settle outstanding awards, all such awards will become fully vested and exercisable immediately prior to the consummation of the change in control. In addition, upon a change in control the vesting of all awards granted to our non-employee directors will accelerate and such awards will become exercisable (to the extent applicable) in full prior to the consummation of the change of control at such times and on such conditions as the committee determines.

Adjustment. In the event of a change in the number of outstanding shares of our common stock without consideration by reason of a stock dividend, extraordinary dividend or distribution, recapitalization, stock split, reverse stock split, subdivision, combination, consolidation reclassification, spin-off or similar change in our capital structure, appropriate proportional adjustments will be made to the number of shares reserved for issuance under our 2019 Plan; the exercise prices, number and class of shares subject to outstanding options or SARs; the number and class of shares subject to other outstanding awards; and any applicable maximum award limits with respect to incentive stock options.

Clawback; transferability. All awards will be subject to clawback or recoupment pursuant to any compensation clawback or recoupment policy adopted by our board of directors or required by law during the term of service of the award holder, to the extent set forth in such policy or applicable agreement. Except in limited circumstances, awards granted under our 2019 Plan may generally not be transferred in any manner prior to vesting other than by will or by the laws of descent and distribution.

Amendment and termination. Our board of directors may amend our 2019 Plan at any time, subject to stockholder approval as may be required. Our 2019 Plan will terminate ten years from the date our board of directors adopts the plan, unless it is terminated earlier by our board of directors. No termination or amendment of the 2019 Plan may adversely affect any then-outstanding award without the consent of the affected participant, except as is necessary to comply with applicable laws.

401(k) plan

We sponsor a retirement savings plan, or 401(k) plan, that is intended to qualify for favorable tax treatment under Section 401(a) of the Code, and contains a cash or deferred feature that is intended to meet the requirements of Section 401(k) of the Code. U.S. employees who have attained at least 21 years of age are generally eligible to participate in the 401(k) plan following two months of service, subject to certain criteria. Participants may make pre-tax and certain after-tax (Roth) salary deferral contributions to the plan from their eligible earnings up to the statutorily prescribed annual limit under the Code. Participants who are 50 years of age or older may contribute additional amounts based on the statutory limits for catch-up contributions. Participant contributions are held in trust as required by law. No minimum benefit is provided under the plan. An employee's interest in his or her salary deferral contributions is 100% vested when contributed. We have the ability to make discretionary matching and profit share contributions under the plan but have not done so to date. Any such discretionary employer contributions would vest in equal, annual installments over 4 years and may be subject to other eligibility requirements.

Other benefits

Our named executive officers are eligible to participate in our employee benefit plans on the same basis as our other employees, including our health and welfare plans.

Limitations on liability and indemnification matters

Our restated certificate of incorporation that will become effective in connection with the completion of this offering contains provisions that limit the liability of our directors for monetary damages to the fullest extent permitted by the Delaware General Corporation Law, or DGCL. Consequently, our directors will not be personally liable to us or our stockholders for monetary damages for any breach of fiduciary duties as directors, except liability for:

- any breach of the director's duty of loyalty to us or our stockholders;
- any act or omission not in good faith or that involves intentional misconduct or a knowing violation of law;
- unlawful payments of dividends or unlawful stock repurchases or redemptions as provided in Section 174 of the DGCL; or
- any transaction from which the director derived an improper personal benefit.

Our restated certificate of incorporation and our restated bylaws that will become effective in connection with the completion of this offering require us to indemnify our directors and officers to the maximum extent not prohibited by the DGCL and allow us to indemnify other employees and agents as set forth in the DGCL.

We have entered, and intend to continue to enter, into separate indemnification agreements with our directors, officers and certain of our key employees, in addition to the indemnification provided for in our restated certificate of incorporation and restated bylaws. These agreements, among other things, require us to indemnify our directors, officers and key employees for certain expenses, including attorneys' fees, judgments, penalties, fines and settlement amounts actually incurred by these individuals in any action or proceeding arising out of their service to us or any of our subsidiaries or any other company or enterprise to which these individuals provide services at our request. Subject to certain limitations, our indemnification agreements also require us to advance expenses incurred by our directors, officers and key employees for the defense of any action for which indemnification is required or permitted.

We believe that these indemnification provisions and agreements are necessary to attract and retain qualified directors, officers and key employees. We also maintain directors' and officers' liability insurance.

The limitation of liability and indemnification provisions in our restated certificate of incorporation and restated bylaws may discourage stockholders from bringing a lawsuit against our directors and officers for breach of their fiduciary duty. They may also reduce the likelihood of derivative litigation against our directors and officers, even though an action, if successful, might benefit us and other stockholders. Further, a stockholder's investment may be adversely affected to the extent that we pay the costs of settlement and damage awards against directors and officers as required by these indemnification provisions.

At present, there is no pending litigation or proceeding involving any of our directors or executive officers as to which indemnification is required or permitted, and we are not aware of any threatened litigation or proceeding that may result in a claim for indemnification.

Insofar as indemnification for liabilities arising under the Securities Act of 1933, as amended, or Securities Act, may be permitted to directors, executive officers or persons controlling us, we have been informed that, in the opinion of the SEC, such indemnification is against public policy as expressed in the Securities Act and is therefore unenforceable.

Certain relationships and related party transactions

In addition to the compensation arrangements, including any employment, termination of employment and change in control arrangements, with our directors and executive officers, including those discussed in the sections entitled “Management” and “Executive compensation,” the following is a description of each transaction since January 1, 2016 and each currently proposed transaction in which:

- we have been or are to be a participant;
- the amounts involved exceeded or will exceed $120,000; and
- any of our directors, executive officers or holders of more than 5% of our capital stock, or an affiliate or immediate family member of the foregoing persons, had or will have a direct or indirect material interest.

Other than as described below, there have not been, nor are there any currently proposed, transactions or series of similar transactions to which we have been or will be a party other than compensation arrangements, which are described where required under the section entitled “Executive compensation.”

Equity financings

Series A

In July 15, 2015, we sold an aggregate of 24,456,520 shares of our Series A convertible preferred stock at a purchase price of $0.2392 per share for an aggregate purchase price of approximately $5.8 million. In July 2016, we sold an aggregate of 12,541,806 additional shares of our Series A convertible preferred stock at a purchase price of $0.2392 per share for an aggregate purchase price of approximately $3.0 million. In February 2017, we sold an aggregate of 12,541,806 additional shares of our Series A convertible preferred stock at a purchase price of $0.2392 per share for an aggregate purchase price of approximately $3.0 million.

Simple Agreement for Future Equity

In October 2017, we issued, to Apple Tree Partners IV, L.P., rights to purchase certain shares of our capital stock for an aggregate purchase price of $3,000,000, or Purchase Amount, pursuant to a Simple Agreement for Future Equity, or SAFE. The entire Purchase Amount and all other obligations under the SAFE converted into 7,839,038 shares of our Series A-2 convertible preferred stock, which is described below.

Series A-2

In January 2018, we sold an aggregate of 40,501,698 shares of our Series A-2 convertible preferred stock at a purchase price of $0.3827 per share for an aggregate purchase price of approximately $15.5 million. In September 2018, we sold an aggregate of 35,275,672 additional shares of our Series A-2 convertible preferred stock at a purchase price of $0.3827 per share for an aggregate purchase price of approximately $13.5 million.

Series B

In October 2018, we sold an aggregate of 100,267,372 shares of our Series B convertible preferred stock at a purchase price of $0.8976 per share for an aggregate purchase price of approximately $90 million.

The following table summarizes the Series A, Series A-2 and Series B convertible preferred stock purchased by members of our board of directors or their affiliates and holders of more than five percent of our outstanding capital stock:

Name of stockholder	Series	Shares of convertible preferred stock	Total purchase price ($)
Apple Tree Partners, IV, L.P.(1)	A	49,540,132	11,849,999.57
Apple Tree Partners, IV, L.P.(1)	A-2	75,777,370	28,999,999.50
Apple Tree Partners, IV, L.P.(1)	B	27,852,049	24,999,999.18
RTW Master Fund(2)	B	24,173,938	21,698,526.75
RTW Innovation Master Fund, Ltd.(2)	B	3,678,111	3,301,472.43

1. Apple Tree Partners, IV, L.P., or ATP IV, holds more than five percent of our outstanding capital stock. Seth L. Harrison, M.D., a member of our board of directors, is the founder and managing partner of ATP IV and Samuel W. Hall, Ph.D., a member of our board of directors, is a principal at ATP IV.

2. Entities associated with RTW Investments, or RTW, hold more than 5% of our outstanding capital stock.

Amended and restated investors' rights agreement

We have entered into a second amended and restated investors' rights agreement, or the IRA, dated October 22, 2018, with certain holders of our convertible preferred stock, including entities with which certain of our directors are affiliated. Additionally, the IRA provides for a participation right to affiliates of RTW Master Fund and Apple Tree Partners IV, L.P., holders of more than five percent of our common stock, to purchase a specified percentage of shares of common stock in this offering at the public offering price. The IRA further provides that, under certain circumstances in which such entities are unable to participate in this offering, we are required to offer them shares of our common stock through a separate private placement to be concurrent with this offering. Under the IRA, these stockholders are also entitled to rights with respect to the registration of their shares following this offering under the Securities Act of 1933, as amended. For a description of these registration rights, see the section entitled "Description of capital stock—Registration rights."

Equity grants to executive officers and directors

We have granted stock options to our executive officers and certain directors, as more fully described in the sections entitled "Executive compensation" and "Management—Non-employee director compensation," respectively.

Director and executive officer compensation

Please see the sections entitled "Management—Non-employee director compensation" and "Executive compensation" for information regarding the compensation of our directors and executive officers.

Employment agreements

We have entered into employment agreements with our executive officers. For more information regarding these agreements, see the section entitled "Executive compensation—Employment agreements."

Consulting agreement

In October 2014, we entered into a consulting agreement with Adrian R. Krainer, who is also an employee of Cold Spring Harbor Laboratory, 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 made payments of $100,000 during each of the years ended December 31, 2018, 2017 and 2016 for such consulting services. The initial term of this agreement was five years and may be extended by the mutual consent of us and Professor Krainer.

Indemnification agreements

In connection with this offering, we intend to enter into new indemnification agreements with each of our directors and executive officers. The indemnification agreements, our restated certificate of incorporation and our restated bylaws will require us to indemnify our directors to the fullest extent not prohibited by Delaware law. Subject to certain limitations, our restated bylaws also require us to advance expenses incurred by our directors and officers. For more information regarding these agreements, see the section entitled “Executive compensation—Limitations on liability and indemnification matters” for information on our indemnification arrangements with our directors and executive officers.

Policies and procedures for related party transactions

In connection with this offering, we intend to adopt a written related person transactions policy that provides that our executive officers, directors, nominees for election as a director, beneficial owners of more than 5% of our common stock, and any members of the immediate family of and any entity affiliated with any of the foregoing persons, are not permitted to enter into a material related person transaction with us without the review and approval of our audit committee, or a committee composed solely of independent directors in the event it is inappropriate for our audit committee to review such transaction due to a conflict of interest. We expect the policy to provide that any request for us to enter into a transaction with an executive officer, director, nominee for election as a director, beneficial owner of more than 5% of our common stock or with any of their immediate family members or affiliates in which the amount involved exceeds $120,000 will be presented to our audit committee (or the committee composed solely of independent directors, if applicable) for review, consideration and approval. In approving or rejecting any such proposal, we expect that our audit committee (or the committee composed solely of independent directors, if applicable) will consider the relevant facts and circumstances available and deemed relevant to the audit committee (or the committee composed solely of independent directors, if applicable), including, but not limited to, whether the transaction is on terms no less favorable than terms generally available to an unaffiliated third party under the same or similar circumstances and the extent of the related person’s interest in the transaction.

Principal stockholders

The following table and accompanying footnotes set forth certain information with respect to the beneficial ownership of our common stock at March 15, 2019, and as adjusted to reflect the shares of common stock to be issued and sold in this offering, for:

- each of our directors;
- each of our named executive officers;
- all of our current directors and executive officers as a group; and
- each person, or group of affiliated persons, who beneficially owned more than five percent of our outstanding shares of common stock.

We have determined beneficial ownership in accordance with the rules of the SEC, and the information is not necessarily indicative of beneficial ownership for any other purpose. Except as indicated by the footnotes below, we believe, based on information furnished to us, that the persons and entities named in the table below have sole voting and sole investment power with respect to all shares of common stock that they beneficially owned, subject to applicable community property laws.

Beneficial ownership prior to this offering is based on 234,413,489 shares of common stock outstanding as of March 15, 2019, assuming the automatic conversion of all outstanding shares of our convertible preferred stock into common stock in connection with this offering. Beneficial ownership after this offering is based on shares of common stock outstanding, assuming (i) the automatic conversion of all outstanding shares of our convertible preferred stock into common stock as described above and (ii) the issuance of shares of common stock in this offering. In computing the number of shares of common stock beneficially owned by a person and the percentage ownership of that person, we deemed to be outstanding all shares of common stock subject to options held by that person or entity that are currently exercisable or that will become exercisable within 60 days of March 15, 2019. We did not deem these shares outstanding, however, for the purpose of computing the percentage ownership of any other person.

Unless otherwise indicated, the address of each beneficial owner listed in the table below is c/o Stoke Therapeutics, Inc., 45 Wiggins Avenue, Bedford, Massachusetts, 01730.

	Beneficial ownership prior to this offering		Beneficial ownership after this offering	
Name of beneficial owner	**Number**	**Percent**	**Number**	**Percent**
Directors and named executive officers:				
Edward M. Kaye, M.D.(1)	3,185,412	1.3%		%
Huw M. Nash, Ph.D.(2)	3,005,271	1.3		
Barry S. Ticho, M.D., Ph.D., FACC(3)	1,014,777	*		
Seth L. Harrison, M.D.(4)	153,169,551	65.3		
Samuel W. Hall, Ph.D.	—	—		
Adrian R. Krainer, Ph.D.(5)	4,068,592	1.7		
Arthur A. Levin, Ph.D.(6)	283,022	*		
Arthur O. Tzianabos, Ph.D.(7)	102,358	*		
All executive officers and directors as a group (10 persons)(8)	165,425,280	68.2		
Other 5% stockholders:				
Apple Tree Partners IV, L.P.(4)	153,169,551	65.3		
Entities affiliated with RTW Investments, L.P.(9)	27,852,049	11.9		

* Represents beneficial ownership of less than one percent.

(1) Represents 3,185,412 shares underlying options to purchase common stock that are exercisable within 60 days of March 15, 2019.

(2) Represents 3,005,271 shares underlying options to purchase common stock that are exercisable within 60 days of March 15, 2019.

(3) Represents 1,014,777 shares underlying options to purchase common stock that are exercisable within 60 days of March 15, 2019.

(4) Represents 153,169,551 shares of common stock held by Apple Tree Partners IV, L.P., or ATP IV. ATP III GP, Ltd., or ATP III, is the sole general partner of ATP IV. Seth L. Harrison, M.D., a member of our board of directors, is the sole director of ATP III and may be deemed to have sole voting and dispositive power over the shares held by ATP IV. The address of ATP IV is 230 Park Avenue, Suite 2800, New York, New York 10169.

(5) Represents (i) 4,025,943 shares of common stock and (ii) 42,649 shares underlying options to purchase common stock that are exercisable within 60 days of March 15, 2019.

(6) Represents (i) 178,880 shares of common stock held by Arthur A. Levin, Trustee, Butler-Levin Revocable Trust and (ii) 104,142 shares underlying options to purchase common stock that are exercisable within 60 days of March 15, 2019.

(7) Represents 102,358 shares underlying options to purchase common stock that are exercisable within 60 days of March 15, 2019.

(8) Represents (i) 157,374,374 shares of common stock and (ii) 8,050,906 shares underlying options to purchase common stock that are exercisable within 60 days of March 15, 2019.

(9) Represents (i) 24,173,938 shares of common stock held by RTW Master Fund, Ltd., or RTW Master Fund, and (ii) 3,678,111 shares of common stock held by RTW Innovation Master Fund, Ltd., or RTW Innovation Fund. RTW Investments, LP, or RTW Investments, is the manager of RTW Master Fund and RTW Innovation Fund. Roderick Wong, M.D. is the managing partner and chief investment officer of RTW Investments and has sole voting and investment control over the shares held by each of RTW Master Fund and RTW Innovation Fund. The address of RTW Investments is 412 West 15th Street, Floor 9, New York, New York 10011.

Description of capital stock

The following description summarizes the most important terms of our capital stock, as they will be in effect following this offering. Because it is only a summary, it does not contain all the information that may be important to you. We expect to adopt a restated certificate of incorporation and restated bylaws that will become effective upon the completion of this offering, and this description summarizes provisions that are expected to be included in these documents. For a complete description, you should refer to our restated certificate of incorporation and restated bylaws, which are included as exhibits to the registration statement of which this prospectus forms a part, and to the applicable provisions of Delaware law.

Upon the completion of this offering, our authorized capital stock will consist of shares of common stock, $0.0001 par value per share, and shares of undesignated preferred stock, $0.0001 par value per share.

Pursuant to the provisions of our current certificate of incorporation all of the outstanding convertible preferred stock will automatically convert into common stock in connection with the completion of this offering. Our Series A convertible preferred stock will convert at a ratio of 1:1, our Series A-2 convertible preferred stock will convert at a ratio of 1:1, and our Series B convertible preferred stock will convert at a ratio of 1:1. Assuming the effectiveness of this conversion as of December 31, 2018, there were shares of our common stock issued, held by approximately stockholders of record, and no shares of our convertible preferred stock outstanding. Our board of directors is authorized, without stockholder approval, to issue additional shares of our capital stock.

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. See the section entitled “Dividend policy.”

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 will be able to elect all of our directors. Our restated certificate of incorporation will establish a classified board of directors, to be divided into three classes with staggered three-year terms. Only one class of directors will be 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

Immediately prior to the completion of this offering, each outstanding share of preferred stock will be converted into common stock at a ratio of 1:1.

Following the completion of this offering, our board of directors will be authorized, subject to limitations prescribed by Delaware law, to issue 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 will also be 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.

Stock options

As of December 31, 2018, we had outstanding options to purchase an aggregate 34,663,530 shares of our common stock, with a weighted-average exercise price of $0.12.

Registration rights

Pursuant to the terms of our amended and restated investors' rights agreement, immediately following this offering, the holders of 225,584,874 shares of our common stock will be entitled to rights with respect to the registration of these shares under the Securities Act of 1933, as amended, or the Securities Act, as described below. We refer to these shares collectively as registrable securities.

Form S-1 registration rights

Beginning 180 days after the completion of this offering, the holders of at least a majority of the then-outstanding registrable securities may make a request to us for the registration under the Securities Act of registrable securities if the aggregate price to the public of the shares offered is at least $10.0 million. Within ten (10) days following such request, we are obligated to provide notice of such request to all stockholders, other than the initiating holders, to file a registration statement under the Securities Act covering all registrable securities that the initiating holders requested to be registered and any additional registrable securities requested to be included in such registration by any other holders. We are only required to file two registration statements that are declared effective upon exercise of these demand registration rights. We may postpone taking action with respect to such filing not more than once during any 12-month period for a total period of not more than 120 days, if after receiving a request for registration, we furnish to the holders requesting such registration a certificate signed by our Chief Executive Officer stating that, in the good faith judgment of our board of directors, it would be materially detrimental to us and our stockholders for such registration statement to be effected at such time.

The underwriters of any underwritten offering will have the right to limit the number of shares registered by these holders if they determine that marketing factors require limitation, in which case the number of shares to be registered will be apportioned, in proportion (as nearly as practicable), to the number of registrable securities owned by each holder or in such other proportion as shall mutually be agreed to by all such selling

Holders. However, the number of shares to be registered by these holders cannot be reduced unless all other securities are first entirely excluded from the underwriting.

Form S-3 registration rights

Any holder or group of holders of at least 20% of then-outstanding registrable securities can request that we register all or part of their shares on Form S-3 if we are eligible to file a registration statement on Form S-3 and if the aggregate price to the public of the shares offered is at least $1.0 million. The stockholders may only require us to effect two registration statements on Form S-3 in a 12-month period. We may postpone taking action with respect to such filing not more than once during any 12-month period for a total period of not more than 120 days, if after receiving a request for registration, we furnish to the holders requesting such registration a certificate signed by our Chief Executive Officer stating that, in the good faith judgment of our board of directors, it would be materially detrimental to us and our stockholders for such registration statement to be effected at such time.

The underwriters of any underwritten offering will have the right to limit the number of shares registered by these holders if they determine that marketing factors require limitation, in which case the number of shares to be registered will be apportioned, in proportion (as nearly as practicable), to the number of registrable securities owned by each holder or in such other proportion as shall mutually be agreed to by all such selling Holders. However, the number of shares to be registered by these holders cannot be reduced unless all other securities are first entirely excluded from the underwriting.

Piggyback registration rights

If we register any of our securities for public sale, holders of then-outstanding registrable securities or their permitted transferees will have the right to include their registrable securities in the registration statement. However, this right does not apply to a registration relating to employee benefit plans, a registration relating to a corporate reorganization, a registration on a form that does not include substantially the same information as would be required to be included in a registration statement covering the sale of registrable securities or a registration in which the only common stock being registered is common stock issuable upon conversion of debt securities that are being registered.

The underwriters of any underwritten offering will have the right to limit the number of shares registered by these holders if they determine that marketing factors require limitation, in which case the number of shares to be registered will be apportioned to the selling holders, in proportion (as nearly as practicable), to the number of registrable securities owned by each selling holder or in such other proportion as shall mutually be agreed to by all such selling Holders. However, the number of shares to be registered by these holders cannot be reduced (i) unless all other securities (other than securities to be sold by us) are first entirely excluded from the offering, (ii) below 25% of the total number of securities included in such offering, unless such offering is the initial public offering, in which case the selling holders may be excluded further if the underwriters make the determination for a limitation and no other stockholder’s securities are included in such offering.

Expenses of registration rights

We generally will pay all expenses, other than underwriting discounts and commissions.

Expiration of registration rights

The registration rights described above will expire, with respect to any particular holder of these rights, on the earlier of the fifth anniversary of this offering or with respect to each holder, such time following this offering as all registrable securities of such holder may be sold within a three-month period pursuant to Rule 144.

Anti-takeover provisions

The provisions of Delaware General Corporation Law, or DGCL, our restated certificate of incorporation and our restated bylaws, as we expect they will be in effect upon the completion of this offering, 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. We believe that the benefits of increased protection of our potential ability to negotiate with an unfriendly or unsolicited acquirer outweigh the disadvantages of discouraging a proposal to acquire us because negotiation of these proposals could result in an improvement of their terms.

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. We expect the existence of this provision to have an anti-takeover effect with respect to transactions our board of directors does not approve in advance. We also anticipate that Section 203 may also discourage attempts that might result in a premium over the market price for the shares of common stock held by stockholders.

Restated certificate of incorporation and restated bylaw provisions

Our restated certificate of incorporation and our restated bylaws, as we expect they will be in effect upon the completion of this offering, 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 will 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 will 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. See the section entitled “Management—Board composition.”
- *Stockholder action; special meetings of stockholders.* Our restated certificate of incorporation will provide 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 will 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 will 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 will 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 will not provide for cumulative voting.
- *Directors removed only for cause.* Our restated certificate of incorporation will provide 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 would require 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 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 will provide 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, 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

Upon the completion of this offering, the transfer agent and registrar for our common stock will be . The transfer agent's address is , and its telephone number is .

Nasdaq Global Market listing

We intend to apply to list our common stock on the Nasdaq Global Market under the symbol "STOK."

Shares eligible for future sale

Prior to this offering, there has been no public market for our common stock, and we cannot predict the effect, if any, that market sales of shares of our common stock or the availability of shares of our common stock for sale will have on the market price of our common stock prevailing from time to time. Nevertheless, sales of substantial amounts of our common stock, including shares issued upon exercise of outstanding options, in the public market following this offering could adversely affect market prices prevailing from time to time and could impair our ability to raise capital through the sale of our equity securities.

Upon the completion of this offering, we will have a total of shares of our common stock outstanding, assuming (i) the automatic conversion of all outstanding shares of our convertible preferred stock into an aggregate of shares of our common stock and (ii) the issuance of shares of common stock in this offering. Of these outstanding shares, all of the shares of common stock sold in this offering will be freely tradable, except that any shares purchased in this offering by our affiliates, as that term is defined in Rule 144 under the Securities Act of 1933, as amended, or the Securities Act, can only be sold in compliance with the Rule 144 limitations described below or in compliance with the lock-up agreements.

The remaining outstanding shares of our common stock will be deemed “restricted securities” as defined in Rule 144. Restricted securities may be sold in the public market only if they are registered under the Securities Act or if they qualify for an exemption from registration under Rule 144 or Rule 701 promulgated under the Securities Act, which rules are summarized below. In addition, substantially all of our security holders have, or will have, entered into market standoff agreements with us or lock-up agreements with the underwriters under which they have agreed, subject to specific exceptions, not to sell any of our stock for at least 180 days following the date of this prospectus, as described below. As a result of these agreements and the provisions of our amended and restated investors’ rights agreement described above under the section entitled “Description of capital stock—Registration rights,” subject to the provisions of Rule 144 or Rule 701, shares will be available for sale in the public market as follows:

- beginning on the date of this prospectus, all of the shares sold in this offering will be immediately available for sale in the public market; and
- beginning 181 days after the date of this prospectus, additional shares will become eligible for sale in the public market, of which shares will be held by affiliates and subject to the volume and other restrictions of Rule 144, as described below.

Lock-up/market standoff agreements

All of our directors and officers and substantially all of our security holders are, or will be, subject to lock-up agreements or market standoff provisions that prohibit them from offering for sale, selling, contracting to sell, granting any option for the sale of, transferring or otherwise disposing of any shares of our common stock, options to acquire shares of our common stock or any security or instrument related to our common stock, or entering into any swap, hedge or other arrangement that transfers any of the economic consequences of ownership of our common stock, for a period of 180 days following the date of this prospectus without the prior written consent of J.P. Morgan Securities LLC, subject to certain exceptions. See the section entitled “Underwriting.”

Rule 144

In general, under Rule 144 as currently in effect, once we have been subject to public company reporting requirements for at least 90 days, a person who is not deemed to have been one of our affiliates for purposes of the Securities Act at any time during the three months preceding a sale and who has beneficially owned the

shares proposed to be sold for at least six months, including the holding period of any prior owner other than our affiliates, is entitled to sell those shares without complying with the manner of sale, volume limitation or notice provisions of Rule 144, subject to compliance with the public information requirements of Rule 144. If such a person has beneficially owned the shares proposed to be sold for at least one year, including the holding period of any prior owner other than our affiliates, then that person would be entitled to sell those shares without complying with any of the requirements of Rule 144.

In general, under Rule 144, as currently in effect, our affiliates or persons selling shares on behalf of our affiliates are entitled to sell upon expiration of the lock-up and market standoff agreements described above, within any three-month period, a number of shares that does not exceed the greater of:

- 1% of the number of shares of our common stock then outstanding, which will equal approximately shares immediately after this offering; or
- the average reported weekly trading volume of our common stock during the four calendar weeks preceding the filing of a notice on Form 144 with respect to that sale.

Sales under Rule 144 by our affiliates or persons selling shares on behalf of our affiliates are also subject to certain manner of sale provisions and notice requirements and to the availability of current public information about us.

Rule 701

Rule 701 generally allows a stockholder who purchased shares of our common stock pursuant to a written compensatory plan or contract and who is not deemed to have been an affiliate of our company during the immediately preceding three months to sell these shares in reliance upon Rule 144, but without being required to comply with the public information, holding period, volume limitation or notice provisions of Rule 144. Rule 701 also permits affiliates of our company to sell their Rule 701 shares under Rule 144 without complying with the holding period requirements of Rule 144. All holders of Rule 701 shares, however, are required by that rule to wait until 90 days after the date of this prospectus before selling those shares pursuant to Rule 701 and are subject to the lock-up and market standoff agreements described above.

Form S-8 registration statement

In connection with this offering, we intend to file a registration statement on Form S-8 under the Securities Act covering all of the shares of our common stock subject to outstanding options and the shares of our common stock reserved for issuance under our stock plans. We expect to file this registration statement as soon as permitted under the Securities Act. However, the shares registered on Form S-8 may be subject to the volume limitations and the manner of sale, notice and public information requirements of Rule 144 and will not be eligible for resale until expiration of the lock-up and market standoff agreements to which they are subject.

Registration rights

We have granted demand, piggyback and Form S-3 registration rights to certain of our stockholders to sell our common stock. Registration of the sale of these shares under the Securities Act would result in these shares becoming freely tradable without restriction under the Securities Act immediately upon the effectiveness of the registration, except for shares purchased by affiliates. For a further description of these rights, see the section entitled “Description of capital stock—Registration rights.”

Material U.S. federal income tax consequences to non-U.S. holders

The following summary describes the material U.S. federal income tax consequences of the acquisition, ownership and disposition of our common stock acquired in this offering by Non-U.S. Holders (as defined below). This discussion does not address all aspects of U.S. federal income taxes, does not discuss the potential application of the alternative minimum tax or Medicare contribution tax on net investment income and does not deal with state or local taxes, U.S. federal gift and estate tax laws, except to the limited extent provided below, or any non-U.S. tax consequences that may be relevant to Non-U.S. Holders in light of their particular circumstances.

Special rules different from those described below may apply to certain Non-U.S. Holders that are subject to special treatment under the Code, such as:

- insurance companies, banks and other financial institutions;
- tax-exempt organizations (including private foundations) and tax-qualified retirement plans;
- foreign governments and international organizations;
- broker-dealers and traders in securities;
- U.S. expatriates and certain former citizens or long-term residents of the United States;
- persons required for U.S. federal income tax purposes to conform the timing of income accruals to their financial statements under Section 451(b) of the Code;
- persons that own, or are deemed to own, more than 5% of our capital stock;
- “controlled foreign corporations,” “passive foreign investment companies” and corporations that accumulate earnings to avoid U.S. federal income tax;
- persons that hold our common stock as part of a “straddle,” “hedge,” “conversion transaction,” “synthetic security” or integrated investment or other risk reduction strategy;
- persons who do not hold our common stock as a capital asset within the meaning of Section 1221 of the Code (generally, for investment purposes); and
- partnerships and other pass-through entities, and investors in such pass-through entities (regardless of their places of organization or formation).

Such Non-U.S. Holders are urged to consult their own tax advisors to determine the U.S. federal, state, local and other tax consequences that may be relevant to them.

Furthermore, the discussion below is based upon the provisions of the Code, and U.S. Treasury Regulations, rulings and judicial decisions thereunder as of the date hereof, and such authorities may be repealed, revoked or modified, possibly retroactively, and are subject to differing interpretations which could result in U.S. federal income tax consequences different from those discussed below. We have not requested a ruling from the Internal Revenue Service, or the IRS, with respect to the statements made and the conclusions reached in the following summary, and there can be no assurance that the IRS will agree with such statements and conclusions or will not take a contrary position regarding the tax consequences described herein, or that any such contrary position would not be sustained by a court.

PERSONS CONSIDERING THE PURCHASE OF OUR COMMON STOCK PURSUANT TO THIS OFFERING SHOULD CONSULT THEIR OWN TAX ADVISORS CONCERNING THE U.S. FEDERAL INCOME TAX CONSEQUENCES OF

ACQUIRING, OWNING AND DISPOSING OF OUR COMMON STOCK IN LIGHT OF THEIR PARTICULAR SITUATIONS AS WELL AS ANY CONSEQUENCES ARISING UNDER THE LAWS OF ANY OTHER TAXING JURISDICTION, INCLUDING ANY STATE, LOCAL OR NON-U.S. TAX CONSEQUENCES OR ANY U.S. FEDERAL NON-INCOME TAX CONSEQUENCES, AND THE POSSIBLE APPLICATION OF TAX TREATIES.

For the purposes of this discussion, a “Non-U.S. Holder” is a beneficial owner of common stock that is not a U.S. Holder or a partnership for U.S. federal income tax purposes. A “U.S. Holder” means a beneficial owner of our common stock that is, for U.S. federal income tax purposes, (a) an individual citizen or resident of the United States, (b) a corporation (or other entity taxable as a corporation for U.S. federal income tax purposes), created or organized in or under the laws of the United States, any state thereof or the District of Columbia, (c) an estate the income of which is subject to U.S. federal income taxation regardless of its source, or (d) a trust if it (1) is subject to the primary supervision of a court within the United States and one or more U.S. persons (within the meaning of Section 7701(a)(30) of the Code) have the authority to control all substantial decisions of the trust or (2) has a valid election in effect under applicable U.S. Treasury Regulations to be treated as a U.S. person.

If you are an individual non-U.S. citizen, you may, in some cases, be deemed to be a resident alien (as opposed to a nonresident alien) by virtue of being present in the United States for at least 31 days in the calendar year and for an aggregate of at least 183 days during a three-year period ending in the current calendar year. Generally, for this purpose, all the days present in the current year, one-third of the days present in the immediately preceding year, and one-sixth of the days present in the second preceding year, are counted.

Resident aliens are generally subject to U.S. federal income tax as if they were U.S. citizens. Individuals who are uncertain of their status as resident or nonresident aliens for U.S. federal income tax purposes are urged to consult their own tax advisors regarding the U.S. federal income tax consequences of the ownership or disposition of our common stock.

Distributions

We do not expect to make any distributions on our common stock in the foreseeable future. If we do make distributions on our common stock, however, such distributions made to a Non-U.S. Holder of our common stock will constitute dividends for U.S. tax purposes to the extent paid out of our current or accumulated earnings and profits (as determined under U.S. federal income tax principles). Distributions in excess of our current and accumulated earnings and profits will constitute a return of capital that is applied against and reduces, but not below zero, a Non-U.S. Holder’s adjusted tax basis in our common stock. Any remaining excess will be treated as gain realized on the sale or exchange of our common stock as described below under the section entitled “—Gain on disposition of our common stock.”

Any distribution on our common stock that is treated as a dividend paid to a Non-U.S. Holder that is not effectively connected with the holder’s conduct of a trade or business in the United States will generally be subject to withholding tax at a 30% rate or such lower rate as may be specified by an applicable income tax treaty between the United States and the Non-U.S. Holder’s country of residence. To obtain a reduced rate of withholding under a treaty, a Non-U.S. Holder generally will be required to provide the applicable withholding agent with a properly executed IRS Form W-8BEN, IRS Form W-8BEN-E or other appropriate form, certifying the Non-U.S. Holder’s entitlement to benefits under that treaty. Such form must be provided prior to the payment of dividends and must be updated periodically. If a Non-U.S. Holder holds stock through a financial institution or other agent acting on the holder’s behalf, the holder will be required to provide appropriate documentation to such agent. The holder’s agent may then be required to provide certification to the applicable withholding agent, either directly or through other intermediaries. If you are eligible for a reduced rate of U.S. withholding tax under an income tax treaty, you should consult with your own tax advisor to determine if you are able to obtain a refund of any excess amounts withheld by timely filing an appropriate claim for a refund with the IRS.

We generally are not required to withhold tax on dividends paid to a Non-U.S. Holder that are effectively connected with the holder's conduct of a trade or business within the United States (and, if required by an applicable income tax treaty, are attributable to a permanent establishment that the holder maintains in the United States) if a properly executed IRS Form W-8ECI, stating that the dividends are so connected, is furnished to us (or, if stock is held through a financial institution or other agent, to the applicable withholding agent). In general, such effectively connected dividends will be subject to U.S. federal income tax on a net income basis at the regular graduated rates applicable to U.S. persons. A corporate Non-U.S. Holder receiving effectively connected dividends may also be subject to an additional "branch profits tax," which is imposed, under certain circumstances, at a rate of 30% (or such lower rate as may be specified by an applicable treaty) on the corporate Non-U.S. Holder's effectively connected earnings and profits, subject to certain adjustments.

See also the section below entitled "—Foreign accounts" for additional withholding rules that may apply to dividends paid to certain foreign financial institutions or non-financial foreign entities.

Gain on disposition of our common stock

Subject to the discussions below under the sections entitled "—Backup withholding and information reporting" and "—Foreign accounts," a Non-U.S. Holder generally will not be subject to U.S. federal income or withholding tax with respect to gain realized on a sale or other disposition of our common stock unless (a) the gain is effectively connected with a trade or business of the holder in the United States (and, if required by an applicable income tax treaty, is attributable to a permanent establishment that the holder maintains in the United States), (b) the Non-U.S. Holder is a nonresident alien individual and is present in the United States for 183 or more days in the taxable year of the disposition and certain other conditions are met, or (c) we are or have been a "United States real property holding corporation" within the meaning of Code Section 897(c)(2) at any time within the shorter of the five-year period preceding such disposition or the holder's holding period in the common stock.

If you are a Non-U.S. Holder described in (a) above, you will be required to pay tax on the net gain derived from the sale at the regular graduated U.S. federal income tax rates applicable to U.S. persons. Corporate Non-U.S. Holders described in (a) above may also be subject to the additional branch profits tax at a 30% rate or such lower rate as may be specified by an applicable income tax treaty. If you are an individual Non-U.S. Holder described in (b) above, you will be required to pay a flat 30% tax on the gain derived from the sale, which gain may be offset by U.S. source capital losses (even though you are not considered a resident of the United States), provided you have timely filed U.S. federal income tax returns with respect to such losses. With respect to (c) above, in general, we would be a United States real property holding corporation if U.S. real property interests as defined in the Code and the U.S. Treasury Regulations comprised (by fair market value) at least half of our worldwide real property interests plus our other assets used or held for use in a trade or business. We believe that we are not, and do not anticipate becoming, a United States real property holding corporation. However, there can be no assurance that we will not become a United States real property holding corporation in the future. Even if we are treated as a U.S. real property holding corporation, gain realized by a Non-U.S. Holder on a disposition of our common stock will not be subject to U.S. federal income tax so long as (1) the Non-U.S. Holder owned, directly, indirectly or constructively, no more than five percent of our common stock at all times within the shorter of (i) the five-year period preceding the disposition or (ii) the holder's holding period and (2) our common stock is regularly traded on an established securities market, such as Nasdaq. However, there can be no assurance that our common stock will qualify as regularly traded on an established securities market.

U.S. federal estate tax

The estates of nonresident alien individuals generally are subject to U.S. federal estate tax on property with a U.S. situs. Because we are a U.S. corporation, our common stock will be U.S. situs property and, therefore, will

be included in the taxable estate of a nonresident alien decedent, unless an applicable estate tax treaty between the United States and the decedent's country of residence provides otherwise. The terms "resident" and "nonresident" are defined differently for U.S. federal estate tax purposes than for U.S. federal income tax purposes. Investors are urged to consult their own tax advisors regarding the U.S. federal estate tax consequences of the ownership or disposition of our common stock.

Backup withholding and information reporting

Generally, we or certain financial middlemen must report information to the IRS with respect to any dividends we pay on our common stock including the amount of any such dividends, the name and address of the recipient, and the amount, if any, of tax withheld. A similar report is sent to the holder to whom any such dividends are paid. Pursuant to tax treaties or certain other agreements, the IRS may make its reports available to tax authorities in the recipient's country of residence.

Dividends paid by us (or our paying agents) to a Non-U.S. Holder may also be subject to U.S. backup withholding. U.S. backup withholding generally will not apply to a Non-U.S. Holder who provides a properly executed IRS Form W-8BEN or IRS Form W-8BEN-E, as applicable, or otherwise establishes an exemption, provided that the applicable withholding agent does not have actual knowledge or reason to know the holder is a U.S. person.

Under current U.S. federal income tax law, U.S. information reporting and backup withholding requirements generally will apply to the proceeds of a disposition of our common stock effected by or through a U.S. office of any broker, U.S. or non-U.S., unless the Non-U.S. Holder provides a properly executed IRS Form W-8BEN or IRS Form W-8BEN-E, as applicable, or otherwise meets documentary evidence requirements for establishing non-U.S. person status or otherwise establishes an exemption. Generally, U.S. information reporting and backup withholding requirements will not apply to a payment of disposition proceeds to a Non-U.S. Holder where the transaction is effected outside the United States through a non-U.S. office of a non-U.S. broker. Information reporting and backup withholding requirements may, however, apply to a payment of disposition proceeds if the broker has actual knowledge, or reason to know, that the holder is, in fact, a U.S. person. For information reporting purposes, certain brokers with substantial U.S. ownership or operations will generally be treated in a manner similar to U.S. brokers.

Backup withholding is not an additional tax. If backup withholding is applied to you, you should consult with your own tax advisor to determine whether you have overpaid your U.S. federal income tax, and whether you are able to obtain a tax refund or credit of the overpaid amount.

Foreign accounts

In addition, U.S. federal withholding taxes may apply under legislation common known as the Foreign Account Tax Compliance Act, or FATCA, on certain types of payments, including dividends paid to non-U.S. financial institutions and certain other non-U.S. entities. Specifically, a 30% withholding tax may be imposed on dividends on our common stock paid to a "foreign financial institution" or a "non-financial foreign entity" (each as defined in the Code), unless (1) the foreign financial institution agrees to undertake certain diligence and reporting obligations, (2) the non-financial foreign entity either certifies it does not have any "substantial United States owners" (as defined in the Code) or furnishes identifying information regarding each substantial United States owner, or (3) the foreign financial institution or non-financial foreign entity otherwise qualifies for an exemption from these rules. The 30% federal withholding tax described in this paragraph cannot be reduced under an income tax treaty with the United States. If the payee is a foreign financial institution and is subject to the diligence and reporting requirements in (1) above, it must enter into an agreement with the U.S. Department of the Treasury requiring, among other things, that it undertake to identify accounts held by certain "specified United States persons" or "United States-owned foreign entities" (each as defined in the

Code), annually report certain information about such accounts, and withhold 30% on certain payments to non-compliant foreign financial institutions and certain other account holders. Under proposed U.S. Treasury Regulations promulgated by the Treasury Department on December 13, 2018, which state that taxpayers may rely on the proposed Treasury Regulations until final Treasury Regulations are issued, this withholding tax will not apply to the gross proceeds from any sale or disposition of our common stock. Foreign financial institutions located in jurisdictions that have an intergovernmental agreement with the United States governing FATCA may be subject to different rules.

Prospective investors should consult their tax advisors regarding the potential application of withholding under FATCA to their investment in our common stock.

EACH PROSPECTIVE INVESTOR SHOULD CONSULT ITS OWN TAX ADVISOR REGARDING THE TAX CONSEQUENCES OF PURCHASING, HOLDING AND DISPOSING OF OUR COMMON STOCK, INCLUDING THE CONSEQUENCES OF ANY PROPOSED CHANGE IN APPLICABLE LAW, AS WELL AS TAX CONSEQUENCES ARISING UNDER ANY STATE, LOCAL, NON-U.S. OR U.S. FEDERAL NON-INCOME TAX LAWS SUCH AS ESTATE AND GIFT TAX.

Underwriting

We are offering the shares of common stock described in this prospectus through a number of underwriters. J.P. Morgan Securities LLC, Cowen and Company, LLC and Credit Suisse Securities (USA) LLC are acting as joint book-running managers of the offering and as representatives of the underwriters. We have entered into an underwriting agreement with the representatives. Subject to the terms and conditions of the underwriting agreement, we have agreed to sell to the underwriters, and each underwriter has severally agreed to purchase, at the initial public offering price less the underwriting discounts and commissions set forth on the cover page of this prospectus, the number of shares of common stock listed next to its name in the following table:

Name	Number of shares
J.P. Morgan Securities LLC	
Cowen and Company, LLC	
Credit Suisse Securities (USA) LLC	
Canaccord Genuity LLC	
Total	

The underwriters are committed to purchase all the common shares offered by us if they purchase any shares. The underwriting agreement also provides that if an underwriter defaults, the purchase commitments of non-defaulting underwriters may also be increased or the offering may be terminated.

The underwriters propose to offer the common shares directly to the public at the initial public offering price set forth on the cover page of this prospectus and to certain dealers at that price less a concession not in excess of $ per share. Any such dealers may resell shares to certain other brokers or dealers at a discount of up to $ per share from the initial public offering price. After the initial offering of the shares to the public, if all of the common shares are not sold at the initial public offering price, the underwriters may change the offering price and the other selling terms. Sales of shares made outside of the United States may be made by affiliates of the underwriters. The offering of shares by the underwriters is subject to receipt and acceptance and subject to the underwriters' right to reject any order in whole or in part.

The underwriters have an option to buy up to additional shares of common stock from us to cover sales of shares by the underwriters which exceed the number of shares specified in the table above. The underwriters have 30 days from the date of this prospectus to exercise this option to purchase additional shares. If any shares are purchased with this option to purchase additional shares, the underwriters will purchase shares in approximately the same proportion as shown in the table above. If any additional shares of common stock are purchased, the underwriters will offer the additional shares on the same terms as those on which the shares are being offered.

The underwriting fee is equal to the public offering price per share of common stock less the amount paid by the underwriters to us per share of common stock. The underwriting fee is $ per share. The following table shows the per share and total underwriting discounts and commissions to be paid to the underwriters assuming both no exercise and full exercise of the underwriters' option to purchase additional shares.

	Without option to purchase additional shares exercise	With full option to purchase additional shares exercise
Per Share	$	$
Total	$	$

We estimate that the total expenses of this offering, including registration, filing and listing fees, printing fees and legal and accounting expenses, but excluding the underwriting discounts and commissions, will be approximately $. We have agreed to reimburse the underwriters for expenses of up to $ related to clearance of this offering with the Financial Industry Regulatory Authority, or FINRA.

A prospectus in electronic format may be made available on the web sites maintained by one or more underwriters, or selling group members, if any, participating in this offering. The underwriters may agree to allocate a number of shares to underwriters and selling group members for sale to their online brokerage account holders. Internet distributions will be allocated by the representatives to underwriters and selling group members that may make Internet distributions on the same basis as other allocations.

We have agreed that we will not (i) offer, pledge, announce the intention to sell, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase or otherwise dispose of, directly or indirectly, or file with the SEC a registration statement under the Securities Act of 1933, as amended, or the Securities Act, relating to, any shares of our common stock or securities convertible into or exchangeable or exercisable for any shares of our common stock, or publicly disclose the intention to make any offer, sale, pledge, disposition or filing, or (ii) enter into any swap or other arrangement that transfers all or a portion of the economic consequences associated with the ownership of any shares of common stock or any such other securities (regardless of whether any of these transactions are to be settled by the delivery of shares of common stock or such other securities, in cash or otherwise), in each case without the prior written consent of J.P. Morgan Securities LLC for a period of 180 days after the date of this prospectus, other than the shares of our common stock to be sold hereunder and any shares of our common stock issued upon the exercise of options granted under our existing equity incentive plans.

Our directors, executive officers and shareholders have entered into lock-up agreements with the underwriters prior to the commencement of this offering pursuant to which each of these persons or entities, with limited exceptions, for a period of 180 days after the date of this prospectus, may not, without the prior written consent of J.P. Morgan Securities LLC, (1) offer, pledge, announce the intention to sell, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, or otherwise transfer or dispose of, directly or indirectly, any shares of our common stock or any securities convertible into or exercisable or exchangeable for our common stock (including, without limitation, common stock or such other securities which may be deemed to be beneficially owned by such directors, executive officers, managers and members in accordance with the rules and regulations of the SEC and securities which may be issued upon exercise of a stock option or warrant) or (2) enter into any swap or other agreement that transfers, in whole or in part, any of the economic consequences of ownership of the common stock or such other securities, whether any such transaction described in clause (1) or (2) above is to be settled by delivery of common stock or such other securities, in cash or otherwise, or (3) make any demand for or exercise any right with respect to the registration of any shares of our common stock or any security convertible into or exercisable or exchangeable for our common stock.

The restrictions described in the immediately preceding paragraph do not apply to, among other items, transfers or dispositions of shares of common stock:

- as a bona fide gift, including bona fide gifts to a charity or educational institution, or for bona fide estate planning purposes;
- to any trust for the direct or indirect benefit of the party subject to the lock-up restrictions or the immediate family of such person;
- to any corporation, partnership, limited liability company or other entity under the ownership of the party subject to the lock-up restrictions or the immediate family of such person;

- by will, other testamentary document or intestate succession to the legal representative, heir, beneficiary or a member of the immediate family of the party subject to the lockup restrictions;
- as distributions to partners, members or stockholders of the party subject to the lock-up restrictions; and
- as transfers to affiliates, investment funds or other entities controlled or managed by the party subject to the lock-up restrictions; and

provided that in the case of any transfer or distribution pursuant to the six subclauses above, (i) each transferee, donee or distributee shall sign and deliver a lock-up letter in the form executed by the party subject to the lock up restrictions and (ii) no filing or other public announcement under Section 16(a)of the Exchange Act of 1934, as amended, or the Exchange Act, shall be required or shall be voluntarily made during the restricted period (other than a filing on Form 5 or a required filing on a Schedule 13F or 13G);

- the transfer pursuant to a bona fide third-party tender offer, merger, consolidation or other similar transaction made to all holders of our common stock involving a change of control; provided that in the event such tender offer, merger, consolidation or other such transaction is not completed, the shares of our common stock shall remain subject to the lock-up restrictions;
- the exercise of outstanding warrants or options to purchase shares of common stock granted under any stock incentive plan or stock purchase plan of ours, provided that the underlying shares shall continue to be subject to the lock-up restrictions;
- the establishment of a trading plan pursuant to Rule 10b5-1 under the Exchange Act for the transfer of shares of common stock, provided that (i) such plan does not provide for the transfer of shares of common stock during the restricted period and (ii) no filing under the Exchange Act or other public announcement shall be required or voluntarily made by or on behalf of the party subject to the lock-up restrictions regarding the establishment of such plan;
- the transfer or disposition of shares of common stock acquired in this offering or on the open market following this offering, provided that no filing under the Exchange Act or other public announcement shall be required or voluntarily made in connection with such transfer or disposition during the restricted period (other than a required filing on a Schedule 13F or 13G);
- transfers or surrenders to us of shares of common stock pursuant to any contractual arrangement that provides us with an option to repurchase such shares in connection with the termination of the party subject to the lock-up's employment or service relationship with us, or pursuant to a right of first refusal with respect to transfers of such shares of common stock or other securities, or on a cashless or "net exercise" basis or to cover tax withholding obligations of the party subject to the lock-up, in connection with the vesting or exercise of such shares of common stock or other securities, provided that any filing under Section 16 of the Exchange Act shall clearly indicate in the footnotes thereto that the filing relates to such circumstances described above and no other public announcement shall be required or voluntarily made in connection with such transfers or surrenders; and
- transfers or dispositions of shares of common stock by operation of law pursuant to a qualified domestic order or in connection with a divorce settlement or other court order, provided that the recipient of such shares shall execute and deliver to J.P. Morgan Securities LLC a lock-up letter in the form executed by the party subject to the lock-up restrictions, provided, further that any filing under Section 16 of the Exchange Act shall clearly indicate in the footnotes that the filing relates to the circumstances described above and no other public announcement shall be required or voluntarily made in connection with such transfer or disposition.

We have agreed to indemnify the several underwriters against certain liabilities, including liabilities under the Securities Act.

We will apply to have our common stock approved for listing on Nasdaq under the symbol “STOK.”

In connection with this offering, the underwriters may engage in stabilizing transactions, which involves making bids for, purchasing and selling shares of common stock in the open market for the purpose of preventing or retarding a decline in the market price of the common stock while this offering is in progress. These stabilizing transactions may include making short sales of the common stock, which involves the sale by the underwriters of a greater number of shares of common stock than they are required to purchase in this offering, and purchasing shares of common stock on the open market to cover positions created by short sales. Short sales may be “covered” shorts, which are short positions in an amount not greater than the underwriters’ option to purchase additional shares referred to above, or may be “naked” shorts, which are short positions in excess of that amount. The underwriters may close out any covered short position either by exercising their option to purchase additional shares, in whole or in part, or by purchasing shares in the open market. In making this determination, the underwriters will consider, among other things, the price of shares available for purchase in the open market compared to the price at which the underwriters may purchase shares through the option to purchase additional shares. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the common stock in the open market that could adversely affect investors who purchase in this offering. To the extent that the underwriters create a naked short position, they will purchase shares in the open market to cover the position.

The underwriters have advised us that, pursuant to Regulation M of the Securities Act, they may also engage in other activities that stabilize, maintain or otherwise affect the price of the common stock, including the imposition of penalty bids. This means that if the representatives of the underwriters purchase common stock in the open market in stabilizing transactions or to cover short sales, the representatives can require the underwriters that sold those shares as part of this offering to repay the underwriting discount received by them.

These activities may have the effect of raising or maintaining the market price of the common stock or preventing or retarding a decline in the market price of the common stock, and, as a result, the price of the common stock may be higher than the price that otherwise might exist in the open market. If the underwriters commence these activities, they may discontinue them at any time. The underwriters may carry out these transactions on the Nasdaq in the over-the-counter market or otherwise.

Prior to this offering, there has been no public market for our common stock. The initial public offering price will be determined by negotiations between us and the representatives of the underwriters. In determining the initial public offering price, we and the representatives of the underwriters expect to consider a number of factors including:

- the information set forth in this prospectus and otherwise available to the underwriters;
- our prospects and the history and prospects for the industry in which we compete;
- an assessment of our management;
- our prospects for future earnings;
- the general condition of the securities markets at the time of this offering;
- the recent market prices of, and demand for, publicly traded common stock of generally comparable companies; and
- other factors deemed relevant by the underwriters and us.

Neither we nor the underwriters can assure investors that an active trading market will develop for our common shares, or that the shares will trade in the public market at or above the initial public offering price.

Other relationships

The underwriters and their respective affiliates are full service financial institutions engaged in various activities, which may include sales and trading, commercial and investment banking, advisory, investment management, investment research, principal investment, hedging, market making, brokerage and other financial and non-financial activities and services. Certain of the underwriters and their respective affiliates may in the future provide various commercial banking, financial advisory or investment banking advice or other services in the ordinary course of their business, for which they will receive customary fees and commissions. In addition, from time to time, certain of the underwriters and their respective affiliates, officers, directors and employees may effect transactions for their own account or the account of customers, and hold on behalf of themselves or their customers, long or short positions in our debt or equity securities or loans, and may do so in the future. The underwriters and their respective affiliates may also communicate independent investment recommendations, market color or trading ideas and/or publish or express independent research views in respect of our securities and may at any time hold, or recommend to clients that they should acquire, long and/or short positions in our securities.

Selling restrictions

General

Other than in the United States, no action has been taken by us or the underwriters that would permit a public offering of the securities offered by this prospectus in any jurisdiction where action for that purpose is required. The securities offered by this prospectus may not be offered or sold, directly or indirectly, nor may this prospectus or any other offering material or advertisements in connection with the offer and sale of any such securities be distributed or published in any jurisdiction, except under circumstances that will result in compliance with the applicable rules and regulations of that jurisdiction. Persons into whose possession this prospectus comes are advised to inform themselves about and to observe any restrictions relating to the offering and the distribution of this prospectus. This prospectus does not constitute an offer to sell or a solicitation of an offer to buy any securities offered by this prospectus in any jurisdiction in which such an offer or a solicitation is unlawful.

Canada

The shares may be sold only to purchasers purchasing, or deemed to be purchasing, as principal that are accredited investors, as defined in National Instrument 45-106 *Prospectus Exemptions* or subsection 73.3(1) of the *Securities Act* (Ontario), and are permitted clients, as defined in National Instrument 31-103 *Registration Requirements, Exemptions and Ongoing Registrant Obligations*. Any resale of the shares must be made in accordance with an exemption from, or in a transaction not subject to, the prospectus requirements of applicable securities laws.

Securities legislation in certain provinces or territories of Canada may provide a purchaser with remedies for rescission or damages if this prospectus (including any amendment thereto) contains a misrepresentation, provided that the remedies for rescission or damages are exercised by the purchaser within the time limit prescribed by the securities legislation of the purchaser's province or territory. The purchaser should refer to any applicable provisions of the securities legislation of the purchaser's province or territory for particulars of these rights or consult with a legal advisor.

Pursuant to section 3A.3 of National Instrument 33-105 *Underwriting Conflicts* (NI 33-105), the representatives are not required to comply with the disclosure requirements of NI 33-105 regarding underwriter conflicts of interest in connection with this offering.

European Economic Area

In relation to each Member State of the European Economic Area (each, a "Relevant Member State"), no offer of shares may be made to the public in that Relevant Member State other than:

A. to any legal entity which is a qualified investor as defined in the Prospectus Directive;

B. to fewer than 100 or, if the Relevant Member State has implemented the relevant provision of the 2010 PD Amending Directive, 150, natural or legal persons (other than qualified investors as defined in the Prospectus Directive), as permitted under the Prospectus Directive, subject to obtaining the prior consent of the representatives; or

C. in any other circumstances falling within Article 3(2) of the Prospectus Directive,

provided that no such offer of shares shall require the Company or the representatives to publish a prospectus pursuant to Article 3 of the Prospectus Directive or supplement a prospectus pursuant to Article 16 of the Prospectus Directive.

Each person in a Relevant Member State who initially acquires any shares or to whom any offer is made will be deemed to have represented, acknowledged and agreed that it is a "qualified investor" within the meaning of the law in that Relevant Member State implementing Article 2(1)(e) of the Prospectus Directive. In the case of any shares being offered to a financial intermediary as that term is used in Article 3(2) of the Prospectus Directive, each such financial intermediary will be deemed to have represented, acknowledged and agreed that the shares acquired by it in the offer have not been acquired on a non-discretionary basis on behalf of, nor have they been acquired with a view to their offer or resale to, persons in circumstances which may give rise to an offer of any shares to the public other than their offer or resale in a Relevant Member State to qualified investors as so defined or in circumstances in which the prior consent of the representatives has been obtained to each such proposed offer or resale.

The Company, the representatives and their affiliates will rely upon the truth and accuracy of the foregoing representations, acknowledgements and agreements.

This prospectus has been prepared on the basis that any offer of shares in any Relevant Member State will be made pursuant to an exemption under the Prospectus Directive from the requirement to publish a prospectus for offers of shares. Accordingly, any person making or intending to make an offer in that Relevant Member State of shares which are the subject of the offering contemplated in this prospectus may only do so in circumstances in which no obligation arises for the Company or any of the underwriters to publish a prospectus pursuant to Article 3 of the Prospectus Directive in relation to such offer. Neither the Company nor the underwriters have authorized, nor do they authorize, the making of any offer of shares in circumstances in which an obligation arises for the Company or the underwriters to publish a prospectus for such offer.

For the purpose of the above provisions, the expression "an offer to the public" in relation to any shares in any Relevant Member State means the communication in any form and by any means of sufficient information on the terms of the offer and the shares to be offered so as to enable an investor to decide to purchase or subscribe the shares, as the same may be varied in the Relevant Member State by any measure implementing the Prospectus Directive in the Relevant Member State and the expression "Prospectus Directive" means Directive 2003/71/EC (including the 2010 PD Amending Directive, to the extent implemented in the Relevant Member States) and includes any relevant implementing measure in the Relevant Member State and the expression "2010 PD Amending Directive" means Directive 2010/73/EU.

Hong Kong

The shares may not be offered or sold by means of any document other than (i) in circumstances that do not constitute an offer to the public within the meaning of the Companies Ordinance (Cap. 32, Laws of Hong Kong), or (ii) to "professional investors" within the meaning of the Securities and Futures Ordinance (Cap. 571, Laws of Hong Kong) and any rules made thereunder, or (iii) in other circumstances that do not result in the document being a "prospectus" within the meaning of the Companies Ordinance (Cap. 32, Laws of Hong Kong), and no advertisement, invitation or document relating to the shares may be issued or may be in the possession of any person for the purpose of issue (in each case whether in Hong Kong or elsewhere), which is directed at, or the contents of which are likely to be accessed or read by, the public in Hong Kong (except if permitted to do so under the laws of Hong Kong) other than with respect to shares that are or are intended to be disposed of only to persons outside Hong Kong or only to "professional investors" within the meaning of the Securities and Futures Ordinance (Cap. 571, Laws of Hong Kong) and any rules made thereunder.

Japan

The securities have not been and will not be registered under the Financial Instruments and Exchange Law of Japan, or the Financial Instruments and Exchange Law, and each underwriter has agreed that it will not offer or sell any securities, directly or indirectly, in Japan or to, or for the benefit of, any resident of Japan (which term, as used in this prospectus means any person resident in Japan, including any corporation or other entity organized under the laws of Japan) or to others for re-offering or resale, directly or indirectly, in Japan or to a resident of Japan, except pursuant to an exemption from the registration requirements of, and otherwise in compliance with, the Financial Instruments and Exchange Law and any other applicable laws, regulations and ministerial guidelines of Japan.

Singapore

This prospectus has not been registered as a prospectus with the Monetary Authority of Singapore. Accordingly, this prospectus and any other document or material in connection with the offer or sale, or invitation for subscription or purchase, of the shares may not be circulated or distributed, nor may the shares be offered or sold, or be made the subject of an invitation for subscription or purchase, whether directly or indirectly, to persons in Singapore other than (i) to an institutional investor under Section 274 of the Securities and Futures Act, Chapter 289 of Singapore, or the SFA, (ii) to a relevant person, or any person pursuant to Section 275(1A), and in accordance with the conditions specified in Section 275 of the SFA or (iii) otherwise pursuant to, and in accordance with the conditions of, any other applicable provision of the SFA.

Where the shares are subscribed or purchased under Section 275 by a relevant person that is: (a) a corporation (which is not an accredited investor) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor; or (b) a trust (where the trustee is not an accredited investor) whose sole purpose is to hold investments and each beneficiary is an accredited investor, shares, debentures and units of shares and debentures of that corporation or the beneficiaries' rights and interest in that trust shall not be transferable for six months after that corporation or that trust has acquired the shares under Section 275 except: (1) to an institutional investor under Section 274 of the SFA or to a relevant person, or any person pursuant to Section 275(1A), and in accordance with the conditions specified in Section 275 of the SFA; (2) where no consideration is given for the transfer; or (3) by operation of law.

Switzerland

The shares may not be publicly offered in Switzerland and will not be listed on the SIX Swiss Exchange, or SIX, or on any other stock exchange or regulated trading facility in Switzerland. This document has been prepared

without regard to the disclosure standards for issuance prospectuses under art. 652a or art. 1156 of the Swiss Code of Obligations or the disclosure standards for listing prospectuses under art. 27 ff. of the SIX Listing Rules or the listing rules of any other stock exchange or regulated trading facility in Switzerland. Neither this document, nor any other offering or marketing material relating to the shares or this offering, may be publicly distributed or otherwise made publicly available in Switzerland. Neither this document nor any other offering or marketing material relating to this offering, the Company, or the shares has been or will be filed with or approved by any Swiss regulatory authority. In particular, this document will not be filed with, and the offer of shares will not be supervised by, the Swiss Financial Market Supervisory Authority FINMA, or FINMA, and the offer of shares has not been and will not be authorized under the Swiss Federal Act on Collective Investment Schemes, or CISA. The investor protection afforded to acquirers of interests in collective investment schemes under the CISA does not extend to acquirers of shares.

United Arab Emirates

This prospectus relates to an Exempt Offer in accordance with the Offered Securities Rules of the Dubai Financial Services Authority, or DFSA. This prospectus is intended for distribution only to persons of a type specified in the Offered Securities Rules of the DFSA. It must not be delivered to, or relied on by, any other person. The DFSA has no responsibility for reviewing or verifying any documents in connection with Exempt Offers. The DFSA has not approved this prospectus nor taken steps to verify the information set forth herein and has no responsibility for this prospectus. The shares to which this prospectus relates may be illiquid and/or subject to restrictions on their resale. Prospective purchasers of the shares offered should conduct their own due diligence on the shares. If you do not understand the contents of this prospectus, you should consult an authorized financial advisor.

United Kingdom

This document is being distributed only to, and is directed only at, and any offer subsequently made may only be directed at persons who are “qualified investors” (as defined in the Prospectus Directive) (i) who have professional experience in matters relating to investments falling within Article 19 (5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005, as amended (the “Order”) and/or (ii) who are high net worth companies (or persons to whom it may otherwise be lawfully communicated) falling within Article 49 (2) (a) to (d) of the Order (all such persons together being referred to as “relevant persons”).

Any person in the United Kingdom that is not a relevant person should not act or rely on the information included in this document or use it as basis for taking any action. In the United Kingdom, any investment or investment activity that this document relates to may be made or taken exclusively by relevant persons. Any person in the United Kingdom that is not a relevant person should not act or rely on this document or any of its contents.

Legal matters

The validity of the shares of common stock offered by this prospectus will be passed upon for us by Fenwick & West LLP, San Francisco, California. Certain legal matters relating to the offering will be passed upon for the underwriters by Davis Polk & Wardwell LLP, New York, New York. Fenwick & West LLP beneficially owns an aggregate of 25,125 shares of our common stock.

Experts

The consolidated financial statements of Stoke Therapeutics, Inc. as of December 31, 2018 and 2017, and for each of the years in the two-year period ended December 31, 2018, have been included herein and in the registration statement in reliance upon the report of KPMG LLP, an independent registered public accounting firm, appearing elsewhere herein, and upon the authority of said firm as experts in accounting and auditing.

Where you can find additional information

We have filed with the SEC a registration statement on Form S-1 under the Securities Act of 1933, as amended, with respect to the shares of common stock offered hereby. This prospectus, which constitutes a part of the registration statement, does not contain all of the information set forth in the registration statement or the exhibits filed therewith. For further information about us and the common stock offered hereby, reference is made to the registration statement and the exhibits filed therewith. Statements contained in this prospectus concerning the contents of any contract or any other document are not necessarily complete. If a contract or document has been filed as an exhibit to the registration statement, please see the copy of the contract or document that has been filed for the complete contents of that contract or document. Each statement in this prospectus relating to a contract or document filed as an exhibit is qualified in all respects by the filed exhibit. The exhibits to the registration statement should be reviewed for the complete contents of these contracts and documents.

We currently do not file periodic reports with the SEC. Upon the completion of this offering, we will be required to file periodic reports, proxy statements and other information with the SEC pursuant to the Securities Exchange Act of 1934, as amended. The SEC maintains a website that contains reports, proxy and information statements and other information regarding registrants that file electronically with the SEC. The address of the website is www.sec.gov.

We also maintain a website at www.stoketherapeutics.com. Upon completion of this offering, you may access these materials at our website free of charge as soon as reasonably practicable after they are electronically filed with, or furnished to, the SEC. The information contained in, or that can be accessed through, our website is not part of, and is not incorporated into, this prospectus.

Index to 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 (together, the Company) as of December 31, 2018 and 2017, the related consolidated statements of operations, stockholders' equity (deficit), and cash flows for each of the years in the two-year period ended December 31, 2018, 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, 2018 and 2017, and the results of its operations and its cash flows for each of the years in the two-year period ended December 31, 2018, 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 and in accordance with auditing standards generally accepted in the United States of America. 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, MA
March 26, 2019

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

	As of December 31,	
	2018	**2017**
Assets		
Current assets:		
Cash and cash equivalents	$105,399	$ 1,797
Prepaid expenses and other current assets	548	113
Interest receivable	196	—
Total current assets	106,143	1,910
Restricted cash	204	56
Property and equipment, net	1,192	473
Total assets	$107,539	$ 2,439
Liabilities and stockholders' equity (deficit)		
Current liabilities:		
Accounts payable	$ 1,071	$ 141
Accrued and other current liabilities	1,396	574
Simple agreement for future equity	—	3,000
Total current liabilities	2,467	3,715
Long term liabilities	4	16
Total liabilities	2,471	3,731
Commitments and contingencies (Note 7)		
Stockholders' equity (deficit)		
Convertible Preferred Stock, par value of $0.0001 per share; 225,584,874 and 59,575,576 shares authorized, 225,584,874 and 49,540,132 shares issued and outstanding as of December 31, 2018 and 2017, respectively; aggregate liquidation preference of $130,850 at December 31, 2018	23	5
Common stock, par value of $0.0001 per share; 278,527,249 and 79,000,000 shares authorized, 7,236,019 and 6,665,733 shares issued and outstanding as of December 31, 2018 and 2017, respectively	1	1
Additional paid-in capital	130,754	11,891
Accumulated deficit	(25,710)	(13,189)
Total stockholders' equity (deficit)	105,068	(1,292)
Total liabilities and stockholders' equity (deficit)	$107,539	$ 2,439

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

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

	Year Ended December 31,	
	2018	**2017**
Revenue	$ —	$ —
Operating expenses:		
Research and development	8,371	3,598
General and administrative	4,410	1,956
Total operating expenses	12,781	5,554
Loss from operations	(12,781)	(5,554)
Other income (expense):		
Interest income	270	—
Other expense, net	(10)	(4)
Total other income (expense)	260	(4)
Net loss	(12,521)	$ (5,558)
Net loss per share attributable to common stockholders—basic and diluted	$ (1.77)	$ (0.83)
Weighted average common shares outstanding—basic and diluted	7,056,159	6,665,733

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				
	Shares	Amount	Shares	Amount	Additional paid-in capital	Accumulated deficit	Stockholders' equity (Deficit)
Balance as of December 31, 2016	36,998,326	$ 4	6,665,733	$ 1	$ 8,891	$ (7,631)	$ 1,265
Stock-based compensation	—	—	—	—	26	—	26
Issuance of convertible Preferred Stock, net of issuance costs of $25	12,541,806	1	—	—	2,974	—	2,975
Net loss	—	—	—	—	—	(5,558)	(5,558)
Balance as of December 31, 2017	49,540,132	5	6,665,733	1	11,891	(13,189)	(1,292)
Stock-based compensation	—	—	—	—	240	—	240
Issuance of common stock	—	—	570,286	—	19	—	19
Issuance of convertible Preferred Stock, net of issuance costs of $378	176,044,742	18	—	—	118,604	—	118,622
Net loss	—	—	—	—	—	(12,521)	(12,521)
Balance as of December 31, 2018	225,584,874	$ 23	7,236,019	$ 1	$ 130,754	$ (25,710)	$ 105,068

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,	
	2018	**2017**
Cash flows from operating activities:	$ (12,521)	$(5,558)
Net loss		
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation	214	113
Stock-based compensation	240	26
Loss on disposal of property and equipment	10	4
Changes in assets and liabilities:		
Prepaid expenses and other current assets	(632)	(72)
Accounts payable and accrued liabilities	1,735	100
Deferred rent	(10)	3
Net cash used in operating activities	(10,964)	(5,384)
Cash flows from investing activities:		
Purchases of property and equipment	(935)	(113)
Proceeds from sale of property and equipment	10	—
Net cash used in investing activities	(925)	(113)
Cash flows from financing activities:		
Proceeds from simple agreement for future equity	—	3,000
Proceeds from issuance of convertible Preferred Stock	116,000	3,000
Preferred Stock issuance costs	(378)	(25)
Proceeds from the issuance of common stock	19	—
Other	(2)	(1)
Net cash provided by financing activities	115,639	5,974
Net increase in cash, cash equivalents and restricted cash	103,750	477
Cash, cash equivalents and restricted cash—beginning of year	1,853	1,376
Cash, cash equivalents and restricted cash—end of year	$105,603	$ 1,853
Supplemental disclosure of non-cash investing and financing activities:		
Property and equipment included in accrued expenses and accounts payable	$ 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 subsidiaries
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.

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 as of and for the year ended December 31, 2018, 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 future viability of the Company beyond that date is dependent on its ability to raise additional capital to finance its operations.

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 generally accepted accounting principles (GAAP), and include the accounts of Stoke Therapeutics, Inc. and its wholly-owned subsidiary. All intercompany transactions between and among 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 our 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 account and money market accounts.

Restricted cash

At December 31, 2018, restricted cash consisted of money market accounts collateralizing a letter of credit issued as a security deposit in connection with the Company's lease 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,	
	2018	**2017**
Cash and cash equivalents	$ 105,399	1,797
Restricted cash	204	56
	$ 105,603	1,853

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

Accounting Standards Codification (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 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.

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. 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, 2018 and 2017.

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.

Rent expense

The Company's real estate operating lease provides 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 lease. 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, 2018 and 2017, 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 reduces 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 this offering, (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 2016-02, *Leases* (Topic 842), with guidance regarding the accounting for and disclosure of leases. The update requires lessees to recognize all leases, including operating leases, with a term greater than 12 months on the consolidated balance sheet. This update also requires lessees and lessors to disclose key information about their leasing transactions. This guidance will be effective for public companies for annual and interim periods beginning after December 15, 2018. For all other entities, this standard is effective for annual reporting periods beginning after December 15, 2019, and interim periods within annual periods beginning after December 15, 2020. The Company will adopt this standard on January 1, 2020. While the Company expects the implementation of ASU 2016-02 to result in the recognition of right-of-use assets and lease liabilities for leased facilities, the Company is still evaluating the impact that the adoption of ASU 2016-2 will have on its consolidated financial statements.

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.

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

There were no assets or liabilities carried at fair value on a recurring basis as of December 31, 2018. As of December 31, 2017, the Company had a $3,000 Simple Agreement for Future Equity (SAFE) obligation, which represents a Level 3 measurement within the fair value hierarchy.

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, 2018			
	Level 1	**Level 2**	**Level 3**	**Total**
Cash equivalents:				
Money market funds	$105,399	$ —	$ —	$105,399
Total	$105,399	$ —	$ —	$105,399

	Fair value measurements as of December 31, 2017			
	Level 1	**Level 2**	**Level 3**	**Total**
Cash equivalents:				
Money market funds	$ 1,797	$ —	$ —	$1,797
Total	$ 1,797	$ —	$ —	$1,797
Debt:				
Simple agreement for future equity	$ —	$ —	$ 3,000	$3,000
Total	$ —	$ —	$ 3,000	$3,000

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, 2018 and 2017.

The following table presents a roll-forward of the fair value of the SAFE for which fair value is determined by Level 3 inputs:

Balance as of January 1, 2017	$ —
Initial fair value	3,000
Fair value adjustment	—
Balance as of December 31, 2017	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 7,839,038 Preferred Stock received ($3,000). Given the proximity of the conversion of the SAFE to the financial reporting period end, the fair value of the SAFE as of December 31, 2017 was also determined to be equal to the fair value of the Preferred Stock, of $3,000, received on conversion.

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,	
	2018	2017
Laboratory equipment	$ 1,485	$ 583
Furniture and fixtures	—	20
Leasehold improvements	—	5
Office equipment	70	37
Construction in progress	16	—
	1,571	645
Less accumulated depreciation	(379)	(172)
	$ 1,192	$ 473

Depreciation expense was $214 and $113 for the years ended December 31, 2018 and 2017, respectively.

5. Accrued and other current liabilities

Accrued and other current liabilities consisted of the following:

	As of December 31,	
	2018	2017
Accrued employee compensation costs	$ 901	$ 382
Accrued professional	200	102
Accrued research and development costs	234	70
Accrued other	61	20
	$ 1,396	$ 574

6. Simple agreement for future equity

In October 2017, the Company entered into a simple agreement for future equity (the SAFE) with an investor, receiving $3,000 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). Issue costs of $21 related to the SAFE were recorded as a general and administrative expense for the year ended December 31, 2017 in the accompanying consolidated statements of operations. 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 7,839,038 shares of Series A-2 convertible Preferred Stock (Series A-2 Preferred).

7. Commitments and contingencies

Operating lease

In December 2015, the Company entered into an agreement to lease its facility under a non-cancellable operating lease that expires December 2019. The lease includes two renewal options, each for five-year terms and at fair market value upon exercise. The lease contains escalating rent clauses which require higher rent payments in future years. The Company expenses rent on a straight-line basis over the term of the lease. The lease was terminated by the Company, effective December 31, 2018, without early termination fees or any additional obligation to the landlord.

In August 2018, the Company entered into an agreement to sublease approximately 23,000 square feet of space for a term of three years. Lease terms are triple net lease commencing at $886 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 $231 per annum, with 2.5% annual base rent increases plus operating expenses, real estate taxes, utilities and janitorial fees. The Company expects to occupy this space in the first half of 2019.

As of December 31, 2018, the future minimum payments for operating leases are as follows:

2019	$1,051
2020	1,149
2021	1,102
2022	71
2023	—
Thereafter	—
	$3,373

Rent expense incurred under operating leases was approximately $326 and $235 for the years ended December 31, 2018 and 2017, 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 made payments of $100 in each of the years ended December 31, 2018 and 2017, respectively, for such consulting services. The initial term of this agreement was five years and may be 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 1,640,608 shares of common stock valued based on an independent appraisal at approximately $65. 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 low double-digit percentage of the sublicense revenue to CSHL, which may be reduced to a low double-digit 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 $10, which amount is creditable against any owed royalty or milestone payments. The maximum aggregate potential milestone payments payable total approximately $900. 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, 2018 and 2017.

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 55 pounds sterling (approximately $72 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 400 pounds sterling (approximately $508 as of December 31, 2018). As of December 31, 2018, and 2017, the Company has recorded no liabilities under the Southampton Agreement.

Sponsored research agreement

In December 2017, the Company entered into a sponsored research agreement with the University of Michigan (the University of Michigan Agreement) to fund research conducted at the University of Michigan through November 2018. The budget for the scope of work described in the research agreement was $428. In December 2018, the University of Michigan Agreement was renewed and extended through November 2020 with a budget for the scope of work of $624. The costs incurred by the Company under the University of Michigan Agreement are recorded as research and development expense and expensed in the period in which they are incurred. Research and development spending under the University of Michigan Agreement was $428 and $12 for years ended December 31, 2018 and 2017, respectively.

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, 2018, 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 225,584,874 shares of $0.0001 par value convertible preferred stock, 49,540,132 are designated Series A convertible preferred stock (Series A Preferred), 75,777,370 are designated Series A-2 Preferred and 100,267,372 are designated Series B convertible preferred stock (Series B Preferred) (collectively, the Preferred Stock). 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, January 1, 2017	36,998,326	$ 8,750	—	$ —	—	$ —	36,998,326	$ 8,750
Issuance, net of issuance costs of $25	12,541,806	2,975	—	—	—	—	12,541,806	2,975
Balance, December 31, 2017	49,540,132	11,725	—	—	—	—	49,540,132	11,725
Issuance upon conversion of SAFE	—	—	7,839,038	3,000	—	—	7,839,038	3,000
Issuance, net of issuance costs of $120	—	—	67,938,332	25,880	—	—	67,938,332	25,880
Issuance, net of issuance costs of $258	—	—	—	—	100,267,372	89,742	100,267,372	89,742
Balance, December 31, 2018	49,540,132	$ 11,725	75,777,370	$ 28,880	100,267,372	$ 89,742	225,584,874	$ 130,347

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 $0.8976 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, $0.2392 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 $0.3827 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 unless elected otherwise by the requisite holders of Preferred Stock.

9. Common stock

In June 2014, the Company issued 5,000,000 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. Vested shares as of December 31, 2018 and 2017 were 5,000,000 and 4,444,444 shares, respectively. In July 2015, the Company issued 1,640,608 shares of common stock to CSHL in exchange for an exclusive license to a patent (Note 7).

The holders of record of the shares of common stock, exclusively and as a separate class, shall be entitled to elect two directors of the Company. The holders of the common stock and one Preferred Stock investor, voting together as a single class on an as-if-converted basis, shall be entitled to elect two directors and the holders of the common stock and the Preferred Stock, voting together as a single class on an as-if-converted basis, shall be entitled to elect one director.

10. 2014 equity incentive plan

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 6,756,555 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 45,706,365 shares.

In 2016, the Company granted options to purchase 5,087,712 shares of common stock to certain of its employees, and directors. The options vest over three to four years and are exercisable at a per share price equal to the fair value of the common stock on the grant date.

In 2017, the Company granted options to purchase 1,427,379 shares of common stock to certain of its employees and directors. The options vest over four years and are exercisable at a per share price equal to the fair value of the common stock on the grant date.

In 2018, the Company granted options to purchase 29,536,111 shares of common stock to certain of its employees, and directors. The options vest over four years and are exercisable at a per share price equal to the fair value of the common stock on the grant date.

As of December 31, 2018, there were 11,042,826 shares available for future issuance under the 2014 Plan.

As there is not a public market for the Company's common stock, the Company has determined the volatility for options granted in 2017 based on a study of reported data for a guideline group of companies that issued options with substantially similar terms. The risk-free interest rate is based on a zero-coupon United States Treasury instrument with terms consistent with the expected life of the stock options. The Company has not paid and does not anticipate paying cash dividends on shares of common stock; therefore, the expected dividend yield is assumed to be zero.

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

	Number of shares	Weighted average exercise price	Weighted average remaining contractual life (years)	Aggregate intrinsic value[1]
Outstanding as of December 31, 2016	4,993,022	$ 0.04	9.1	$ —
Granted	1,427,379	0.04		
Forfeited or expired	(596,644)	0.04		
Outstanding as of December 31, 2017	5,823,757	0.04	8.0	—
Granted	29,536,111	0.13		
Exercised	(570,286)	0.04		
Forfeited or expired	(126,052)	0.04		
Outstanding as of December 31, 2018	34,663,530	0.12	8.9	3,436
Exercisable as of December 31, 2018	8,867,025	0.06	8.1	1,437

(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, 2018 and 2017.

The weighted average grant date fair value per share of stock options granted during the years ended December 31, 2018 and 2017 was $0.08 and $0.04, respectively. The aggregate intrinsic value of stock options exercised during the year ended December 31, 2018 was $100.

The aggregate grant date fair value of stock options granted during the years ended December 31, 2018 and 2017 was approximately $2,335 and $57, respectively.

Stock-based compensation

The Company recorded stock-based compensation expense of $240 and $26 during the years ended December 31, 2018 and 2017, respectively. As of December 31, 2018, there was $1,986 of unrecognized compensation cost related to unvested stock-based compensation arrangements granted under the 2014 Plan.

The compensation is expected to be recognized over a weighted average period of 4 years as of December 31, 2018.

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,	
	2018	2017
Research and development	$ 117	$ 7
General and administrative	123	19
	$ 240	$ 26

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 year ended December 31, 2018:

	Year ended December 31,	
	2018	2017
Risk-free interest rate	2.67%—2.84%	2.27%
Expected dividend yield	0%	0%
Expected life	6.25—6.375 years	6.25—6.375 years
Expected volatility	57%—60%	65%

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,	
	2018	2017
Numerator:		
Net loss	$ (12,521)	$ (5,558)
Denominator:		
Weighted-average number of common shares, basic and diluted	7,056,159	6,665,733
Net loss per common share attributable to common stockholders, basic and diluted	$ (1.77)	$ (0.83)

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:

	Year ended December 31,	
	2018	2017
Preferred Stock	225,584,874	49,540,132
Options to purchase common stock	34,663,530	5,823,757
	260,248,404	55,363,889

12. Income taxes

Among other provisions, the TCJA reduces the historical U.S. federal corporate income tax rate from a top rate of 35% to a newly enacted flat rate of 21% beginning January 1, 2018. At the date the new legislation is enacted, under ASC 740, *Income Taxes*, the Company is required to recognize the effects of the change in tax law and rates on its deferred tax assets and liabilities as a charge to income tax expense. As a result of the above TCJA and the revaluation of deferred tax assets and liabilities at December 31, 2017, the Company recognized a decrease in its deferred tax assets of $1,506. This reduction in the Company's deferred tax assets has been offset by a coinciding reduction in the associated valuation allowance, resulting in no additional tax expense.

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,	
	2018	2017
Expected income tax benefit at the federal statutory rate	21.0	34.0
State income taxes, net of federal benefit	6.2	5.0
Non-deductible items	(0.3)	(1.7)
Research and development credit, net	0.9	6.7
Tax rate reductions due to the TCJA	0.0	(27.2)
Other	0.1	0.0
Change in valuation allowance	(27.9)	(16.8)
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,	
	2018	2017
Deferred tax assets:		
Federal and state net operating loss carryforwards	$ 6,637	$ 3,380
Research and development tax credits	778	654
Other	210	92
Gross deferred tax assets	7,625	4,126
Less: valuation allowance	(7,625)	(4,126)
Net deferred tax assets	$ —	$ —

As of December 31, 2018 and 2017, the Company had federal net operating loss carryforwards of $24,372 and $12,476, 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, 2018 and 2017, the Company had state net operating loss carry forwards of $24,030 and $12,293, respectively, which may be available to reduce future taxable income and expire at various dates beginning in 2034. In addition, at December 31, 2018 and 2017, the Company had federal research and development tax credit carryforwards of $443 and $172, respectively, and state research and development tax credit carry forwards of $425 and $241, 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 $7,625 and $4,126 was established at December 31, 2018 and 2017, respectively. The change in the valuation allowance was an increase of $3,499 and $932 in 2018 and 2017, 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, 2018, and 2017 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.

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, 2018 and 2017.

14. Subsequent events

The Company has evaluated subsequent events through the issuance date of these consolidated financial statements.

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shares

Common stock

Prospectus

J.P. Morgan

Cowen

Credit Suisse

Canaccord Genuity

, 2019

PART II

Information not required in prospectus

Item 13. Other expenses of issuance and distribution.

The following table sets forth all costs and expenses, other than underwriting discounts and commissions, paid or payable by the Registrant in connection with the sale of the common stock being registered. All amounts shown are estimates except for the SEC registration fee, the FINRA filing fee and the Nasdaq listing fee:

	Amount paid or to be paid
SEC registration fee	$ *
FINRA filing fee	15,500
Nasdaq listing fee	*
Printing and engraving expenses	*
Legal fees, Blue Sky fees and expenses	*
Accounting fees and expenses	*
Transfer agent and registrar fees and expenses	*
Miscellaneous expenses	*
Total	$ *

* To be completed by amendment.

Item 14. Indemnification of directors and officers.

Section 145 of the Delaware General Corporation Law, or DGCL, authorizes a court to award, or a corporation's board of directors to grant, indemnity to directors and officers under certain circumstances and subject to certain limitations. The terms of Section 145 of the DGCL are sufficiently broad to permit indemnification under certain circumstances for liabilities, including reimbursement of expenses incurred, arising under the Securities Act of 1933, as amended, or the Securities Act.

As permitted by the DGCL, the Registrant's restated certificate of incorporation to be effective in connection with the completion of this offering contains provisions that eliminate the personal liability of its directors for monetary damages for any breach of fiduciary duties as a director, except liability for the following:

- any breach of the director's duty of loyalty to the Registrant or its stockholders;
- acts or omissions not in good faith or that involve intentional misconduct or a knowing violation of law;
- under Section 174 of the DGCL (regarding unlawful dividends and stock purchases); or
- any transaction from which the director derived an improper personal benefit.

As permitted by the DGCL, the Registrant's restated bylaws to be effective in connection with the completion of this offering, provide that:

- the Registrant is required to indemnify its directors and executive officers to the fullest extent permitted by the DGCL, subject to limited exceptions;
- the Registrant may indemnify its other employees and agents as set forth in the DGCL;

- the Registrant is required to advance expenses, as incurred, to its directors and executive officers in connection with a legal proceeding to the fullest extent permitted by the DGCL, subject to limited exceptions; and
- the rights conferred in the restated bylaws are not exclusive.

Prior to the completion of this offering, the Registrant intends to enter into indemnification agreements with each of its current directors and executive officers to provide these directors and executive officers additional contractual assurances regarding the scope of the indemnification set forth in the Registrant's restated certificate of incorporation and restated bylaws and to provide additional procedural protections. There is no pending litigation or proceeding involving a director or executive officer of the Registrant for which indemnification is sought. Reference is also made to the underwriting agreement to be filed as Exhibit 1.1 to this registration statement, which provides for the indemnification of executive officers, directors and controlling persons of the Registrant against certain liabilities. The indemnification provisions in the Registrant's restated certificate of incorporation, restated bylaws and the indemnification agreements entered into or to be entered into between the Registrant and each of its directors and executive officers may be sufficiently broad to permit indemnification of the Registrant's directors and executive officers for liabilities arising under the Securities Act.

The Registrant has directors' and officers' liability insurance for securities matters.

Item 15. Recent sales of unregistered securities.

The following lists set forth information regarding all securities sold or granted by the Registrant from April 26, 2016 through April 26, 2019 that were not registered under the Securities Act, and the consideration, if any, received by the Registrant for such securities:

(a) Stock Option Grants

From April 26, 2016 through April 26, 2019, the Registrant has granted to its employees, directors, consultants and other service providers options to purchase an aggregate of 38,093,234 shares of common stock under its 2014 Equity Incentive Plan, or 2014 Plan, with exercise prices ranging from $0.04 to $0.45 per share.

From April 26, 2016 through April 26, 2019, employees, directors, consultants and other service providers of the Registrant exercised options granted under the 2014 Plan for an aggregate of 2,384,224 shares of common stock with exercise prices ranging from $0.04 to $0.22 per share for an aggregate exercise price of $113,141.

(b) Preferred Stock

In July 2016, the Registrant issued and sold an aggregate of 12,541,806 additional shares of Series A convertible preferred stock, at a purchase price of $0.2392 per share, for an aggregate purchase price of approximately $3 million. In February 2017, we sold an aggregate of 12,541,806 additional shares of our Series A convertible preferred stock, at a purchase price of $0.2392 per share, for an aggregate purchase price of approximately $3 million. Upon the completion of this offering, these shares of Series A convertible preferred stock will convert into 25,083,612 shares of common stock.

Between January and September 2018, the Registrant issued and sold to an investor an aggregate of 75,777,370 shares of Series A-2 convertible preferred stock, at a purchase price of $0.3827 per share, for an aggregate purchase price of $29,000,000. Upon the completion of this offering, these shares of Series A-2 convertible preferred stock will convert into 75,777,370 shares of common stock.

On October 22, 2018, the Registrant issued and sold to 14 investors an aggregate of 100,267,372 shares of Series B convertible preferred stock, at a purchase price of $0.8976 per share, for an aggregate purchase price of $89,999,994. Upon the completion of this offering, these shares of Series B convertible preferred stock will convert into 100,267,372 shares of common stock.

(c) Simple Agreement for Future Equity

In October 2017, we issued rights to purchase certain shares of our capital stock at a purchase price of $3,000,000, or Purchase Amount, pursuant to a Simple Agreement for Future Equity, or SAFE. The entire Purchase Amount and all other obligations under the SAFE converted into 7,839,038 shares of our Series A-2 convertible preferred stock in January 2018.

Unless otherwise stated, the sales of the above securities were deemed to be exempt from registration under the Securities Act in reliance on Section 4(a)(2) of the Securities Act (or Regulation D or Regulation S promulgated thereunder), or Rule 701 promulgated under Section 3(b) of the Securities Act, as transactions by an issuer not involving any public offering or pursuant to benefit plans and contracts relating to compensation as provided under Rule 701. The recipients of the securities in each of these transactions represented their intentions to acquire the securities for investment only and not with a view to or for sale in connection with any distribution thereof, and appropriate legends were placed on the stock certificates issued in each of the foregoing transactions.

None of the foregoing transactions involved any underwriters, underwriting discounts or commissions or any public offering, and the Registrant believes each transaction was exempt from the registration requirements of the Securities Act as stated above. All recipients of the foregoing transactions either received adequate information about the Registrant or had access, through their relationships with the Registrant, to such information. Furthermore, the Registrant affixed appropriate legends to the share certificates and instruments issued in each foregoing transaction setting forth that the securities had not been registered and the applicable restrictions on transfer.

Item 16. Exhibits and financial statement schedules.

(a) Exhibits.

Exhibit Number	Description of document
1.1*	Form of Underwriting Agreement.
3.1+	Amended and Restated Certificate of Incorporation, as amended to date, as currently in effect.
3.2*	Form of Restated Certificate of Incorporation to be effective upon the completion of this offering.
3.3+	Amended and Restated Bylaws, as amended to date, as currently in effect.
3.4*	Form of Restated Bylaws to be effective upon the completion of this offering.
4.1*	Form of Common Stock Certificate.
4.2+	Amended and Restated Investors' Rights Agreement, dated October 22, 2018, by and among the Registrant and certain of its stockholders.
5.1*	Opinion of Fenwick & West LLP.
10.1*	Form of Indemnification Agreement with directors and officers.
10.2+	2014 Equity Incentive Plan, as amended, and forms of award agreements.
10.4*	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.
10.5*	Lease Agreement, dated August 20, 2018, by and between Homology Medicines, Inc., and the Registrant.
10.6+	Lease Agreement dated January 2, 2019, by and between MIT 139 Main Street Leasehold LLC., and the Registrant.
10.7*	License Agreement, dated July 31, 2015, by and between Cold Spring Harbor Laboratory and the Registrant.
10.8*	License Agreement, dated April 18, 2016, by and between the University of Southampton and the Registrant.
10.9*	Employment Agreement, dated October 20, 2017, by and between the Registrant and Edward M. Kaye.
10.10*	Employment Agreement, dated November 20, 2015, by and between the Registrant and Huw M. Nash.
10.11*	Employment Agreement, dated September 11, 2017, by and between the Registrant and Barry J. Ticho.
10.12*	Employment Agreement, dated January 16, 2018, by and between the Registrant and Gene Liau.
10.13*	Employment Agreement, dated February 12, 2019, by and between the Registrant and Stephen J. Tulipano.
10.14*	Consulting Agreement, dated October 24, 2014, by and between the Registrant and Adrian R. Krainer.
21.1+	Subsidiaries of the Registrant.
23.1*	Consent of KPMG, an independent registered public accounting firm.
23.2*	Consent of Fenwick & West LLP (included in Exhibit 5.1).
23.3*	Consent of Health Advances LLC.
24.1	Power of Attorney (included in the signature page to this registration statement).

* To be filed by amendment.
\+ Previously submitted

(b) Financial Statement Schedules.

No financial statement schedules are provided because the information called for is not required or is shown either in the financial statements or notes.

Item 17. Undertakings.

The undersigned Registrant hereby undertakes to provide to the underwriters at the completion specified in the underwriting agreement, certificates in such denominations and registered in such names as required by the underwriters to permit prompt delivery to each purchaser.

Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, officers and controlling persons of the Registrant pursuant to the foregoing provisions, or otherwise, the Registrant has been advised that in the opinion of the SEC such indemnification is against public policy as expressed in the Securities Act and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the Registrant of expenses incurred or paid by a director, officer or controlling person of the Registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the Registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Securities Act and will be governed by the final adjudication of such issue.

The undersigned Registrant hereby undertakes that:

(1) For purposes of determining any liability under the Securities Act, the information omitted from the form of prospectus filed as part of this registration statement in reliance upon Rule 430A and contained in a form of prospectus filed by the Registrant pursuant to Rule 424(b)(1) or (4) or 497(h) under the Securities Act shall be deemed to be part of this registration statement as of the time it was declared effective.

(2) For the purpose of determining any liability under the Securities Act, each post-effective amendment that contains a form of prospectus shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

Signatures

Pursuant to the requirements of the Securities Act of 1933, as amended, the Registrant has duly caused this registration statement on Form S-1 to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of Bedford, State of Massachusetts, on the day of , 2019.

STOKE THERAPEUTICS, INC.

By: _____
Edward M. Kaye, M.D.
Chief Executive Officer

Power of attorney

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below hereby constitutes and appoints Edward M. Kaye and Stephen J. Tulipano, and each of them, as his true and lawful attorneys-in-fact, proxies and agents, each with full power of substitution and resubstitution and full power to act without the other, for him in any and all capacities, to sign any and all amendments to this registration statement (including post-effective amendments or any abbreviated registration statement and any amendments thereto filed pursuant to Rule 462(b) increasing the number of securities for which registration is sought), and to file the same, with all exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact, proxies and agents full power and authority to do and perform each and every act and thing requisite and necessary to be done in connection therewith, as fully for all intents and purposes as he or she might or could do in person, hereby ratifying and confirming all that said attorneys-in-fact, proxies and agents, or their or his or her substitute or substitutes, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Act of 1933, as amended, this registration statement on Form S-1 has been signed by the following persons in the capacities and on the dates indicated.

Signature	Title	Date
Edward M. Kaye, M.D.	Chief Executive Officer (Principal Executive Officer)	, 2019
Stephen J. Tulipano	Chief Financial Officer (Principal Accounting and Financial Officer)	, 2019
Samuel W. Hall, Ph.D.	Director	, 2019
Seth L. Harrison, M.D.	Director	, 2019
Adrian R. Krainer, Ph.D.	Director	, 2019
Arthur A. Levin, Ph.D.	Director	, 2019
Arthur O. Tzianabos, Ph.D.	Director	, 2019