

**UNITED STATES**  
**SECURITIES AND EXCHANGE COMMISSION**  
**WASHINGTON, DC 20549**

**FORM 10-K**

(Mark One)

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

For the fiscal year ended December 31, 2021 OR

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

For the transition period from \_\_\_\_\_ to \_\_\_\_\_

Commission File Number: 001-39041

**Satsuma Pharmaceuticals, Inc.**

(Exact Name of Registrant as Specified in its Charter)

**Delaware**

(State or other jurisdiction of incorporation or organization)  
400 Oyster Point Boulevard, Suite 221

South San Francisco, CA  
(Address of principal executive offices)

**81-3039831**

(I.R.S. Employer Identification No.)

**94080**  
(Zip Code)

Registrant's telephone number, including area code: (650) 410-3200  
Securities registered pursuant to Section 12(b) of the Act:

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

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

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes  No

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. Yes  No

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

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

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

Large accelerated filer	<input type="checkbox"/>	Accelerated filer	<input type="checkbox"/>
Non-accelerated filer	<input checked="" type="checkbox"/>	Smaller reporting company	<input checked="" type="checkbox"/>
		Emerging growth company	<input checked="" type="checkbox"/>

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

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

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes  No

The aggregate market value of the voting stock and non-voting common stock held by non-affiliates of the registrant, based on the closing price of a share of the registrant's common stock on June 30, 2021 as reported by the Nasdaq Global Market on such date, was approximately \$159 million. Shares of common stock held by each executive officer and director and by each other person who may be deemed to be an affiliate of the registrant, have been excluded from this computation. The determination of affiliate status for this purpose is not necessarily a conclusive determination for other purposes.

As of March 11, 2022, the registrant had 31,545,564 shares of common stock, \$0.0001 par value per share, outstanding.

**DOCUMENTS INCORPORATED BY REFERENCE**

Portions of the registrant's definitive Proxy Statement relating to the 2022 Annual Meeting of Stockholders are incorporated herein by reference in Part III of this Annual Report on Form 10-K to the extent stated herein. The proxy statement will be filed with the Securities and Exchange Commission within 120 days of the registrant's fiscal year ended December 31, 2021.

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## SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K contains “forward-looking statements” within the meaning of Section 21E of the Securities Exchange Act of 1934, as amended, or Exchange Act. We have based these forward-looking statements largely on our current expectations and projections about future events and financial trends affecting the financial condition of our business. Forward-looking statements should not be read as a guarantee of future performance or results, and will not necessarily be accurate indications of the times at, or by, which such performance or results will be achieved. Forward-looking statements are based on information available at the time those statements are made and/or management’s good faith beliefs as of that time with respect to future events, and are subject to risks and uncertainties that could cause actual performance or results to differ materially from those expressed in or suggested by the forward-looking statements.

Forward-looking statements include all statements that are not historical facts. In some cases, you can identify forward-looking statements by terms such as “may,” “might,” “will,” “objective,” “intend,” “should,” “could,” “can,” “would,” “expect,” “believe,” “anticipate,” “project,” “target,” “design,” “estimate,” “predict,” “potential,” “plan” or the negative of these terms, or similar expressions and comparable terminology intended to identify forward-looking statements. These statements reflect our current views with respect to future events and are based on assumptions and subject to risks and uncertainties, including those set forth under the section titled “Risk Factors” and elsewhere in this report. Forward-looking statements include, but are not limited to, statements about:

- our expectations with regard to the data to be derived from our ongoing and planned clinical trials and timing of expected data announcements;
  - the timing or likelihood of regulatory filings and approvals for STS101;
  - our expectations regarding the potential market size and size of the potential patient populations for STS101, if approved for commercial use;
  - our clinical and regulatory development plans for STS101;
  - the implementation of our business model and strategic plans for our business and STS101;
  - the impacts of the COVID-19 pandemic on our operations;
  - our plans and expectations for the further clinical development of STS101;
  - our commercialization, marketing and manufacturing plans and expectations;
  - the pricing and reimbursement of STS101, if approved;
  - the scope of protection we are able to establish and maintain for intellectual property rights covering STS101, including the projected terms of patent protection;
  - estimates of our expenses, future revenue, capital requirements, our needs for additional financing and our ability to obtain additional capital;
  - the timing of commencement of future nonclinical studies and clinical trials and research and development programs;
  - our future financial performance; and
  - developments and projections relating to our competitors and our industry, including competing therapies and procedures.
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All forward-looking statements are based on information available to us on the date of this Annual Report on Form 10-K and we will not update any of the forward-looking statements after the date of this Annual Report on Form 10-K, except as required by law. Our actual results could differ materially from those discussed in this Annual Report on Form 10-K. The forward-looking statements contained in this Annual Report on Form 10-K, and other written and oral forward-looking statements made by us from time to time, are subject to certain risks and uncertainties that could cause actual results to differ materially from those anticipated in the forward-looking statements, and you should not regard these statements as a representation or warranty by us or any other person that we will achieve our objectives and plans in any specified time frame, or at all. Factors that might cause such a difference include, but are not limited to, those discussed in the following discussion and within Part I, Item 1A “Risk Factors” of this Annual Report on Form 10-K.

In addition, statements that “we believe” and similar statements reflect our beliefs and opinions on the relevant subject. These statements are based upon information available to us as of the date of this Annual Report on Form 10-K, and although we believe such information forms a reasonable basis for such statements, such information may be limited or incomplete, and our statements should not be read to indicate that we have conducted a thorough inquiry into, or review of, all potentially available relevant information. These statements are inherently uncertain and investors are cautioned not to unduly rely upon these statements.

### **Trademarks**

All brand names or trademarks appearing in this report are the property of their respective holders. Solely for convenience, our trademarks and tradenames referred to in this report may appear without the ® and ™ symbol, 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.

*Unless the context requires otherwise, references in this report to “Satsuma” the “Company,” “we,” “us,” and “our” refer to Satsuma Pharmaceuticals, Inc.*

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## **Risk Factor Summary**

*Below is a summary of the principal factors that make an investment in our common stock speculative or risky. This summary does not address all of the risks that we face. Additional discussion of the risks summarized in this risk factor summary, and other risks that we face, can be found below under the heading "Risk Factors" and should be carefully considered, together with other information in this Annual Report on Form 10-K and our other filings with the Securities and Exchange Commission (SEC) before making investment decisions regarding our common stock.*

- We are a clinical-stage biopharmaceutical company with a limited operating history and no products approved for commercial sale. We have incurred significant losses since our inception, and we anticipate that we will continue to incur significant losses for the foreseeable future, which, together with our limited operating history, makes it difficult to assess our prospects.
- We will require substantial additional financing to achieve our goals, and a failure to obtain this capital when needed on acceptable terms, or at all, could force us to delay, limit, reduce or terminate our product development or commercialization efforts.
- Our business is entirely dependent on the successful development, regulatory approval and commercialization of STS101, our only product candidate under development.
- Previously, in our Phase 3 EMERGE study, STS101 did not demonstrate a statistically significant difference as compared to placebo on either of the co-primary endpoints.
- Clinical development involves a lengthy and expensive process with an uncertain outcome, and delays can occur for a variety of reasons outside of our control.
- We may be unable to obtain regulatory approval for STS101 under applicable regulatory requirements. The denial or delay of any such approval would delay commercialization of STS101 and adversely impact our potential to generate revenue, our business and our results of operations.
- If we encounter difficulties with patient enrollment or completion in our clinical trials, our clinical development activities could be delayed or otherwise adversely affected.
- The ongoing COVID-19 pandemic and outbreak in the United States may adversely affect our business.
- STS101 may cause undesirable side effects or have other properties that could delay or prevent its regulatory approval, limit the commercial profile of an approved label, or result in significant negative consequences following marketing approval, if any.
- We may be unable to rely on Section 505(b)(2) of the Federal Food, Drug and Cosmetic Act (FDCA), which could result in a longer development program and more costly trials than we anticipate.
- Even if STS101 obtains regulatory approval, it may fail to achieve broad market acceptance.
- We face, and will continue to face, significant competition in an environment of rapid technological and scientific change and our failure to effectively compete may prevent us from achieving significant market penetration for STS101, if approved. Most of our competitors have significantly greater resources than we have and we may not be able to successfully compete.
- The successful commercialization of STS101 will depend in part on the extent to which governmental authorities, private health insurers, and other third-party payors provide coverage, adequate reimbursement levels and implement pricing policies favorable for it. Failure to obtain or maintain coverage and adequate reimbursement for STS101, if approved, could limit our ability to market our product and decrease our ability to generate revenue.

ITEM 1. BUSINESS

Overview

BUSINESS

Overview

We are a clinical-stage biopharmaceutical company developing a novel therapeutic product for the acute treatment of migraine. Our product candidate, STS101, is a drug-device combination of a proprietary dry-powder formulation of dihydroergotamine mesylate, or DHE, which is designed to be quickly and easily self-administered with a proprietary pre-filled, single-use, nasal delivery device. DHE products have long been recommended as a first-line therapeutic option for the acute treatment of migraine and have significant advantages over other therapeutics for many patients. However, broad use has been limited by invasive and burdensome administration and/or sub-optimal clinical performance of available injectable and liquid nasal spray products. STS101 is specifically designed to deliver the clinical advantages of DHE while overcoming these shortcomings. If approved, we believe STS101 has the potential to be an important and differentiated option for the acute treatment of migraine that can address the unmet needs of many people living with migraines.

In March 2021, we announced an updated development plan for STS101 that was informed by our analyses of data from our STS101 Phase 3 EMERGE efficacy trial in which STS101 demonstrated favorable numerical trends but did not achieve statistical significance versus placebo on the study's co-primary endpoints. Our updated development plan for STS101 included a Phase 1 trial, which we completed in June 2021; a Phase 3 efficacy trial (the SUMMIT trial), which we initiated in June 2021 and is currently ongoing; and continuation of the open-label, Phase 3 long-term safety trial of STS101 (the ASCEND trial). The SUMMIT trial is a randomized, double-blind, placebo-controlled Phase 3 trial designed to evaluate the efficacy, safety and tolerability of a single dose of STS101 5.2 mg in the acute treatment of migraine in approximately 1,400 subjects. We expect topline results from the ASCEND trial in the second half of 2022 and SUMMIT trial in the fourth quarter of 2022. If the SUMMIT and ASCEND trials are successful, we plan to file a new drug application, or NDA, for STS101 with the U.S. Food and Drug Administration, or FDA, in the first quarter of 2023.

In September 2020, we announced topline results from the EMERGE Phase 3 efficacy trial of STS101. The EMERGE trial was a randomized, double-blind, placebo-controlled trial in 1,201 subjects designed to evaluate the efficacy, safety and tolerability of a single dose of STS101 (3.9 mg or 5.2 mg) in the acute treatment of migraine. Although both STS101 dose strengths evaluated in the EMERGE trial showed favorable numerical differences versus placebo on the pre-specified co-primary endpoints of freedom from pain and freedom from most bothersome symptom (from among photophobia, phonophobia and nausea) at two hours post-administration, these differences did not achieve statistical significance for either dosage strength. Both dosage strengths of STS101 did, however, demonstrate significant effects (nominal p-value <0.05) on both freedom from pain and most bothersome symptom endpoints by three hours post-administration and later time points. In addition, STS101 demonstrated significant effects on multiple, pre-specified secondary efficacy endpoints. Both STS101 dose strengths were generally well-tolerated in the EMERGE trial, with low adverse event rates and no serious adverse events reported.

Based on our analyses and review of EMERGE trial results and other data, including preliminary results from our ongoing open-label, Phase 3 long-term safety trial of STS101 5.2 mg, (the ASCEND trial), we believe we have identified and taken steps to address the key reasons why STS101 did not achieve statistical significance on co-primary endpoints at the two-hour post-administration time point in the EMERGE trial. Our analyses suggest a significant proportion of subjects in EMERGE who self-administered STS101 to treat their migraine attacks may not have achieved and sustained target DHE plasma concentrations due to under-delivery of STS101. We believe we have addressed the under-delivery issue by (i) introducing improved instructions for STS101 use and training of subjects in our clinical trials and (ii) making several minor modifications to the STS101 delivery device to improve its performance. We refer to the modified and improved STS101 delivery device as the "second-generation" device. We believe other factors also contributed to a negative outcome in the EMERGE trial, including: (i) early data entry by subjects in the electronic diary device due to device alarm programming; (ii) high proportions of subjects and

treated migraine attacks with characteristics associated with poor treatment outcomes, and in particular, high proportions of subjects with pain of severe intensity immediately prior to treatment with study medication; and (iii) a high placebo response rate, particularly in light of the severe symptomology of the migraine attacks treated by subjects in the trial.

In August 2020, we initiated our ASCEND Phase 3 long-term safety trial, in which we have enrolled more than 480 subjects with migraine who treat their migraine attacks with STS101 on an as-needed basis for up to 12 months. Our plan is to fulfill the target subject exposure requirements previously communicated to us by the FDA (at least 150 subjects completing six months of treatment and potentially at least 50 subjects completing 12 months of treatment) using investigational product incorporating the second-generation STS101 delivery device. To date, subjects in the ASCEND trial have treated a total of more than 6,000 migraine attacks with STS101 5.2 mg. STS101 has been generally well-tolerated, with low adverse event rates reported. We expect topline results from the ASCEND trial in the second half of 2022.

If the SUMMIT and ASCEND trials are successful, we plan to file an NDA for STS101 with the FDA in the first quarter of 2023.

Migraine is a chronic and debilitating neurological disorder characterized by attacks of often severe headache and accompanying neurological symptoms lasting four to 72 hours. More than 90% of individuals suffering from migraine attacks are unable to work or function normally during a migraine attack, with many experiencing comorbid conditions such as depression, anxiety and insomnia. Based on reported prevalence data, approximately 39 million individuals in the United States and over 100 million individuals in Europe suffer from migraine. With a global prevalence of greater than one billion, migraine ranks as the world's third most prevalent illness, the sixth highest specific cause of disability worldwide, and the leading cause of disability in people under 50 years of age. In addition, migraine is the second leading cause of disability worldwide in terms of number of years lost to disability. It has been estimated that migraine results in up to \$36 billion in healthcare and lost productivity costs and up to 157 million lost workdays annually in the United States. Despite its high prevalence and burden, migraine remains a highly underdiagnosed and undertreated illness due to lack of awareness, stigma and the inherent limitations of currently available therapies.

Acute treatments for migraine are categorized as non-specific therapies, including nonsteroidal anti-inflammatory drugs (NSAIDs) and acetaminophen, and migraine-specific therapies, such as triptans, ergot alkaloids (including DHE-based products), oral calcitonin gene-related peptide (CGRP) antagonists (gepants), and lasmiditan, an oral 5-HT<sub>1F</sub> agonist (ditan). Lasmiditan and two gepants, ubrogepant and rimegepant, were approved in late 2019 and early 2020 by the FDA, and commercial introductions of these new products in the United States commenced in early 2020.

The acute migraine prescription market is large and growing at an accelerating rate. In 2021 approximately 18.1 million prescriptions were written in the United States for acute migraine-specific therapies, and prescription volumes for acute migraine-specific therapies grew by 8% versus 2020 (rimegepant was approved by the FDA in May 2021 for the additional indication of migraine prevention and prescription figures noted include both acute and preventive uses.). This figure excludes prescriptions for non-specific therapies and therefore likely significantly understates the total number of prescriptions written for the acute treatment of migraine. Oral triptans are currently the predominant class of drug for acute treatment of migraine, accounting for approximately 83% of migraine-specific acute therapy prescriptions. However, triptans have been reported to have a number of shortcomings, including that they have inconsistent efficacy across patients and migraine types, require early treatment, cause various side effects, may cause medication overuse headache, or MOH, and have slow and variable onset of action and short duration of effect that necessitates retreatment.

The migraine prescription market growth in 2021 is attributed primarily to the introductions in 2020 of rimegepant and ubrogepant, which together accounted for more than one billion dollars in net sales in the United States in 2021. Ubrogapant and rimegepant have outperformed the initial projections of industry analysts. We believe these trends reflect the large size of the migraine patient population, the significant unmet need among people with migraine for new and improved acute treatments, and the large potential commercial opportunity for such products. In addition, we believe the prospects for continued and sustained market growth are favorable given that migraine is under-diagnosed and under-treated. Further, given that none of the currently available treatment options adequately achieve the American Headache Society's defined goals for the acute treatment of migraine for a

significant percentage of migraine patients, we believe many patients will continue to experience high unmet need and seek new and better treatment options.

DHE products have long been recommended as a first-line therapeutic option for the acute treatment of migraine and have significant clinical advantages over other therapeutics, including triptans, for many patients. However, approved DHE products have drawbacks that have resulted in limited clinical use. For instance, injectable DHE, while effective, has invasive administration requirements, and in the case of intravenous (IV) delivery, generally must be administered by a healthcare provider, typically in the hospital or clinic setting, requires specialized equipment and may often result in side effects, in particular, nausea and vomiting. Similarly, intramuscular (IM) and or subcutaneous (SC) injections are invasive, require administration via injection by the patient, caregiver or healthcare provider and patients typically prefer non-injectable therapies. DHE liquid nasal sprays have complex, time-consuming and burdensome administration, as well as high variability and slow absorption that may result in inconsistent and sub-optimal clinical performance. Additionally, DHE plasma levels achievable with DHE liquid nasal sprays may not be sufficient for robust efficacy for many patients. Further, due to DHE's low oral bioavailability, there are no approved oral DHE products in the United States.

We designed STS101 to be a reliable and convenient DHE product capable of delivering the clinical advantages of DHE while overcoming the shortcomings of existing DHE products. We believe the key attributes of STS101 may provide significant advantages over existing acute treatments for migraine and result in robust and consistent clinical performance, thereby facilitating broad adoption and use. These attributes are primarily the result of our proprietary dry-powder formulation, which incorporates a mucoadhesive drug carrier and engineered drug particle technologies, and our proprietary nasal delivery device. These key STS101 attributes include:

- *Rapidly achieving and sustaining target plasma concentrations.* In our Phase 1 clinical trials, STS101 rapidly achieved and sustained target DHE plasma concentrations and demonstrated an overall pharmacokinetic (PK) profile that we believe has the potential to result in robust anti-migraine activity.
- *Low PK variability.* In our Phase 1 clinical trials, STS101 demonstrated significantly lower variability in peak DHE plasma concentration and DHE exposure as compared to Migranal® (DHE liquid nasal spray), which we believe may lead to more reliable clinical performance.
- *Quick and convenient self-administration.* STS101 utilizes a convenient, patient-friendly, single-use, nasal delivery device designed to enable self-administration of a full dose of DHE into a single nostril in a matter of seconds. The pre-filled device is pocket-sized and more compact than available DHE liquid nasal spray products, enabling portability and discreet use, and requires no assembly or priming. Our primary market research with migraine patients and physicians indicates they view these features as important and desirable. In addition, our STS101 dry-powder formulation has demonstrated favorable stability properties (including, insensitivity to light, heat or oxygen) that we expect will enable storage across a wide range of temperatures and conditions.
- *Well tolerated.* To date, in our Phase 1 PK trials in healthy volunteers and Phase 3 clinical trials in which more than 1,000 subjects with migraine have treated more than 7,000 migraine attacks with STS101 5.2 mg, STS101 has been generally well-tolerated, with low adverse event rates reported. Importantly, STS101 does not exhibit the rapid and high peak concentrations associated with delivery of DHE by IV injection, which may often result in side effects, in particular, nausea and vomiting.

We believe the foregoing attributes of STS101 could lead to it having a favorable clinical profile as compared to IV, IM or SC delivery of DHE and DHE liquid nasal spray products.



The STS101 administration procedure is shown in the figure below:



Although STS101 rapidly achieved and sustained targeted DHE plasma concentrations and demonstrated low pharmacokinetic variability in our Phase 1 PK trials, our analyses of data from the Phase 3 EMERGE trial suggest a significant proportion of subjects in EMERGE who self-administered STS101 to treat their migraine attacks may not have achieved and sustained target DHE plasma concentrations due to under-delivery of STS101. We believe we have successfully addressed this under-delivery issue by introducing improved instructions for STS101 use and training of subjects in our clinical trials and making several minor modifications to the STS101 delivery device to improve its performance. Based on extensive testing and performance characterization of the improved STS101 delivery devices, we believe the improved devices have more robust performance and are easier for patients to use, thereby potentially mitigating the risk of under-delivery.

The faster a DHE product can produce the threshold DHE plasma concentration necessary for a therapeutic response, the more quickly following administration it may be able to exert anti-migraine effects and therapeutic response. At the same time, we believe that rapid and high peak DHE plasma concentrations that greatly exceed the levels required for threshold a therapeutic response level may result in adverse side effects. For example, IV delivery of DHE has demonstrated peak DHE plasma concentrations of 50 ng/ml or more within several minutes of administration, and is reported to more frequently result in side effects (including nausea and vomiting, increases in blood pressure, flushing, dizziness, extremity pain, and abnormal skin sensations) than delivery of DHE by other routes of administration, such as IM or SC injection, nasal or pulmonary, which exhibit much lower peak DHE plasma concentrations that generally have not been reported to exceed approximately 3 to 4 ng/ml. Based on data from our STS101 clinical trials and from published DHE PK and clinical efficacy trials, we estimate that achieving DHE plasma concentrations between 1.0 ng/ml and approximately 2.5 to 3.5 ng/ml within approximately 15 to 30 minutes after dosing may result in clinically significant therapeutic response rates by two hours or earlier after dosing and low side effect rates as compared with IV DHE delivery. As demonstrated in our Phase 1 clinical trials, administration of STS101 5.2 mg resulted in DHE plasma concentrations rising rapidly, with mean peak DHE plasma concentrations reaching 2.2 ng/ml at 30 minutes after dosing.

Our management team has extensive pharmaceutical industry experience in drug development, regulatory approval, manufacturing, reimbursement, commercialization and finance from their prior roles at other pharmaceutical and biotechnology companies, including ALZA, AstraZeneca, Athena Neurosciences, Elan Pharmaceuticals, GlaxoSmithKline, Ilypsa, Immunex, Jazz Pharmaceuticals, Johnson & Johnson, Pearl Therapeutics, Protagonist Therapeutics, Relypsa, Roivant Sciences, and Wyeth Laboratories. Collectively, our management team has materially contributed to the clinical development, registration and/or commercialization of over 50 approved drug products, including 15 drug-device combination products, 13 of which are delivered via inhalation.

## Our Strategy

Our strategy is to develop and commercialize STS101 and address the significant unmet medical needs of a large number of people living with migraine. Key elements of our strategy include:

- *Advance STS101 through clinical development and regulatory approval for the acute treatment of migraine.* In March 2021, we announced an updated development plan for STS101 that was informed by our analyses of data from our STS101 Phase 3 EMERGE efficacy trial in which STS101 demonstrated favorable numerical trends but did not achieve statistical significance versus placebo on the study's co-primary endpoints. Our updated development plan for STS101 included a Phase 1 trial, which we completed in June 2021; our SUMMIT Phase 3 efficacy trial, which we initiated in June 2021 and is currently ongoing; and continuation of the ongoing open-label, ASCEND Phase 3 long-term safety trial of STS101. The SUMMIT trial is a randomized, double-blind, placebo-controlled Phase 3 trial designed to evaluate the efficacy, safety and tolerability of a single dose of STS101 5.2 mg as an acute treatment for migraine in approximately 1,400 subjects. We expect topline results from the ASCEND trial in the second half of 2022 and SUMMIT trial in the fourth quarter of 2022. If the SUMMIT and ASCEND trials are successful, we plan to file an NDA, for STS101 with the FDA in the first quarter of 2023.
- *Maximize commercial potential of STS101.* In June 2021, we initiated the SUMMIT Phase 3 efficacy trial utilizing a randomized, double-blind, placebo-controlled design similar to that of the EMERGE trial and as typically required by the FDA to support product-specific efficacy claims in product labeling and promotional materials. We believe that approved product labeling for STS101 including results from the SUMMIT trial may differentiate STS101 from competing products and increase its commercial potential. We may also conduct additional clinical trials and consider additional headache indications for STS101 to maximize its commercial potential.
- *Commercialize STS101 in the United States.* If approved, we plan to commercialize STS101 in the United States by building a specialized sales organization focusing on headache specialists, as well as general neurologists and primary care physicians who frequently prescribe migraine therapeutics.
- *Pursue market opportunities for STS101 outside the United States with one or more partners.* We believe there is a significant market opportunity for STS101 in markets outside the United States. To address these markets, we plan to seek one or more ex-U.S. partners who can commercialize STS101, subject to foreign regulatory approval.

## Migraine Overview

Migraine is a chronic and debilitating neurological disorder characterized by attacks of often severe headache and accompanying neurological symptoms lasting four to 72 hours. More than 90% of individuals suffering from migraine are unable to work or function normally during a migraine attack, with many experiencing comorbid conditions such as depression, anxiety and insomnia. Failure to effectively treat migraine attacks can lead to disease progression, increased frequency of attacks and greater migraine-related disability. Migraine is often accompanied by one or more of the following disabling symptoms:

- extreme sensitivity to light, sound, touch or smell;
- nausea and/or vomiting;
- dizziness;
- visual disturbances;
- tingling or numbness in the extremities or face; and
- neck pain.

Based on reported prevalence data, approximately 39 million individuals in the United States and over 100 million individuals in Europe suffer from migraine. With a global prevalence of greater than one billion, migraine ranks as the world's third most prevalent illness, the sixth highest specific cause of disability worldwide, and the leading cause of disability in people under 50 years of age. In addition, migraine is the second leading cause

of disability worldwide in terms of number of years lost to disability. It has been estimated that migraine results in up to \$36 billion in healthcare and lost productivity costs and up to 157 million lost workdays annually in the United States. Despite its high prevalence and burden, migraine remains a highly underdiagnosed and undertreated illness due to lack of awareness, stigma and the inherent limitations of currently available therapies.

The underlying causes of migraine are not well understood; however, both genetics and environmental factors appear to be relevant. Further, the underlying biology of migraine is complex and multifactorial, and it is believed that migraine susceptibility arises from genetic predisposition to generalized neuronal hyperexcitability. During a migraine attack, hyperexcitable neurons cause the release of various vasoactive, pro-inflammatory and neuroactive substances, including calcitonin gene-related peptide (CGRP), substance P, histamine, inducible nitric oxide synthase (iNOS), cyclooxygenase-2 (COX-2) and serotonin, leading to vasodilation, neurogenic inflammation and neurological symptoms, including headache and pain.

Migraine treatment can generally be categorized as either acute or preventive. Treatment guidelines indicate that all patients should be offered acute treatment, which is focused on stopping the migraine attack quickly and restoring the patient's ability to function with minimal side effects. In addition to receiving acute treatments, a subset of patients (typically those with more severe and/or frequent migraine attacks) may also receive preventive treatment, which is focused on reducing the frequency, duration or severity of migraine attacks or the associated disability caused by such attacks. Historically, preventive therapies, such as anti-convulsants, beta blockers and onabotulinumtoxinA injections, have lacked strong efficacy for many patients, have been associated with significant side effects or required burdensome administration. The recent development and introduction of anti-CGRP therapeutics as a new class of preventive therapy is raising awareness of the treatment opportunities in migraine and may lead to an increase in the number patients being diagnosed and treated for migraine. However, these new therapies do not alleviate the need for acute therapies, as such products that have been approved to date on average result in patients experiencing a reduction of only two migraine days per month. Despite its high prevalence and burden, migraine remains an underdiagnosed and undertreated illness due to lack of awareness, stigma and the inherent limitations of currently available therapies.

### **Current Acute Treatment Paradigm**

Patients typically seek acute treatment for migraine to relieve pain and associated symptoms. The current treatment guidelines from the American Headache Society define the five goals of acute therapy as:

- Rapid and consistent freedom from pain and associated symptoms without recurrence;
- Restored ability to function;
- Minimal need for repeat dosing or rescue medications;
- Optimal self-care and reduced subsequent use of resources (e.g., emergency room visits, diagnostic imaging, healthcare provider and ambulatory infusion center visits); and
- Minimal or no side effects.

Acute treatments are typically administered orally, via injection or nasally. Orally-administered acute treatments have significant limitations, including relatively slow onset of effect due to the time required for absorption of the drug from the gastrointestinal tract following ingestion. During a migraine attack, absorption of orally-administered treatments can be delayed due to gastric stasis, which commonly occurs in people with migraine both during and between attacks. In addition, orally-administered acute treatments are inappropriate for the many migraine patients who experience significant nausea or vomiting with their attacks or who have trouble swallowing orally-administered medications. Injectable therapies, while often offering the fastest means of achieving therapeutic plasma levels of the administered drug product, often require the involvement of a healthcare provider, can be difficult to self-administer and typically result in greater side effects than non-injectable therapies. As a result, patients generally prefer non-injectable therapies over injectable therapies. While nasal administration of acute treatments has the potential to address certain of these limitations by facilitating rapid absorption of drug from the linings of the nasal passages into the bloodstream while simultaneously limiting side effects, currently available and development-stage nasally-administered acute treatments have drawbacks and limitations. These drawbacks and limitations may include one or more of the following:

- Efficacy that is comparable or only incrementally better than orally-administered acute treatments;
- Partial or variable absorption in the nose, with the remaining fraction of drug delivered into the nasal passage running down the back of the throat and being swallowed with potential for any subsequent absorption in the gastrointestinal tract to be poor or delayed;
- Variable pharmacokinetics (PK), resulting in inconsistent and sub-optimal clinical performance and perceived lack of reliability;
- For liquid nasal spray formulations, the administered drug product often drips out of the nose and runs-off down the back of throat, which can result in unpleasant taste;
- Non-intuitive and cumbersome administration procedures, including the need for assembly, priming and multiple administrations (sprays or insufflations) over time in order to deliver a full dose. For example, this is the case with Migranal DHE mesylate liquid nasal spray, for which the self-administration procedure requires four sprays, one in each nostril initially, followed by an additional spray in each nostril 15 minutes later, to administer a full dose; and
- Large size, which reduces practicality of transport for patients and ability to discreetly self-administer.

Acute treatments are categorized as non-specific therapies, including NSAIDs and acetaminophen, and migraine-specific therapies, such as triptans, ergot alkaloids (including DHE-based products), gepants and a ditan. Non-specific therapies are generally recommended for the acute treatment of migraine with mild to moderate pain, and migraine-specific therapies are generally recommended for the acute treatment of migraine with moderate to severe pain. However, none of the currently available treatment options adequately achieve the acute treatment goals for a significant percentage of migraine patients.

## **Triptans**

Oral triptans are currently the predominant class of drug for acute treatment of migraine, accounting for approximately 83% of migraine-specific acute therapy prescriptions, or over 15 million prescriptions in the United States in 2021. Triptans are serotonergic agonists, typically with selective activity on a limited number of serotonergic receptors, including the 5-HT<sub>1B</sub> and 5-HT<sub>1D</sub> receptors. While widely prescribed, triptans have been reported to have low treatment persistence, with up to 66% of patients never refilling their initial triptan prescriptions. A substantial majority of patients who discontinue triptans cite a lack of efficacy and side effects as the reasons for discontinuation. Triptans have been reported to have a number of shortcomings, including being inconsistent and having sub-optimal efficacy, leading to side effects and medication overuse headaches, having early treatment requirements that only allow for a short therapeutic window, and having a slow and variable onset of action and short duration of effect.

## Oral CGRP Receptor Agonists (gepants)

First commercially introduced in the United States in early 2020, the gepants are a class of orally-administered, migraine-specific acute treatments that act as antagonists of the calcitonin gene-related peptide receptor. Two gepant products, ubrogepant and rimegepant, are currently approved in the United States for the acute treatment of migraine and together accounted for more than one billion dollars in 2021 net sales in the United States. \* These gepant products accounted for up to 12% of migraine-specific acute therapy prescriptions in the United States in 2021, and in the month of December 2021 captured up to a 15% share of these prescriptions (in May 2021, rimegepant was approved by the FDA for the additional indication of migraine prevention; thus, portions of preceding net revenue and prescription figures are attributable to preventive use of rimegepant). We believe these trends reflect the large size of the migraine patient population, the significant unmet need among people with migraine for new and improved acute treatments and the large potential commercial opportunity for such products. The safety and tolerability of the gepants is reported to be favorable, and because gepants are thought to act by mechanisms other than vasoconstriction, recommended use is not restricted to patients who do not have cardiovascular risk factors or disease, as is the case for triptan and ergot alkaloid products (including DHE) due to their vasoconstrictive actions. The efficacy of the gepants, however, is reported to be modest in comparison with the triptans and potentially not meaningfully greater than that of simple analgesics than can be purchased without a prescription.

## DHE

DHE products have long been recommended as a first-line therapeutic option for the acute treatment of migraine. DHE has broader pharmacological activity than triptans across multiple receptor types, including serotonergic, adrenergic and dopaminergic receptors, represses CGRP release, and is thought to inhibit neuroinflammation and central sensitization via adrenergic receptors. In addition, DHE has a long pharmacodynamic half-life thought to be attributed to slow receptor dissociation. Because of its differentiated clinical attributes, many headache specialists consider DHE to be a preferred treatment for many difficult-to-treat migraine types, including severe migraine, migraine with allodynia, migraine upon awakening, fast onset migraine, prolonged and recurrent migraine attacks, including menstrual-related migraine, and migraine attacks requiring late treatment (i.e., more than one hour after onset of attack). In addition, DHE is considered a standard-of-care treatment for medication-overuse headache, or MOH, and for status migrainosus, which is a condition characterized by debilitating migraine attacks that last more than 72 hours. Given the complexity of migraine biology and the redundancy and interdependence of migraine disease pathways, DHE's activity across multiple receptors is thought to offer the potential for better responses for many migraine patients.

DHE has a number of differentiating clinical attributes providing advantages for the acute treatment of migraine, including:

- *Effective in patients who are non-responsive or refractory to triptan therapy.* Published data indicate that approximately half of all patients who have previously failed to adequately respond to triptan therapy, do respond to DHE therapy.
- *Effective in migraine attacks with allodynia.* Allodynia is present in up to two-thirds of migraine attacks, and its presence is associated with poor response to triptans and most other acute treatments. DHE, however, has demonstrated strong efficacy in migraine attacks in which allodynia is present.
- *Effective irrespective of when administered during the time course of a migraine attack.* Unlike triptans and certain other acute treatments for migraine, which are most effective when administered within one hour of onset of pain, DHE remains effective when administered late after onset of attack.
- *Low risk of headache recurrence.* DHE has been demonstrated in head-to-head controlled studies to have significantly lower headache recurrence rates than available triptan therapies.
- *Lower risk of causing MOH.* DHE is thought to have a lower potential for causing MOH with frequent use and, unlike triptan class therapies, currently approved DHE products do not contain a label warning for MOH potential.

Due to its chemical properties and structure, DHE has low bioavailability (approximately 1%) when administered orally and, as a result, oral forms have generally not been effective for the acute treatment of migraine. There are currently no approved oral DHE treatments in the United States. Approved DHE products include injectable and liquid nasal spray dosage forms, which have drawbacks that have resulted in limited clinical use.

Due to DHE's vasoconstrictive effects, DHE products are not recommended for use in patients with cardiovascular risk factors. In addition, approved DHE products carry a "black box" warning in their labels for a risk that the coadministration of DHE and certain other drugs, including specific antivirals and antibiotics, may result in elevated levels of DHE, potentially causing vasospasm that may result in inadequate blood flow to the extremities or the brain. Unless we can successfully demonstrate by conducting drug-drug interaction studies and potentially additional studies that the coadministration of DHE and certain other drugs does not result in drug-drug interactions, the FDA is likely to require the label for STS101, if approved, to include such warning, and this could result in STS101 not achieving its full commercial potential.

### ***Injectable DHE***

IV delivery is the fastest means of achieving plasma concentration levels of DHE that we estimate to be necessary to effectively treat a migraine attack, with anti-migraine responses reported as quickly as 15-20 minutes following administration. IV-delivered DHE is typically administered by a healthcare provider in a hospital, clinic or infusion center setting, which is expensive and requires the patient to travel to one of these locations while suffering from a migraine attack. Because IV delivery of DHE results in rapid achievement of high DHE plasma levels, side effects are more common with IV administration than with other routes of administration, with nausea and vomiting being particularly common and typically requiring coadministration of anti-nausea medication. DHE can also be administered by IM or SC injection. However, IM and SC administration require a patient, caregiver or healthcare provider to use proper technique during a migraine attack to draw the correct dose of DHE solution for injection from a vial or glass ampule into a syringe and then inject the solution into the muscle or subcutaneous layer of the skin. Although generally considered effective, the challenges of injectable DHE and the fact that migraine patients typically prefer non-injectable therapies for acute treatment of attacks make injectable DHE a less favored treatment option for many people with migraine.

### ***DHE Liquid Nasal Sprays***

DHE may also be delivered via liquid nasal spray. However, DHE liquid nasal spray products have a number of limitations and complexities related to their liquid formulation and delivery devices, which may include:

- high pharmacokinetic variability and slow absorption;
- inability to achieve DHE plasma levels sufficient for robust efficacy;
- complex administration procedures, including requirements for vial-opening, assembly, priming and administration of multiple sprays into both nostrils, that are burdensome and time-consuming for patients to perform;
- relatively large physical size;
- stringent storage requirements and potential for limited shelf life due to the liquid DHE formulation being sensitive to light, heat and oxygen;
- packaging that results in some patients experiencing injury while preparing to self-administer; and
- utilization of hydrofluoroalkane propellants that are potent greenhouse gases.

Headache specialists articulate a need for a patient-friendly, self-administered, non-injected DHE product that consistently and reliably provides the rapid, durable and robust efficacy that is currently available only with injectable DHE therapies. Given the differentiated clinical features of DHE, we believe DHE, if made available in a non-injectable dosage form that is well tolerated, facilitates quick and convenient administration and delivers rapid and sustained achievement of therapeutic concentrations with low variability, could provide significant benefits over existing acute treatments for migraine and help a large number of people living with migraine achieve better treatment outcomes.

## Our Solution: STS101 for the Acute Treatment of Migraine

STS101 is an investigational drug-device combination of a proprietary dry-powder formulation of DHE administered by a proprietary pre-filled, single-use, nasal delivery device. STS101 is specifically designed to deliver the clinical advantages of DHE while overcoming the shortcomings that have limited the utility of DHE for the acute treatment of migraine. The proprietary and foundational dry-powder formulation and nasal delivery device technologies incorporated in STS101 were developed over more than 15 years by a dedicated team at Shin Nippon Biomedical Laboratories, Ltd., or SNBL.

Subsequent to licensing such technology from SNBL, we advanced the development of STS101 by developing and optimizing the STS101 formulation, establishing analytical methods and scalable and commercial-scale manufacturing performed in accordance with good manufacturing practices, conducting extensive analytical characterization of STS101 and its components, and completing toxicology studies in accordance with good laboratory practices. The manufacturing processes we established employ standard technologies that are commonly utilized in the pharmaceutical industry for the manufacture of approved drug and drug-device combination products, and we are establishing commercial-scale manufacturing capability for STS101 via relationships with third-party contract manufacturing organizations, or CMOs.



We designed STS101 to be a reliable easy-to-use and convenient DHE product capable of delivering the clinical advantages of DHE while overcoming the shortcomings of existing DHE products. We believe the key attributes of STS101 may provide significant advantages over existing acute treatments for migraine and result in robust and consistent clinical performance, thereby facilitating broad adoption and use. These attributes are primarily the result of our proprietary dry-powder formulation, which incorporates a mucoadhesive drug carrier and engineered drug particle technologies, and our proprietary nasal delivery device. These key STS101 attributes include:

- *Rapidly achieving and sustaining target plasma concentrations.* In our Phase 1 clinical trials, STS101 rapidly achieved and sustained target DHE plasma concentrations and demonstrated an overall pharmacokinetic (PK) profile that we believe has the potential to result in robust anti-migraine activity.
- *Low PK variability.* In our Phase 1 clinical trials, STS101 demonstrated significantly lower variability in peak DHE plasma concentration and DHE exposure as compared to Migranal, which we believe, may lead to more reliable clinical performance.
- *Quick and convenient self-administration.* STS101 utilizes a convenient, patient-friendly, single-use, nasal delivery device designed to enable self-administration of a full dose of DHE into a single nostril in a matter of seconds. The pre-filled device is pocket-sized and more compact than available DHE liquid nasal spray products, enabling portability and discreet use, and requires no assembly or priming. Our primary market research with migraine patients and physicians indicates they view these features as important and desirable. In addition, the STS101 dry-powder formulation has demonstrated favorable stability properties (including, insensitivity to light, heat or oxygen) that we expect will enable storage across a wide range of temperatures and conditions.
- *Well tolerated.* To date, in our Phase 1 PK trials in healthy volunteers and Phase 3 clinical trials in which more than 1,000 subjects with migraine have treated more than 7,000 migraine attacks with STS101 5.2

mg, STS101 has been generally well-tolerated, with low adverse event rates reported. Importantly, STS101 does not exhibit the rapid and high peak concentrations associated with IV delivery of DHE, which may often result in side effects, in particular, nausea and vomiting.

We believe the foregoing attributes of STS101 offer the potential for a favorable clinical profile as compared to IV, IM or SC delivery of DHE and DHE mesylate liquid nasal spray products.

Although STS101 rapidly achieved and sustained targeted DHE plasma concentrations and demonstrated low pharmacokinetic variability in our Phase 1 PK trials, our analyses of data from the Phase 3 EMERGE trial suggest a significant proportion of subjects in EMERGE who self-administered STS101 to treat their migraine attacks may not have achieved and sustained target DHE plasma concentrations due to under-delivery of STS101. We believe we have addressed this under-delivery issue by introducing improved instructions for STS101 use and training of subjects in our clinical trials and making several minor modifications to the STS101 delivery device to improve its performance.

The faster a DHE product can produce the threshold DHE plasma concentration necessary for a therapeutic response, the more quickly following administration it may be able to exert anti-migraine effects and therapeutic response. At the same time, we believe that rapid and high peak DHE plasma concentrations that greatly exceed the levels required for threshold a therapeutic response level may result in adverse side effects. For example, IV delivery of DHE has demonstrated peak DHE plasma concentrations of 50 ng/ml or more within several minutes of administration, and is reported to more frequently result in side effects (including nausea and vomiting, increases in blood pressure, flushing, dizziness, extremity pain, and abnormal skin sensations) than delivery of DHE by other routes of administration, such as IM or SC injection, nasal or pulmonary, which exhibit much lower peak DHE plasma concentrations that generally have not been reported to exceed approximately 3 to 4 ng/ml. Based on data from our STS101 clinical trials and from published DHE PK and clinical efficacy trials, we estimate that achieving DHE plasma concentrations between 1.0 ng/ml and approximately 2.5 to 3.5 ng/ml within approximately 15 to 30 minutes after dosing may result in clinically significant therapeutic response rates by two hours or earlier after dosing and low side effect rates as compared with IV DHE delivery. As demonstrated in our Phase 1 clinical trials, administration of STS101 5.2 mg resulted in DHE plasma concentrations rising rapidly, with mean peak DHE plasma concentrations reaching 2.2 ng/ml at 30 minutes after dosing.

The STS101 administration procedure is shown in the figure below:





## Development Plan and Regulatory Pathway

Our development plan for STS101 is informed by published FDA guidance as well as our discussions with the FDA. Based on written feedback provided by the FDA, we believe the results of our completed Phase 1 PK clinical trials and our ongoing ASCEND Phase 3 safety trial, if successful, could be sufficient to support FDA approval of STS101 for the acute treatment of migraine headaches with or without aura. However, we believe positive results from a Phase 3 efficacy trial, if included in approved product labeling, would differentiate STS101 from competing products and increase its commercial potential. With the objective of demonstrating efficacy results to include in STS101 approved product labeling, we initiated in June 2021 the SUMMIT Phase 3 efficacy trial. SUMMIT utilizes a randomized, double-blind, placebo-controlled design similar to that of the EMERGE trial and as typically required by the FDA to support product-specific efficacy claims in product labeling and promotional materials. Whereas EMERGE was a three-arm trial (STS101 5.2 mg, STS101 3.9 mg and placebo) that enrolled approximately 400 subjects per arm, SUMMIT is a two-arm trial (STS101 5.2 mg and placebo) designed to enroll approximately 700 subjects per arm. The larger size of the SUMMIT trial provides greater statistical power to detect a potential treatment effect of STS101 5.2 mg versus placebo. We may also conduct additional clinical trials and consider additional headache indications for STS101 to maximize its commercial potential.

Because DHE is well characterized and previously approved, we intend to seek FDA marketing approval of STS101 under Section 505(b)(2) of the Federal Food, Drug and Cosmetic Act, which provides an alternate path to FDA approval for modifications to formulations of products previously approved by the FDA. Section 505(b)(2) permits the filing of an NDA where at least some of the information required for approval comes from non-clinical studies and clinical trials not conducted by or for the applicant and for which the applicant has not obtained a right of reference. By utilizing this pathway, and based on our discussions with the FDA, we believe we would be able to forego a Phase 2 clinical trial of STS101 by establishing that STS101 has comparative bioavailability to a reference listed drug with the PK results of one or more of our Phase 1 clinical trials.

In the United States, we intend to pursue a 505(b)(2) NDA for STS101 referencing the NDAs for D.H.E. 45 (DHE mesylate injectable solution) and Migranal (DHE mesylate liquid nasal spray). Migranal has no therapeutic equivalents (other than an authorized generic and three third-party generics) and is not covered under any unexpired patents that could delay approval of our NDA. We believe this development strategy could provide both an expeditious and cost-efficient approval pathway for STS101 in the United States.

In Europe, our regulatory strategy is to pursue marketing approval STS101 based on results of the clinical trials we complete in the United States, assuming such trials adequately establish the efficacy and safety of STS101. Based on feedback we have received from regulatory agencies in several European countries following scientific advice meetings, we believe our U.S. clinical program for STS101, if successful, could support marketing approval of STS101 in Europe. However, because European countries generally do not offer applicants regulatory pathways analogous to the U.S. 505(b)(2) pathway, some or all regulators in Europe could require us to successfully complete certain non-clinical studies prior to granting marketing approval for STS101.

### STS101 Clinical Trials

We have reported results from two Phase 1 clinical trials of STS101 in healthy volunteers, the first conducted in 2018 and the second in 2021. In both trials, STS101 demonstrated rapid and sustained DHE plasma concentrations, low pharmacokinetic variability, and a generally favorable safety and tolerability profile. We believe the overall pharmacokinetic profile demonstrated by STS101 5.2 mg in these trials should result in robust anti-migraine activity and a favorable safety and tolerability profile.

### EMERGE: Phase 3 Efficacy Trial

Our Phase 3 EMERGE efficacy trial was a multi-center, single-dose, randomized, double-blind, placebo-controlled, parallel group study to evaluate the efficacy, safety, and tolerability of single doses of STS101 in the acute treatment of migraine in approximately 1,140 subjects. After establishing eligibility, study participants were randomized (1:1:1) to receive one of three treatments: STS101 DHE 3.9 mg, STS101 DHE 5.2 mg or matching placebo. After randomization, the trial participants were instructed to treat their next migraine attack of moderate or severe pain severity with the allocated blinded study medication. All study participants were trained multiple times

in the STS101 administration procedure prior to use, and we provided each participant with an electronic device preloaded with diary software designed to capture relevant trial data.

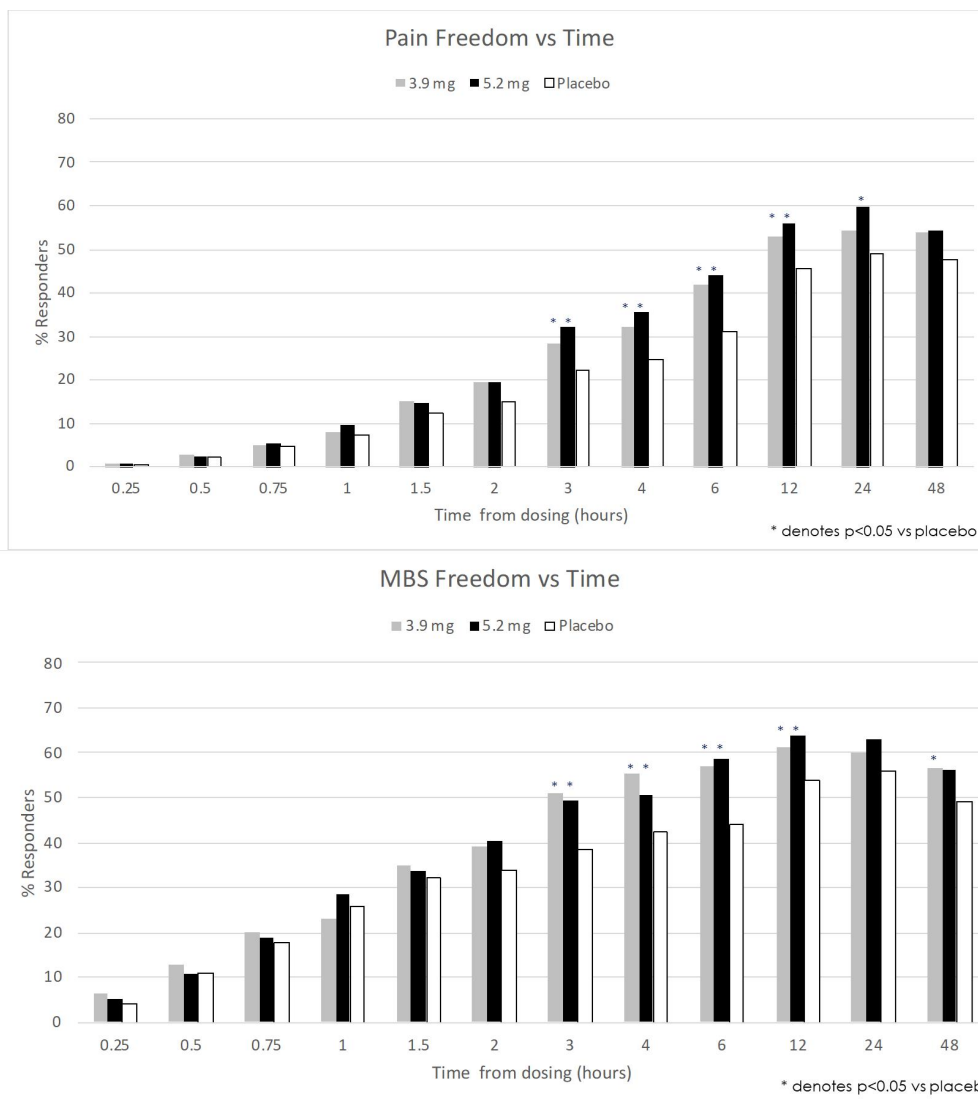
We completed enrollment in our EMERGE Phase 3 trial in May 2020, randomizing 1,201 subjects with migraine to one of two STS101 dosage strengths or placebo. In September 2020, we announced topline data from the EMERGE trial. Although STS101 3.9 mg and 5.2 mg showed favorable numerical differences versus placebo on the pre-specified co-primary endpoints of freedom from pain and freedom from most bothersome symptom (from among photophobia, phonophobia and nausea) at two hours post-administration, these differences did not achieve statistical significance (p-value <0.05) for either dosage strength. The table below summarizes the results of STS101 on the co-primary endpoints in the EMERGE trial.

<b>EMERGE Co-primary Endpoints*:</b>	<b>3.9 mg</b>	<b>5.2 mg</b>	<b>Placebo</b>
Subjects**	n=354	n=353	n=358
<b>Freedom from Pain at 2 hours</b>			
Number of subjects	69/354	68/353	53/358
% responders	<b>19.5%</b>	<b>19.3%</b>	<b>14.8%</b>
Difference vs Placebo	4.7%	4.5%	
p-value	0.10	0.11	---
<b>Freedom from Most Bothersome Symptom at 2 hours</b>			
Number of subjects	133/340	139/343	119/353
% responders	<b>39.1%</b>	<b>40.5%</b>	<b>33.7%</b>
Difference vs Placebo	5.4%	6.8%	
p-value	0.14	0.06	---

\* Per the EMERGE trial Statistical Analysis Plan, subjects who did not report efficacy data for the 2-hour post-treatment time point were imputed to be non-responders, irrespective of response status as of the last time point prior to 2 hours when efficacy data was reported.

\*\* All randomized subjects with a qualifying migraine attack who took study medication and provided efficacy data for at least one time point at or before two hours post-administration of study medication

As illustrated below, both dose strengths of STS101 did, however, demonstrate significant effects (nominal p-value < 0.05) on both freedom from pain and most bothersome symptom endpoints by three hours post-dose and later time points. In addition, STS101 demonstrated significant effects on multiple, pre-specified secondary efficacy endpoints.



Both STS101 dose strengths were generally well-tolerated in the EMERGE trial, with low adverse event rates and no drug-related serious adverse events reported. The most common treatment-emergent adverse events were nasal discomfort, dysgeusia, rhinorrhea, nasal congestion, and nausea. The most frequent nasal adverse event (discomfort) occurred in less than 6% of all trial participants who administered STS101.

We conducted multiple post-hoc analyses to determine why STS101 did not achieve statistical significance on co-primary endpoints in the EMERGE trial, and believe we have identified the key reasons. Our analyses suggest a significant proportion of subjects in EMERGE who self-administered STS101 to treat their migraine attacks may not have achieved and sustained target DHE plasma concentrations due to under-delivery of STS101. We believe we have addressed the under-delivery issue by (i) introducing improved instructions for STS101 use and training of

subjects in our clinical trials and (ii) making several minor modifications to the STS101 delivery device to improve its performance. We believe other factors also contributed to a negative outcome in the EMERGE trial, including: (i) early data entry by subjects in the electronic diary device due to device alarm programming; (ii) high proportions of subjects and treated migraine attacks with characteristics associated with poor treatment outcomes, and in particular, high proportions of subjects with pain of severe intensity immediately prior to treatment with study medication; and (iii) a high placebo response rate, particularly in light of the severe symptomology of the migraine attacks treated by subjects in the trial. We have taken steps that we believe will mitigate these issues in the ongoing SUMMIT Phase 3 efficacy trial of STS101.

### **ASCEND: Phase 3 Safety Trial**

In August 2020, we initiated our ASCEND trial, in which we have enrolled more than 480 subjects with migraine who treat their migraine attacks with STS101 on an as-needed basis for up to 12 months. As part of our efforts to address the STS101 under-delivery issue that we identified during our post-hoc analyses of the EMERGE trial results, we have introduced over the course of the ASCEND trial (and instituted in the SUMMIT trial) improvements to the instructions for STS101 use and training of subjects, as well as STS101 investigational product incorporating the minor modifications we have made to the STS101 delivery device to improve its performance. Based on our analyses of STS101 devices used by ASCEND subjects in treating their migraine attacks, which have demonstrated improved delivery performance, we believe the aforementioned measures we have implemented in the ASCEND and SUMMIT trials have addressed the under-delivery issue we saw in the EMERGE trial.

Our plan is to fulfill the target subject exposure requirements previously communicated to us by the FDA in writing (at least 150 subjects completing six months of treatment and potentially at least 50 subjects completing 12 months of treatment) using investigational product incorporating the improved second-generation STS101 delivery device. To date, subjects in the ASCEND trial have treated a total of more than 6,000 migraine attacks with STS101 5.2 mg. STS101 has been generally well-tolerated, with low adverse event rates. We expect topline results from the ASCEND trial in the second half of 2022.

### **SUMMIT Phase 3 Efficacy Trial**

In June 2021, we initiated the SUMMIT Phase 3 efficacy trial, a randomized, double-blind, placebo-controlled Phase 3 trial designed to evaluate the efficacy, safety and tolerability of a single dose of STS101 5.2 mg as an acute treatment for migraine in approximately 1,400 subjects. The SUMMIT trial utilizes investigational product that incorporates the modified and improved STS101 delivery device and improved instructions for STS101 use and training of subjects. In addition, we have made several modifications to the SUMMIT trial design and conduct, which, together with the improved STS101 delivery device and instructions for STS101 use and training, we believe will address the key reasons why STS101 did not achieve statistical significance on the co-primary endpoints in the EMERGE trial. We expect topline results from the SUMMIT trial in the fourth quarter of 2022.

If the SUMMIT and ASCEND trials are successful, we plan to file an NDA, for STS101 with the FDA in the first quarter of 2023.

### **Additional Trials**

To date, we and SNBL have completed preliminary human factors studies that we believe support self-administration of STS101 in the outpatient setting for the treatment of migraine and validate the STS101 instructions for use. We anticipate conducting further human factors studies, including a human factors validation study.

We may undertake additional clinical trials with STS101 to enhance its clinical profile. For example, unless we can successfully demonstrate by conducting drug-drug interaction studies and potentially additional studies that the coadministration of STS101 and certain other drugs does not result in drug-drug interactions, the FDA is likely to require a “black box” warning in the label for STS101, if approved, in line with the warnings that are included in the labels for other approved DHE products.

Because migraine affects adolescents (12 to 17 years of age) and children (six to eleven years of age), pediatric studies are required under the Federal Food, Drug, Cosmetic Act, or the FDCA. To address such

requirements, we designed an initial pediatric study plan, or iPSP, consistent with the FDA guidance *Migraine: Developing Drugs for Acute Treatment* (February 2018) and the FDA has agreed with our plan to request a waiver of clinical studies in children under age six. We are working with the FDA to finalize the iPSP, and to our knowledge the FDA has not previously required initiation of pediatric studies for any drug for the acute treatment of migraine prior to its approval in the adult population, there can be no assurance that the FDA will ultimately grant our proposed waiver and/or deferrals. As a result, we could be required to conduct pediatric studies in such patient populations prior to or following any approval of STS101. Under the pediatric exclusivity provision of the FDCA, if FDA issues a written request for the pediatric studies and they are conducted pursuant to the written request, STS101 could qualify for an additional six months of marketing exclusivity. Moreover, if the conducted iPSP leads to an approval of STS101 for pediatric migraine patients, then this population could use STS101.

## **Manufacturing**

Our manufacturing and regulatory teams have substantial experience in manufacturing process development, registration and the commercial manufacture of drug-device combination products, including inhalation-route drug-device combination products. We do not have internal manufacturing facilities and all of our manufacturing processes, which must comply with current good manufacturing practices, or cGMP, are outsourced to third party CMOs, with oversight by our internal managers. We own or have contracted to purchase certain equipment, including plastic component molds, semi-custom automated filling and assembly equipment, and semi-custom packaging equipment, for our third-party CMOs to utilize in the manufacture of STS101 or its components. We rely on third-party CMOs to produce sufficient quantities of drug product for use in clinical trials. We intend to continue this practice for any future clinical trials and production of STS101, if approved, for commercial sale.

We selected processes for manufacturing of STS101 that we believe are readily scalable and transferable, and all of our STS101 manufacturing processes employ standard technologies that are commonly utilized in the pharmaceutical industry for the manufacture of approved drug and drug-device combination products. However, certain processes for the manufacture of STS101 involve trade secrets and/or require custom or semi-custom equipment that is not available for off-the-shelf purchase, requires substantial investment, and/or has long lead times associated with its design, manufacture, delivery, installation and qualification.

The drug substance of STS101 is supplied by a drug substance manufacturer, which has extensive experience manufacturing the STS101 drug substance under cGMP, has an active Drug Master File, or DMF, registered with FDA, and has the capacity to meet our anticipated clinical and commercial supply needs. We believe there are additional drug substance manufacturers with active DMFs registered with the FDA that could potentially serve as back-up suppliers for us.

## **Commercial Operations**

If approved, we plan to commercialize STS101 in the United States by building a specialized sales organization focusing on headache specialists, as well as general neurologists and primary care physicians who are high prescribers of migraine therapeutics. Outside the United States, we intend to establish commercialization strategies for STS101 as we approach possible commercial approval in each market, which may include collaborations with other companies.

## **Competition**

The pharmaceutical industry is highly competitive, with a number of established, large pharmaceutical companies, as well as many smaller companies. Many of these companies have greater financial resources, marketing capabilities and experience in obtaining regulatory approvals for product candidates. If approved for the acute treatment of migraine, we anticipate that STS101 would compete against other marketed migraine therapies for the acute treatment of migraine and may compete with products currently under development by other companies.

In 2021, approximately 18.1 million prescriptions for migraine-specific acute therapies were written in the United States. This figure excludes prescriptions of non-specific therapies, such as nonsteroidal anti-inflammatory

drugs (NSAIDs) and acetaminophen, and thus likely understates the total number of prescriptions written for the acute treatment of migraine. The majority of the prescriptions written were for generic triptans. There are seven FDA-approved triptan molecules available in branded and branded generic/generic oral dosage forms, and two of these molecules are also available in injectable and/or liquid nasal spray dosage forms that may have faster onset of action than oral dosage forms. With respect to DHE products, we will compete with Bausch Health's Migranal DHE liquid nasal spray and its authorized and third-party generic equivalents as well as the branded injectable DHE product and its generic equivalents. In addition, in September 2021 Impel NeuroPharma announced FDA approval of a DHE liquid nasal spray product that utilizes the same liquid formulation and container closure system as Migranal, but with a different propellant-powered, single-use delivery device that requires a multi-step vial-opening, assembly and priming procedure. Impel NeuroPharma received FDA approval for its DHE liquid nasal spray product on the basis of a clinical development program that included only a comparative pharmacokinetic study and an open-label, uncontrolled, repeat-dose safety trial (and not a randomized, controlled, double-blinded Phase 3 efficacy study which the FDA typically requires to support any product-specific marketing claims relating to efficacy). Impel NeuroPharma has recently commenced commercialization of its DHE liquid nasal spray product in the U.S. We believe the Impel product has many of the same limitations as Migranal, does not significantly improve DHE absorption or pharmacokinetics as compared with Migranal to an extent that we believe likely to be clinically relevant, and has not been evaluated for efficacy in any randomized, controlled, double-blinded efficacy trial.

We also face competition from newer oral migraine-specific acute treatments that have been recently approved by FDA and commercially introduced in 2020 such as Eli Lilly's lasmiditan, a ditan, and two gepants, Abbvie's ubrogepant and Biohaven's rimegepant. Because rimegepant, ubrogepant, and lasmiditan are thought to act by mechanisms other than vasoconstriction, recommended use is not restricted to patients who do not have cardiovascular risk factors or disease, as is the case for triptan and ergot alkaloid products (including DHE) due to their vasoconstrictive actions. Although the labels for rimegepant, ubrogepant and lasmiditan do not limit use to patients without cardiovascular risk factors or disease, we believe these products have disadvantages. For example, lasmiditan has been reported to commonly cause central nervous system adverse events such as dizziness, somnolence and paresthesia, and the lasmiditan label includes warnings for driving impairment and operation of machinery for at least eight hours after taking a lasmiditan dose, central nervous system depression, serotonin syndrome, and medication overuse headache. Additionally, because lasmiditan has shown potential for abuse and dependence, the U.S. Drug Enforcement Agency, or DEA, has designated lasmiditan as a controlled substance; this designation imposes licensing and documentation requirements upon prescribers and as well restricts distribution. With ubrogepant and rimegepant, reported efficacy is modest in comparison with efficacy historically reported with triptan and DHE products. Moreover, prescribing of ubrogepant, and to a lesser extent rimegepant, may be complicated by the potential for interactions with a variety of prescription and over-the-counter medicines, vitamins and herbal supplements, with this potential necessitating dose adjustment of or contraindication to ubrogepant.

Although we believe STS101 and our development strategy has potential advantages over DHE liquid nasal sprays and other anti-migraine treatments, there can be no assurance that STS101, if approved, will be able to successfully compete against these products.

There are many pharmaceutical companies, biotechnology companies, public and private universities, government agencies and research organizations actively engaged in research and development of products which may target the same markets as STS101. We expect any future products we develop to compete on the basis of, among other things, product efficacy and safety, time to market, price, extent of adverse side effects experienced and convenience of administration and drug delivery. One or more of our competitors may develop products based upon the principles underlying our proprietary technologies earlier than us, obtain approvals for such products from the FDA more rapidly than us or develop alternative products or therapies that are safer, more effective and/or more cost effective than any future products developed by us. We also expect to face competition in our efforts to identify appropriate collaborators or partners to help commercialize STS101 in our target commercial areas outside the United States. Many of these companies have greater financial resources, marketing capabilities and experience in obtaining regulatory approvals for product candidates.

## **Intellectual Property**

Our commercial success depends in part on our ability to obtain and maintain proprietary protection for STS101, manufacturing and process discoveries, and other know how, to operate without infringing the proprietary

rights of others, and to prevent others from infringing our proprietary rights. Our policy is to seek to protect our proprietary position by, among other methods, filing U.S. and foreign patent applications related to our proprietary technology, inventions and improvements that are important to the development and implementation of our business. We also rely on trade secrets, know how, continuing technological innovation and potential in licensing opportunities to develop and maintain our proprietary position.

With regard to STS101, we have patents and applications to formulations, dosages, devices, and methods of use. As of December 31, 2020, we own or have exclusive license rights under more than sixty U.S. patents and foreign patents and pending applications. In the U.S., we own or have exclusive license rights under ten issued U.S. patents relating to STS101 with estimated expiration dates ranging from 2023 until the end of 2039 (absent any adjustments or extensions of term). Recently issued U.S. patents relating to STS101 that we own or are exclusively licensed under include U.S. Patent 10,758,532, issued September 1, 2020 and U.S. Patent 10,792,253, issued October 6, 2020. If issued, we project future patents resulting from pending U.S. patent applications relating to STS101 will expire between 2033 and 2040 (absent any adjustments or extensions of term). As of December 31, 2020, all but one issued U.S. and foreign patents relating to STS101 were exclusively licensed from SNBL. The pending U.S. and foreign patent applications relating to STS101 are solely owned by us or exclusively licensed from SNBL.

The patent portfolio for STS101 is directed to cover formulations, dosages, devices, and methods of treatment. This patent portfolio includes issued U.S. patents, pending U.S. patent applications and corresponding foreign national and regional counterpart patents and patent applications. As of December 31, 2020, all except one of the issued US patents were exclusively licensed from SNBL. Royalties on products covered by this exclusive license are payable on a product-by-product and country-by-country basis until the latter of the expiration of the last-to-expire patent covering such product and the ten-year anniversary of the first commercial sale of such product in such country. For more information on the SNBL License, see the section titled “Business—Licenses and Collaborations.” We own U.S. patent applications relating to the formulations, dosages, devices and methods of use for DHE and related compounds in the treatment and prevention of headache.

The terms of patents and patent applications, if issued, relating to STS101 in other jurisdictions (including Europe, Japan, China, India, Canada, Australia, Brazil, Korea, Mexico, Russia), if the appropriate maintenance, renewal, annuity and other government fees are paid, are expected to expire between 2025 and 2039. We also protect our proprietary technology and processes, in part, by confidentiality and invention assignment agreements with our employees, consultants, scientific advisors and other contractors. These agreements may be breached, and we may not have adequate remedies for any breach. In addition, our trade secrets may otherwise become known or be independently discovered by competitors. To the extent that our employees, consultants, scientific advisors or other contractors use intellectual property owned by others in their work for us, disputes may arise as to the rights in related or resulting know how and inventions.

Our commercial success will also depend in part on not infringing the proprietary rights of third parties. It is uncertain whether the issuance of any third-party patent would require us to alter our development or commercial strategies, alter our drugs or processes, obtain licenses or cease certain activities. Our breach of any license agreements or failure to obtain a license to proprietary rights that we may require to develop or commercialize our future drugs may have a material adverse impact on us. If third parties prepare and file patent applications in the United States that also claim technology to which we have rights, we may have to participate in interference proceedings in the United States Patent and Trademark Office, or USPTO, to determine priority of invention.

## **Licenses and Collaborations**

In June 2016, we and SNBL, entered into a licensing and assignment agreement, or the SNBL License, which was amended and restated in December 2016 and further amended in January 2017, April 2017, October 2017, and May 2020. We currently rely and intend to continue to rely on the SNBL License for purposes of our development and potential commercialization of STS101. From the time we entered into the SNBL License until the consummation of our Series A convertible preferred stock financing in December 2016, we were a subsidiary of SNBL and SNBL continues to hold over 5% of our outstanding capital stock. Under the SNBL License, SNBL assigned to us certain patent rights and know-how that are directed to SNBL’s proprietary nasal drug delivery technology, including its proprietary nasal delivery device, or the Device, and formulation technologies, for use with

DHE, or the DHE Product. SNBL granted to us an exclusive, worldwide, royalty-bearing, sublicensable license, under certain patent rights and know-how, other than the assigned patent rights and know-how, to develop, make, use, and commercialize DHE Products in the field of treatment, prevention or prophylaxis of all indications and human medical conditions, as well as the products consisting of the Device used to deliver a combination of DHE and one or more active pharmaceutical ingredients other than DHE, or DHE Combination Products, in the field of treatment, prevention or prophylaxis of migraine and non-migraine headaches. We granted to SNBL a non-exclusive, royalty-free, sublicensable license, under our rights in improvements to the Device, to develop, make, use, and commercialize products and devices other than DHE Products and DHE Combination Products. During the term of the SNBL License, we, SNBL, and our and SNBL's affiliates are not permitted to develop or commercialize, or to enable third parties to develop or commercialize, a product containing DHE as an active ingredient for delivery through nasal tissues or the respiratory system, other than pursuant to the SNBL License. We will be responsible, at our cost, for the development, manufacture and commercialization of DHE Products and DHE Combination Products under the SNBL License. We are required to use commercially reasonable efforts to develop and commercialize at least one such product, initially in the United States.

Under the SNBL License, in 2016 we reimbursed SNBL for approximately \$80,000 of costs relating to our incorporation and prosecution and maintenance of the product-specific patents. We also agreed to make royalty payments based on a low single-digit percentage of worldwide net sales of DHE Products and DHE Combination Products, payable on a product-by-product and country-by-country basis until the latest of the expiration of the last-to-expire patent covering such product and the ten-year anniversary of the first commercial sale of such product in such country. The royalty payments are subject to reductions based on royalties paid to any third party under a license to such third party's patent rights.

We have the sole right to control the prosecution and maintenance of, and to enforce, the patent rights that SNBL assigned to us. SNBL has the first right to control the prosecution and maintenance of the patent rights that SNBL licensed to us. We have step in rights if SNBL does not continue such prosecution and maintenance. We also have the first right to enforce such licensed patent rights with respect to certain infringing products. If we do not bring an action to enforce such patents against infringing activities that involve such infringing products, SNBL has the right to bring such an action.

The SNBL License continues on a country-by-country and product-by-product basis until the expiration of the obligation to pay royalties with respect such product and country. We may terminate the SNBL License in its entirety without cause on ninety days' prior written notice. SNBL may terminate the SNBL License for our material breach that remains uncured for ninety days. SNBL may also terminate the SNBL License if we challenge the licensed patents, or if we assist any third party in challenging such patents. In addition, SNBL has the right to terminate the license agreement upon our insolvency.

#### **Government Regulation**

The FDA and other regulatory authorities at federal, state, and local levels, as well as in foreign countries, extensively regulate, among other things, the research, development, testing, manufacture, storage, recordkeeping, approval, labeling, marketing and promotion, distribution, post-approval monitoring and reporting, sampling, and import and export of products, such as those we are developing. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations require the expenditure of substantial time and financial resources.

Our product candidate, STS101, is subject to regulation in the United States as a drug-device combination product. If marketed individually, the drug component and the propriety device component would be subject to different regulatory pathways and would require approval of independent marketing applications by the FDA. A combination product, however, is assigned to a Center within FDA that will have primary jurisdiction over the product's regulation based on a determination of the combination product's primary mode of action, which is the single mode of action that provides the most important therapeutic action. In the case of STS101, the FDA has confirmed that the primary mode of action is attributable to the drug component of the product. Accordingly, STS101 will be regulated as a drug product by the FDA's Center for Drug Evaluation and Research, or CDER, which will have primary jurisdiction over premarket development and approval. We plan to seek approval of STS101 through an NDA submitted to CDER through the 505(b)(2) approval pathway. We do not expect that the



FDA will require separate marketing authorization for the proprietary device constituent of STS101. However, the drug delivery device component of STS101 will be subject to consulting review by FDA's Center for Devices and Radiological Health, and we will be required to comply with applicable provisions of the medical device Quality System Regulation as part of ensuring STS101 complies with cGMP. The FDA will also require that we conduct human factors studies to support approval of STS101. To date, we and SNBL have completed preliminary human factors studies that we believe support self-administration of STS101 in the outpatient setting for the treatment of migraine and validate the STS101 instructions for use that we are utilizing. We anticipate conducting further human factors studies, including a human factors validation study.

## **U.S. Drug Regulation**

In the United States, the FDA regulates drugs under the FDCA and its implementing regulations. FDA approval is required before any new unapproved drug or dosage form, including a new use or new formulation of a previously approved drug, can be marketed in the United States. Drugs are also subject to other federal, state and local statutes and regulations. Failure to comply with applicable FDA or other requirements may subject a company to a variety of administrative or judicial sanctions, such as FDA clinical holds, refusal to approve pending applications, withdrawal of an approval, warning or untitled letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, civil penalties and criminal prosecution.

The process required by the FDA before product candidates may be marketed in the United States generally involves the following:

- completion of preclinical laboratory tests and animal studies, all performed in accordance with the FDA's Good Laboratory Practice, or GLP, regulations;
- submission to the FDA of an IND, which must become effective before human clinical studies may begin and must be updated annually or when significant changes are made;
- approval by an independent institutional review board, or IRB, representing each clinical site before a clinical study may be initiated;
- performance of adequate and well-controlled human clinical trials in accordance with good clinical practice, or GCP, regulations to establish the safety and efficacy of the product candidate for each proposed indication;
- preparation of and submission to the FDA of an NDA;
- satisfactory completion of an FDA advisory committee review, if applicable;
- a determination by the FDA within 60 days of its receipt of an NDA to file the application for review;
- satisfactory completion of an FDA pre-approval inspection of the manufacturing facility(ies) where the product is manufactured to assess compliance with current good manufacturing practice, or cGMP, regulations, and of selected clinical investigation sites to assess compliance with GCP; and
- FDA review and approval of an NDA to permit commercial marketing of the product for its particular labeled uses in the United States.

### ***Preclinical and Clinical Studies***

The preclinical and clinical testing and approval process can take many years and the actual time required to obtain approval, if any, may vary substantially based upon the type, complexity and novelty of the product or condition being treated.

Preclinical tests include laboratory evaluation of product chemistry, formulation and toxicity, as well as animal studies to assess the characteristics and potential safety and efficacy of the product. The conduct of preclinical tests must comply with federal regulations and requirements, including GLP. The results of preclinical testing are submitted to the FDA as part of an IND along with other information, including information about product chemistry, manufacturing and controls and any available human data or literature to support use of the

product in humans. Long-term preclinical tests, such as animal tests of reproductive toxicity and carcinogenicity, may continue after the IND is submitted.

The central focus of an IND submission is on the general investigational plan and the protocol(s) for human studies. An IND must become effective before human clinical trials may begin. An IND will automatically become effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or questions related to the proposed clinical studies. In such a case, the IND may be placed on clinical hold and the IND sponsor and the FDA must resolve any outstanding concerns or questions before clinical studies can begin. A separate submission to an existing IND must also be made for each successive clinical trial conducted during product development along with any subsequent changes to the investigational plan.

Clinical studies involve the administration of the investigational new drug to human subjects under the supervision of qualified investigators in accordance with GCPs, which include the requirement that all research subjects provide their informed consent for participation in each clinical study. Clinical studies are conducted under protocols detailing, among other things, the objectives of the study, the parameters to be used in monitoring safety and the efficacy criteria to be evaluated. A protocol for each clinical study and any subsequent protocol amendments must be submitted to the FDA as part of the IND. Additionally, approval must also be obtained from each clinical study site's IRB before a study may be initiated at the site, and the IRB must monitor the study until completed. Sponsors of clinical trials generally must register and report ongoing clinical studies and clinical study results to public registries, including the website maintained by the U.S. National Institutes of Health, ClinicalTrials.gov.

For purposes of NDA approval, human clinical trials are typically divided into three or four phases. Although the phases are usually conducted sequentially, they may overlap or be combined.

- Phase 1. The drug is initially introduced into healthy human subjects or into subjects with the target disease or condition. These studies are designed to evaluate the safety, dosage tolerance, metabolism and pharmacologic actions of the drug in humans, the side effects associated with increasing doses, and if possible, to gain early evidence on effectiveness.
- Phase 2. The drug is administered to a limited population of subjects with the target disease or condition to evaluate dosage tolerance and optimal dosage, identify possible adverse side effects and safety risks and preliminarily evaluate efficacy.
- Phase 3. The drug is administered to an expanded population of subjects with the target disease or condition, generally at geographically dispersed clinical study sites to generate enough data to statistically evaluate dosage, clinical effectiveness and safety, to establish the overall benefit-risk relationship of the investigational product and to provide an adequate basis for product approval.
- Phase 4. In some cases, the FDA may condition approval of an NDA for a product candidate on the sponsor's agreement to conduct additional clinical studies after approval. In other cases, a sponsor may voluntarily conduct additional clinical studies after approval to gain more information about the drug. Such post-approval studies are typically referred to as Phase 4 clinical studies.

The FDA, the IRB or the clinical study sponsor may suspend or terminate a clinical study at any time on various grounds, including a finding that the research subjects are being exposed to an unacceptable health risk. We may also suspend or terminate a clinical study based on evolving business objectives and/or competitive climate.

Concurrent with clinical trials, companies may complete additional animal studies and develop additional information about the characteristics of the product candidate, and must finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the product and, among other things, must include methods for testing the identity, strength, quality and purity of the final product. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the product does not undergo unacceptable deterioration over its shelf life.

### ***Submission of an NDA to the FDA***

Assuming successful completion of all required testing in accordance with all applicable regulatory requirements, the results of product development and testing are submitted to the FDA in the form of an NDA requesting approval to market the product for one or more indications. The submission of an NDA requires payment of a substantial application user fee to the FDA, unless a waiver or exemption applies.

An NDA must include all relevant data available from pertinent preclinical and clinical studies, including negative or ambiguous results as well as positive findings, together with detailed information relating to the product's chemistry, manufacturing, controls and proposed labeling, among other things. Data can come from company-sponsored clinical studies intended to test the safety and effectiveness of a use of a product, or from a number of alternative sources, including studies initiated by investigators. To support marketing approval, the data submitted must be sufficient in quality and quantity to establish the safety and effectiveness of the investigational product to the satisfaction of the FDA.

The 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. The FDA may request additional information rather than accept an application for filing. In this event, the application must be resubmitted with the additional information and is subject to payment of additional user fees. The resubmitted application is also subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in-depth substantive review. Under the Prescription Drug User Fee Act, or PDUFA, the FDA has agreed to certain performance goals in the review of NDAs through a two-tiered classification system, standard review and priority review. Priority review designation is given to drugs that offer major advances in treatment, or provide a treatment where no adequate therapy exists. According to PDUFA performance goals, the FDA endeavors to review applications subject to standard review within ten to twelve months, whereas the FDA's goal is to review priority review applications within six to eight months, depending on whether the drug is a new molecular entity.

The FDA may refer applications for novel drug products or drug products which present difficult questions of safety or efficacy to an advisory committee for review, evaluation and recommendation as to whether the application should be approved and under what conditions.

Before approving an NDA, the FDA typically will inspect the facility or facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, the FDA will typically inspect one or more clinical sites to assure that relevant study data was obtained in compliance with GCP requirements.

After the FDA evaluates the NDA and conducts inspections of manufacturing facilities, it may issue an approval letter or a complete response letter. A complete response letter indicates that the review cycle of the application is complete and the application is not ready for approval. A tentative approval may be issued for an NDA submitted under Section 505(b)(2) of the FDCA if the sponsor must await the expiration of applicable patents or other exclusivity covering the previously approved product referenced in the application before obtaining final approval. A complete response letter generally outlines the deficiencies in the submission and may require substantial additional testing or information in order for the FDA to reconsider the application. Even with submission of this additional information, the FDA may ultimately decide that an application does not satisfy the regulatory criteria for approval. If, or when, the deficiencies have been addressed to the FDA's satisfaction in a resubmission of the application, the FDA will issue an approval letter. An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications.

As a condition of NDA approval, the FDA may require a Risk Evaluation and Mitigation Strategy, or REMS, program to help ensure that the benefits of the drug outweigh its risks. If the FDA determines a REMS program is necessary during review of the application, the drug sponsor must agree to the REMS plan at the time of approval. For 505(b)(2) NDAs, FDA will typically require a REMS if the reference product is required to have a REMS. A REMS program may be required to include various elements, such as a medication guide or patient package insert, a communication plan to educate healthcare providers of the drug's risks, or other elements to assure safe use, such as limitations on who may prescribe or dispense the drug, dispensing only under certain circumstances, special

monitoring and the use of patient registries. In addition, all REMS programs must include a timetable to periodically assess the strategy following implementation.

Further, product approval may require substantial post-approval testing and surveillance to monitor the drug's safety and efficacy, and the FDA has the authority to prevent or limit further marketing of a product based on the results of these post-marketing programs. Once granted, product approvals may be withdrawn if compliance with regulatory standards is not maintained or problems are identified following initial marketing. Moreover, changes to the conditions established in an approved application, including changes in indications, labeling or manufacturing processes or facilities may require submission and FDA approval of a new NDA or NDA supplement before the changes can be implemented. An NDA supplement for a new indication typically requires clinical data similar to that supporting the original approval, and the FDA uses similar procedures in reviewing supplements as it does in reviewing original applications.

### ***Post-Approval Requirements***

Once an NDA is approved, a product will be subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to drug listing and registration, recordkeeping, periodic reporting, product sampling and distribution, adverse event reporting and advertising, marketing and promotion. Drugs may be marketed only for the approved indications and in accordance with the provisions of the approved labeling. While physicians may prescribe for off-label uses, manufacturers may only promote for the approved indications and in accordance with the provisions of the approved label. However, companies may share truthful and not misleading information that is otherwise consistent with a product's FDA approved labeling. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability.

After approval, most changes to the approved product, such as adding new indications or other labeling claims, are subject to prior FDA review and approval. There also are continuing user fee requirements, under which FDA assesses an annual program fee for each product identified in an approved NDA. 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 the FDA and certain state agencies. Registration with the FDA subjects entities to periodic unannounced and announced inspections by the FDA and these state agencies, during which the agency inspects manufacturing facilities to assess compliance with cGMPs. FDA regulations also require investigation and correction of any deviations from cGMP and impose reporting requirements upon us and any third-party manufacturers that we may decide to use. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain compliance with cGMP and other aspects of regulatory compliance.

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

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

The FDA may also require post-approval studies and clinical trials if the FDA finds that scientific data, including information regarding related drugs, deem it appropriate. The purpose of such studies would be to assess a known serious risk or signals of serious risk related to the drug or to identify an unexpected serious risk when available data indicate the potential for a serious risk. The FDA may also require a labeling change if it becomes aware of new safety information that it believes should be included in the labeling of a drug.

## **The Hatch-Waxman Amendments**

### ***ANDA Approval Process***

The Hatch-Waxman Amendments established abbreviated FDA approval procedures for drugs that are shown to be equivalent to proprietary drugs previously approved by the FDA through its NDA process. Approval to market and distribute these drugs is obtained by filing an abbreviated new drug application, or ANDA, with the FDA.

An ANDA is a comprehensive submission that contains, among other things, data and information pertaining to the active pharmaceutical ingredient, drug product formulation, specifications and stability of the generic drug, as well as analytical methods, manufacturing process validation data and quality control procedures. Premarket applications for generic drugs are termed abbreviated because they generally do not include preclinical and clinical data to demonstrate safety and effectiveness. Instead, a generic applicant must demonstrate that its product is bioequivalent to the innovator drug. In certain situations, an applicant may obtain ANDA approval of a generic product with a strength or dosage form that differs from a referenced innovator drug pursuant to the filing and approval of an ANDA suitability petition. The FDA will approve the generic product as suitable for an ANDA application if it finds that the generic product does not raise new questions of safety and effectiveness as compared to the innovator product. A product is not eligible for ANDA approval if the FDA determines that it is not equivalent to the referenced innovator drug or is intended for a different use, and it is not otherwise subject to an approved suitability petition. However, such a product might be approved under an NDA, with supportive data from clinical trials.

### ***505(b)(2) NDAs***

As an alternative path to FDA approval for modifications to formulations or uses of products previously approved by the FDA, an applicant may submit an NDA under Section 505(b)(2) of the FDCA. Section 505(b)(2) was enacted as part of the Hatch-Waxman Amendments and permits the filing of an NDA where at least some of the information required for approval comes from studies not conducted by, or for, the applicant. If the 505(b)(2) applicant can establish that reliance on FDA's previous findings of safety and effectiveness is scientifically appropriate, it may eliminate the need to conduct certain preclinical or clinical studies of the new product. The FDA may also require companies to perform additional studies or measurements, including clinical trials, to support the change from the approved reference drug. The FDA may then approve the new product candidate for all, or some, of the label indications for which the reference drug has been approved, as well as for any new indication sought by the 505(b)(2) applicant.

### ***Orange Book Listing***

In seeking approval for a drug through an NDA, including a 505(b)(2) NDA, applicants are required to list with the FDA certain patents whose claims cover the applicant's product. Upon approval of an NDA, each of the patents listed in the application for the drug is then published in the Orange Book. Any applicant who files an ANDA seeking approval of a generic equivalent version of a drug listed in the Orange Book or a 505(b)(2) NDA referencing a drug listed in the Orange Book must certify to the FDA that (1) no patent information on the drug product that is the subject of the application has been submitted to the FDA; (2) such patent has expired; (3) the date on which such patent expires; or (4) such patent is invalid or will not be infringed upon by the manufacture, use or sale of the drug product for which the application is submitted. This last certification is known as a paragraph IV certification. A notice of the paragraph IV certification must be provided to each owner of the patent that is the subject of the certification and to the holder of the approved NDA to which the ANDA or 505(b)(2) application refers. The applicant may also elect to submit a "section viii" statement certifying that its proposed label does not contain (or carves out) any language regarding the patented method-of-use rather than certify to a listed method-of-use patent.

If the reference NDA holder and patent owners assert a patent challenge directed to one of the Orange Book listed patents within 45 days of the receipt of the paragraph IV certification notice, the FDA is prohibited from approving the application until the earlier of 30 months from the receipt of the paragraph IV certification expiration of the patent, settlement of the lawsuit or a decision in the infringement case that is favorable to the applicant. The ANDA or 505(b)(2) application also will not be approved until any applicable non-patent exclusivity listed in the Orange Book for the reference drug has expired.

### ***Non-Patent Exclusivity***

In addition to patent exclusivity, NDA holders may be entitled to a period of non-patent exclusivity, during which the FDA cannot approve an ANDA or 505(b)(2) application that relies on the listed drug. For example, a pharmaceutical manufacturer may obtain five years of non-patent exclusivity upon NDA approval of a new chemical entity, or NCE, which is a drug that contains an active moiety that has not been approved by FDA in any other NDA.

A non-NCE drug, including one approved under Section 505(b)(2), may qualify for a three-year period of exclusivity for a particular condition of approval or change to a previously approved product, such as a new formulation or method of administration for a previously approved product, if one or more new clinical studies (other than bioavailability or bioequivalence studies) was essential to the approval of the application and was conducted or sponsored by the applicant. Should this occur, the FDA would be precluded from approving any ANDA or 505(b)(2) application for the protected modification until after that three-year exclusivity period has concluded. However, unlike NCE exclusivity, the FDA can accept an application and begin the review process during the exclusivity period. A drug approved under Section 505(b)(2) may also be eligible for pediatric exclusivity if the FDA issues a Written Request for one or more pediatric studies, the manufacturer conducts the studies and submits written reports to the FDA, and such studies meet the conditions of the Written Request. If granted, pediatric exclusivity extends any existing marketing exclusivity or patent protection for the product by an additional six months.

### ***International Regulation***

In addition to regulations in the United States, we could become subject to a variety of foreign regulations regarding development, approval, commercial sales and distribution of our products if we seek to market STS101 in other jurisdictions. Whether or not we obtain FDA approval for a product, we must obtain the necessary approvals by the comparable 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 can involve additional product testing and additional review periods, and the time may be longer or shorter than that required to obtain FDA approval. The requirements governing, among other things, the conduct of clinical trials, product licensing, pricing and reimbursement vary greatly from country to country. Regulatory approval in one country does not ensure regulatory approval in another, but a failure or delay in obtaining regulatory approval in one country may negatively impact the regulatory process in others. If we fail to comply with applicable foreign regulatory requirements, we may be subject to fines, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecution.

### ***Other Healthcare Laws***

Pharmaceutical companies are subject to additional healthcare regulation and enforcement by the federal government and by authorities in the states and foreign jurisdictions in which they conduct their business. Such laws include, without limitation, U.S. federal and state fraud and abuse laws, including anti-kickback, false claims, civil monetary penalties laws, consumer protection and transparency laws as well as similar foreign laws in the jurisdictions outside the U.S. For example, the federal Anti-Kickback Statute prohibits, among other things, individuals or entities from knowingly and willfully offering, paying, soliciting or receiving remuneration, directly or indirectly, overtly or covertly, in cash or in kind to induce or in return for purchasing, leasing, ordering or arranging for or recommending the purchase, lease or order of any item or service reimbursable under Medicare, Medicaid or other federal healthcare programs. A person or entity does not need to have actual knowledge of this statute or specific intent to violate it in order to have committed a violation. The federal civil and criminal false claims laws, including the civil False Claims Act, prohibit, among other things, any individual or entity from knowingly presenting, or causing to be presented, a false claim for payment to the federal government or knowingly

making, using or causing to be made or used a false record or statement material to a false or fraudulent claim to the federal government. In addition, the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the civil False Claims Act.

The federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, created additional federal civil and criminal statutes that prohibit, among other things, knowingly and willfully executing a scheme to defraud any healthcare benefit program. Similar to the U.S. federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the healthcare fraud statute implemented under HIPAA or specific intent to violate it in order to have committed a violation. The federal Physician Payments Sunshine Act requires certain manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children’s Health Insurance Program, with specific exceptions, to report annually to CMS information related to payments or other transfers of value made to physicians, certain other healthcare professionals beginning in 2022, and teaching hospitals, and applicable manufacturers and applicable group purchasing organizations to report annually to CMS ownership and investment interests held by physicians and their immediate family members.

Similar state and local laws and regulations may also restrict business practices in the pharmaceutical industry, such as state anti-kickback and false claims laws, which may apply to business practices, including but not limited to, research, distribution, sales and marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers, or by patients themselves; state laws that require pharmaceutical companies to comply with the pharmaceutical industry’s voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government, or otherwise restrict payments that may be made to healthcare providers and other potential referral sources; state laws and regulations that require drug manufacturers to file reports relating to pricing and marketing information or which require tracking gifts and other remuneration and items of value provided to physicians, other healthcare providers and entities; and state and local laws that require the registration of pharmaceutical sales representatives.

Violation of any of these laws or any other governmental regulations that apply may result in penalties, including, without limitation, administrative, civil and criminal penalties, damages, fines, disgorgement, integrity oversight and reporting obligations, the curtailment or restructuring of operations, exclusion from participation in governmental healthcare programs and imprisonment.

### **Data Privacy and Security Laws**

Pharmaceutical companies may be subject to U.S. federal and state health information privacy, security and data breach notification laws, which may govern the collection, use, disclosure and protection of health-related and other personal information. In the U.S., HIPAA imposes privacy, security and breach reporting obligations with respect to individually identifiable health information upon “covered entities” (health plans, health care clearinghouses and certain health care providers), and their respective business associates, individuals or entities that create, receive, maintain or transmit protected health information in connection with providing a service for or on behalf of a covered entity. HIPAA mandates the reporting of certain breaches of health information to HHS, affected individuals and if the breach is large enough, the media. Entities that are found to be in violation of HIPAA as the result of a breach of unsecured PHI, a complaint about privacy practices or an audit by the Department of Health and Human Services, or HHS, may be subject to significant civil, criminal and administrative fines and penalties and/or additional reporting and oversight obligations if required to enter into a resolution agreement and corrective action plan with HHS to settle allegations of HIPAA non-compliance. Even when HIPAA does not apply, according to the Federal Trade Commission or the FTC, failing to take appropriate steps to keep consumers’ personal information secure constitutes unfair acts or practices in or affecting commerce in violation of Section 5(a) of the Federal Trade Commission Act, or the FTCA, 15 U.S.C § 45(a). The FTC expects a company’s data security measures to be reasonable and appropriate in light of the sensitivity and volume of consumer information it holds, the size and complexity of its business, and the cost of available tools to improve security and reduce vulnerabilities. Individually identifiable health information is considered sensitive data that merits stronger safeguards. The FTC’s guidance for appropriately securing consumers’ personal information is similar to what is required by the HIPAA Security Rule.

In addition, certain state laws govern the privacy and security of health information in certain circumstances, some of which are more stringent, broader in scope or offer greater individual rights with respect to protected health information, or PHI, than HIPAA and many of which may differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts. Failure to comply with these laws, where applicable, can

result in the imposition of significant civil and/or criminal penalties and private litigation. For example, California recently enacted legislation, the California Consumer Privacy Act, or CCPA, which went into effect January 1, 2020. The CCPA, among other things, creates new data privacy obligations for covered companies and provides new privacy rights to California residents, including the right to opt out of certain disclosures of their information. The CCPA also creates a private right of action with statutory damages for certain data breaches, thereby potentially increasing risks associated with a data breach. Although the law includes limited exceptions, including for “protected health information” maintained by a covered entity or business associate, it may regulate or impact our processing of personal information depending on the context.

European Union member states, the United Kingdom, Switzerland and other jurisdictions have also adopted data protection laws and regulations, which impose significant compliance obligations. In the EEA and the United Kingdom, the collection and use of personal data, including clinical trial data, is governed by the provisions of the General Data Protection Regulation, or GDPR. The GDPR became effective on May 25, 2018, repealing its predecessor directive and increasing responsibility and liability of pharmaceutical companies in relation to the processing of personal data of EU data subjects. The GDPR, together with national legislation, regulations and guidelines of the EU member states and the United Kingdom governing the processing of personal data, impose strict obligations and restrictions on the ability to collect, analyze and transfer personal data, including health data from clinical trials and adverse event reporting. In particular, these obligations and restrictions concern the consent of the individuals to whom the personal data relates, the information provided to the individuals, the transfer of personal data out of the EEA or the United Kingdom, security breach notifications, security and confidentiality of the personal data and imposition of substantial potential fines for breaches of the data protection obligations. European data protection authorities may interpret the GDPR and national laws differently and impose additional requirements, which add to the complexity of processing personal data in or from the EEA or United Kingdom. Guidance on implementation and compliance practices are often updated or otherwise revised.

### **Coverage and Reimbursement**

Sales of any pharmaceutical product depend, in part, on the extent to which such product will be covered by third-party payors, such as federal, state and foreign government healthcare programs, commercial insurance and managed healthcare organizations, and the level of reimbursement for such product by third-party payors. No uniform policy exists for coverage and reimbursement for products exists among U.S. third-party payors. Therefore, decisions regarding the extent of coverage and amount of reimbursement to be provided are made on a plan-by-plan basis. The process for determining whether a third-party payor will provide coverage for a product typically is separate from the process for setting the price of such product or for establishing the reimbursement rate that the payor will pay for the product once coverage is approved. Third-party payors may limit coverage to specific products on an approved list, also known as a formulary, which might not include all of the FDA-approved products for a particular indication, or place products at certain formulary levels that result in lower reimbursement levels and higher cost-sharing obligation imposed on patients. One third-party payor’s decision to cover a particular medical product or service does not ensure that other payors will also provide coverage for the medical product or service. As a result, the coverage determination process will often require us to provide scientific and clinical support for the use of our products to each payor separately and can be a time-consuming process, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance. Existing acute treatments for migraine are generally covered or reimbursed by third-party payers and, based on preliminary primary market research we have conducted with certain third-party payers, we believe that STS101, if approved, would qualify for coverage and reimbursement substantially similar to other branded acute treatments for migraine; however, such research is preliminary and we cannot guarantee the availability of coverage or adequacy of reimbursement at this time.

In international markets, reimbursement and healthcare payment systems vary significantly by country, and many countries have instituted price ceilings on specific products and therapies. For example, the European Union provides options for its member states to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. A member state may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. Pharmaceutical products may face competition from lower-priced products in foreign countries that have placed price controls on pharmaceutical products. Furthermore, there can be no assurance that a product will be considered medically reasonable and necessary for a specific indication, that a product will be considered cost-effective by third-party



payors, that an adequate level of reimbursement will be established even if coverage is available or that the third-party payors' reimbursement policies will not adversely affect the ability to sell a product profitably.

## Healthcare Reform

In the United States and certain foreign jurisdictions, there have been, and we expect there will continue to be, a number of legislative and regulatory changes to the healthcare system. By way of example, in the United States, in March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or collectively the ACA, was signed into law, which substantially changed the way healthcare is financed by both governmental and private insurers and significantly affected the pharmaceutical industry. The ACA contained a number of provisions, including those governing enrollment in federal healthcare programs, reimbursement adjustments and changes to fraud and abuse laws. Additionally, the ACA increased the minimum level of Medicaid rebates payable by manufacturers of brand name drugs from 15.1% to 23.1% of the average manufacturer price; required collection of rebates for drugs paid by Medicaid managed care organizations; required manufacturers to participate in a coverage gap discount program, under which they must agree to offer 70% point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D; imposed a non-deductible annual fee on pharmaceutical manufacturers or importers who sell certain "branded prescription drugs" to specified federal government programs, implemented a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted, or injected; expanded eligibility criteria for Medicaid programs; creates 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 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.

Since its enactment, there have been judicial, executive and Congressional challenges to certain aspects of the ACA. For example, in 2017, Congress enacted the Tax Cuts and Jobs Act, which eliminated 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." On December 14, 2018, a U.S. District Court Judge in the Northern District of Texas, or the Texas District Court Judge, ruled that the individual mandate is a critical and inseparable feature of the ACA, and therefore, because it was repealed as part of the Tax Cuts and Jobs Act, the remaining provisions of the ACA are invalid as well. On December 18, 2019, the U.S. Court of Appeals for the 5th Circuit ruled that the individual mandate was unconstitutional and remanded the case back to the District Court to determine whether the remaining provisions of the ACA are invalid as well. The U.S. Supreme Court is currently reviewing the case, although it is unclear how Supreme Court will rule. It is also unclear how, and other efforts, if any, to challenge, repeal or replace the ACA will impact the ACA.

Other legislative changes have been proposed and adopted since the ACA was enacted, including aggregate reductions of Medicare payments to providers of 2% per fiscal year and reduced payments to several types of Medicare providers, which will remain in effect through 2030, with the exception of a temporary suspension from May 1, 2020 through March 31, 2021, absent additional congressional action. Moreover, there has recently 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 legislation designed, among other things, to bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs and reform government program reimbursement methodologies for pharmaceutical products. Individual states in the United States have also become increasingly active in implementing regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures and, in some cases, mechanisms to encourage importation from other countries and bulk purchasing. Furthermore, there has been increased interest by third party payors and governmental authorities in reference pricing systems and publication of discounts and list prices.

## **Employees and Human Capital Resources**

As of December 31, 2021, we had 21 employees, all of whom were full-time. None of our employees is represented by a labor union or a collective bargaining agreement. We consider our relationship with our employees to be good.

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

## **Segment Information**

We have one primary business activity and operate one reportable segment.

## **Facilities**

Our corporate headquarters are located in South San Francisco, California, where we lease approximately 4,148 square feet of office space pursuant to a lease dated January 9, 2018, which continues through October 31, 2022. We are in the process of negotiating an extension on this lease. In addition, we lease approximately 5,043 square feet of office space in Research Triangle Park, North Carolina pursuant to a lease dated August 1, 2019, which continues through July 31, 2025. We believe these facilities are sufficient for our near-term needs, and expect to expand to new and/or additional space as we grow. We believe the biotechnology environment in the South San Francisco area offers suitable additional space on commercially reasonable terms to enable our expansion.

## **Legal Proceedings**

We are not currently involved in any litigation or legal proceedings that, in management's opinion, are likely to have any material adverse effect on our company.

## **Corporate Information**

We were founded on June 21, 2016 as a Delaware corporation under the name Satsuma Pharmaceuticals, Inc. Our principal executive offices are located at 400 Oyster Point Boulevard, Suite 221, South San Francisco, CA 94080, and our telephone number is (650) 410-3200. Our website address is [www.satsumarx.com](http://www.satsumarx.com). The information on, or that can be accessed through, our website is not incorporated by reference in this annual report on Form 10-K or in any other filings we make with the Securities and Exchange Commission, or SEC. We have included our website address as an inactive textual reference only.

## **Available Information**

We make available on or through our website certain reports and amendments to those reports that we file with or furnish to the SEC in accordance with the Securities Exchange Act of 1934, as amended. These include our annual reports on Form 10-K, our quarterly reports on Form 10-Q, and our current reports on Form 8-K, and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Exchange Act. We make this information available on or through our website free of charge as soon as reasonably practicable after we electronically file the information with, or furnish it to, the SEC. The SEC maintains a website that contains reports, proxy and information statements, and other information regarding our filings, at [www.sec.gov](http://www.sec.gov). The information on, or that can be accessed through, our website is not incorporated by reference into this Annual Report on Form 10-K or any other filings we make with the SEC.

## ITEM 1A. RISK FACTORS

### RISK FACTORS

*Our business involves significant risks, some of which are described below. You should carefully consider these risks, as well as the other information in this Annual Report on Form 10-K, including our audited financial statements and the related notes and “Management’s Discussion and Analysis of Financial Condition and Results of Operations.” The occurrence of any of the events or developments described below could have a material adverse effect on our business, results of operations, financial condition, prospects and stock price. Additional risks and uncertainties not presently known to us or that we currently deem immaterial may also impair our business operations.*

#### Risks Related to Our Business

***We are a clinical-stage biopharmaceutical company with a limited operating history and no products approved for commercial sale. We have incurred significant losses since our inception, and we anticipate that we will continue to incur significant losses for the foreseeable future, which, together with our limited operating history, makes it difficult to assess our prospects.***

Biopharmaceutical product development is a highly speculative undertaking and involves a substantial degree of risk. We are a clinical-stage biopharmaceutical company, and we have only a limited operating history upon which you can evaluate our business and prospects. We have no products approved for commercial sale, have not generated any revenue from product sales and have incurred losses in each year since our inception in June 2016. In addition, we have limited experience and have not yet demonstrated an ability to successfully overcome many of the risks and uncertainties frequently encountered by companies in new and rapidly evolving fields, particularly in the pharmaceutical industry.

In September 2020, we announced topline data from the EMERGE Phase 3 efficacy trial, which randomized 1,201 migraine subjects to one of two STS101 dose strengths or placebo. Although STS101 3.9 mg and 5.2 mg showed favorable numerical differences versus placebo on the pre-specified co-primary endpoints of freedom from pain and freedom from most bothersome symptom (from among photophobia, phonophobia and nausea) at two hours post-administration, these differences did not achieve statistical significance for either dosage strength. In March 2021, we announced an update to our development plan for STS101 that takes into account the findings from our detailed analyses of results and data from our EMERGE efficacy trial. Our updated development plan for STS101 included a Phase 1 trial, which we completed in June 2021, to evaluate the pharmacokinetics, safety and tolerability of STS101 5.2 mg and two higher dose strengths, as well as the new pivotal SUMMIT Phase 3 efficacy trial that we initiated in June 2021, with topline results expected in the fourth quarter of 2022.

We have limited or no experience as a company conducting Phase 3 clinical trials, submitting applications for regulatory approvals, such as an NDA, or commercializing any products.

We have had significant operating losses since our inception. Our net losses for the year ended December 31, 2021 and 2020 were approximately \$51.2 million and \$47.6 million, respectively. As of December 31, 2021, we had an accumulated deficit of \$141.7 million. Substantially all of our losses have resulted from expenses incurred in connection with the development of STS101 and general and administrative costs associated with our operations.

STS101 will require substantial additional development time and resources before we would be able to apply for or receive regulatory approvals and begin generating revenue from product sales. In addition, we expect to continue to incur increasing costs associated with operating as a public company. We also do not yet have a sales organization or commercial infrastructure and, accordingly, we will incur significant expenses to establish a sales organization and associated commercial infrastructure in advance of generating any commercial product sales. We expect to continue to incur losses for the foreseeable future, and we anticipate these losses will increase as we continue to develop STS101 through clinical trials and regulatory submissions. Even if we achieve profitability in the future, we may not be able to sustain profitability in subsequent periods. Our prior losses, combined with expected losses, have had and will continue to have an adverse effect on our stockholders’ equity and working

capital.

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

Since our inception, we have invested substantially all of our efforts and financial resources in the development of STS101 for the acute treatment of migraine. We believe that we will continue to expend substantial resources for the foreseeable future in connection with the clinical development of STS101. These expenditures will include costs associated with clinical trials, obtaining regulatory approvals, and manufacturing and supply, as well as commercializing STS101, if approved for sale. In addition, other unanticipated costs may arise. Because the outcome of any clinical trial is highly uncertain, we cannot reasonably estimate the actual amounts necessary to successfully complete the development and commercialization of STS101.

As of December 31, 2021, we had resources consisting of cash, cash equivalents and marketable securities of \$95.8 million. Based on our current operating plan, we believe our existing cash, cash equivalents and marketable securities will be sufficient to fund our planned operations into the second half of 2023. However, our operating plans may change as a result of many factors currently unknown to us, and we may need to seek additional funds sooner than planned. Adequate funding may not be available to us on acceptable terms, or at all, particularly in light of the current COVID-19 pandemic and associated economic uncertainty and potential local and/or global economic recession. In addition, we may seek additional capital due to favorable market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. We do not expect to generate any meaningful revenue unless and until we obtain regulatory approval of and commercialize STS101 or enter into collaborative agreements with third parties, and we do not know when, or if, either will occur. We may seek to raise capital through private or public equity or debt financings, collaborative or other arrangements with corporate sources, or through other sources of financing. Adequate additional funding may not be available to us on acceptable terms, or at all. Our failure to raise capital as and when needed would have a negative impact on our financial condition and our ability to pursue the development and commercialization of STS101.

Our future capital requirements depend on many factors, including:

- the scope, timing, rate of progress, results and costs of our clinical trials for STS101, including our ongoing SUMMIT Phase 3 efficacy, our ongoing ASCEND Phase 3 long-term safety trial and including in connection with any clinical program we may pursue in foreign jurisdictions;
- the scope and costs of manufacturing development and commercial manufacturing activities;
- the cost of building a sales force and associated commercial infrastructure in anticipation of commercializing STS101;
- the cost and timing associated with commercializing STS101, if approved;
- the number and scope of clinical programs we decide to pursue;
- the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims;
- any product liability or other lawsuits related to STS101;
- the extent to which the ongoing COVID-19 pandemic may impact our ongoing or planned clinical trials;
- our efforts to enhance operational systems and our ability to attract, hire and retain qualified personnel, including personnel to support the development of STS101;
- the extent to which we acquire or in-license other product candidates or technologies;
- the payment of royalty payments owed under our existing license agreement;

- our ability to establish and maintain collaborations on favorable terms, if at all;
- the costs associated with being a public company; and
- the timing, receipt and amount of revenues generated by sales of STS101, if approved.

Additional funds may not be available when we need them, on terms that are acceptable to us, or at all. If adequate funds are not available to us on a timely basis, we may be required to:

- delay, limit, reduce or terminate clinical studies or other development activities for STS101; or
- delay, limit, reduce or terminate our efforts to establish manufacturing and sales and marketing capabilities or other activities that may be necessary to commercialize STS101, or reduce our flexibility in developing or maintaining our sales and marketing strategy.

We also could be required to seek funds through arrangements with collaborators or others that may require us to relinquish rights to some of our technologies or STS101 that we would otherwise pursue on our own. We do not expect to realize revenue from sales of STS101 in the foreseeable future, if at all, unless and until STS101 is clinically tested, approved for commercialization and successfully commercialized. To date, we have funded our operations through private placements of convertible preferred stock, a convertible promissory note, long-term debt, and common stock. We will be required to seek additional funding in the future and currently intend to do so through public or private equity offerings or debt financings, credit or loan facilities or a combination of one or more of these funding sources. Our ability to raise additional funds will depend on financial, economic and other factors, many of which are beyond our control. If we raise additional funds by issuing equity securities, including pursuant to the Sales Agreement we entered into with SVB Leerink LLC in October 2020 in connection with our at-the-market offering, our stockholders will suffer dilution and the terms of any financing may adversely affect the rights of our stockholders. In addition, as a condition to providing additional funds to us, future investors may demand, and may be granted, rights superior to those of existing stockholders. Debt financing, if available, is likely to involve restrictive covenants limiting our flexibility in conducting future business activities, and, in the event of insolvency, debt holders would be repaid before holders of our equity securities received any distribution of our corporate assets.

***Our business is entirely dependent on the successful development, regulatory approval and commercialization of STS101, our only product candidate under development.***

We have invested substantially all of our efforts and financial resources in the development of STS101 for the acute treatment of migraine, which has not been approved for sale or commercial use. Currently, STS101 is our only product candidate and we have not licensed, acquired, or invented any other product candidates for pre-clinical or clinical evaluation. This may make an investment in our company riskier than similar companies that have multiple product candidates in active development and that therefore may be able to better sustain a failure of a lead candidate. The success of our business, including our ability to finance our company and generate any revenue in the future, will depend entirely on the successful development, regulatory approval and commercialization of STS101, which may never occur.

As we continue development of STS101, our research and development expenses may increase substantially, as we seek to advance STS101 through clinical development, manufacturing and regulatory approval, and prepare for commercialization of STS101, if approved. We may have inadequate financial or other resources to advance STS101 through the clinical trial process, depending on the requirements of the FDA. In addition, our clinical development program for STS101 may not lead to regulatory approval from the FDA and similar foreign regulatory agencies if we fail to demonstrate in ongoing or future trials that STS101 is safe and effective, and we may therefore fail to commercialize STS101. The challenge of establishing STS101 as being safe and effective may be even more difficult given the failure of STS101 to demonstrate statistically significant effects as compared to placebo on the co-primary endpoints of our EMERGE trial. Even if approved, we may fail to obtain differentiated product labeling for STS101 as compared to other available dihydroergotamine mesylate, or DHE, products for migraine and, as a result, our commercial prospects may be impaired. Further, STS101 may not receive regulatory approval even if it is successful in planned and future clinical trials. Any failure to obtain regulatory approval of STS101 would have a material and adverse impact on our business. Even if we successfully obtain regulatory approvals to market STS101,

our revenue will be dependent, in part, upon the size of the markets in the territories for which we gain regulatory approval. If the markets or patient subsets that we are targeting are not as significant as we estimate, we may not generate significant revenues from sales of STS101, even if approved.

The clinical and commercial success of STS101 may depend on a number of factors, including the following:

- our ability to successfully address the issues that we believe resulted in the EMERGE trial not achieving statistical significance on the co-primary endpoints, including, but not limited to, the DHE under-delivery we observed;
- the ability of the STS101 5.2 mg dose strength that we selected for our Phase 3 clinical trial program to demonstrate adequate efficacy, safety and tolerability in the ACSEND and SUMMIT Phase 3 clinical trials;
- our ability to raise any additional required capital on acceptable terms, or at all;
- timely completion of our clinical trials, which may be significantly slower or cost more than we currently anticipate and will depend substantially upon the performance of third-party contractors;
- our ability to successfully conduct and complete clinical studies in the COVID-19 pandemic environment, and to adequately control for any factors introduced by the pandemic that may potentially affect the outcomes of our clinical studies;
- whether we are required by the FDA or similar foreign regulatory agencies to conduct additional clinical trials or other studies beyond those planned to support approval of STS101;
- our ability to consistently manufacture STS101 on a timely basis;
- our ability, and the ability of any third parties with whom we contract, to remain in good standing with regulatory agencies and develop, validate and maintain commercially viable manufacturing processes that are compliant with current good manufacturing practices, or cGMPs;
- our ability to demonstrate to the satisfaction of the FDA and similar foreign regulatory authorities the safety, efficacy and acceptable risk-benefit profile of STS101;
- the prevalence, duration and severity of potential side effects or other safety issues experienced with STS101;
- the timely receipt of necessary marketing approvals from the FDA and similar foreign regulatory authorities;
- achieving and maintaining, and, where applicable, ensuring that our third-party contractors achieve and maintain, compliance with our contractual obligations and with all regulatory requirements applicable to STS101;
- the differentiation of STS101 from other available DHE products and other acute treatments of migraine, and the willingness of physicians, operators of hospitals and clinics and patients to adopt and utilize STS101;
- our ability to successfully develop a commercial strategy and thereafter commercialize STS101 in the United States and internationally, if approved for marketing, sale and distribution in such countries and territories, whether alone or in collaboration with others;
- the availability of coverage and adequate reimbursement from managed care plans, private insurers, government payors (such as Medicare and Medicaid and similar foreign authorities) and other third-party payors for STS101;

- patients' willingness to pay out-of-pocket for STS101 in the absence of coverage and/or adequate reimbursement from third-party payors;
- the convenience of the administration of STS101;
- acceptance by physicians, payors and patients of the benefits, safety and efficacy of STS101, if approved;
- patient demand for STS101, if approved;
- our ability to establish and enforce intellectual property rights in and to STS101; and
- our ability to avoid third-party patent interference, intellectual property challenges or intellectual property infringement claims.

These factors, many of which are beyond our control, could cause us to experience significant delays or an inability to obtain regulatory approvals or commercialize STS101. Even if regulatory approvals are obtained, we may never be able to successfully commercialize STS101. Accordingly, we cannot provide assurances that we will be able to generate sufficient revenue through the sale of STS101 to continue our business or achieve profitability. In addition, disruptions caused by the COVID-19 pandemic may increase the likelihood that we encounter such difficulties or delays in initiating, enrolling, conducting or completing our planned clinical trials.

While the scope of regulatory approval generally is similar in other countries, in order to obtain separate regulatory approval in other countries we must comply with numerous and varying regulatory requirements of such countries regarding safety and efficacy. Other countries also have their own regulations governing, among other things, requirements for nonclinical studies, clinical trials and commercial sales, as well as pricing and distribution of STS101, and we may be required to expend significant resources to obtain regulatory approval and to comply with ongoing regulations in these jurisdictions. Regulatory approval in one country does not ensure regulatory approval in another, but a failure or delay in obtaining regulatory approval in one country may have a negative effect on the regulatory process in others.

***STS101 failed to demonstrate a statistically significant difference as compared to placebo on either of the co-primary endpoints in our first pivotal efficacy trial.***

In September 2020, we announced topline data from the EMERGE Phase 3 efficacy trial. Although topline data showed numerical differences in favor of STS101 3.9 mg and 5.2 mg versus placebo on the pre-specified co-primary endpoints of freedom from pain and freedom from most bothersome symptom (from among photophobia, phonophobia and nausea) at two hours post-administration, these differences did not achieve statistical significance for either dose strength. Both dose strengths of STS101 did, however, demonstrate significant effects on both freedom from pain and most bothersome symptom by three hours post-dose and later time points. Both STS101 dose strengths were well-tolerated in the EMERGE efficacy trial, with low adverse event rates and no serious adverse events reported.

Based on our analyses and review of EMERGE efficacy trial results and other data, including preliminary results from the ongoing ASCEND safety trial, we believe we have identified and have taken steps in our updated development plan to address the key reasons that STS101 did not achieve statistical significance versus placebo on the co-primary endpoints at two hours post-administration in the EMERGE efficacy trial. Our analyses suggest a significant proportion of subjects in EMERGE who self-administered STS101 to treat their migraine attacks may not have achieved and sustained targeted DHE concentrations due to under-delivery of STS101. We believe we have addressed this under-delivery issue through a combination of introducing improved instructions for STS101 use and subject training in our clinical trials and by making several minor modifications to the second-generation STS101 delivery device to improve its performance. We also believe other factors contributed to a negative outcome in the

EMERGE efficacy trial, and we believe we have taken appropriate steps to mitigate these issues in the ongoing SUMMIT efficacy trial through modifications to the trial design and conduct. However, these efforts may prove to be ineffective and there can be no assurance that the measures we have taken or plan to take will result in successful outcomes in our future clinical trials of STS101, including our ongoing SUMMIT efficacy trial, or be sufficient to obtain regulatory approval.

In addition, we may not be able to obtain regulatory approval for and successfully commercialize STS101 without conducting further clinical trials in addition to those trials that are ongoing or planned, and there can be no assurance that the results of any ongoing, planned or additional clinical trials will be sufficient to obtain regulatory approval or support successful commercialization. For example, in August 2021, we announced that we plan to enroll approximately 180 additional subjects in the ASCEND trial to ensure adequate exposures and safety are established with STS101 incorporating the second-generation delivery device. While adding these subjects is not expected to affect the overall STS101 development timeline, the FDA may require additional patients or additional studies to evaluate STS101 incorporating the second-generation delivery device.

***The ongoing COVID-19 pandemic and outbreak in the United States may adversely affect our business.***

As a result of the ongoing COVID-19 virus pandemic, we may experience disruptions that could severely impact our business, preclinical studies, clinical trials, and manufacturing activities, including:

- delays or difficulties in enrolling subjects in our clinical trials;
- delays or difficulties in clinical site initiation, including difficulties in recruiting clinical site investigators and clinical site staff;
- delays in the completion of our clinical trials;
- reduced ability to monitor and thereby ensure adequate quality and compliance in the conduct of our clinical trials;
- delays or difficulties in our ability to attract, hire and retain qualified personnel, including personnel to support the commercialization of STS101;
- diversion of healthcare resources away from the conduct of clinical trials;
- interruption of key clinical trial activities due to limitations on travel imposed or recommended by federal or state governments, employers and others or interruption of clinical trial subject visits and study procedures, which may impact the integrity of subject data and clinical study endpoints;
- interruption or delays in the operations of the FDA, which may impact review and approval timelines;
- interruption of, or delays in receiving, supplies of our investigational product from CMOs due to staffing shortages, production slowdowns or stoppages and disruptions in delivery systems;
- interruption of, or delays in completing manufacturing and manufacturing-related activities such as CMO qualification, production equipment manufacture, delivery and qualification, validation of manufacturing processes, manufacture and/or analytical characterization of our product candidate, completion of stability studies and/or manufacture of registration batches of our product candidate required for NDA submission; and
- limitations on employee resources that would otherwise be focused on the conduct of our nonclinical studies, clinical trials and product candidate manufacturing activities, including because of sickness of employees or their families or the desire of employees to avoid contact with large groups of people.

In addition, the spread of COVID-19 coronavirus may negatively impact the trading price of shares of our common stock and could further severely impact our ability to raise additional capital on a timely basis or at all.

The COVID-19 pandemic continues to evolve. The extent to which the outbreak impacts our business and clinical trials will depend on future developments, which are highly uncertain and cannot be predicted with



confidence, such as the duration of the pandemic, travel restrictions and social distancing in the United States and other countries, business closures or business disruptions, equipment and supply shortages, delays in shipping, delays in manufacturing and the effectiveness of actions taken in the United States and other countries to contain and treat the disease.

Furthermore, in response to the COVID-19 pandemic, in March 2020, the FDA announced its intention to temporarily postpone routine surveillance inspections of domestic manufacturing facilities. On July 10, 2020, the FDA announced its intention to restart certain on-site inspections of domestic manufacturing facilities subject to a risk-based prioritization system. The FDA intends to use this risk-based assessment system to identify the categories of regulatory activity that can occur within a given geographic area, ranging from mission critical inspections to resumption of all regulatory activities. Regulatory authorities outside the United States may adopt similar restrictions or other policy measures in response to the COVID-19 pandemic and may experience delays in their regulatory activities. If a prolonged government shutdown occurs, or if global health concerns continue to prevent the FDA or other regulatory authorities from conducting their regular inspections, reviews, or other regulatory activities, it could significantly impact the ability of the FDA or other regulatory authorities to timely review and process our regulatory submissions, which could have a material adverse effect on our business

***Clinical development involves a lengthy and expensive process with an uncertain outcome, and delays can occur for a variety of reasons outside of our control.***

Clinical development is expensive and can take many years to complete, and its outcome is inherently uncertain. Failure can occur at any time during the clinical trial process. For example, in September 2020, we announced topline data from the EMERGE trial. Although STS101 3.9 mg and 5.2 mg showed favorable numerical differences versus placebo on the pre-specified co-primary endpoints of freedom from pain and freedom from most bothersome symptom (from among photophobia, phonophobia and nausea) at two hours post-administration, these differences did not achieve statistical significance for either dosage strength. In addition, we may experience delays in initiating or completing our ongoing, planned, or future trials of STS101. Furthermore, we cannot be certain that studies or trials for STS101 will begin on time, not require redesign, enroll an adequate number of subjects on time or be completed on schedule, if at all. Clinical trials can be delayed or terminated for a variety of reasons, including delays or failures related to:

- the COVID-19 pandemic, including its impact on the providers of healthcare services, such as the healthcare clinics and institutions where we conduct our ongoing clinical trials and may conduct planned clinical trials;
- the FDA or comparable foreign regulatory authorities disagreeing as to the design or implementation of our clinical trials;
- delays in obtaining regulatory authorization to commence a trial;
- reaching agreement on acceptable terms with prospective contract research organizations, or CROs, and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- obtaining institutional review board, or IRB, approval at each trial site;
- recruiting an adequate number of suitable patients to participate in a trial;
- having subjects complete a trial or return for post-treatment follow-up;
- clinical sites deviating from trial protocol or dropping out of a trial;
- addressing subject safety concerns that arise during the course of a trial;
- adding a sufficient number of clinical trial sites; or

- obtaining sufficient quantities of STS101 for use in clinical trials from third-party suppliers on a timely basis.

We may experience numerous adverse or unforeseen events during, or as a result of, preclinical studies and clinical trials that could delay or prevent our ability to receive marketing approval or commercialize STS101, including:

- we may receive feedback from regulatory authorities that requires us to modify the design of our clinical trials;
- clinical trials of STS101 may produce negative or inconclusive results (for example, in the EMERGE trial, STS101 did not achieve statistical significance versus placebo on pre-specified co-primary endpoints), and we may decide, or regulators may require us, to conduct additional clinical trials or abandon our development program for STS101;
- the number of subjects required for clinical trials of STS101 may be larger than we anticipate, enrollment in these clinical trials may be slower than we anticipate or participants may drop out of these clinical trials at a higher rate than we anticipate;
- clinical trial participants may not comply with study protocol procedures and instructions;
- we or our third-party contractors may fail to comply with regulatory requirements, fail to maintain adequate quality controls, or be unable to produce sufficient product supply to conduct and complete clinical trials of STS101 in a timely manner, or at all;
- we or our investigators might have to suspend or terminate clinical trials of STS101 for various reasons, including non-compliance with regulatory requirements, a finding that STS101 has undesirable side effects or other unexpected characteristics, or a finding that the participants are being exposed to unacceptable health risks;
- the cost of clinical trials of STS101 may be greater than we anticipate;
- the quality of STS101 or other materials necessary to conduct clinical trials of STS101 may be insufficient or inadequate;
- regulators may revise the requirements for approving STS101, or such requirements may not be as we anticipate; and
- future collaborators may conduct clinical trials in ways they view as advantageous to them but that are sub-optimal for us.

If we are required to conduct additional clinical trials or other testing of STS101 beyond those that we currently contemplate, including for purposes of demonstrating the potential efficacy of STS101, if we are unable to successfully complete clinical trials of STS101 or other testing, if the results of these trials or tests are not positive or are only moderately positive or if there are safety concerns, we may:

- incur unplanned costs;
- be delayed in obtaining marketing approval for STS101 or not obtain marketing approval at all;
- obtain marketing approval in some countries and not in others;
- obtain marketing approval for indications or patient populations that are not as broad as intended or desired;

- obtain marketing approval with labeling that includes significant use or distribution restrictions or safety warnings, including boxed warnings;
- be subject to additional post-marketing testing requirements, which could be expensive and time consuming; or
- have the treatment removed from the market after obtaining marketing approval.

We could also encounter delays if a clinical trial is suspended or terminated by us, by the IRBs of the institutions in which such trials are being conducted or by the FDA or other regulatory authorities. Such authorities may suspend or terminate a clinical trial due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA or other regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a product candidate, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial.

Further, conducting clinical trials in foreign countries, as we could do for STS101, presents additional risks that may delay completion of our clinical trials. These risks include the failure of enrolled subjects in foreign countries to adhere to clinical protocol as a result of differences in healthcare services or cultural customs, managing additional administrative burdens associated with foreign regulatory schemes, as well as political and economic risks relevant to such foreign countries.

Principal investigators for our clinical trials may serve as scientific advisors or consultants to us from time to time and may receive cash or equity compensation in connection with such services. If these relationships and any related compensation result in perceived or actual conflicts of interest, or a regulatory authority concludes that the financial relationship may have affected the interpretation of the trial, the integrity of the data generated at the applicable clinical trial site may be questioned and the utility of the clinical trial itself may be jeopardized, which could result in the delay or rejection of the marketing application we submit. Any such delay or rejection could prevent or delay us from commercializing STS101.

If any of our clinical trials of STS101 are unsuccessful, delayed or terminated, its commercial prospects may be harmed, and our ability to generate revenues from sales of STS101 will be delayed or not realized at all. In addition, any delays in completing our clinical trials may increase our costs, slow down our STS101 development and approval process and jeopardize our ability to commence product sales and generate revenues. Any of these occurrences may significantly harm our business, financial condition and prospects. In addition, many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of STS101. If STS101 generally proves to be ineffective, unsafe or commercially unviable, it would have a material and adverse effect on our business, financial condition, results of operations and prospects.

***We may be unable to obtain regulatory approval for STS101 under applicable regulatory requirements. The denial or delay of any such approval would delay commercialization of STS101 and adversely impact our potential to generate revenue, our business and our results of operations.***

We as a company have not previously submitted an NDA or any other marketing application to the FDA or similar filings to comparable foreign regulatory authorities. An NDA or other similar regulatory filing requesting approval to market a product candidate must include extensive preclinical and clinical data and supporting information to establish that the product candidate is safe, effective, pure and potent for each desired indication. The NDA or other similar regulatory filing must also include significant information regarding the chemistry, manufacturing and controls for the product.

The research, testing, manufacturing, labeling, approval, sale, marketing and distribution of pharmaceutical products are subject to extensive regulation by the FDA and other regulatory authorities in the United States and other countries, and such regulations differ from country to country. We are not permitted to market STS101 in the United States or in any foreign countries until it receives the requisite approval from the applicable regulatory

authorities of such jurisdictions.

The FDA or any foreign regulatory bodies can delay, limit or deny approval of STS101 for many reasons, including:

- our inability to demonstrate to the satisfaction of the FDA or the applicable foreign regulatory body that STS101 is safe and effective for the requested indication;
- the FDA's or the applicable foreign regulatory agency's disagreement with our trial protocol or the interpretation of data from preclinical studies or clinical trials;
- our inability to demonstrate that the clinical and other benefits of STS101 outweigh any safety or other perceived risks; the FDA's or the applicable foreign regulatory agency's requirement for additional preclinical studies or clinical trials;
- the FDA's or the applicable foreign regulatory agency's non-approval of the formulation, labeling or specifications of STS101;
- the FDA's or the applicable foreign regulatory agency's failure to approve our manufacturing processes and facilities or the facilities of third-party manufacturers upon which we rely; or
- the potential for approval policies or regulations of the FDA or the applicable foreign regulatory agencies to significantly change in a manner rendering our clinical data insufficient for approval.

Of the large number of pharmaceutical products in development, only a small percentage successfully complete the FDA or other regulatory bodies' approval processes and are commercialized.

Even if we eventually complete clinical testing and receive approval from the FDA or applicable foreign agencies for STS101, the FDA or the applicable foreign regulatory agency may grant approval contingent on the performance of costly additional clinical trials, which may be required after approval. The FDA or the applicable foreign regulatory agency also may approve STS101 for a more limited indication or a narrower patient population than we originally requested, and the FDA or applicable foreign regulatory agency, may not approve it with the labeling that we believe is necessary or desirable for its successful commercialization.

In addition, because migraine affects adolescents (12 to 17 years of age) and children (6 to 11 years of age), pediatric studies are required under the Federal Food, Drug, Cosmetic Act, or the FDCA. To address such requirements, we designed an initial pediatric study plan, or iPSP, consistent with the FDA guidance *Migraine: Developing Drugs for Acute Treatment* (February 2018). We are awaiting FDA final agreement with the iPSP and plan to initiate after completing development of STS101 for acute treatment of migraine in adults.

Any delay in obtaining, or inability to obtain, applicable regulatory approval would delay or prevent commercialization of STS101 and would materially adversely impact our business and prospects.

***If we encounter difficulties with patient enrollment or completion in our clinical trials, our clinical development activities could be delayed or otherwise adversely affected.***

The timely completion of clinical trials in accordance with their protocols depends, among other things, on our ability to enroll a sufficient number of subjects who remain in the study until its conclusion. We may experience difficulties in patient enrollment in our clinical trials for a variety of reasons, including as a result of the availability of approved preventive and acute treatments for migraine. The enrollment of subjects depends on many additional factors, including:

- the patient eligibility criteria defined in the protocol;

- the general willingness of subjects to enroll in the trial;
- the sample size of the subjects required for analysis of the trial’s primary endpoints;
- the proximity of subjects to trial sites;
- the design of the trial;
- our ability to recruit clinical trial investigators with the appropriate competencies and experience;
- clinicians’ and patients’ perceptions as to the potential advantages of the product candidate being studied in relation to other available therapies, including any new therapies that may be approved for the indications we are investigating;
- the clinical site’s ability to obtain and maintain patient consents;
- subjects may elect not to participate in future trials of STS101 given STS101 did not achieve statistical significance versus placebo on pre-specified co-primary endpoints in the EMERGE trial; and
- clinical trial participants may not comply with study protocol procedures and instructions.

Our clinical trials may also compete with other clinical trials for product candidates that seek to treat migraine, and this competition will reduce the number and types of subjects available to us, because some subjects who might have opted to enroll in our trials may instead opt to enroll in a trial being conducted by one of our competitors. Since the number of qualified clinical investigators is limited, we may conduct some of our clinical trials at the same clinical trial sites that some of our competitors use, which will reduce the number of subjects who are available for our clinical trials in such clinical trial sites.

Delays in patient enrollment may result in increased costs or may affect the timing or outcome of the planned clinical trials, which could prevent completion of these trials and adversely affect our ability to advance the development of STS101. Furthermore, the COVID-19 pandemic could significantly affect patient enrollment and completion in our ongoing and planned clinical trials to an extent that we have not anticipated. Although subjects in our EMERGE trial were generally able to complete their scheduled visits and we were able to collect the essential data from those visits, there can be no assurances that our experience with our ASCEND safety trial, our SUMMIT efficacy trial, or any planned or future clinical trials will be the same or similar or that the COVID-19 pandemic will not have a significant impact on our ability to complete our ASCEND and SUMMIT clinical trials and enroll subjects in any planned or future clinical trials.

***STS101 may cause undesirable side effects or have other properties that could delay or prevent its regulatory approval, limit the commercial profile of an approved label, or result in significant negative consequences following marketing approval, if any.***

The results of our clinical trials may show that STS101 may cause undesirable side effects, which could interrupt, delay or halt clinical trials, resulting in the denial of regulatory approval by the FDA and other regulatory authorities. In light of widely publicized events concerning the safety risk of certain drug products, regulatory authorities, members of Congress, the Government Accounting Office, medical professionals and the general public have raised concerns about potential drug safety issues. These events have resulted in the withdrawal of drug products, revisions to drug labeling that further limit use of the drug products and establishment of risk management programs that may, for instance, restrict distribution of drug products. The increased attention to drug safety issues may result in a more cautious approach by the FDA to clinical trials. Data from clinical trials may receive greater scrutiny with respect to safety, which may make the FDA or other regulatory authorities more likely to terminate clinical trials before completion, or require longer or additional clinical trials that may result in substantial additional expense and a delay or failure in obtaining approval or approval for a more limited indication than originally sought.

Although STS101 has generally been well-tolerated in our clinical trials to date, with low adverse event rates reported, if unacceptable side effects arise in our ongoing ASCEND safety trial, our ongoing SUMMIT efficacy trial, or any other trials we may conduct in the future, we, the FDA, or the IRBs at the institutions in which our studies are conducted could suspend or terminate our clinical trials or the FDA or comparable foreign regulatory authorities could order us to cease clinical trials or deny approval of STS101 for its targeted indications.

Treatment-related side effects in our clinical trials or in the use of approved DHE products could also affect patient recruitment or the ability or willingness of enrolled subjects to complete any of our clinical trials, and/or result in potential product liability claims. In addition, if undesirable side effects caused by other available DHE products or DHE products in development, the development and successful commercialization of STS101, if approved, could be negatively affected. The active pharmaceutical ingredient in STS101 (DHE) is contraindicated for patients with certain pre-existing conditions and the labels of approved DHE products warn against use by patients with cardiovascular risk factors. These contraindications and warnings could limit the use of STS101 following marketing approval, if approved, or cause undesirable side effects in patients who use STS101 despite these warnings. For example, we received a single report of a treatment-related serious adverse event in an ASCEND trial participant. This adverse event was consistent with a side effect described in prescribing information for DHE and other vasoconstrictive agents, such as triptans. The adverse event occurred following the subject's sixth use of study medication, and no further occurrences were reported with six subsequent uses of study medication by the subject. Investigation determined the subject's medical history, which the subject did not disclose to the trial site, included DHE contraindications and fulfilled key trial exclusion criteria that are disqualifying for trial participation. In addition, approved DHE products carry a "black box" warning in their labels for a risk that the coadministration of DHE and certain other drugs, including specific antivirals and antibiotics, may result in elevated levels of DHE in the blood, potentially causing vasospasm that may result in inadequate blood flow to the extremities or the brain. Unless we can successfully demonstrate by conducting drug-drug interaction studies and potentially additional studies that the coadministration of DHE and certain other drugs does not result in drug-drug interactions, the FDA is likely to require the label for STS101, if approved, to include such warning, and this could result in STS101 not achieving its full commercial potential. Treatment-related side effects in our clinical trials or in the use of approved DHE products could also affect patient recruitment or the ability of enrolled subjects to complete any of our clinical trials or result in potential product liability claims.

If STS101 receives marketing approval and we or others later identify undesirable side effects caused by STS101 or by other DHE products, a number of potentially significant negative consequences could result, including:

- regulatory authorities may withdraw their approval of STS101;
- we may be required to recall the STS101 or change the way it is administered to patients;
- additional restrictions may be imposed on the marketing of the STS101 or the manufacturing processes for STS101 or any component thereof;
- regulatory authorities may require the addition of labeling statements, such as a "black box" warning or a contraindication similar to those that are currently included with the labels of DHE products;
- we may be required to implement a Risk Evaluation and Mitigation Strategy, or create a Medication Guide outlining the risks of such side effects for distribution to patients;
- we could be sued and held liable for harm caused to patients;
- STS101 may become less competitive; and
- our reputation may suffer.

Any of the foregoing events could prevent us from achieving or maintaining market acceptance of the particular product candidate, if approved, and result in the loss of significant revenues to us, which would materially

and adversely affect our results of operations and business.

***We may be unable to rely on Section 505(b)(2) of the Federal Food, Drug and Cosmetic Act (FDCA), which could result in a longer development program and more costly trials than we anticipate.***

We may not be able to seek FDA marketing approval of STS101 under Section 505(b)(2) of the FDCA. Section 505(b)(2), if applicable to us, would allow any NDA we file with the FDA to rely in part on data in the public domain or the FDA's prior conclusions regarding the safety and effectiveness of approved DHE products. Under Section 505(b)(2), the development and approval of STS101 could potentially be expedited by decreasing the overall scope of work we must do ourselves so as to enable an STS101 NDA submission based on Phase 3 efficacy and/or safety trial data combined with a demonstration of pharmacokinetic comparability of STS101 to one or more approved DHE products (i.e., reference listed drugs). Although we believe both our Phase 1 trials have established the pharmacokinetic comparability of STS101 5.2 mg to DHE reference listed drugs, if we are unable to rely on Section 505(b)(2), the development program for STS101 would be longer than we expect, and we would also have to conduct more costly trials than we anticipate, which would harm our business.

***STS101 is a drug-device combination product, which may result in additional regulatory risks.***

Our finished drug product and nasal delivery device will be regulated as a drug-device combination product. There may be additional regulatory risks for drug-device combination products. We may experience delays in obtaining regulatory approval of STS101 given the increased complexity of the review process when approval of the product and a delivery device is sought under a single marketing application. In the United States, each component of a combination product is subject to the requirements established by the FDA for that type of component, whether a drug, biologic or device. The delivery system device will be subject to FDA device requirements regarding design, performance and validation as well as human factors testing, among other things. We implemented several minor modifications to the second-generation STS101 delivery device to improve its performance and we cannot be certain these changes will not result in additional regulatory risks. Delays in or failure of the studies conducted by us, or failure of our company, our collaborators, if any, or our third-party providers or suppliers to obtain or maintain regulatory approval could result in increased development costs, delays in or failure to obtain regulatory approval, and associated delays in STS101 reaching the market.

***Interim, "topline" and preliminary data from our clinical trials that we announce or publish from time to time may change as more patient data become available and are subject to audit and verification procedures that could result in material changes in the final data.***

From time to time, we may publicly disclose preliminary or topline data from our preclinical studies and clinical trials, which is based on a preliminary analysis of then-available data, and the results and related findings and conclusions are subject to change following a more comprehensive review of the data related to the particular study or trial. We also make assumptions, estimations, calculations and conclusions as part of our analyses of data, and we may not have received or had the opportunity to fully and carefully evaluate all data. As a result, the topline or preliminary results that we report may differ from future results of the same studies, or different conclusions or considerations may qualify such results, once additional data have been received and fully evaluated. Topline data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, topline data should be viewed with caution until the final data are available.

From time to time, we may also disclose interim data from our nonclinical studies and clinical trials. Interim data from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available. Adverse differences between preliminary or interim data and final data could significantly harm our business prospects. Further, disclosure of interim data by us or by our competitors could result in volatility in the price of our common stock.

Further, others, including regulatory agencies, may not accept or agree with our assumptions, estimates, calculations, conclusions or analyses or may interpret or weigh the importance of data differently, which could impact the value of the particular program, the approvability or commercialization of the particular product candidate or product and our company in general. In addition, the information we choose to publicly disclose regarding a particular study or clinical trial is based on what is typically extensive information, and you or others

may not agree with what we determine is material or otherwise appropriate information to include in our disclosure.

If the interim, topline, or preliminary data that we report differ from actual results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for, and commercialize, our product candidates may be harmed, which could harm our business, operating results, prospects or financial condition.

***Even if STS101 obtains regulatory approval, it may fail to achieve broad market acceptance.***

Even if STS101 receives FDA or other regulatory approvals, its commercial success will depend significantly on the extent to which it is adopted, prescribed by physicians and used by patients. The degree of market acceptance of STS101, if approved, will depend on a number of factors, including:

- the safety and efficacy of STS101 as compared to other available acute therapies for treatment of migraine;
- patient satisfaction with the results and administration of STS101 and overall treatment experience, including, the ease and convenience of administration of STS101;
- the clinical indications for which STS101 is approved and patient demand for approved products that treat those indications;
- our ability to manufacture and release adequate commercial supplies on a timely basis;
- the availability of coverage and adequate reimbursement from managed care plans, private insurers, government payors (such as Medicare and Medicaid) and other third-party payors for STS101;
- the cost of treatment with STS101 in relation to alternative treatments and patients' willingness to pay out-of-pocket for the product, if approved, in the absence of coverage and/or adequate reimbursement from third-party payors;
- acceptance by physicians, operators of hospitals and clinics and patients of the product as a safe, effective and easy to administer treatment;
- physician and patient willingness to adopt a new therapy over other available preventive and acute therapies for treatment of migraine;
- the prevalence and severity of side effects;
- limitations or warnings contained in the FDA-approved labeling for STS101, such as a "black box" warning or a contraindication similar to those that are currently included with the labels of DHE products;
- the willingness of physicians, operators of hospitals and clinics and patients to utilize or adopt our product as a solution, particularly in light of STS101's failure to demonstrate statistically significant effectiveness in our EMERGE trial;
- the effectiveness of our sales, marketing and distribution efforts;
- adverse publicity about STS101 or favorable publicity about competitive products;
- patients' willingness to take a dry-powder intranasal medication;
- potential product liability claims; and



- global economic conditions.

We cannot assure you that STS101, if approved, will achieve broad market acceptance among physicians and patients. Any failure by STS101, if approved, to achieve market acceptance or commercial success would adversely affect our results of operations.

***We face, and will continue to face, significant competition in an environment of rapid technological and scientific change and our failure to effectively compete may prevent us from achieving significant market penetration for STS101, if approved. Most of our competitors have significantly greater resources than we have and we may not be able to successfully compete.***

The pharmaceutical industry is highly competitive, with a number of established, large pharmaceutical companies, as well as many smaller companies. Many of these companies have greater financial resources, marketing capabilities and experience in obtaining regulatory approvals for product candidates. There are many pharmaceutical companies, biotechnology companies, public and private universities, government agencies and research organizations actively engaged in research and development of products which may target the same markets as STS101. For instance, companies actively marketing branded products or that have products in late-stage development for the acute treatment or prevention of migraine which may directly or indirectly compete with STS101 include, but are not limited to, Teva Pharmaceutical Industries, Eli Lilly, Novartis, Abbvie, Biohaven, Lundbeck, Amgen, and a number of smaller companies, including Impel NeuroPharma, Axsome Therapeutics, Amneal Pharmaceuticals, and Zosano Pharma. As well, generic products for the acute treatment or prevention of migraine may directly or indirectly compete with STS101. We expect STS101 to compete on the basis of, among other things, product efficacy and safety, price, extent of adverse side effects experienced and convenience of administration. One or more of our competitors may develop and commercialize competing products that incorporate technologies similar to our proprietary technologies earlier than us, obtain approvals for such products from the FDA more rapidly than us or develop alternative products or therapies that are safer, more effective and/or more cost effective than STS101.

The market in which we will compete with STS101 is currently dominated by generic triptan products, and also includes other DHE products, newer oral migraine-specific acute treatments and preventive treatments. The majority of the prescriptions written for the acute treatment of migraine are for generic triptans. There are seven FDA-approved triptan molecules available in branded and branded generic/generic oral dose forms, and two of these molecules are also available in injectable and/or liquid nasal spray dose forms that may have faster onset of action than oral dose forms.

With respect to DHE products, we will compete with Bausch Health's Migranal and several generic versions thereof, which are DHE liquid nasal spray products, as well as branded and generic DHE injectable products. In addition, Impel NeuroPharma recently received FDA approval for and launched a DHE liquid nasal spray product, utilizing the same liquid formulation and container closure system as Migranal, but with a different propellant-powered, single-use delivery device. There can be no assurance that STS101 will be able to successfully compete against such products, if approved.

We also face competition from newer oral migraine-specific acute treatments that have been approved by FDA and commercially introduced in 2020 such as Eli Lilly's lasmiditan, a ditan, and two gepants, Abbvie's ubrogepant and Biohaven's rimegepant. Because lasmiditan, ubrogepant, and rimegepant are thought to act by mechanisms other than vasoconstriction, recommended use is not restricted to patients who do not have cardiovascular risk factors or disease, as is the case for triptan and ergot alkaloid products (including DHE) due to their vasoconstrictive actions. Although the labels for lasmiditan, ubrogepant and rimegepant do not limit use to patients without cardiovascular risk factors or disease, we believe these products have disadvantages. For example, lasmiditan has been reported to commonly cause central nervous system adverse events such as dizziness, somnolence and paresthesia, and the lasmiditan label includes warnings for driving impairment and operation of machinery for at least eight hours after taking a lasmiditan dose, central nervous system depression, serotonin syndrome, and medication overuse headache. Additionally, because lasmiditan has shown potential for abuse and dependence, the U.S. Drug Enforcement Agency, or DEA, has designated lasmiditan as a controlled substance; this designation imposes licensing and documentation requirements upon prescribers and as well restricts distribution. With ubrogepant and rimegepant, reported efficacy is modest in comparison with efficacy historically reported with

triptan and DHE products.

Many of our competitors have significantly greater financial, technical, manufacturing, marketing, sales and supply resources and experience than we do. If we successfully obtain approval for STS101, we will face competition based on many different factors, including the safety and effectiveness of STS101, the ease with which STS101 can be administered and the extent to which patients accept the nasal route of administration, the timing and scope of regulatory approvals for STS101, the availability and cost of manufacturing, marketing and sales capabilities, price, reimbursement coverage and patent position. Competing products could present superior treatment alternatives, including by being more effective, safer, less expensive or marketed and sold more effectively than STS101. Competitive products may make any products we develop obsolete or noncompetitive before we recover the expense of developing and commercializing STS101. Such competitors could also recruit our employees, which could negatively impact our level of expertise and our ability to execute our business plan. For additional information regarding our competition, see “Business—Competition.”

***The successful commercialization of STS101 will depend in part on the extent to which governmental authorities, private health insurers, and other third-party payors provide coverage, adequate reimbursement levels and implement pricing policies favorable for it. Failure to obtain or maintain coverage and adequate reimbursement for STS101, if approved, could limit our ability to market our product and decrease our ability to generate revenue.***

The availability of coverage and adequacy of reimbursement by managed care plans, governmental healthcare programs, such as Medicare and Medicaid, private health insurers and other third-party payors are essential for most patients to be able to afford medical services and pharmaceutical products that receive FDA approval. Our ability to achieve acceptable levels of coverage and reimbursement for STS101 by third-party payors will have an effect on our ability to successfully commercialize it. A decision by a third-party payor not to cover or separately reimburse for STS101, could reduce physician utilization if approved. Assuming there is coverage for STS101 by a third-party payor, the resulting reimbursement payment rates may not be adequate or may require co-payments that patients find unacceptably high. We cannot be sure that coverage and reimbursement in the United States, the European Union or elsewhere will be available for STS101 and any reimbursement that may become available may not be adequate or may be decreased or eliminated in the future.

Moreover, increasing efforts by governmental and other third-party payors in the United States and abroad to cap or reduce healthcare costs have resulted in increasing challenges to prices charged for pharmaceutical products and services, and many third-party payors may refuse to provide coverage and adequate reimbursement for particular drugs when an equivalent generic drug, biosimilar or a less expensive therapy is available. It is possible that a third-party payor may consider STS101 as substitutable and only offer to reimburse patients for the less expensive product, if any. For example, there are currently generic versions of both DHE liquid nasal spray products and DHE injectable products, with which we may compete. Even if we show improved efficacy or improved convenience of administration with STS101, pricing of existing third-party therapeutics may limit the amount we will be able to charge for it. These third-party payors may deny or revoke the reimbursement status of STS101, if approved, or establish prices for it at levels that are too low to enable us to realize an appropriate return on our investment. If reimbursement is not available or is available only at limited levels, we may not be able to successfully commercialize STS101.

No uniform policy for coverage and reimbursement for products exists among third-party payors in the United States. Therefore, coverage and reimbursement for products can differ significantly from payor to payor. As a result, the coverage determination process is often a time-consuming and costly process that may require us to provide scientific and clinical support for the use of STS101 to each payor separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance. Furthermore, rules and regulations regarding reimbursement change frequently, in some cases on short notice, and we believe that changes in these rules and regulations are likely.

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 and other countries will likely put pressure on the pricing and usage of medical products. In many countries, the prices of medical products are subject to varying price control mechanisms as part of national health systems.

Other countries allow companies to fix their own prices for medical 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 STS101. Accordingly, in markets outside the United States, the reimbursement for STS101 may be reduced compared with the United States and may be insufficient to generate commercially-reasonable revenue and profits.

***We currently have no sales organization. If we are unable to establish sales capabilities on our own or through third parties, we may not be able to market and sell STS101 effectively in the United States and foreign jurisdictions, if approved, or generate product revenue.***

We currently do not have a marketing or sales organization. In order to commercialize STS101, if approved, in the United States and foreign jurisdictions, we must build our marketing, sales, distribution, managerial and other non-technical capabilities or make arrangements with third parties to perform these services, and we may not be successful in doing so. If STS101 receives regulatory approval, we expect to establish a sales organization in the United States with technical expertise and supporting marketing and distribution capabilities to commercialize it, which will be expensive and time consuming. We have no prior experience as a company in the marketing, sale and distribution of pharmaceutical products and there are significant risks involved in building and managing a sales organization, including our ability to hire, retain, and incentivize qualified individuals, generate sufficient sales leads, provide adequate training to sales and marketing personnel, and effectively manage a geographically dispersed sales and marketing team. Any failure or delay in the development of our internal sales, marketing and distribution capabilities would adversely impact the commercialization of STS101. We may choose to collaborate with third parties that have direct sales forces and established distribution systems, either to augment our own sales force and distribution systems or in lieu of our own sales force and distribution systems. If we are unable to enter into such arrangements on acceptable terms or at all, we may not be able to successfully commercialize STS101. If we are not successful in commercializing STS101, either on our own or through arrangements with one or more third parties, we may not be able to generate product revenue and we would incur significant additional losses.

***We rely, and intend to continue to rely, on qualified third parties to supply all components of STS101. As a result, we are dependent on several third parties, most of which are sole source suppliers, for the manufacture of STS101 and our supply chain, and if we experience problems with any of these suppliers, or they fail to comply with applicable regulatory requirements or to supply sufficient quantities at acceptable quality levels or prices, or at all, it would materially and adversely affect our business.***

We do not own or operate manufacturing facilities for clinical or commercial manufacture of either the proprietary dry-powder formulation of DHE component of STS101 or the proprietary pre-filled, single-use, nasal delivery device, including the drug substance and packaging. We have limited personnel with experience in drug-device product manufacturing and we lack the capabilities to manufacture either the drug or device components of STS101 on a clinical or commercial scale. We currently outsource all manufacturing and packaging of STS101 to third parties, and we do not plan to own or operate our own manufacturing and packaging facilities. There can be no assurance that our clinical development product supplies will not be limited, interrupted, or of satisfactory quality or continue to be available at acceptable prices. In particular, any replacement of any of our third-party suppliers could require significant effort and expertise because there may be a limited number of qualified replacements. In addition, we may encounter issues with transferring technology to a new third-party manufacturer, and we may encounter regulatory delays if we need to move the manufacturing of our products from one third-party manufacturer to another. Some of the third parties on which we rely may also be adversely impacted by COVID-19 or other unforeseen events and public health emergencies, and the foregoing challenges could be compounded as a result.

In addition, we do not currently have long-term commercial supply agreements with third-party manufacturers for either the formulation or device components of STS101 or the STS101 finished product. We may be unable to enter into agreements for commercial supply with all third-party manufacturers, or may be unable to do so on acceptable terms. Even if we enter into these agreements or, for those agreements that we have already entered into, the various manufacturers utilized for STS101 will likely be single source suppliers to us for a significant period of time. We may not be able to establish additional sources of supply for STS101 prior to commercialization. Certain of such suppliers are subject to regulatory requirements covering manufacturing, testing, quality control and record keeping relating to STS101, and are subject to pre-approval and ongoing inspections by the regulatory agencies. Failure by any of our suppliers to comply with applicable regulations may result in long delays and interruptions to

our manufacturing capacity while we seek to secure another supplier that meets all regulatory requirements.

Reliance on third-party manufacturers entails risks to which we would not be subject if we manufactured STS101 ourselves, including:

- reliance on the third parties for regulatory compliance, quality assurance and hazardous materials handling;
- the possible breach of the manufacturing and quality agreements by the third parties because of factors beyond our control;
- the possibility of termination or nonrenewal of the agreements by the third parties because of our breach of the manufacturing agreement or based on their own business priorities; and
- with respect to any manufacturers with which we do not have a long-term agreement, the possibility that the manufacturer decides to stop supplying to us or changes the price or other terms of supply.

Any of these factors could cause the delay of required approvals or commercialization of STS101, could prevent us from commercializing it successfully, could cause the suspension of initiation or completion of clinical trials and regulatory submissions, and could lead to higher product costs.

In addition, the facilities used by our CMOs to manufacture STS101 are subject to various regulatory requirements and may be subject to the inspection of the FDA or other regulatory authorities. We do not directly control manufacturing at our CMOs, and are completely dependent on them for compliance with current regulatory requirements. If our CMOs cannot successfully manufacture components of finished product that conforms to our specifications and the regulatory requirements of the FDA or comparable regulatory authorities in foreign jurisdictions, we may not be able to rely on them for the manufacture of STS101. In addition, we have limited control over the ability of our CMOs to maintain adequate quality control, quality assurance and qualified personnel. If the FDA or a comparable foreign regulatory authority finds our facilities or those of our CMOs inadequate for the manufacture of STS101 or if such facilities are subject to enforcement action in the future or are otherwise inadequate, we may need to find alternative manufacturing facilities, which would significantly impact our ability to develop, obtain regulatory approval for or commercialize STS101 and the timing of any such approval and commercialization. We implemented several minor modifications to the STS101 delivery device to improve its performance and we cannot be certain these changes will not result in additional regulatory risks. In addition, if any of our CMOs are adversely impacted by COVID-19 or other unforeseen events and public health emergencies, or if such events impede the ability of the FDA or a comparable regulatory authority to inspect the facilities used by our CMOs to manufacture STS101, which could delay our ability to seek approval or commercialize STS101.

Our CMOs may experience manufacturing difficulties due to resource constraints or as a result of labor disputes or unstable political environments.

Additionally, due to COVID-19 pandemic we may experience interruption of, or delays in completing manufacturing and manufacturing-related activities such as CMO qualification, production equipment manufacture, delivery and qualification, validation of manufacturing processes, manufacture and/or analytical characterization of our product candidate, completion of stability studies and/or manufacture of registration batches of our product candidate required for NDA submission. If our CMOs were to encounter any of these difficulties, our ability to provide STS101 to subjects in clinical trials, or to provide product for the treatment of patients once approved, would be jeopardized.

***We rely, and intend to continue to rely, on third-party suppliers for materials used in the manufacture of STS101, and the loss of third-party suppliers or their inability to supply us with adequate key materials could harm our business.***

We currently do not have the ability to independently conduct any clinical trials. We rely, and intend to continue to rely, on third-party suppliers, most of which are sole source suppliers, for certain key materials required

for the production of the DHE dry-powder formulation of STS101. Our dependence on these third-party suppliers and the challenges we may face in obtaining adequate supplies of these materials involve several risks, including limited control over pricing, availability, quality and delivery schedules. As a small company, our negotiation leverage is limited and we are likely to get lower priority than other companies or purchasers that are larger than we are. We cannot be certain that our suppliers will continue to provide us with the quantities of these key materials that we require or satisfy our anticipated specifications and quality requirements. Some of these third parties may also be adversely impacted by COVID-19 or other unforeseen events and public health emergencies. Any supply interruption in limited or sole sourced key materials could materially harm the manufacture of STS101 until a new source of supply, if any, could be identified and qualified. We may be unable to find a sufficient alternative supplier in a reasonable time or on commercially reasonable terms. Any performance failure on the part of our suppliers could delay the development and potential commercialization of STS101, including limiting supplies necessary for clinical trials and regulatory approvals, which would have a material adverse effect on our business.

***We rely, and intend to continue to rely, on third parties in the conduct of all of our clinical trials. If these third parties do not successfully carry out their contractual duties, fail to comply with applicable regulatory requirements or meet expected deadlines, we may be unable to obtain regulatory approval for STS101.***

The FDA and comparable foreign regulatory authorities in other jurisdictions require us to comply with regulations and standards, commonly referred to as good clinical practice, or GCP, requirements for conducting, monitoring, recording and reporting the results of clinical trials, in order to ensure that the data and results are scientifically credible and accurate and that the trial subjects are adequately informed of the potential risks of participating in clinical trials. We rely on medical institutions, clinical investigators, contract laboratories and other third parties, such as CROs and consultants, to conduct GCP-compliant clinical trials of STS101 properly and on time. While we have agreements with these third parties, we monitor and control only certain aspects of their activities and have limited influence over their actual performance and the amount or timing of resources that they devote to our programs. Third parties with whom we contract may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical trials or other drug development activities that could harm our competitive position. The third parties with whom we contract for execution of our clinical trials play a significant role in the conduct of these trials and the subsequent collection and analysis of data. Although we rely on these third parties to conduct portions of our clinical trials, we remain responsible for ensuring that each of our clinical trials is conducted in accordance with its investigational plan and protocol and applicable laws and regulations, and our reliance on these third parties does not relieve us of our regulatory responsibilities. These challenges have been made more difficult by the COVID-19 pandemic and resulting shelter-in-place and stay-at-home restrictions, which are driving greater dependency on electronic monitoring of our clinical trial sites. Such monitoring could prove to be less reliable and could increase data privacy and cybersecurity risks.

If the third parties conducting our clinical trials do not adequately perform their contractual duties or obligations, experience significant business challenges, disruptions or failures, do not meet expected deadlines, terminate their agreements with us or need to be replaced, or if the quality or accuracy of the data they obtain is compromised due to their failure to adhere to our protocols or to GCPs, or for any other reason, we may need to enter into new arrangements with alternative third parties. This could be difficult, costly or impossible, and clinical trials may need to be extended, delayed, terminated or repeated. As a result, we may not be able to obtain regulatory approval in a timely fashion, or at all, for STS101, our results our business and results of operations and the commercial prospects for STS101 would be harmed, our costs could increase, and our ability to generate revenues could be delayed.

***We will need to increase the size of our organization, and we may experience difficulties in managing growth.***

As of December 31, 2021, we had 21 full-time employees. We will need to continue to expand our managerial, operational, financial and other resources in order to manage our operations and clinical trials, continue our development activities and commercialize STS101. Our management and personnel, systems and facilities currently in place may not be adequate to support this future growth. Our need to effectively execute our growth strategy requires that we:

- effectively manage our clinical trials and the development of STS101;

- identify, recruit, retain, incentivize and integrate additional employees, including sales personnel;
- manage our internal development and operational efforts effectively while carrying out our contractual obligations to third parties; and
- continue to improve our operational, financial and management controls, reporting systems and procedures.

We may be unable to successfully implement these tasks, which could have a material adverse effect on our business, results of operations, financial condition, prospects and stock price.

***We may conduct additional clinical trials and consider additional headache indications for STS101 to enhance its commercial potential; however, these trials may not produce results necessary to enable additional commercial potential or enhancement of its label.***

In addition to our pursuit of initial regulatory approval and successful commercialization of STS101 in the United States, we may conduct additional clinical trials and consider additional headache indications for STS101 to expand its commercial potential, including by potentially conducting clinical programs outside the United States. However, any positive results from our ongoing, planned or future clinical trials of STS101 and results from clinical testing by third parties of other DHE products and product candidates, may not be predictive of the results of any such additional clinical trials. Therefore, there can be no assurance that we will ever be successful enhancing the commercial potential of STS101 or expanding its label.

***Any future collaboration arrangements that we may enter into, may not be successful, which could significantly limit the likelihood of receiving the potential economic benefits of the collaboration and adversely affect our ability to develop and commercialize STS101.***

- To the extent that we pursue collaborations relating to STS101 in the future, we may face significant competition in seeking appropriate collaborators and may not be able to ultimately enter into collaborations. Moreover, any such collaboration arrangements may be complex and time-consuming to negotiate, document, implement and maintain and challenging to manage. We may not be successful in our efforts with any such collaborator and we may never receive any milestone or royalty payments under any such agreements. Further, the terms of any collaborations or other arrangements that we may establish, may not be favorable to us.
- The success of any collaboration arrangement will depend heavily on the efforts and activities of our collaborators. Collaborations are subject to numerous risks, which may include risks that:
- collaborators have significant discretion in determining the efforts and resources that they will apply to collaborations;
- collaborators may not pursue development and commercialization of STS101 or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in their strategic focus due to their acquisition of competitive products or their internal development of competitive products, availability of funding or other external factors, such as a business combination that diverts resources or creates competing priorities;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial, abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with STS101;
- we could grant exclusive rights to our collaborators that would prevent us from collaborating with others;
- collaborators may not properly maintain or defend our intellectual property rights or may use our intellectual property or proprietary information in a way that gives rise to actual or threatened

- litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential liability;
- collaborations may be terminated, and, if terminated, this may result in a need for additional capital to pursue further development or commercialization of STS101;
  - disputes may arise with respect to the ownership of any intellectual property developed pursuant to our collaborations;
  - a collaborator's sales and marketing activities or other operations may not be in compliance with applicable laws, resulting in civil or criminal proceedings;
  - disputes may arise between us and a collaborator that causes the delay or termination of the development or commercialization of STS101 or that results in costly litigation or arbitration that diverts our management's attention and resources; and
  - collaborators may be adversely impacted by COVID-19 or other unforeseen events and public health emergencies.

***If we engage in future acquisitions or strategic partnerships, this may increase our capital requirements, dilute our stockholders, cause us to incur debt or assume contingent liabilities, and subject us to other risks.***

We may evaluate various acquisitions and strategic partnerships, including licensing or acquiring complementary products, intellectual property rights, technologies, or businesses. Any potential acquisition or strategic partnership may entail numerous risks, including:

- increased operating expenses and cash requirements;
- the assumption of additional indebtedness or contingent and unforeseen liabilities;
- the issuance of our equity securities;
- assimilation of operations, intellectual property and products of an acquired company, including difficulties associated with integrating new personnel;
- the diversion of our management's attention from our existing product programs and initiatives in pursuing such a strategic merger or acquisition;
- retention of key employees, the loss of key personnel, and uncertainties in our ability to maintain key business relationships;
- risks and uncertainties associated with the other party to such a transaction, including the prospects of that party and their existing products or product candidates and regulatory approvals; and
- our inability to generate revenue from acquired technology and/or products sufficient to meet our objectives in undertaking the acquisition or even to offset the associated acquisition and maintenance costs.

In addition, if we undertake acquisitions, we may issue dilutive securities, assume or incur debt obligations, incur large one-time expenses and acquire intangible assets that could result in significant future amortization expense. Moreover, we may not be able to locate suitable acquisition opportunities and this inability could impair our ability to grow or obtain access to technology or products that may be important to the development of our business.

***Our business involves the use of hazardous materials and we and our third-party manufacturers and suppliers must comply with environmental laws and regulations, which can be expensive and restrict how we do***

*business.*

Our third-party manufacturers' and suppliers' activities involve the controlled storage, use and disposal of hazardous materials owned by us, including the components of STS101 and other hazardous compounds. We and any third-party manufacturers and suppliers we engage are subject to numerous federal, state and local environmental, health and safety laws, regulations and permitting requirements, including those governing laboratory procedures; the generation, handling, use, storage, treatment, and disposal of hazardous and regulated materials and wastes; the emission and discharge of hazardous materials into the ground, air and water; and employee health and safety. Our operations involve the use of hazardous and flammable materials, including chemicals and biological materials. Our operations also produce hazardous waste. In some cases, these hazardous materials and various wastes resulting from their use are stored at our contract manufacturers' facilities pending their use and disposal. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination, which could cause an interruption of our commercialization efforts, research and development efforts and business operations, environmental damage resulting in costly clean-up and liabilities under applicable laws and regulations governing the use, storage, handling and disposal of these materials and specified waste products.

Although we believe that the safety procedures utilized by our third-party manufacturers for handling and disposing of these materials generally comply with the standards prescribed by these laws and regulations, we cannot guarantee that this is the case or eliminate the risk of accidental contamination or injury from these materials. Under certain environmental laws, we could be held responsible for costs relating to any contamination at our current or past facilities and at third-party facilities. In such an event, we may be held liable for any resulting damages and such liability could exceed our resources and state or federal or other applicable authorities may curtail our use of certain materials and/or interrupt our business operations. Furthermore, environmental laws and regulations are complex, change frequently and have tended to become more stringent. We cannot predict the impact of such changes and cannot be certain of our future compliance.

Compliance with applicable environmental laws and regulations may be expensive, and current or future environmental laws and regulations may impair our research, product development and manufacturing efforts. In addition, we cannot entirely eliminate the risk of accidental injury or contamination from these materials or wastes..

### **Risks Related to Intellectual Property**

***Our success depends on our ability to protect our intellectual property and our proprietary technologies.***

Our commercial success depends in part on our ability to obtain and maintain patent protection and trade secret protection for STS101, proprietary technologies and their uses as well as our ability to operate without infringing upon the proprietary rights of others. We generally seek to protect our proprietary position by filing patent applications in the United States and abroad related to STS101, proprietary technologies and their uses that are important to our business. Our patent applications cannot be enforced against third parties practicing the technology claimed in such applications unless, and until, patents issue from such applications, and then only to the extent the issued claims cover the technology in appropriate jurisdictions. There can be no assurance that our patent applications or those of our licensors will result in additional patents being issued or that issued patents will afford sufficient protection against competitors with similar technology, nor can there be any assurance that the patents issued will not be infringed, designed around or invalidated by third parties. Even issued patents may later be found invalid or unenforceable or may be modified or revoked in proceedings instituted by third parties before various patent offices or in courts. The degree of future protection for our proprietary rights is uncertain. Only limited protection may be available and may not adequately protect our rights or permit us to gain or keep any competitive advantage. For example, we do not have a patent covering the composition of matter for DHE, the active ingredient in STS101. If we do not adequately protect our intellectual property and proprietary technology, competitors may be able to use STS101 and proprietary technologies and erode or negate any competitive advantage we may have, which could have a material adverse effect on our financial condition and results of operations.

We have applied, and we intend to continue applying, for patents covering aspects of STS101, proprietary technologies and their uses that we deem appropriate. However, we may not be able to apply for patents on certain aspects of STS101, proprietary technologies and their uses in a timely fashion, at a reasonable cost, in all jurisdictions, or at all, and any potential patent coverage we obtain may not be sufficient to prevent substantial competition.



We own or have an exclusive license under more than sixty U.S. and foreign patents and pending applications. In the U.S., we own or have exclusive license rights under 10 issued U.S. patents relating to STS101 that have expiration dates (absent any adjustments or extensions of term) as late as 2039. We believe the breadth of our patent estate reflects the highly innovative and differentiated nature of our proprietary dry-powder nasal delivery and formulation technologies. With the exception of one issued U.S. patent and several issued or allowed patents in the European Union and Japan that we own, all of our rights under issued U.S. and foreign patents relating to STS101 are exclusively licensed from SNBL.

We cannot be certain that the claims in any of our patent applications will be considered patentable by the USPTO, courts in the United States or by the patent offices and courts in foreign countries, nor can we be certain that the claims in issued patents relating to STS101 will not be found invalid or unenforceable if challenged.

The patent application process is subject to numerous risks and uncertainties, and there can be no assurance that we or any of our actual or potential future collaborators will be successful in protecting STS101, proprietary technologies and their uses by obtaining and defending patents. These risks and uncertainties include the following:

- the USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other provisions during the patent process, the noncompliance with which can result in abandonment or lapse of a patent or patent application, and partial or complete loss of patent rights in the relevant jurisdiction;
- patent applications may not result in any patents being issued;
- patents owned or in-licensed by us may be challenged, invalidated, modified, revoked, circumvented, found to be unenforceable or otherwise may not provide any competitive advantage;
- our competitors, many of whom have substantially greater resources than we do and many of whom have made significant investments in competing technologies, may seek or may have already filed for or obtained patents that will limit, interfere with or eliminate our ability to make, use and sell STS101;
- other parties may have designed around our claims or developed technologies that may be related or competitive to our platform, may have filed or may file patent applications and may have received or may receive patents that overlap or conflict with our patent applications, either by claiming the same compositions, methods or devices or by claiming subject matter that could dominate our patent position;
- any successful opposition or other post-grant challenges to any patents owned by or licensed to us could result in revocation or amendment to our patents so that they no longer cover STS101;
- because patent applications in the United States and most other countries are confidential for a period of time after filing, we cannot be certain that we or our licensors were the first to file any patent application related to STS101, proprietary technologies and their uses;
- an interference proceeding can be provoked by a third party or instituted by the USPTO to determine who was the first to invent any of the subject matter covered by the patent claims of our applications for any application with an effective filing date before March 16, 2013;
- there may be significant pressure on the U.S. government and international governmental bodies to limit the scope of patent protection both inside and outside the United States for disease treatments that prove successful, as a matter of public policy regarding worldwide health concerns; and
- countries other than the United States may have patent laws less favorable to patentees than those upheld by U.S. courts, allowing foreign competitors a better opportunity to create, develop and market competing product candidates.

The patent position of pharmaceutical companies generally is highly uncertain, involves complex legal and factual questions, and has been the subject of much litigation in recent years. Moreover, the patent prosecution process is also 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. 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. Although we enter into non-disclosure and confidentiality agreements with parties who have access to patentable aspects of our research and development output, such as our employees, corporate collaborators, outside scientific

collaborators, CROs, contract manufacturers, consultants, advisors and other third parties, any of these parties may breach such agreements and disclose such output before a patent application is filed, thereby jeopardizing our ability to seek patent protection.

The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our patents, if issued, or the patent rights that we license from others, may be challenged in the courts or patent offices in the United States and abroad. Once granted, patents may remain open to opposition, interference, re-examination, post-grant review, *inter partes* review, nullification or derivation action in court or before patent offices or similar proceedings for a given period after allowance or grant, during which time third parties can raise objections against such initial grant. Such challenges may result in 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 products, or limit the duration of the patent protection of STS101. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our intellectual property may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

Our ability to enforce our patent rights depends on our ability to detect infringement. It may be difficult to detect infringers who do not advertise the components or methods that are used in connection with their products and services. Moreover, it may be difficult or impossible to obtain evidence of infringement in a competitor's or potential competitor's product or service. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded if we were to prevail may not be commercially meaningful.

In addition, proceedings to enforce or defend our patents could put our patents at risk of being invalidated, held unenforceable or interpreted narrowly. Such proceedings could also provoke third parties to assert claims against us or licensor Shin Nippon Biomedical Laboratories, Ltd., or SNBL, which we have agreed to indemnify under certain circumstances, including that some or all of the claims in one or more of our patents are invalid or otherwise unenforceable. If any of our patents covering STS101 are invalidated or found unenforceable, or if a court found that valid, enforceable patents held by third parties covered STS101, our competitive position could be harmed or we could be required to incur significant expenses to enforce or defend our rights. If we initiate lawsuits to protect or enforce our patents, or litigate against third-party claims, such proceedings would be expensive and would divert the attention of our management and technical personnel.

The degree of future protection for our proprietary rights is uncertain, and we cannot ensure that:

- any of our patents, or any of our pending patent applications, if issued, or those of our licensors, will include claims having a scope sufficient to protect STS101;
- any of our pending patent applications or those of our licensors may issue as patents;
- others will not or may not be able to make, use, offer to sell, or sell products that are the same as or similar to our own but that are not covered by the claims of the patents that we own or license;
- we will be able to successfully commercialize STS101 on a substantial scale, if approved, before the relevant patents that we own or license expire;
- we were the first to make the inventions covered by each of the patents and pending patent applications that we own or license;
- we or our licensors were the first to file patent applications for these inventions;
- others will not develop similar or alternative technologies that do not infringe the patents we own or license;
- any of the patents we own or license will be found to ultimately be valid and enforceable;
- any patents issued to us or our licensors will provide a basis for an exclusive market for our commercially viable products or will provide us with any competitive advantages;
- a third party may not challenge the patents we own or license and, if challenged, a court would hold that such patents are valid, enforceable and infringed;

- the patents of others will not have an adverse effect on our business;
- our competitors do not conduct research and development activities in countries where we do not have enforceable patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;
- we will develop additional proprietary technologies or products that are separately patentable; or
- our commercial activities or products will not infringe upon the patents of others.

To the extent we obtain licenses from or collaborate with third parties, 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 third parties, or such activities, if controlled by us, may require the input of such third parties. We may also require the cooperation of our licensors and collaborators to enforce any licensed patent rights, and such cooperation may not be provided. Therefore, these patents and applications may not be prosecuted and enforced in a manner consistent with the best interests of our business. Moreover, if we do obtain necessary licenses, we will likely have obligations under those licenses, and any failure to satisfy those obligations could give our licensor the right to terminate the license. Termination of a necessary license, or expiration of licensed patents or patent applications, could have a material adverse impact on our business.

***The lives of our patents may not be sufficient to effectively protect STS101 and our business.***

Patents have a limited lifespan. In the United States, the natural expiration of a patent is generally 20 years after its first effective non-provisional filing date. Although various extensions may be available, the life of a patent, and the protection it affords, is limited. Even if patents covering STS101, proprietary technologies and their uses are obtained, once the patent life has expired, we may be open to competition. In addition, although upon issuance in the United States a patent's life can be increased based on certain delays caused by the USPTO, this increase can be reduced or eliminated based on certain delays caused by the patent applicant during patent prosecution. Given the amount of time required for the development, testing and regulatory review of STS101, patents protecting it might expire before or shortly after it is commercialized. If we do not have sufficient patent life to protect STS101, proprietary technologies and their uses, our business and results of operations will be adversely affected.

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

We rely on the protection of our trade secrets, including unpatented know-how, technology and other proprietary information. We have taken steps to protect our trade secrets and unpatented know-how, including entering into confidentiality agreements with third parties, and confidentiality and inventions agreements with employees, consultants and advisors. In addition to contractual measures, we try to protect the confidential nature of our proprietary information using commonly accepted physical and technological security measures. 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, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. In addition, such security measures may not provide adequate protection for our proprietary information, for example, in the case of misappropriation of a trade secret by an employee, consultant, customer or third party with authorized access. Our security measures may not prevent an employee, consultant or customer from misappropriating our trade secrets and providing them to a competitor, and recourse we take against such misconduct may not provide an adequate remedy to protect our interests fully. Monitoring unauthorized uses and disclosures is difficult, and we do not know whether the steps we have taken to protect our proprietary technologies will be effective. Unauthorized parties may also attempt to copy or reverse engineer certain aspects of STS101 that we consider proprietary. 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. Even though we use commonly accepted security measures, the criteria for protection of trade secrets can vary among different jurisdictions.

Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. In addition, some courts inside and outside the United States are less willing or unwilling to protect trade secrets. Moreover, third parties may still obtain this information or may

come upon this or similar information independently, and we would have no right to prevent them from using that technology or information to compete with us. Trade secrets will over time be disseminated within the industry through independent development, the publication of journal articles and the movement of personnel skilled in the art from company to company or academic to industry scientific positions. Though our agreements with third parties typically restrict the ability of our advisors, employees, collaborators, licensors, suppliers, third-party contractors and consultants to publish data potentially relating to our trade secrets, our agreements may contain certain limited publication rights. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent such competitor from using that technology or information to compete with us, which could harm our competitive position. Because from time to time we expect to rely on third parties in the development, manufacture, and distribution of STS101, we must, at times, share trade secrets with them. Despite employing the contractual and other security precautions described above, the need to share trade secrets increases the risk that such trade secrets become known by our competitors, are inadvertently incorporated into the technology of others, or are disclosed or used in violation of these agreements. If any of these events occurs or if we otherwise lose protection for our trade secrets, the value of this information may be greatly reduced and our competitive position would be harmed. If we do not apply for patent protection prior to such publication or if we cannot otherwise maintain the confidentiality of our proprietary technology and other confidential information, then our ability to obtain patent protection or to protect our trade secret information may be jeopardized.

***Our rights to develop and commercialize STS101 are subject in part to the terms and conditions of a license granted to us by SNBL. The patent protection, prosecution and enforcement for STS101 may be dependent on third parties.***

We currently are reliant upon a license of certain patent rights and proprietary technology pursuant to a licensing and assignment agreement we entered with SNBL in June 2016, or the SNBL License. Such rights and technology are important or necessary to the development of STS101. This and other licenses we may enter into in the future may not provide adequate rights to use such intellectual property and technology in all relevant fields of use or in all territories in which we may wish to develop or commercialize our technology and products in the future. As a result, we may not be able to develop and commercialize our technology and products in fields of use and territories for which we are not granted rights pursuant to such licenses.

Licenses to additional third-party technology that may be required for our development programs may not be available in the future or may not be available on commercially reasonable terms, which could have a material adverse effect on our business and financial condition.

In some circumstances, we may not have the right to control the preparation, filing, prosecution and enforcement of patent applications, or to maintain the patents, covering technology that we license from third parties. In addition, in some instances, the SNBL License requires us to negotiate in good faith a strategy with respect to infringement, and in some instances, SNBL retains the sole right to initiate and control some infringing activities, before we can enforce patent rights. Therefore, we cannot be certain that SNBL or any future licensors or collaborators will prosecute, maintain, enforce and defend such intellectual property rights in a manner consistent with the best interests of our business, including by taking reasonable measures to protect the confidentiality of know-how and trade secrets, or by paying all applicable prosecution and maintenance fees related to intellectual property registrations for STS101. We also cannot be certain that our licensors have drafted or prosecuted the patents and patent applications licensed to us in compliance with applicable laws and regulations, which may affect the validity and enforceability of such patents or any patents that may issue from such applications. If they fail to do so, this could cause us to lose rights in any applicable intellectual property that we in-license, and as a result our ability to develop and commercialize STS101 may be adversely affected and we may be unable to prevent competitors from making, using and selling competing products.

The SNBL License imposes a low single-digit royalty on net sales of STS101 along with certain other obligations on us, and any future licenses, if required, likely will impose various royalty payments, milestones, and other obligations on us. If we fail to comply with any of these obligations, we may be required to pay damages and the licensor may have the right to terminate the license. Termination by the licensor would cause us to lose valuable rights, and could prevent us from developing and commercializing STS101 and proprietary technologies. Our business would suffer if any current or future licenses terminate, if the licensors fail to abide by the terms of the license, if the licensors fail to enforce licensed patents against infringing third parties, if the licensed patents or other rights are found to be invalid or unenforceable, or if we are unable to enter into necessary licenses on acceptable

terms. Furthermore, if any current or future licenses terminate, or if the underlying patents fail to provide the intended exclusivity, competitors or other third parties may gain the freedom to seek regulatory approval of, and to market, products identical to ours. Moreover, our licensors may own or control intellectual property that has not been licensed to us and, as a result, we may be subject to claims, regardless of their merit, that we are infringing or otherwise violating the licensor's rights. In addition, while we cannot currently determine the amount of the royalty obligations we would be required to pay on sales of future products, if any, the amounts may be significant. The amount of our future royalty obligations will depend on the technology and intellectual property we use in products that we successfully develop and commercialize, if any. Therefore, even if we successfully develop and commercialize STS101, we may be unable to achieve or maintain profitability.

***Litigation or other proceedings or third-party claims of intellectual property infringement could require us to spend significant time and money and could prevent us from selling our products.***

Our commercial success depends significantly on our ability to operate without infringing the patents and other proprietary rights of third parties. However, our research, development and commercialization activities may be subject to claims that we infringe or otherwise violate patents or other intellectual property rights owned or controlled by third parties. Claims by third parties that we infringe their proprietary rights may result in liability for damages or prevent or delay our developmental and commercialization efforts. We cannot assure you that our operations do not, or will not in the future, infringe existing or future patents.

Other entities may have or obtain patents or proprietary rights that could limit our ability to make, use, sell, offer for sale or import STS101 or impair our competitive position. There is a substantial amount of litigation, both within and outside the United States, involving patent and other intellectual property rights in the pharmaceutical and biotechnology industries, including patent infringement lawsuits, interferences, oppositions, reexaminations, *inter partes* review proceedings and post-grant review proceedings before the USPTO and/or corresponding foreign patent offices. Numerous third-party U.S. and foreign issued patents and pending patent applications exist in the fields of STS101. There may be third-party patents or patent applications with claims to materials, formulations, methods of manufacture or methods for treatment related to the use or manufacture of STS101.

Furthermore, the scope of a patent claim is determined by an interpretation of the law, the written disclosure in a patent and the patent's prosecution history and can involve other factors such as expert opinion. Our interpretation of the relevance or the scope of claims in a patent or a pending application may be incorrect, which may negatively impact our ability to market STS101. Further, we may incorrectly determine that our technologies or STS101 are not covered by a third-party patent or may incorrectly predict whether a third party's pending patent application will issue with claims of relevant scope. Our determination of the expiration date of any patent in the United States or abroad that we consider relevant may be incorrect, which may negatively impact our ability to develop and market STS101.

As the pharmaceutical industry expands and more patents are issued, the risk increases that STS101 may be subject to claims of infringement of the patent rights of third parties. Our competitors in both the United States and abroad, many of which have substantially greater resources and have made substantial investments in patent portfolios and competing technologies, may have applied for or obtained or may in the future apply for and obtain, patents that will prevent, limit or otherwise interfere with our ability to make, use and sell STS101. We do not always conduct independent reviews of pending patent applications of and patents issued to third parties.

Patent applications in the United States and elsewhere are typically published approximately 18 months after the earliest filing for which priority is claimed, with such earliest filing date being commonly referred to as the priority date. Certain U.S. applications that will not be filed outside the United States can remain confidential until patents issue. In addition, patent applications in the United States and elsewhere can be pending for many years before issuance, or unintentionally abandoned patents or applications can be revived. Furthermore, pending patent applications that have been published can, subject to certain limitations, be later amended in a manner that could cover our technologies, STS101 or the use of STS101. As such, there may be applications of others now pending or recently revived patents of which we are unaware. These applications may later result in issued patents, or the revival of previously abandoned patents, that will prevent, limit or otherwise interfere with our ability to make, use or sell STS101. Because patent applications are maintained as confidential for a certain period of time, until the relevant application is published we may be unaware of third-party patents that may be infringed by

commercialization of STS101, and cannot be certain that we were the first to file a patent application related to a product candidate or technology. Moreover, because patent applications can take many years to issue, there may be currently-pending patent applications that may later result in issued patents that STS101 may infringe. In addition, identification of third-party patent rights that may be relevant to our technology is difficult because patent searching is imperfect due to differences in terminology among patents, incomplete databases and the difficulty in assessing the meaning of patent claims. Any claims of patent infringement asserted by third parties would be time consuming and could:

- result in costly litigation;
- divert the time and attention of our technical personnel and management;
- cause development delays;
- prevent us from commercializing STS101 until the asserted patent expires or is held finally invalid or not infringed in a court of law;
- require us to develop non-infringing technology, which may not be possible on a cost-effective basis;
- require us to pay damages to the party whose intellectual property rights we may be found to be infringing, which may include treble damages if we are found to have been willfully infringing such intellectual property;
- require us to pay the attorney's fees and costs of litigation to the party whose intellectual property rights we may be found to be infringing; and/or
- require us to enter into royalty or licensing agreements, which may not be available on commercially reasonable terms, or at all.

Although no third-party has asserted a claim of patent infringement against us as of the date of this report, others may hold proprietary rights that could prevent STS101 from being marketed. Any patent-related legal action against us claiming damages and seeking to enjoin commercial activities relating to STS101 or processes could subject us to potential liability for damages, including treble damages if we were determined to willfully infringe, and require us to obtain a license to manufacture or market STS101. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business. We cannot predict whether we would prevail in any such actions or that any license required under any of these patents would be made available on commercially acceptable terms, if at all. Even if such licenses are available, we could incur substantial costs related to royalty payments for licenses obtained from third parties, which could negatively affect our gross margins, and the rights may be non-exclusive, which could give our competitors access to the same technology or intellectual property rights licensed to us. In addition, we cannot be certain that we could redesign STS101 or processes to avoid infringement, if necessary. Accordingly, an adverse determination in a judicial or administrative proceeding, or the failure to obtain necessary licenses, could prevent us from developing and commercializing STS101, which could harm our business, financial condition and operating results. In addition, intellectual property litigation, regardless of its outcome, may cause negative publicity and could prohibit us from marketing or otherwise commercializing STS101.

If we collaborate with third parties in the development of technology in the future, our collaborators may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to litigation or potential liability. Further, collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability. Also, we may be obligated under our agreements with our collaborators, licensors, suppliers and others to indemnify and hold them harmless for damages arising from intellectual property infringement by us.

***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. Further, issued patents relating to STS101 could be found invalid or unenforceable if challenged in court.***

Competitors may infringe our intellectual property rights or those of our licensors. To prevent infringement or

unauthorized use, we may be required to file infringement claims, which can be expensive and time-consuming. In addition, in a patent infringement proceeding, a court may decide that a patent we own or in-license is not valid, is unenforceable and/or is not infringed. If we or any of our potential future collaborators were to initiate legal proceedings against a third party to enforce a patent directed at STS101, the defendant could counterclaim that our patent is invalid and/or unenforceable in whole or in part. In patent litigation in the United States, defendant counterclaims alleging invalidity and/or unenforceability are commonplace. Grounds for a validity challenge include an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness or non-enablement. Grounds for an unenforceability assertion could include an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO or made a misleading statement during prosecution. Third parties may also raise similar claims before the USPTO, even outside the context of litigation. Similar mechanisms for challenging the validity and enforceability of a patent exist in ex-U.S. patent offices and may result in the revocation, cancellation, or amendment of any ex-U.S. patents we hold in the future. The outcome following legal assertions of invalidity and unenforceability is unpredictable, and prior art could render our patents or those of our licensors invalid. If a defendant were to prevail on a legal assertion of invalidity and/or unenforceability, we would lose at least part, and perhaps all, of the patent protection on such product candidate. Such a loss of patent protection would have a material adverse impact on our business. Interference or derivation proceedings provoked by third parties or brought by us or declared by the USPTO may be necessary to determine the priority of inventions with respect to our patents or patent applications or those of our licensors. An unfavorable outcome could require us to cease using the related technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms or at all, or if a non-exclusive license is offered and our competitors gain access to the same technology. Our defense of litigation or interference proceedings may fail and, even if successful, may result in substantial costs and distract our management and other employees. In addition, the uncertainties associated with litigation could have a material adverse effect on our ability to raise the funds necessary to continue our clinical trials, continue our research programs, license necessary technology from third parties or enter into development or manufacturing partnerships that would help us bring STS101 to market.

Even if resolved in our favor, litigation or other legal proceedings relating to our intellectual property rights may cause us to incur significant expenses, and could distract our technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing or distribution activities. We may not have sufficient financial or other resources to conduct such litigation or proceedings adequately. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could compromise our ability to compete in the marketplace.

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. There could also 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, it could have a material adverse effect on the price of our common stock.

***We may fail to comply with our obligations under the SNBL License or any future agreements pursuant to which we may license or otherwise acquire intellectual property rights or technology, which could result in the loss of rights or technology that are material to our business.***

Our business is dependent on the SNBL License for certain patent rights and know-how that are directed to SNBL's proprietary nasal drug delivery technology, including its proprietary nasal delivery device and formulation technologies, for use with DHE. Our rights under the SNBL License and any license for intellectual property or technology that we may enter into in the future are and will be subject to the continuation of and our compliance with the terms of these agreements. Disputes may arise regarding our rights to intellectual property licensed to us from a third party, including but not limited to:

- the scope of rights granted under the license agreement and other interpretation-related issues;
- the extent to which our technology and processes infringe on intellectual property of the licensor that is not subject to the licensing agreement;
- the sublicensing of patent and other rights;
- our diligence obligations under the license agreement and what activities satisfy those diligence obligations;
- the ownership of inventions and know-how resulting from the creation or use of intellectual property by us, alone or with our licensors and collaborators;
- the scope and duration of our payment obligations;
- our rights upon termination of such agreement; and
- the scope and duration of exclusivity obligations of each party to the agreement.

Any disputes over intellectual property and other rights under the SNBL License could prevent or impair our ability to maintain the license on acceptable terms and our ability to successfully develop and commercialize STS101. In addition, if we fail to comply with our obligations under the SNBL License, it may be terminated or the scope of our rights under it may be reduced and we might be unable to develop, manufacture or market STS101.

***We may be subject to claims challenging the inventorship or ownership of our patents and other intellectual property.***

We may also be subject to claims that former employees, collaborators or other third parties have an ownership interest in our patents or other intellectual property. In addition, we may face claims by third parties that our agreements with employees, contractors or consultants obligating them to assign intellectual property to us are ineffective or in conflict with prior or competing contractual obligations of assignment, which could result in ownership disputes regarding intellectual property we have developed or will develop and interfere with our ability to capture the commercial value of such intellectual property. Litigation may be necessary to defend against these and other claims challenging inventorship or ownership. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights. Such an outcome could have a material adverse effect on our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and distraction to management and other employees.

**Risks Related to Government Regulation**

***Even if we obtain regulatory approval for STS101, STS101 will remain subject to regulatory scrutiny.***

If STS101 is approved, it will be subject to ongoing regulatory requirements for manufacturing, labeling, packaging, storage, advertising, promotion, sampling, record-keeping, conduct of post-marketing studies, and submission of safety, efficacy, and other post-market information, including both federal and state requirements in the United States and requirements of comparable foreign regulatory authorities.

Manufacturers and manufacturers' facilities are required to comply with extensive FDA and comparable foreign regulatory authority requirements, including ensuring that quality control and manufacturing procedures conform to cGMP regulations. As such, we and our contract manufacturers will be subject to continual review and inspections to assess compliance with cGMP and adherence to commitments made in any approved marketing application. Accordingly, we and others with whom we work must continue to expend time, money, and effort in all areas of regulatory compliance, including manufacturing, production, and quality control.

We will have to comply with requirements concerning advertising and promotion for STS101. Promotional communications with respect to prescription drugs are subject to a variety of legal and regulatory restrictions and must be consistent with the information in the product's approved label. As such, we may not promote STS101 for indications or uses for which they do not have approval. However, companies may share truthful and not misleading information that is otherwise consistent with a product's FDA approved labeling. We also must submit new or



supplemental applications and obtain approval for certain changes to STS101, if approved, product labeling, or manufacturing process. We could also be asked to conduct post-marketing clinical studies to verify the safety and efficacy of STS101 in general or in specific patient subsets. An unsuccessful post-marketing study or failure to complete such a study could result in the withdrawal of marketing approval.

If we discover previously unknown problems with STS101, such as adverse events of unanticipated severity or frequency, or problems with the facility where STS101 is manufactured, or if the FDA disagrees with the promotion, marketing or labeling of STS101, the FDA may impose restrictions on it or us, including requiring withdrawal of it from the market. If we fail to comply with applicable regulatory requirements, the FDA and other regulatory authorities may, among other things:

- issue warning letters;
- impose civil or criminal penalties;
- suspend or withdraw regulatory approval;
- suspend any of our ongoing clinical studies;
- refuse to approve pending applications or supplements to approved applications;
- impose restrictions on our operations, including closing our contract manufacturers' facilities; or
- require a product recall, seizure or detention.

Any government action or investigation of alleged violations of law could require us to expend significant time and resources in response, and could generate negative publicity. Any failure to comply with ongoing regulatory requirements may significantly and adversely affect our ability to commercialize and generate revenue from STS101. If regulatory sanctions are applied or if regulatory approval is withdrawn, the value of our company and our operating results will be adversely affected.

Moreover, the policies of the FDA and of other regulatory authorities may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of STS101. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative or executive action, either in the United States or abroad. In addition, 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 could lose any marketing approval that we may have obtained and we may not achieve or sustain profitability.

***If STS101 obtains regulatory approval, competitors could enter the market with generic versions, which may result in a material decline in sales of affected products.***

Under the Hatch-Waxman Amendments to the Federal Food, Drug and Cosmetic Act, or FDCA, a pharmaceutical manufacturer may file an abbreviated new drug application, or ANDA, seeking approval of a generic version of an approved drug product. A manufacturer may also submit an NDA under section 505(b)(2) of the FDCA, which may be for a new or improved version of the originally approved drug product. The Hatch-Waxman Amendments also provide for certain periods of regulatory exclusivity, which preclude FDA acceptance or approval of an ANDA or 505(b)(2) NDA for specific timeframes. In addition to this non-patent exclusivity, an NDA holder may have patents claiming the active ingredient, product formulation or an approved use of the drug, which would be listed in the FDA publication, "Approved Drug Products with Therapeutic Equivalence Evaluations," known as the Orange Book. If there are patents listed in the Orange Book for a product, a generic or 505(b)(2) applicant that seeks to market its product before expiration of the patents must include in their applications what is known as a "Paragraph IV" certification, challenging the validity or enforceability of, or claiming non-infringement of, the listed patent or patents. Notice of the certification must be given to the patent owner and NDA holder and if, within 45 days of receiving notice, either the patent owner or NDA holder sues for patent infringement, approval of the ANDA or 505(b)(2) NDA is stayed for up to 30 months.

Accordingly, if STS101 is approved, including through the 505(b)(2) pathway, competitors could file ANDAs for generic versions of STS101. If there are patents listed for STS101 in the Orange Book, those ANDAs would be

required to include a certification as to each listed patent indicating whether the ANDA applicant does or does not intend to challenge the patent. We cannot predict which, if any, patents in our current portfolio or patents we may obtain in the future will be eligible for listing in the Orange Book, how any generic competitor would address such patents, whether we would sue on any such patents, or the outcome of any such suit.

We may not be successful in securing or maintaining proprietary patent protection for STS101. Moreover, if any of our owned or in-licensed patents that are listed in the Orange Book are successfully challenged by way of a Paragraph IV certification and subsequent litigation, STS101 could immediately face generic competition and its sales would likely decline rapidly and materially.

***The successful commercialization of STS101 will depend in part on the extent to which governmental authorities, private health insurers, managed care plans and other third-party payors provide coverage, adequate reimbursement levels and implement pricing policies favorable for STS101. Failure to obtain or maintain coverage and adequate reimbursement for STS101, if approved, could limit our ability to market those products and decrease our ability to generate revenue.***

The availability of coverage and adequacy of reimbursement by governmental healthcare programs, such as Medicare and Medicaid, private health insurers, managed care plans and other third-party payors are essential for most patients to be able to afford medical services and pharmaceutical products such as STS101 that receive FDA approval. Our ability to achieve acceptable levels of coverage and reimbursement by third-party payors for our products will have an effect on our ability to successfully commercialize STS101.

No uniform policy for coverage and reimbursement for products exists among third-party payors in the United States. Therefore, coverage and reimbursement for products can differ significantly from payor to payor. The process for determining whether a third-party payor will provide coverage for a product typically is separate from the process for setting the price of such product or for establishing the reimbursement rate that the payor will pay for the product once coverage is approved. Third-party payors may limit coverage to specific products on an approved list, also known as a formulary, which might not include all of the FDA-approved products for a particular indication, or place products at certain formulary levels that result in lower reimbursement levels and higher cost-sharing obligation imposed on patients. One third-party payor's decision to cover a particular medical product or service does not ensure that other payors will also provide coverage for the medical product or service. As a result, the coverage determination process will often require us to provide scientific and clinical support for the use of our products to each payor separately and can be a time-consuming process, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance. We cannot be sure that coverage will be available for any product that we may develop. A decision by a third-party payor not to cover STS101 could reduce physician utilization of our products once approved and adversely affect our business, financial condition, results of operations and prospects.

Assuming there is coverage for our products by a third-party payor, the resulting reimbursement payment rates may not be adequate or may require co-payments that patients find unacceptably high. Furthermore, rules and regulations regarding reimbursement change frequently, in some cases on short notice, and we believe that changes in these rules and regulations are likely. Third-party payors increasingly are challenging prices charged for pharmaceutical products and services, and many third-party payors may refuse to provide coverage and adequate reimbursement for particular drugs or biologics when an equivalent generic drug, biosimilar or a less expensive therapy is available. It is possible that a third-party payor may consider STS101 as substitutable and only offer to reimburse patients for the less expensive product. For example, there are currently generic versions of both DHE liquid nasal spray products and DHE injectable products, which we may compete with. Even if we show improved efficacy or improved convenience of administration with STS101, pricing of other third-party therapeutics may limit the amount we will be able to charge for our products. These third-party payors may deny or revoke the reimbursement status of our products, if approved, or establish prices for our products at levels that are too low to enable us to realize an appropriate return on our investment. If reimbursement is not available, is decreased or eliminated in the future, or is available only at limited levels, we may not be able to successfully commercialize our products and may not be able to obtain a satisfactory financial return on our products.

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 and other countries has and will continue to put pressure on the pricing and usage of our products, if any. In many countries, the prices of medical products are subject to varying price control mechanisms as part of national health systems. Other countries allow companies to fix their own prices for medical 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 products. Accordingly, in markets outside the United States, the reimbursement for our products may be reduced compared with the United States and may be insufficient to generate commercially reasonable revenue and profits.

***Our business operations and current and future relationships with investigators, healthcare professionals, consultants, third-party payors, patient organizations and customers will be subject to applicable healthcare regulatory laws, which could expose us to penalties.***

Our business operations and current and future arrangements with investigators, healthcare professionals, consultants, third-party payors, patient organizations and customers, may expose us to broadly applicable fraud and abuse and other healthcare laws. These laws may constrain the business or financial arrangements and relationships through which we conduct our operations, including how we research, market, sell and distribute STS101, if approved. Such laws include, but are not limited to:

- the U.S. federal Anti-Kickback Statute, which prohibits, among other things, persons or entities from knowingly and willfully soliciting, offering, receiving or providing any remuneration (including any kickback, bribe, or certain rebate), directly or indirectly, overtly or covertly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, lease, order or recommendation of, any good, facility, item or service, for which payment may be made, in whole or in part, under any U.S. federal healthcare program, such as Medicare and Medicaid. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;
- the U.S. federal civil monetary penalty and civil and criminal false claims laws, including the civil federal False Claims Act, which can be enforced through civil whistleblower or qui tam actions, which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, to the U.S. federal government, claims for payment or approval that are false or fraudulent, knowingly making, using or causing to be made or used, a false record or statement material to a false or fraudulent claim, or from knowingly making a false statement to avoid, decrease or conceal an obligation to pay money to the U.S. federal government. Pharmaceutical manufacturers can cause false claims to be presented to the U.S. federal government by engaging in impermissible marketing practices, such as the off-label promotion of a product for an indication for which it has not received FDA approval. In addition, the government may assert that a claim including items and services resulting from a violation of the U.S. federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the civil False Claims Act;
- HIPAA, which 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 knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement, in connection with the delivery of, or payment for, healthcare benefits, items or services. Similar to the U.S. federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the healthcare fraud statute implemented under HIPAA or specific intent to violate it in order to have committed a violation;
- the FDCA, which prohibits, among other things, the adulteration or misbranding of drugs, biologics and medical devices;
- the U.S. Physician Payments Sunshine Act and its implementing regulations, which requires certain manufacturers of drugs, devices, biologics and medical supplies that are reimbursable under Medicare, Medicaid, or the Children's Health Insurance Program, with specific exceptions, to report annually to the government information related to certain payments and other transfers of value to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), certain other health care professionals beginning in 2022, and teaching hospitals, as well as ownership and investment interests held by the physicians described above and their immediate family members;

- federal consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers;
- analogous U.S. state laws, including: state anti-kickback and false claims laws, which may apply to our business practices, including but not limited to, research, distribution, sales and marketing arrangements and claims involving healthcare items or services reimbursed by any third-party payor, including private insurers; state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the U.S. federal government, or otherwise restrict payments that may be made to healthcare providers and other potential referral sources; state laws that require drug manufacturers to file reports relating to pricing and marketing information, which requires tracking gifts and other remuneration and items of value provided to healthcare professionals and entities; and state and local laws requiring the registration of pharmaceutical sales representatives;
- the U.S. Foreign Corrupt Practices Act of 1977, as amended, which prohibits, among other things, U.S. companies and their employees and agents from authorizing, promising, offering, or providing, directly or indirectly, corrupt or improper payments or anything else of value to foreign government officials, employees of public international organizations and foreign government owned or affiliated entities, candidates for foreign political office, and foreign political parties or officials thereof; and
- similar healthcare and data protection laws in the European Union and other jurisdictions, including reporting requirements detailing interactions with and payments to healthcare providers.

Ensuring that our internal operations and future business arrangements with third parties comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices do not comply with current or future statutes, regulations, agency guidance or case law involving applicable fraud and abuse or other healthcare laws. If our operations are found to be in violation of any of the laws described above or any other governmental laws that may apply to us, we may be subject to significant penalties, including civil, criminal and administrative penalties, damages, fines, exclusion from government-funded healthcare programs, such as Medicare and Medicaid or similar programs in other countries or jurisdictions, integrity oversight and reporting obligations to resolve allegations of non-compliance, disgorgement, imprisonment, contractual damages, reputational harm, diminished profits and the curtailment or restructuring of our operations. If any of the physicians or other providers or entities with whom we expect to do business are found to not be in compliance with applicable laws, they may be subject to significant criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs and imprisonment, which could affect our ability to operate our business. Further, defending against any such actions can be costly, time-consuming and may require significant personnel resources. Therefore, even if we are successful in defending against any such actions that may be brought against us, our business may be impaired.

***Enacted and future healthcare legislation may increase the difficulty and cost for us to obtain marketing approval of and commercialize STS101 and may affect the prices we may set.***

In the United States, the European Union and other jurisdictions, there have been, and we expect there will continue to be, a number of legislative and regulatory changes and proposed changes to the healthcare system that could affect our future results of operations. In particular, there have been and continue to be a number of initiatives at the U.S. federal and state levels that seek to reduce healthcare costs and improve the quality of healthcare. For example, in March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or collectively the ACA, was enacted, which substantially changed the way healthcare is financed by both governmental and private payors. Among the provisions of the ACA, those of greatest importance to the pharmaceutical and biotechnology industries include the following:

- an annual, non-deductible fee payable by any entity that manufactures or imports certain branded prescription drugs and biologic agents (other than those designated as orphan drugs), which is apportioned among these entities according to their market share in certain government healthcare programs;
- an increase to the minimum Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program and an extension the rebate program to individuals enrolled in Medicaid managed care

organizations;

- a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected;
- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to certain individuals with income at or below 133% of the federal poverty level, thereby potentially increasing a manufacturer's Medicaid rebate liability;
- a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D;
- 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
- establishment of a Center for Medicare Innovation at the Centers for Medicare & Medicaid Services, or CMS, to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending.

Since its enactment, there have been judicial, executive and Congressional challenges to certain aspects of the ACA. For example, the Tax Cuts and Jobs Act of 2017, or the Tax Act, which includes a provision that entered into effect on January 1, 2019, that repeals 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." On December 14, 2018, a U.S. District Court Judge in the Northern District of Texas, or Texas District Court Judge, ruled that the individual mandate is a critical and inseparable feature of the ACA, and therefore, because it was repealed as part of the Tax Act, the remaining provisions of the ACA are invalid as well. On December 18, 2019, the U.S. Court of Appeals for the 5th Circuit ruled that the individual mandate was unconstitutional and remanded the case back to the District Court to determine whether the remaining provisions of the ACA are invalid as well. The U.S. Supreme Court is currently reviewing the case, although it is unclear when a decision will be made or how the Supreme Court will rule. In addition, there may be other efforts to challenge, repeal or replace the ACA. We are continuing to monitor any changes to the ACA that, in turn, may potentially impact our business in the future.

In addition, other legislative changes have been proposed and adopted in the United States since the ACA was enacted. In August 2011, the Budget Control Act of 2011, among other things, led to aggregate reductions of Medicare payments to providers of 2% per fiscal year. These reductions went into effect in April 2013 and, due to subsequent legislative amendments to the statute, will remain in effect through 2030, with the temporary suspension from May 1, 2020 through September 30, 2021, unless additional action is taken by Congress.

Moreover, payment methodologies may be subject to changes in healthcare legislation and regulatory initiatives. For example, CMS may develop new payment and delivery models, such as bundled payment models. In addition, recently there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several U.S. Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under government payor programs, and review the relationship between pricing and manufacturer patient programs. The likelihood of success of these and other measures initiated by the former Trump administration is unclear, particularly in light of the new Biden administration. We expect that additional U.S. federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that the U.S. federal government will pay for healthcare products and services, which could result in reduced demand for STS101 or additional pricing pressures.

Individual states in the United States have also increasingly passed legislation and implemented 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. Legally-mandated price controls on payment amounts by third-party payors or other restrictions could harm our business,

results of operations, financial condition and prospects. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other healthcare programs. Furthermore, there has been increased interest by third-party payors and governmental authorities in reference pricing systems and publication of discounts and list prices.

In the European Union, similar political, economic and regulatory developments may affect our ability to profitably commercialize STS101, if approved. In addition to continuing pressure on prices and cost containment measures, legislative developments at the European Union or member state level may result in significant additional requirements or obstacles that may increase our operating costs. The delivery of healthcare in the European Union, including the establishment and operation of health services and the pricing and reimbursement of medicines, is almost exclusively a matter for national, rather than European Union, law and policy. National governments and health service providers have different priorities and approaches to the delivery of health care and the pricing and reimbursement of products in that context. In general, however, the healthcare budgetary constraints in most European Union member states have resulted in restrictions on the pricing and reimbursement of medicines by relevant health service providers. Coupled with ever-increasing European Union and national regulatory burdens on those wishing to develop and market products, this could prevent or delay marketing approval of STS101, restrict or regulate post-approval activities and affect our ability to commercialize STS101, if approved. In markets outside of the United States and European Union, reimbursement and healthcare payment systems vary significantly by country, and many countries have instituted price ceilings on specific products and therapies.

We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action in the United States, the European Union or any other jurisdiction. For example, the results of the 2020 presidential election may impact our business and industry. Namely, the Trump administration took several executive actions, including the issuance of a number of Executive Orders, that could impose significant burdens on, or otherwise materially delay, the FDA's ability to engage in routine regulatory and oversight activities such as implementing statutes through rulemaking, issuance of guidance, and review and approval of marketing applications. It is difficult to predict whether or how these executive actions will be implemented, or whether they will be rescinded and replaced under the Biden administration. The policies and priorities of a new administration are unknown and could materially impact the regulations governing our product candidates. If we or any third parties we may engage are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we or such third parties are not able to maintain regulatory compliance, STS101 may lose any regulatory approval that may have been obtained and we may not achieve or sustain profitability.

***Changes in and failures to comply with U.S. and foreign privacy and data protection laws, regulations and standards may adversely affect our business, operations and financial performance.***

We are subject to or affected by numerous federal, state and foreign laws and regulations, as well as regulatory guidance, governing the collection, use, disclosure, retention, and security of personal data, such as information that we collect about patients and healthcare providers in connection with clinical trials in the United States and abroad. The global data protection landscape is rapidly evolving, and implementation standards and enforcement practices are likely to remain uncertain for the foreseeable future. This evolution may create uncertainty in our business, affect our or any service providers', contractors' or future collaborators' ability to operate in certain jurisdictions or to collect, store, transfer use and share personal information, necessitate the acceptance of more onerous obligations in our contracts, result in liability or impose additional costs on us. The cost of compliance with these laws, regulations and standards is high and is likely to increase in the future. Any failure or perceived failure by us or our collaborators, service providers and contractors to comply with federal, state or foreign laws or regulation, our internal policies and procedures or our contracts governing processing of personal information could result in negative publicity, diversion of management time and effort and proceedings against us by governmental entities or others. In many jurisdictions, enforcement actions and consequences for noncompliance are rising.

In the United States, California enacted the California Consumer Privacy Act, or the CCPA, on June 28, 2018, which went into effect on January 1, 2020. The CCPA gives California residents expanded rights to access and delete their personal information, opt out of certain personal information sharing, and receive detailed information

about how their personal information is used. The CCPA provides for civil penalties for violations, as well as a private right of action for data breaches that is expected to increase data breach litigation. The CCPA may increase our compliance costs and potential liability. Some observers have noted that the CCPA could mark the beginning of a trend toward more stringent privacy legislation in the United States, which could increase our potential liability and adversely affect our business. Further, on November 3, 2020, the California Privacy Rights Act, or the CPRA, was voted into law by California residents. The CPRA significantly amends the CCPA, and imposes additional data protection obligations on companies doing business in California, including additional consumer rights processes and opt outs for certain uses of sensitive data. It also creates a new California data protection agency specifically tasked to enforce the law, which would likely result in increased regulatory scrutiny of California businesses in the areas of data protection and security. The substantive requirements for businesses subject to the CPRA will go into effect on January 1, 2023, and become enforceable on July 1, 2023.

Our operations abroad may also be subject to increased scrutiny or attention from data protection authorities. Many countries in these regions have established or are in the process of establishing privacy and data security legal frameworks with which we, our collaborators, service providers, including our CRO, and contractors must comply. For example, the European Union General Data Protection Regulation, or the GDPR, went into effect in May 2018 and introduces strict requirements for processing the personal information of individuals within the European Economic Area, or the EEA, and the United Kingdom, including, including clinical trial data. The GDPR has and will continue to increase compliance burdens on us, including by mandating potentially burdensome documentation requirements and granting certain rights to individuals to control how we collect, use, disclose, retain and process information about them. The processing of sensitive personal data, such as physical health condition, may impose heightened compliance burdens under the GDPR and is a topic of active interest among foreign regulators. The GDPR also increases the scrutiny of transfers of personal data from the EEA to the United States and other jurisdictions that the European Commission does not recognize as having “adequate” data protection laws; in July 2020, the Court of Justice of the European Union limited how organizations could lawfully transfer personal data from the EEA to the United States by invalidating the EU-US Privacy Shield and imposing further restrictions on use of the standard contractual clauses, which could increase our costs and our ability to efficiently process personal data from the EEA. In addition, the GDPR provides for more robust regulatory enforcement and fines of up to €20 million or 4% of the annual global revenue of the noncompliant company, whichever is greater. Relatedly, following the United Kingdom’s withdrawal from the EEA and the EU, and the expiry of the transition period, companies will have to comply with the GDPR and the GDPR as incorporated into United Kingdom national law, the latter regime having the ability to separately fine up to the greater of £17.5 million or 4% of global turnover. The relationship between the United Kingdom and the EU in relation to certain aspects of data protection law remains unclear, for example around how data can lawfully be transferred between each jurisdiction, which exposes us to further compliance risk. As we expand into other foreign countries and jurisdictions, we may be subject to additional laws and regulations that may affect how we conduct business.

#### **Risks Related to Ownership of Our Common Stock**

***Our stock price may be volatile and you may not be able to resell shares of our common stock at or above the price you paid.***

The trading price of our common stock may be highly volatile and could be subject to wide fluctuations in response to various factors, including the following:

- announcements with regard to our continued development of STS101;
- announcements with regard to our strategic business and/or financing plans;
- results from, and any delays in, our clinical trials for STS101;
- results of clinical trials of our competitors’ products;
- competition from existing products or new products that may emerge;
- announcements by academic, guideline publishers or other third parties challenging the fundamental premises underlying our approach to treating migraine;
- announcements of regulatory approval or disapproval of STS101;

- failure or discontinuation of any of our research and development programs;
- manufacturing setbacks or delays of or issues with the supply of the materials for STS101;
- announcements relating to future licensing, collaboration or development agreements, including the early termination or failure of an existing strategic collaboration;
- delays in the commercialization of STS101;
- acquisitions and sales of new products, technologies or businesses;
- quarterly variations in our results of operations or those of our future competitors;
- changes in earnings estimates or recommendations by securities analysts;
- announcements by us or our competitors of new products, significant contracts, commercial relationships, acquisitions or capital commitments;
- developments with respect to intellectual property rights;
- our commencement of, or involvement in, litigation;
- changes in financial estimates or guidance, including our ability to meet our future revenue and operating profit or loss estimates or guidance;
- any major changes in our board of directors or management;
- new legislation in the United States or relevant foreign jurisdictions relating to the sale or pricing of pharmaceuticals;
- FDA or other U.S. or foreign regulatory actions affecting us or our industry;
- product liability claims or other litigation or public concern about the safety of STS101 or other DHE products;
- market conditions in the pharmaceutical and biotechnology sectors; and
- general economic conditions in the United States and abroad, including recession or depression resulting from the current COVID-19 pandemic.

In addition, the stock markets in general, and the markets for pharmaceutical and biotechnology stocks in particular, have experienced extreme volatility, including as a result of the COVID-19 pandemic, that may have been unrelated to the operating performance of the issuer. These broad market fluctuations may adversely affect the trading price or liquidity of our common stock. In the past, when the market price of a stock has been volatile, holders of that stock have sometimes instituted securities class action litigation against the issuer. If we were to become involved in securities litigation, we could incur substantial costs and resources and the attention of our management could be diverted from the operation of our business.

***We are an “emerging growth company” and as a result of the reduced disclosure and governance requirements applicable to emerging growth companies, our common stock may be less attractive to investors.***

We are an “emerging growth company,” as defined in Jumpstart Our Business Act of 2012, or the JOBS Act, and we intend to take advantage of certain exemptions from various reporting requirements that are applicable to other public companies that are not emerging growth companies including, but not limited to, not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002, or Section 404, reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements, and exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and obtaining stockholder approval of any golden parachute payments not previously approved. In addition, as an “emerging growth company,” the JOBS Act allows us to delay adoption of new or revised accounting pronouncements applicable to public companies until such pronouncements are made applicable to private companies. We have elected to use this extended transition period under the JOBS Act. As a result, our financial statements may not be comparable to the financial statements of issuers who are required to comply with the effective dates for new or



revised accounting standards that are applicable to public companies, which may make comparison of our financials to those of other public companies more difficult.

We cannot predict if investors will find our common stock less attractive because we will rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile. We may take advantage of these reporting exemptions until we are no longer an emerging growth company. We will remain an emerging growth company until the earlier of (1) December 31, 2024, (2) the last day of the year in which we have total annual gross revenue of at least \$1.07 billion, (3) the last day of the year in which we are deemed to be a “large accelerated filer” as defined in Rule 12b-2 under the Exchange Act, which would occur if the market value of our common stock held by non-affiliates exceeded \$700.0 million as of the last business day of the second fiscal quarter of such year or (4) the date on which we have issued more than \$1.0 billion in non-convertible debt securities during the prior three-year period.

***We incur increased costs as a result of operating as a public company, and our management devotes substantial time to compliance initiatives. We may fail to comply with the rules that apply to public companies, including Section 404, which could result in sanctions or other penalties that would harm our business.***

We incur significant legal, accounting and other expenses as a public company, including costs resulting from public company reporting obligations under the Exchange Act and regulations regarding corporate governance practices. The listing requirements of The Nasdaq Global Market and the rules of the Securities and Exchange Commission, or the SEC, require that we satisfy certain corporate governance requirements relating to director independence, filing annual and interim reports, stockholder meetings, approvals and voting, soliciting proxies, conflicts of interest and a code of conduct. Our management and other personnel devote a substantial amount of time to ensure that we comply with all of these requirements. Moreover, the reporting requirements, rules and regulations associated with being a public company have increased our legal and financial compliance costs and make some activities more time-consuming and costly. Any changes we make to comply with these obligations may not be sufficient to allow us to satisfy our obligations as a public company on a timely basis, or at all. These reporting requirements, rules and regulations, coupled with the increase in potential litigation exposure associated with being a public company, could also make it more difficult for us to attract and retain qualified persons to serve on our board of directors or board committees or to serve as executive officers, or to obtain certain types of insurance, including directors’ and officers’ insurance, on acceptable terms and we may be forced to accept reduced policy limits and coverage or incur substantially higher costs to obtain the same or similar coverage.

We are subject to Section 404 and the related rules of the SEC, which generally require our management and independent registered public accounting firm to report on the effectiveness of our internal control over financial reporting. Beginning with this annual report, Section 404 requires an annual management assessment of the effectiveness of our internal control over financial reporting. However, for so long as we remain an emerging growth company as defined in the JOBS Act, we intend to take advantage of certain exemptions from various reporting requirements that are applicable to public companies that are not emerging growth companies, including, but not limited to, not being required to comply with the auditor attestation requirements of Section 404. Once we are no longer an emerging growth company or, if prior to such date, we opt to no longer take advantage of the applicable exemption, we will be required to include an opinion from our independent registered public accounting firm on the effectiveness of our internal controls over financial reporting. We will remain an emerging growth company until the earlier of (1) December 31, 2024, (2) the last day of the year in which we have total annual gross revenue of at least \$1.07 billion, (3) the last day of the year in which we are deemed to be a “large accelerated filer” as defined in Rule 12b-2 under the Exchange Act, which would occur if the market value of our common stock held by non-affiliates exceeded \$700.0 million as of the last business day of the second fiscal quarter of such year or (4) the date on which we have issued more than \$1.0 billion in non-convertible debt securities during the prior three-year period.

To date, we have never conducted a review of our internal control for the purpose of providing the reports required by these rules. In connection with the contemporaneous audits of our financial statements for the years ended December 31, 2017 and 2018, we identified control deficiencies in the design and operation of our internal control over financial reporting that constituted a material weakness. While we believe we have fully remediated the material weakness in our internal controls, if additional material weaknesses in our internal controls over financial reporting are identified in the future, we may not detect errors on a timely basis and our financial statements may be materially misstated. We or our independent registered public accounting firm may not be able to conclude on an

ongoing basis that we have effective internal control over financial reporting, which could harm our operating results, cause investors to lose confidence in our reported financial information and cause the trading price of our stock to fall. In addition, as a public company we will be required to file accurate and timely quarterly and annual reports with the SEC under the Exchange Act. In order to report our results of operations and financial statements on an accurate and timely basis, we will depend on CROs to provide timely and accurate notice of their costs to us. Any failure to report our financial results on an accurate and timely basis could result in sanctions, lawsuits, delisting of our shares from The Nasdaq Global Market or other adverse consequences that would materially harm to our business.

We are also subject to more stringent state law requirements. For example, on September 30, 2018, the then California Governor Jerry Brown signed into law Senator Bill 826, which generally requires public companies with principal executive offices in California to have a minimum number of females on the company's board of directors. By December 31, 2019, each public company with principal executive offices in California is required to have at least one female on its board of directors. By December 31, 2021, each public company is required to have at least two females on its board of directors if the company has at least five directors, and at least three females on its board of directors if the company has at least six directors. The new law does not provide a transition period for newly listed companies. We do not currently meet the December 31, 2021 requirement.

Additionally, on September 30, 2020, California Governor Gavin Newsom signed into law Assembly Bill 979 (AB 979), which generally requires public companies with principal executive offices in California to include specified numbers of directors from "underrepresented communities." A director from an "underrepresented community" means a director who self-identifies as Black, African American, Hispanic, Latino, Asian, Pacific Islander, Native American, Native Hawaiian, Alaska Native, gay, lesbian, bisexual or transgender. By December 31, 2021, each public company with principal executive offices in California is required to have at least one director from an underrepresented community. By December 31, 2022, a public company with more than four but fewer than nine directors will be required to have a minimum of two directors from underrepresented communities, and a public company with nine or more directors will need to have a minimum of three directors from underrepresented communities. Similar to SB 826, AB 979 does not provide a transition period for newly listed companies. Although we currently meet the December 31, 2021 requirement, there is no guarantee we will continue to do so in the future.

If we fail to comply with SB 826 or AB979, we could be fined by the California Secretary of State, with a \$100,000 fine for the first violation and a \$300,000 for each subsequent violation, and our reputation may be adversely affected.

***If we sell shares of our common stock in future financings, stockholders may experience immediate dilution and, as a result, our stock price may decline.***

We may from time to time issue additional shares of common stock at a discount from the current trading price of our common stock, including pursuant to our 2019 Incentive Award Plan and 2019 Employee Stock Purchase Plan. As a result, our stockholders would experience immediate dilution upon the purchase of any shares of our common stock sold at such discount. In addition, as opportunities present themselves, we may enter into financing or similar arrangements in the future, including the issuance of debt securities, preferred stock or common stock. If we issue common stock or securities convertible into common stock, our common stockholders would experience additional dilution and, as a result, our stock price may decline.

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

We have incurred substantial losses during our history, do not expect to become profitable in the near future, and we may never achieve profitability. To the extent that we continue to incur losses for tax purposes, or NOLs, such NOLs, will carry forward to offset a portion of future taxable income, if any, until such NOLs expire, if subject to expiration. Under current tax law, federal NOLs generated in taxable years beginning after December 31, 2017 may be carried forward indefinitely but may only be used to offset 80% of our taxable income in taxable years beginning after December 31, 2020.

In addition, under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended, if a corporation undergoes an "ownership change," generally defined as a greater than 50 percentage point change (by value) in its

equity ownership by certain stockholders over a rolling three-year period, the corporation's ability to use its pre-change net operating loss carryforwards, or NOLs, and other pre-change tax attributes (such as research and development tax credits) to offset its post-change income or taxes may be limited. If finalized, Treasury Regulations currently proposed under Section 382 of the Code may further limit our ability to utilize our pre-change NOLs or credits if we undergo a future ownership change. Our ability to utilize NOLs and other tax attributes to offset future taxable income or tax liabilities may be currently limited as a result of prior ownership changes, including in connection with our IPO. Similar rules may apply under our state or foreign tax laws. We have not completed a formal study to determine if any ownership changes within the meaning of Section 382 and 383 of the Code have occurred. While we do not believe we have experienced ownership changes in the past, it is possible we have done so, and we may experience ownership changes in the future as a result of subsequent shifts in our stock ownership (some of which shifts are outside our control). If an ownership change has occurred, our ability to use our NOLs or tax credit carryforwards may be restricted, which could require us to pay federal or state income taxes earlier than would be required if such limitations were not in effect. There is also a risk that due to regulatory changes, such as suspensions on the use of NOLs, or other unforeseen reasons, our existing NOLs could expire or otherwise become unavailable to offset future income tax liabilities.

***Provisions in our charter documents and under Delaware law could discourage a takeover that stockholders may consider favorable and may lead to entrenchment of management.***

Our amended and restated certificate of incorporation and amended and restated bylaws contain provisions that could delay or prevent changes in control or changes in our management without the consent of our board of directors. These provisions will include the following:

- a classified board of directors with three-year staggered terms, which may delay the ability of stockholders to change the membership of a majority of our board of directors;
- no cumulative voting in the election of directors, which limits the ability of minority stockholders to elect director candidates;
- the exclusive right of our board of directors to elect a director to fill a vacancy created by the expansion of the board of directors or the resignation, death or removal of a director, which prevents stockholders from being able to fill vacancies on our board of directors;
- the ability of our board of directors to authorize the issuance of shares of preferred stock and to determine the price and other terms of those shares, including preferences and voting rights, without stockholder approval, which could be used to significantly dilute the ownership of a hostile acquiror;
- the ability of our board of directors to alter our amended and restated bylaws without obtaining stockholder approval;
- the required approval of at least 66 2/3% of the shares entitled to vote at an election of directors to adopt, amend or repeal our amended and restated bylaws or repeal the provisions of our amended and restated certificate of incorporation regarding the election and removal of directors;
- a prohibition on stockholder action by written consent, which forces stockholder action to be taken at an annual or special meeting of our stockholders;
- the requirement that a special meeting of stockholders may be called only by our chief executive officer or president or by the board of directors, which may delay the ability of our stockholders to force consideration of a proposal or to take action, including the removal of directors; and
- advance notice procedures that stockholders must comply with in order to nominate candidates to our board of directors or to propose matters to be acted upon at a stockholders' meeting, which may discourage or deter a potential acquiror from conducting a solicitation of proxies to elect the acquiror's own slate of directors or otherwise attempting to obtain control of us.

We are also subject to the anti-takeover provisions contained in Section 203 of the Delaware General Corporation Law. Under Section 203, a corporation may not, in general, engage in a business combination with any holder of 15% or more of its capital stock unless the holder has held the stock for three years or, among other exceptions, the board of directors has approved the transaction. For a description of our capital stock, see "Description of Capital Stock" in our Annual Report on Form 10-K for the year ended December 31, 2020.

***Claims for indemnification by our directors and officers may reduce our available funds to satisfy successful third-party claims against us and may reduce the amount of money available to us.***

Our amended and restated certificate of incorporation and amended and restated bylaws provide that we will indemnify our directors and officers, in each case, to the fullest extent permitted by Delaware law.

In addition, as permitted by Section 145 of the Delaware General Corporation Law, our amended and restated bylaws and our indemnification agreements that we have entered into with our directors and officers provide that:

- We will indemnify our directors and officers for serving us in those capacities or for serving other business enterprises at our request, to the fullest extent permitted by Delaware law. Delaware law provides that a corporation may indemnify such person if such person acted in good faith and in a manner such person reasonably believed to be in or not opposed to the best interests of the registrant and, with respect to any criminal proceeding, had no reasonable cause to believe such person's conduct was unlawful.
- We may, in our discretion, indemnify employees and agents in those circumstances where indemnification is permitted by applicable law.
- We are required to advance expenses, as incurred, to our directors and officers in connection with defending a proceeding, except that such directors or officers shall undertake to repay such advances if it is ultimately determined that such person is not entitled to indemnification.
- We will not be obligated pursuant to our amended and restated bylaws to indemnify a person with respect to proceedings initiated by that person against us or our other indemnitees, except with respect to proceedings authorized by our board of directors or brought to enforce a right to indemnification.
- The rights conferred in our amended and restated bylaws are not exclusive, and we are authorized to enter into indemnification agreements with our directors, officers, employees and agents and to obtain insurance to indemnify such persons.
- We may not retroactively amend our amended and restated bylaw provisions to reduce our indemnification obligations to directors, officers, employees and agents.

***Our amended and restated certificate of incorporation and amended and restated bylaws provide for an exclusive forum in the Court of Chancery of the State of Delaware for certain disputes between us and our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees.***

Our amended and restated certificate of incorporation and amended and restated bylaws provide that the Court of Chancery of the State of Delaware is the exclusive forum for any derivative action or proceeding brought on our behalf, any action asserting a breach of fiduciary duty, any action asserting a claim against us arising pursuant to the Delaware General Corporation Law, our amended and restated certificate of incorporation or our amended and restated bylaws, or any action asserting a claim against us that is governed by the internal affairs doctrine; provided that, the exclusive forum provision will not apply to suits brought to enforce any liability or duty created by the Securities Act or the Exchange Act or any other claim for which the federal courts have exclusive jurisdiction; and provided further that, if and only if the Court of Chancery of the State of Delaware dismisses any such action for lack of subject matter jurisdiction, such action may be brought in another state or federal court sitting in the State of Delaware. Nothing in our amended and restated certificate of incorporation or amended and restated bylaws precludes stockholders that assert claims under the Securities Act or the Exchange Act from bringing such claims in state or federal court, subject to applicable law.

We believe these provisions may benefit us by providing increased consistency in the application of Delaware law and federal securities laws by chancellors and judges, as applicable, particularly experienced in resolving corporate disputes, efficient administration of cases on a more expedited schedule relative to other forums and protection against the burdens of multi-forum litigation. 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, other employees or stockholders, which may discourage lawsuits with respect to such claims, although our stockholders will not be deemed to have waived our compliance with federal securities laws and the rules and

regulations thereunder. If a court were to find the choice of forum provision that will be contained in our amended and 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 adversely affect our business and financial condition.

***We do not currently intend to pay dividends on our common stock, and, consequently, your ability to achieve a return on your investment will depend on appreciation in the price of our common stock.***

We do not currently intend to pay any cash dividends on our common stock for the foreseeable future. Further, we are currently subject to covenants under our Loan Agreement that place restrictions on our ability to pay dividends. We currently intend to invest our future earnings, if any, to fund our growth. Therefore, you are not likely to receive any dividends on your common stock for the foreseeable future. Since we do not intend to pay dividends, your ability to receive a return on your investment will depend on any future appreciation in the market value of our common stock. There is no guarantee that our common stock will appreciate or even maintain the price at which our holders have purchased it.

## **General Risk Factors**

***Unfavorable global economic or political conditions could adversely affect our business, financial condition or results of operations.***

Our results of operations could be adversely affected by general conditions in the global economy and in the global financial markets. A global financial crisis or a global or regional political disruption could cause extreme volatility in the capital markets and lead to diminished liquidity and credit availability, declines in consumer confidence and economic growth, increases in unemployment rates and uncertainty about economic stability. For instance, the recent COVID-19 pandemic has led to a period of considerable uncertainty and volatility. A severe or prolonged economic downturn or political disruption could result in a variety of risks to our business, including weakened demand for STS101, if approved, and our ability to raise additional capital when needed on acceptable terms, if at all. A weak or declining economy or political disruption could also strain our manufacturers or suppliers, possibly resulting in supply disruption, or resulting in the inability of any future customers to pay for STS101, if approved. Any of the foregoing could harm our business and we cannot anticipate all of the ways in which the political or economic climate and financial market conditions could adversely impact our business.

***If product liability lawsuits are brought against us, we may incur substantial liabilities and may be required to limit commercialization of STS101.***

We face an inherent risk of product liability as a result of the planned clinical testing of STS101 and will face an even greater risk if we commercialize it. For example, we may be sued if STS101 allegedly causes injury. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, negligence, strict liability, and a breach of warranty. Claims could also be asserted under state consumer protection acts. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit commercialization of STS101. Even successful defense would require significant financial and management resources. Regardless of the merits or eventual outcome, liability claims may result in:

- decreased demand for STS101;
- injury to our reputation;
- withdrawal of clinical trial participants;
- costs to defend the related litigation;
- a diversion of management's time and our resources;
- substantial monetary awards to trial participants or patients;
- regulatory investigations, product recalls, withdrawals or labeling, marketing or promotional restrictions;

- loss of revenue; and
- the inability to commercialize STS101.

Our inability to obtain and maintain sufficient product liability insurance at an acceptable cost and scope of coverage to protect against potential product liability claims could prevent or inhibit the commercialization of STS101. We currently carry product liability insurance covering our clinical trials, however, any claim that may be brought against us could result in a court judgment or settlement in an amount that is not covered, in whole or in part, by our insurance or that is in excess of the limits of our insurance coverage. Our insurance policies also have various exclusions and deductibles, and we may be subject to a product liability claim for which we have no coverage. We will have to pay any amounts awarded by a court or negotiated in a settlement that exceed our coverage limitations or that are not covered by our insurance, and we may not have, or be able to obtain, sufficient funds to pay such amounts. Moreover, in the future, we may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses. If and when we obtain approval for marketing any dose of STS101, we intend to expand our insurance coverage to include its sale; however, we may be unable to obtain this liability insurance on commercially reasonable terms or at all.

***We depend on our and our third-party suppliers or providers' information technology systems, and any failure of these systems could harm our business. Any real or perceived security breaches, loss of data, and other disruptions or incidents could compromise the privacy, security, integrity or confidentiality of sensitive information related to our business or prevent us from accessing critical information and expose us to liability and reputational harm, which could adversely affect our business, results of operations and financial condition.***

We collect and maintain data and information that is necessary to conduct our business, and we are increasingly dependent on information technology systems and infrastructure to operate our business, including systems infrastructure operated and maintained by our third-party suppliers or providers. In the ordinary course of our business, we collect, store and transmit large amounts of confidential information, including intellectual property, proprietary business information and personal information. It is critical that we do so in a secure manner to maintain the privacy, security, confidentiality and integrity of such confidential information. We have established physical, electronic and organizational measures to safeguard and secure our systems and facilities to prevent an information compromise, and rely on commercially available systems, software, tools, and monitoring to provide security for our information technology systems and the processing, transmission and storage of digital information. We have also outsourced elements of our information technology infrastructure, and as a result a number of third-party vendors may or could have access to our confidential information. Our internal information technology systems and infrastructure, and those of our current and any future collaborators, contractors and consultants and other third parties on which we rely, are vulnerable to damage or unauthorized access or use resulting from computer viruses, malware, natural disasters, terrorism, war, telecommunication and electrical failures, denial-of-service attacks, cyber-attacks or cyber-intrusions over the Internet, hacking, phishing and other social engineering attacks, attachments to emails, persons inside our organization (including employees or contractors), lost or stolen devices, or persons with access to systems inside our organization. These challenges have been made more difficult by the COVID-19 pandemic and resulting shelter-in-place and stay-at-home restrictions, which are driving greater dependency on electronic monitoring of our clinical trial sites. Such monitoring could prove to be less reliable and could increase data privacy and cybersecurity risks.

The risk of a security breach or disruption or data loss, particularly through social engineering attacks, cyber-attacks or cyber-intrusion, including by computer hackers, foreign governments and cyber terrorists, has generally increased as the number, intensity and sophistication of attempted attacks and intrusions from around the world have increased. In addition, the prevalent use of mobile devices that access confidential information increases the risk of data security breaches, which could lead to the loss of confidential information or other intellectual property. The costs to us to mitigate, investigate and respond to potential security incidents, breaches, disruptions, network security problems, bugs, viruses, worms, malicious software programs and security vulnerabilities could be significant, and while we have implemented security measures to protect our data security and information technology systems, our efforts to address these problems may not be successful, and these problems could result in unexpected interruptions, delays, cessation of service and other harm to our business and our competitive position. If such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our product development programs. For example, the loss of clinical trial data from completed or ongoing or planned

clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. Moreover, if a real or perceived security breach affects our systems (or those of our third-party providers or suppliers) or results in the loss of or accidental, unlawful or unauthorized access to, use of, release of or other processing of personally identifiable information or clinical trial data, our reputation could be materially damaged. In addition, such a breach may require notification to governmental agencies, the media or individuals pursuant to various federal and state privacy and security laws, if applicable, including the Health Insurance Portability and Accountability Act of 1996, or HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, and regulations promulgated thereunder, regulations promulgated by the Federal Trade Commission and state breach notification laws. We would also be exposed to a risk of loss, negative publicity, harm to our reputation, governmental investigation and/or enforcement actions, claims or litigation and potential liability, which could materially adversely affect our business, results of operations and financial condition. The global data protection landscape is rapidly evolving, and we may be affected by or subject to new, amended or existing laws and regulations in the future, including as our operations continue to expand or if we begin to operate in foreign jurisdictions.

***Our employees and independent contractors, including principal investigators, consultants, commercial collaborators, service providers and other vendors may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements, which could have an adverse effect on our results of operations.***

We are exposed to the risk that our employees and independent contractors, including principal investigators, consultants, any future commercial collaborators, service providers and other vendors may engage in misconduct or other illegal activity. Misconduct by these parties could include intentional, reckless and/or negligent conduct or other unauthorized activities that violate the laws and regulations of the FDA and other similar regulatory bodies, including those laws that require the reporting of true, complete and accurate information to such regulatory bodies; manufacturing standards; U.S. federal and state fraud and abuse laws, data privacy and security laws and other similar non-U.S. laws; or laws that require the true, complete and accurate reporting of financial information or data. Activities subject to these laws also involve the improper use or misrepresentation of information obtained in the course of clinical trials, the creation of fraudulent data in our preclinical studies or clinical trials, or illegal misappropriation of product, which could result in regulatory sanctions and cause serious harm to our reputation. It is not always possible to identify and deter misconduct by employees and other third-parties, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations. In addition, we are subject to the risk that a person or government could allege such fraud or other misconduct, even if none occurred. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business and financial results, including, without limitation, the imposition of significant civil, criminal and administrative penalties, damages, monetary fines, disgorgement, possible exclusion from participation in Medicare, Medicaid and other U.S. federal healthcare programs or healthcare programs in other jurisdictions, integrity oversight and reporting obligations to resolve allegations of non-compliance, imprisonment, other sanctions, contractual damages, reputational harm, diminished profits and future earnings and curtailment of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

***If our trademarks and trade names are not adequately protected, then we may not be able to build name recognition in our markets of interest and our business may be adversely affected.***

Our unregistered trademarks or trade names may be challenged, infringed, circumvented or declared generic or determined to be infringing on other marks. We may not be able to protect our rights to these trademarks and trade names, which we need to build name recognition among potential partners or customers in our markets of interest. At times, competitors may adopt trade names or trademarks similar to ours, thereby impeding our ability to build brand identity and possibly leading to market confusion. In addition, there could be potential trade name or trademark infringement claims brought by owners of other trademarks or trademarks that incorporate variations of our unregistered trademarks or trade names. Over the long term, if we are unable to establish name recognition based on our trademarks and trade names, then we may not be able to compete effectively and our business may be adversely affected. We may license our trademarks and trade names to third parties, such as distributors. Though these license agreements may provide guidelines for how our trademarks and trade names may be used, a breach of

these agreements or misuse of our trademarks and tradenames by our licensees may jeopardize our rights in or diminish the goodwill associated with our trademarks and trade names. Our efforts to enforce or protect our proprietary rights related to trademarks, trade names, trade secrets, domain names, copyrights or other intellectual property may be ineffective and could result in substantial costs and diversion of resources and could adversely affect our financial condition or results of operations.

***Changes in patent law in the U.S. or in other countries could diminish the value of patents in general, thereby impairing our ability to protect STS101.***

Our patent rights may be affected by developments or uncertainty in U.S. or ex-U.S. patent statutes, patent case laws in USPTO rules and regulations or in the rules and regulations of ex-U.S. patent offices. There are a number of recent changes to the U.S. patent laws that may have a significant impact on our ability to protect our technology and enforce our intellectual property rights. For example, on September 16, 2011, the Leahy-Smith America Invents Act, or Leahy-Smith Act, was signed into law. The Leahy-Smith Act includes a number of significant changes to U.S. patent law. These include provisions that affect the way patent applications will be prosecuted and may also affect patent litigation. In particular, under the Leahy-Smith Act, the United States transitioned in March 2013 to a “first to file” system in which the first inventor to file a patent application will be entitled to the patent. Third parties are allowed to submit prior art before the issuance of a patent by the USPTO, and may become involved in post-grant proceedings including opposition, derivation, reexamination, inter partes review or interference proceedings challenging our patent rights or the patent rights of others. An adverse determination in any such submission, proceeding or litigation could reduce the scope or enforceability of, or invalidate, our patent rights, which could adversely affect our competitive position. This could have a negative impact on some of our intellectual property and could increase uncertainties surrounding obtaining and enforcement or defense of issued patents relating to STS101. In addition, Congress may pass patent reform legislation that is unfavorable to us. The Supreme Court has ruled on several patent cases in recent years, either narrowing the scope of patent protection available in certain circumstances or weakening 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 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 we might obtain in the future.

Similarly, statutory or judicial changes to the patent laws of other countries may increase the uncertainties and costs surrounding the prosecution of patent applications and the enforcement or defense of issued patents.

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

Filing, prosecuting and defending all current and future patents 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 enforcement is not as strong as that in the United States. These products may compete with STS101, and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

The legal systems of many foreign countries do not favor the enforcement of patents and other intellectual property protection, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our proprietary rights. For example, some foreign countries have compulsory licensing laws under which a patent owner must grant licenses to third parties. In addition, some countries limit the enforceability of patents against third parties, including government agencies or government contractors. In these countries, patents may provide limited or no benefit. 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.

***Obtaining and maintaining 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.***

The USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other provisions during the patent process. Periodic maintenance fees, renewal fees, annuity fees and various other governmental fees on patents and/or applications will be due to be paid to the USPTO and various governmental patent agencies outside of the U.S. in several stages over the lifetime of the patents and/or applications. We employ reputable professionals and rely on such third parties to help us comply with these requirements and effect payment of these fees with respect to the patents and patent applications that we own, and if we license intellectual property we may have to rely upon our licensors to comply with these requirements and effect payment of these fees with respect to any patents and patent applications that we license. In many cases, an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with the applicable rules. However, there are situations in which noncompliance can result in abandonment or lapse of a patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, competitors might be able to enter the market earlier than would otherwise have been the case.

***Intellectual property rights do not necessarily address all potential threats to our competitive advantage.***

The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations, and may not adequately protect our business or permit us to maintain our competitive advantage. For example:

- others may be able to make therapies that are similar to ours but that are not covered by the claims of the patents that we own or have exclusively licensed;
- we or our licensors or future collaborators might not have been the first to make the inventions covered by the issued patents or pending patent applications that we own or have exclusively licensed;
- we or our licensors or future collaborators might not have been the first to file patent applications covering certain of our inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights;
- it is possible that our pending patent applications will not lead to issued patents;
- issued patents that we own or have exclusively licensed may be held invalid or unenforceable, as a result of legal challenges by our competitors;
- our competitors might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;
- we may not develop additional proprietary technologies that are patentable; and
- the patents of others may have an adverse effect on our business.

Should any of these events occur, they could significantly harm our business, results of operations and prospects.

***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 or business, 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 stock would be negatively impacted. 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 clinical trials and operating results fail to meet the expectations of analysts, demand for our common stock could decrease and our stock price could decline. If one or more of these analysts cease coverage of us or fail to publish reports on us regularly, we could lose visibility in the financial markets, which in turn could cause our stock price or trading volume to decline.

#### **ITEM 1B. UNRESOLVED STAFF COMMENTS**

None.

#### **ITEM 2. PROPERTIES**

Our corporate headquarters are located in South San Francisco, California, where we lease approximately 4,148 square feet of office space pursuant to a lease dated January 9, 2018, which continues through October 31, 2022. In addition, we lease approximately 5,043 square feet of office space in Research Triangle Park, North Carolina pursuant to a lease dated August 1, 2019, which continues through July 31, 2025. We believe these facilities are sufficient for our near-term needs, and expect to expand to new and/or additional space as we grow. We believe the biotechnology environment in the South San Francisco area offers suitable additional space on commercially reasonable terms to enable our expansion.

#### **ITEM 3. LEGAL PROCEEDINGS**

We are not a party to any material legal proceedings at this time. From time to time, we may be subject to various legal proceedings and claims that arise in the ordinary course of our business activities. Although the results of litigation and claims cannot be predicted with certainty, we do not believe we are party to any claim or litigation the outcome of which, if determined adversely to us, would individually or in the aggregate be reasonably expected to have a material adverse effect on our business. Regardless of the outcome, litigation can have an adverse impact on us because of defense and settlement costs, diversion of management resources and other factors.

#### **ITEM 4. MINE SAFETY DISCLOSURES**

None.

## PART II

### ITEM 5. MARKET FOR REGISTRANT’S COMMON EQUITY, RELATED STOCKHOLDER MATTERS AND ISSUER PURCHASES OF EQUITY SECURITIES

Our common stock has been listed on the Nasdaq Global Market under the symbol “STSA” since September 12, 2019. Prior to this date, there was no public market for our common stock.

#### Holders of Common Stock

As of March 11, 2022, there were approximately 10 records of our common stock. The approximate number of holders is based upon the actual number of holders registered in our records at such date and excludes holders in “street name” or persons, partnerships, associations, corporations, or other entities identified in security positions listings maintained by depository trust companies.

#### Dividend Policy

We have never declared or paid cash dividends on our capital stock. We intend to retain all available funds and any future earnings, if any, to fund the development and expansion of our business and we do not anticipate paying any cash dividends in the foreseeable future. In addition, we are currently subject to covenants under our loan agreement with Silicon Valley Bank that place restrictions on our ability to pay dividends. Any future determination related to dividend policy will be made at the discretion of our board of directors.

#### Securities Authorized for Issuance under Equity Compensation Plans

Information about our equity compensation plans is incorporated herein by reference to Item 12 of Part III of this Annual Report on Form 10-K.

#### Recent Sales of Unregistered Securities

None.

#### Purchases of Equity Securities by the Issuer and Affiliated Purchases

None.



## ITEM 7. MANAGEMENT’S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

*You should read the following discussion and analysis of our financial condition and results of operations together with the section titled “Selected Financial Data” and our financial statements and the related notes included elsewhere in this report. This discussion and analysis and other parts of this report contain forward-looking statements based upon current beliefs, plans and expectations related to future events and our future financial performance that involve risks, uncertainties and assumptions, such as statements regarding our intentions, plans, objectives, expectations, forecasts and projections. Our actual results and the timing of selected events could differ materially from those anticipated in these forward-looking statements as a result of several factors, including those set forth under the section titled “Risk Factors” and elsewhere in this report.*

### Overview

We are a clinical-stage biopharmaceutical company developing a novel therapeutic product for the acute treatment of migraine. Our product candidate, STS101, is a drug-device combination of a proprietary dry-powder formulation of dihydroergotamine mesylate, or DHE, which is designed to be quickly and easily self-administered with a proprietary pre-filled, single-use, nasal delivery device. DHE products have long been recommended as a first-line therapeutic option for the acute treatment of migraine and have significant advantages over other therapeutics for many patients. However, broad use has been limited by invasive and burdensome administration and/or sub-optimal clinical performance of available injectable and liquid nasal spray products. STS101 is specifically designed to deliver the clinical advantages of DHE while overcoming these shortcomings. If approved, we believe STS101 has the potential to be an important and differentiated option for the acute treatment of migraine that can address the unmet needs of many people living with migraines.

In September 2020, we announced topline data from the EMERGE Phase 3 efficacy trial, or EMERGE trial, which randomized 1,201 migraine subjects to one of two STS101 dose strengths or placebo. Although STS101 3.9 mg and 5.2 mg showed favorable numerical differences versus placebo on the pre-specified co-primary endpoints of freedom from pain and freedom from most bothersome symptom (from among photophobia, phonophobia and nausea) at two hours post-administration, these differences did not achieve statistical significance for either dose strength. Both dose strengths of STS101 did, however, demonstrate significant effects on both freedom from pain and most bothersome symptom by three hours post-dose and later time points. Both STS101 dose strengths were well-tolerated in the EMERGE trial, with low adverse event rates and no serious adverse events reported.

In March 2021, we announced an update to our development plan for STS101 that takes into account the findings from our analyses of results from our EMERGE efficacy trial and results from our ongoing ASCEND open-label, Phase 3 long-term safety trial of STS101 5.2 mg, or ASCEND trial. Our updated development plan for STS101 included a Phase 1 trial, which we completed in June 2021, to evaluate the pharmacokinetics, safety and tolerability of STS101 5.2 mg and two higher dose strengths, as well as a new pivotal Phase 3 efficacy trial, or SUMMIT trial, of STS101 5.2 mg that we initiated in June 2021, with topline results expected in the fourth quarter of 2022. If successful, we plan to file an NDA for STS101 in the first quarter of 2023.

Our net losses were \$51.2 million and \$47.6 million for the years ended December 31, 2021 and 2020, respectively. As of December 31, 2021, we had an accumulated deficit of \$141.7 million.

As we continue the development of STS101, our expenses will increase substantially over recent periods, as we advance STS101 through clinical development, manufacturing scale-up and seek to obtain regulatory approval, and prepare for commercialization of STS101, if approved.

Since our inception in June 2016, we have invested substantially all of our efforts and financial resources in the development of STS101 for the acute treatment of migraine. We have incurred significant operating losses to date and expect that our operating expenses will increase significantly as we advance STS101 through clinical development, manufacturing and regulatory approval, and as we prepare for commercialization of STS101, if approved; obtain, maintain, protect and enforce our intellectual property portfolio; and hire additional personnel. In addition, we expect to continue to incur increasing costs associated with operating as a public company.

In October 2020, we entered into a sales agreement (the “Sales Agreement”) with SVB Leerink LLC (“SVB”) to sell shares of our common stock, from time to time, through an at-the-market equity offering program under which SVB will act as its sales agent and pursuant to which we may sell common stock for aggregate gross sales proceeds of up to \$50.0 million. The issuance and sale of shares of common stock by us pursuant to the Sales Agreement is deemed an “at-the-market” offering under the Securities Act of 1933, as amended. SVB is entitled to compensation for its services equal to up to 3.0% of the gross proceeds of any shares of common stock sold through SVB under the Sales Agreement. As of December 31, 2021, we had not received any proceeds from the sale of shares of common stock pursuant to the Sales Agreement.

In February 2021, we entered into a Securities Purchase Agreement with certain purchasers, pursuant to which we agreed to sell and issue to certain purchasers an aggregate of 14,084,507 shares of our common stock at a per share purchase price of \$5.68, the closing price of our common stock on the Nasdaq Global Market on February 26, 2021, for gross proceeds of \$80.0 million (“Private Placement”). We closed the Private Placement in March 2021 and received \$75.2 million in net proceeds after deducting commissions and offering expenses.

We do not have any products approved for sale and have not generated any product revenue since our inception. Our ability to generate product revenue will depend on the successful development and eventual commercialization of STS101. Until such time as we can generate significant revenue from sales of STS101, if ever, we expect to finance our operations through the sale of equity, debt financings or other capital sources, including potential collaborations with other companies or other strategic transactions. Adequate funding may not be available to us on acceptable terms, or at all. If we fail to raise capital or enter into such agreements as and when needed, we may have to significantly delay, scale back, or discontinue the development and commercialization of STS101.

As of December 31, 2021, we had cash, cash equivalents and marketable securities of \$95.8 million. Based on our current operating plans, we believe that those cash, cash equivalents and marketable securities will be sufficient to fund our projected operations for at least 12 months from the issuance of our financial statements as of and for the year ended December 31, 2021 and into the second half of 2023.

## **COVID-19**

COVID-19 has placed strains on the providers of healthcare services, including the healthcare clinics and institutions where we conduct our ongoing clinical trials and may conduct planned clinical trials. To date, we have initiated and enrolled subjects in our planned STS101 clinical trials in accordance with our previously communicated timeline objectives. We will continue to follow FDA guidance on clinical trial conduct during the COVID-19 pandemic, including with respect to remote monitoring of clinical data. To date, subjects in our clinical trials have generally been able to complete their scheduled visits or treatments and we have been able to collect the essential data from those visits or treatments, as well as from the internet-connected electronic diary devices, as applicable, subjects in our trials may use to record efficacy and other key data.

To date, we have not experienced any disruption in our supply of investigational product necessary to conduct our clinical trials and, given our investigational product inventories, believe we will be able to supply the needs of our clinical trials. We are supporting our employees by utilizing remote work when necessary and appropriate, leveraging virtual meeting technology and encouraging employees to follow local guidelines.

The following summarizes our priorities and actions to address the COVID-19 disruption and its impact on our operations:

### *Health & Safety*

- The health and well-being of our employees, subjects in our clinical trials, and staff at our clinical trial sites and supply chain partners is our top priority.
- We have implemented strict measures to ensure and maintain safety, including working remotely when necessary and appropriate, social distancing and enhanced protocols to allow, if deemed necessary, remote monitoring and in-home testing of the subjects participating in our clinical trials.

- We are closely monitoring rapidly evolving conditions throughout the United States and the rest of the world and are adhering to local, state and federal guidelines.

#### *Business Continuity*

- In August 2020, we initiated subject enrollment in our ASCEND safety trial of STS101. While we expect our ASCEND safety trial to benefit from some of the similar design features that enabled our EMERGE efficacy trial to be completed on schedule, there can be no assurance that clinical site initiation and enrollment will not be delayed or otherwise negatively affected. Similarly, there can be no assurance that our recently initiated SUMMIT efficacy trial of STS101 will not be delayed or otherwise negatively affected as a result of the ongoing pandemic.
- We are working closely with our supply chain partners globally to maintain the levels of investigational product and proprietary nasal delivery devices to conduct existing and planned clinical trials, as suppliers support the health and safety of their employees.

### **Components of Operating Results**

#### **Operating Expenses**

##### ***Research and Development Expenses***

All of our research and development expenses consist of expenses incurred in connection with the development of STS101 for the acute treatment of migraine. These expenses include:

- payroll and personnel-related expenses, including salaries, annual cash bonuses, employee benefit costs and stock-based compensation expenses for our research and product development employees;
- fees paid to third parties to conduct preclinical and clinical studies and other research and development activities, including contract research organizations, or CROs, contract manufacturing organizations, or CMOs, consultants, and other service providers; and
- costs for licenses and allocated overhead, including rent, equipment, depreciation, information technology costs and utilities.

We expense both internal and external research and development expenses as they are incurred. We have entered into various agreements with third party vendors and CMOs. Our research and development accruals are estimated based on the level of services performed, progress of the studies, including the phase or completion of events or tasks, and contracted costs. The estimated costs of research and development provided, but not yet invoiced, are included in accrued and other current liabilities on the balance sheet. If the actual timing of the performance of services or the level of effort varies from the original estimates, we adjust the accrual accordingly. Payments made to CROs and CMOs under these arrangements in advance of the performance of the related services are recorded as prepaid expenses and other current assets until the services are rendered. Nonrefundable payments made prior to the receipt of goods or services that will be used or rendered for future research and development activities are deferred and capitalized as prepaid expenses and other current assets on our balance sheet. The capitalized amounts are recognized as expense as the goods are delivered or the related services are performed.

As we continue the development of STS101, our research and development expenses will increase substantially over recent periods, as we seek to advance STS101 through clinical development, manufacturing and regulatory approval, and prepare for commercialization of STS101, if approved. Predicting the timing or the cost to complete our clinical trials or validation of our commercial manufacturing and supply processes is difficult and delays may occur because of many factors, including factors outside of our control. For example, if the FDA or other regulatory authorities were to require us to conduct clinical trials beyond those that we currently anticipate, if we experience significant delays in enrollment in any of our clinical trials or if we experience delays in manufacturing with any of our CMOs, we could be required to expend significant additional financial resources and time on the completion of clinical development. Furthermore, we are unable to predict with any certainty when or if STS101 will receive regulatory approval.

### **General and Administrative Expenses**

General and administrative expenses consist principally of payroll and personnel expenses, including salaries, benefits and stock-based compensation expenses, professional fees for legal, consulting, accounting and tax services, directors and officers insurance, allocated overhead, including rent, debt service, equipment, depreciation, information technology costs, and utilities, and other general operating expenses not otherwise classified as research and development expenses including expenses associated with pre-commercialization activities.

We anticipate that our general and administrative expenses will increase as a result of increased personnel costs, including salaries, benefits and stock-based compensation expenses, expanded infrastructure and higher consulting, legal and accounting services associated with maintaining compliance with stock exchange listing and Securities and Exchange Commission, or SEC, requirements, expenses associated with pre-commercialization activities, investor relations costs and director and officer insurance premiums associated with being a public company.

### **Interest Income**

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

### **Interest Expense**

Interest expense consists primarily of interest related to our long-term debt and accretion of debt discount and debt issuance costs.

## **Results of Operations**

### **Comparison of the Years Ended December 31, 2021 and 2020**

	<b>Year Ended December 31,</b>		<b>Change</b>	<b>% Change</b>
	<b>2021</b>	<b>2020</b>		
Operating expenses:				
Research and development	\$ 37,635	\$ 36,270	\$ 1,365	4%
General and administrative	13,531	12,058	1,473	12%
Loss from operations	(51,166)	(48,328)	(2,838)	6%
Interest income	157	1,115	(958)	(86%)
Interest expense	(163)	(350)	187	(53%)
Net loss	<u>\$ (51,172)</u>	<u>\$ (47,563)</u>	<u>\$ (3,609)</u>	8%

### **Research and Development Expenses**

Research and development expenses increased by \$1.4 million, or 4%, from the year ended December 31, 2020 to the year ended December 31, 2021. The increase was in research and development expenses was primarily due to increase of \$1.2 million in clinical trial costs, which was the net of an increase of \$11.3 million for the SUMMIT efficacy trial, \$3.0 million for the ASCEND safety trial, and \$1.3 million for the STS101 Phase 1 trials offset by decrease of \$14.1 million in EMERGE efficacy trial costs as the EMERGE trial and related costs concluded in December 2020, and a \$0.3 million decrease in clinical consultant costs, as well as increases of \$1.2 million in payroll and personnel expenses, and \$0.2 million in other expenses, partly offset by a decrease of \$1.3 million in manufacturing activities.

### **General and Administrative Expenses**

General and administrative expenses increased by \$1.5 million, or 12%, from the year ended December 31, 2020 to the year ended December 31, 2021. The increase in general and administrative expenses was primarily due to an increase of \$1.1 million of payroll and personnel expenses, including salaries, benefits and stock-based compensation expenses, and an increase of \$1.1 million for directors and officers liability insurance, board fees



including stock based compensation, other services partially offset by a decrease of \$0.6 million in legal and outside consultants.

### ***Interest Income***

Interest income decreased by \$1.0 million, or 86%, from the year ended December 31, 2020 to the year ended December 31, 2021, which was the net result of the significantly lower interest yields on slightly lower average balances for our cash, cash equivalents and marketable securities.

### ***Interest Expense***

Interest expense decreased by \$0.2 million, or 53%, from the year ended December 31, 2020 to the year ended December 31, 2021, which was primarily attributable to the decrease of outstanding debt balances.

## ***Liquidity and Capital Resources; Plan of Operations***

### ***Sources of Liquidity***

We have historically financed our operations primarily through the issuance of common stock in our IPO, and private placements of equity securities and borrowings under its long-term debt facility. We have no products approved for sale, and we have not generated any revenue since inception. We expect to incur significant additional operating losses over at least the next several years.

In October 2020, we entered into the Sales Agreement with SVB to sell shares of our common stock, from time to time, through an at-the-market equity offering program under which SVB will act as its sales agent and pursuant to which we may sell common stock for aggregate gross sales proceeds of up to \$50.0 million. To date we have not received any proceeds from the sale of shares of common stock pursuant to the Sales Agreement.

In February 2021, we entered into a Securities Purchase Agreement with certain purchasers, pursuant to which we agreed to sell and issue to certain purchasers an aggregate of 14,084,507 shares of our common stock at a per share purchase price of \$5.68, the closing price of our common stock on the Nasdaq Global Market on February 26, 2021 for aggregate gross proceeds of approximately \$80.0 million. We closed the Private Placement in March 2021 and received \$75.2 million in net proceeds after deducting commissions and offering expenses.

### ***Credit Facility***

In October 2018, we entered into the Loan Agreement with Silicon Valley Bank. The Loan Agreement provides for loan advances of up to \$10.0 million. We drew down the first advance of \$5.0 million as of the effective date of the Loan Agreement. The remaining \$5.0 million under the facility was never drawn down and is no longer available for draw. The Loan Agreement contains customary affirmative and negative covenants and events of default, including covenants and restrictions that among other things, restrict our ability to incur liens, incur additional indebtedness, make loans and investments, engage in mergers and acquisitions, engage in asset sales or sale and leaseback transactions, and declare dividends or redeem or repurchase capital stock. Interest on the loan advances is payable monthly at a floating per annum rate equal to the greater of 1.5% above the prime rate and 6.5%. Upon the occurrence of an event of default, interest will increase to 5.0% above the rate that is otherwise applicable. Principal on the outstanding loan advance is repayable commencing on December 1, 2019 in 30 monthly payments through maturity. The maturity date of the loan advances is May 1, 2022.

### ***Future Funding Requirements***

We have incurred net losses since our inception. Our net losses were \$51.2 million and \$47.6 million for the years ended December 31, 2021 and 2020, respectively. Based on our current business plan, we believe that our existing cash, cash equivalents and marketable securities will be sufficient to fund our projected operations for at least 12 months from the issuance of our financial statements as of and for the year ended December 31, 2021 and into the second half of 2023.

As we continue the development of STS101, our operating expenses may increase substantially, as we seek to advance STS101 through clinical development, manufacturing and regulatory approval, and prepare for

commercialization of STS101, if approved.

To the extent we continue development of STS101, we will continue to require additional capital to fund operations for the foreseeable future. We do not expect to generate any meaningful revenue unless and until we obtain regulatory approval of and commercialize STS101 or enter into collaborative agreements with third parties, and we do not know when, or if, either will occur. We may seek to raise capital through private or public equity or debt financings, collaborative or other arrangements with corporate sources, or through other sources of financing. Adequate additional funding may not be available to us on acceptable terms, or at all. Our failure to raise capital as and when needed would have a negative impact on our financial condition and our ability to pursue the development and commercialization of STS101. Our need for additional capital will depend on many factors, including:

- the scope, timing, rate of progress, results and costs of our clinical trials for STS101, and most particularly, the SUMMIT Phase 3 efficacy trial for STS101, as well as any clinical program we may pursue in any foreign jurisdictions;
- the number and scope of clinical programs we decide to pursue;
- the scope and costs of manufacturing development and commercial manufacturing activities;
- the cost, timing and outcome of regulatory review of STS101;
- the cost of building a sales force in anticipation of commercialization of STS101;
- the cost and timing associated with commercializing STS101, if approved;
- the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims;
- any product liability or other lawsuits related to STS101;
- our efforts to enhance operational systems and our ability to attract, hire and retain qualified personnel, including personnel to support the commercialization of STS101;
- the extent to which we acquire or in-license other product candidates or technologies;
- the payment of royalty payments owed under our existing license agreement;
- our ability to establish and maintain collaborations on favorable terms, if at all;
- the costs associated with being a public company; and
- the timing, receipt and amount of sales of STS101, if approved.

We are subject to the risks typically related to the development of new product candidates, and we may encounter unforeseen expenses, difficulties, complications, delays and other unknown factors that may adversely affect our business. Despite our implementation of a new development plan for STS101, such plan may change, which could significantly change the costs and timing associated with its development of STS101 and our operations. Furthermore, our operating plans may change in the future, and we will continue to require additional capital to meet operational needs and capital requirements associated with such operating plans. If we raise additional funds by issuing equity securities, our stockholders may experience dilution. Any debt financing into which we enter may impose upon us covenants that restrict our operations, including limitations on our ability to incur liens or additional debt, pay dividends, repurchase our common stock, make certain investments or engage in certain merger, consolidation or asset sale transactions. For example, the Loan Agreement contains many of these restrictions. Any debt financing or additional equity that we raise may contain terms that are not favorable to us or our stockholders. If we are unable to raise additional funds when needed, we may be required to delay, reduce, or terminate our development program and clinical trials. We may also be required to sell or license to others rights to STS101 in certain territories or indications that we would prefer to develop and commercialize ourselves. Adequate additional funding may not be available to us on acceptable terms or at all. See “Risk Factors” for additional risks associated with our substantial capital requirements.

## Summary Statement of Cash Flows

The following table sets forth the primary sources and uses of cash and cash equivalents for each of the periods presented below:

	Year Ended December 31,	
	2021	2020
	(in thousands)	
Net cash (used in) provided by:		
Operating activities	\$ (42,997)	\$ (42,327)
Investing activities	\$ (50,777)	\$ 57,999
Financing activities	\$ 73,283	\$ (2,101)
Net (decrease) increase in cash and cash equivalents	\$ (20,491)	\$ 13,571

### Cash Flows Used in Operating Activities

Net cash used in operating activities was \$43.0 million for the year ended December 31, 2021. Cash used in operating activities was primarily due to the use of funds in our operations to develop STS101, which resulted in a net loss of \$51.2 million, adjusted for a decrease of accounts payable by \$1.2 million and an increase in prepaid expenses and other assets of \$0.9 million, which amounts were partially offset by an increase in accrued and other liabilities of \$3.3 million, stock-based compensation expense of \$5.4 million, net amortization of premiums and discounts on marketable securities of \$0.7 million, loss on disposal of property and equipment of \$0.6 million and depreciation expense of \$0.4 million. The decrease in accounts payable and an increase in prepaid expenses and other assets and accrued and other liabilities were primarily the result of the timing of payments to our vendors.

Net cash used in operating activities was \$42.3 million for the year ended December 31, 2020. Cash used in operating activities was primarily due to the use of funds in our operations to develop STS101, which resulted in a net loss of \$47.6 million, adjusted for a decrease of accounts payable by \$1.6 million, which amounts were partially offset by a decrease in prepaid expenses and other assets of \$1.4 million, an increase in accrued and other liabilities of \$1.0 million, depreciation expense of \$0.2 million, non-cash interest expense and amortization of debt discount and issuance costs of \$0.1 million, net amortization of premiums and discounts on marketable securities of \$0.1 million and stock-based compensation expense of \$4.0 million. The decrease in accounts payable and prepaid expenses and other assets and increase in accrued and other liabilities were primarily the result of the timing of payments to our vendors.

### Cash Flows (Used in) Provided by Investing Activities

Net cash used in investing activities was \$50.8 million for the year ended December 31, 2021, which consisted of purchases of marketable securities of \$88.6 million and purchases of property and equipment of \$2.0 million, which amounts were partially offset by proceeds from maturities of marketable securities of \$39.9 million.

Net cash provided by investing activities was \$58.0 million for the year ended December 31, 2020, which consisted of proceeds from maturities of marketable securities of \$97.2 million, which amounts were partially offset by purchases of marketable securities of \$34.0 million and purchases of property and equipment of \$5.2 million mainly related to construction of the Company's dry powder nasal DHE filling station which is waiting for installation and final acceptance.

### Cash Flows Provided by (Used in) Financing Activities

Net cash provided by financing activities was \$73.3 million for the year ended December 31, 2021, which consisted of \$75.2 million of net cash proceeds from our Private Placement and proceeds from the issuance of common stock under employee plans of \$0.1 million, partially offset by repayment of debt of \$2.0 million.

Net cash used in financing activities was \$2.1 million for the year ended December 31, 2020, which primarily related to repayment of debt of \$2.0 million and payment of offering costs of \$0.2 million, partially offset by proceeds from the exercise of common stock options of \$0.1 million.

### **Contractual Obligations and Commitments**

In October 2018, we entered into the Loan Agreement with Silicon Valley Bank. The maturity date of the loan advances is May 1, 2022. Total future contractual maturities of the loan were \$0.8 million as of December 31, 2021.

We enter into contracts in the normal course of business with third-party contract organizations for clinical trials, manufacturing and testing and providing other services and products for operating purposes. These contracts generally provide for termination following a certain period after notice, and therefore we believe that our non-cancelable obligations under these agreements are not material.

### **Critical Accounting Policies, Significant Judgments and Use of Estimates**

Our financial statements have been prepared in accordance with U.S. 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, the disclosure of contingent assets and liabilities at the date of the financial statements and 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.

While our significant accounting policies are described in more detail in Note 1, Organization and Summary of Significant Accounting Policies, to the financial statements, we believe that the following accounting policy is the most critical to the judgement and estimates used in the preparation of our financial statements.

#### ***Accrued Research and Development***

We monitor the activity under our various agreements with CMOs and other service providers to the extent possible through communication with each service provider, detailed invoice and task completion review, analysis of actual expenses against budget, pre-approval of any changes in scope, and review of contractual terms. Our research and development accruals are estimated based on the level of services performed, progress of the studies, including the phase or completion of events, and contracted costs. These estimates may or may not match the actual services performed by the service providers. Although we do not expect our estimates to be materially different from amounts actually incurred, our understanding of the status and timing of services performed relative to the actual status and timing of services performed may vary and could result in us reporting amounts that are too high or too low in any particular period. The estimated costs of research and development provided, but not yet invoiced, are included in accrued liabilities on the balance sheet. If the actual timing of the performance of services or the level of effort varies from our estimates, we will adjust the accrual or amount of prepaid expenses and other current assets accordingly.

#### **JOBS Act Accounting Election**

The Jumpstart Our Business Startups Act of 2012, or the JOBS Act, permits an “emerging growth company” such as us to take advantage of an extended transition period to comply with new or revised accounting standards applicable to public companies. We have elected to use this extended transition period under the JOBS Act. As a result, our financial statements may not be comparable to the financial statements of issuers who are required to comply with the effective dates for new or revised accounting standards that are applicable to public companies, which may make comparison of our financials to those of other public companies more difficult.

Recent Accounting Pronouncements See “Organization and Summary of Significant Accounting Policies—Recent Accounting Pronouncements” in Note 1 to our financial statements included elsewhere in this Annual Report on Form 10-K for additional information.

**ITEM 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURE ABOUT MARKET RISK**

As of December 31, 2021, we had cash, cash equivalents and marketable securities of \$95.8 million, consisting of interest-bearing money market funds, investments in corporate bonds, asset backed securities and foreign government agency bonds for which the fair value would be affected by changes in the general level of U.S. interest rates. However, due to the short-term maturities and the low-risk profile of our cash equivalents and marketable securities, an immediate 10% change in interest rates would not have a material effect on the fair value of our cash equivalents and marketable securities.

We do not believe that inflation, interest rate changes or exchange rate fluctuations have had a significant impact on our results of operations for any periods presented herein.

**ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA**

**INDEX TO FINANCIAL STATEMENTS**

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## Report of Independent Registered Public Accounting Firm

To the Stockholders and Board of Directors  
Satsuma Pharmaceuticals, Inc.:

### *Opinion on the Financial Statements*

We have audited the accompanying balance sheets of Satsuma Pharmaceuticals, Inc. (the Company) as of December 31, 2021 and 2020, the related statements of operations and comprehensive loss, stockholders' equity, and cash flows for the years then ended, and the related notes (collectively, the financial statements). In our opinion, the financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2021 and 2020, and the results of its operations and its cash flows for each of the years in the two-year period ended December 31, 2021, in conformity with U.S. generally accepted accounting principles.

### *Basis for Opinion*

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

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits, we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

Our audits included performing procedures to assess the risks of material misstatement of the 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 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 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.

San Diego, California  
March 15, 2022

**SATSUMA PHARMACEUTICALS, INC.**  
**Balance Sheets**  
(in thousands, except share and per share amounts)

	December 31,	
	2021	2020
<b>Assets</b>		
Cash and cash equivalents	\$ 15,835	\$ 36,326
Short-term marketable securities	77,315	31,910
Prepaid expenses and other current assets	6,698	5,550
<b>Total current assets</b>	<b>99,848</b>	<b>73,786</b>
Property and equipment, net	6,792	6,473
Long-term marketable securities	2,620	—
Other non-current assets	572	774
<b>Total assets</b>	<b>\$ 109,832</b>	<b>\$ 81,033</b>
<b>Liabilities</b>		
Accounts payable	\$ 1,469	\$ 3,381
Accrued and other current liabilities	5,943	2,675
Current portion of long-term debt	1,080	1,990
<b>Total current liabilities</b>	<b>8,492</b>	<b>8,046</b>
Long-term debt	—	1,042
Other noncurrent liabilities	—	9
<b>Total liabilities</b>	<b>8,492</b>	<b>9,097</b>
Commitments and Contingencies (Note 5)		
<b>Stockholders' equity</b>		
Preferred stock, \$0.0001 par value, 10,000,000 shares authorized as of December 31, 2021 and December 31, 2020; no shares issued and outstanding as of December 31, 2021 and December 31, 2020	—	—
Common stock, \$0.0001 par value, 300,000,000 shares authorized as of December 31, 2021 and December 31, 2020, respectively; 31,545,564 shares and 17,436,978 shares issued and outstanding as of December 31, 2021 and December 31, 2020, respectively	3	2
Additional paid-in-capital	243,115	162,469
Accumulated other comprehensive (loss) income	(42)	29
Accumulated deficit	(141,736)	(90,564)
<b>Total stockholders' equity</b>	<b>101,340</b>	<b>71,936</b>
<b>Total liabilities, preferred stock and stockholders' equity</b>	<b>\$ 109,832</b>	<b>\$ 81,033</b>

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



**SATSUMA PHARMACEUTICALS, INC.**  
**Statements of Operations and Comprehensive Loss**  
**(in thousands, except share and per share amounts)**

	Year Ended December 31,	
	2021	2020
Operating expenses		
Research and development	\$ 37,635	\$ 36,270
General and administrative	13,531	12,058
Total operating expenses	<u>\$ 51,166</u>	<u>\$ 48,328</u>
Loss from operations	(51,166)	(48,328)
Interest income	157	1,115
Interest expense	(163)	(350)
Net loss	<u>\$ (51,172)</u>	<u>\$ (47,563)</u>
Unrealized (loss) gain on marketable securities	(71)	12
Comprehensive loss	<u>\$ (51,243)</u>	<u>\$ (47,551)</u>
Net loss per share attributable to common stockholders, basic and diluted	<u>\$ (1.75)</u>	<u>\$ (2.73)</u>
Weighted-average shares used in computing net loss per share attributable to common stockholders, basic and diluted	<u>29,174,386</u>	<u>17,405,688</u>

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

**SATSUMA PHARMACEUTICALS, INC.**  
**Statements of Stockholders' Equity**  
(in thousands, except share amounts)

	Common Stock		Additional Paid-In Capital	Accumulated Deficit	Accumulated Other Comprehensive Income (Loss)	Total Stockholders' Equity
	Shares	Amount				
<b>Balance at January 1, 2020</b>	17,382,047	2	158,317	(43,001)	17	115,335
Issuance of common stock upon exercise of stock options	35,265	—	82	—	—	82
Stock-based compensation	—	—	4,018	—	—	4,018
Issuance of common stock upon purchases under employee share purchase plan	14,766	—	52	—	—	52
Issuance of common stock upon net exercise of common stock warrants	4,900	—	—	—	—	—
Other comprehensive income	—	—	—	—	12	12
Net loss	—	—	—	(47,563)	—	(47,563)
<b>Balance at December 31, 2020</b>	17,436,978	2	162,469	(90,564)	29	71,936
Issuance of common stock upon exercise of stock options	7,932	—	8	—	—	8
Issuance of common stock in private placement financing, net of issuance costs of \$4,785	14,084,507	1	75,214	—	—	75,215
Stock-based compensation	—	—	5,364	—	—	5,364
Issuance of common stock upon purchases under employee share purchase plan	16,147	—	60	—	—	60
Other comprehensive loss	—	—	—	—	(71)	(71)
Net loss	—	—	—	(51,172)	—	(51,172)
<b>Balance at December 31, 2021</b>	<u>31,545,564</u>	<u>\$ 3</u>	<u>\$ 243,115</u>	<u>\$ (141,736)</u>	<u>\$ (42)</u>	<u>\$ 101,340</u>

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

**SATSUMA PHARMACEUTICALS, INC.**  
**Statements of Cash Flows**  
(in thousands)

	Year Ended December 31,	
	2021	2020
<b>Cash flows from operating activities</b>		
Net loss	\$ (51,172)	\$ (47,563)
Adjustments to reconcile net loss to net cash used in operating activities		
Depreciation	393	239
Loss on disposal of property and equipment	618	—
Non-cash interest expense, and amortization of debt discount and issuance costs	48	102
Amortization of premiums / (accretion of discounts), net on marketable securities	651	83
Stock-based compensation	5,364	4,018
Changes in assets and liabilities		
Prepaid expenses and other assets	(946)	1,455
Accounts payable	(1,212)	(1,625)
Accrued and other current liabilities	3,268	974
Other non-current liabilities	(9)	(10)
Net cash used in operating activities	<u>(42,997)</u>	<u>(42,327)</u>
<b>Cash flows from investing activities</b>		
Purchases of marketable securities	(88,620)	(34,008)
Proceeds from maturities of marketable securities	39,873	97,172
Purchases of property and equipment	(2,030)	(5,165)
Net cash (used in) provided by investing activities	<u>(50,777)</u>	<u>57,999</u>
<b>Cash flows from financing activities</b>		
Repayment of debt	(2,000)	(2,000)
Proceeds from private placement financing, net of issuance costs	75,215	—
Payment of offering costs	—	(235)
Proceeds from issuance of common stock under employee plans	68	134
Net cash provided by (used in) financing activities	<u>73,283</u>	<u>(2,101)</u>
Net (decrease) increase in cash and cash equivalents	(20,491)	13,571
<b>Cash and cash equivalents</b>		
Cash and cash equivalents, at beginning of period	36,326	22,755
Cash and cash equivalents, at end of period	<u>\$ 15,835</u>	<u>\$ 36,326</u>
<b>Supplemental disclosure of cash flow information:</b>		
Cash paid for income taxes	\$ 5	\$ —
Cash paid for interest	\$ 126	\$ 259
<b>Supplemental non-cash investing and financing activities:</b>		
Purchases of property and equipment in accounts payable and accrued and other current liabilities	\$ 24	\$ 724

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

**SATSUMA PHARMACEUTICALS, INC.**  
**Notes to Financial Statements**  
**(in thousands, except share and per share data)**

**1. Organization and Summary of Significant Accounting Policies**

**Description of the Business**

Satsuma Pharmaceuticals, Inc. (the “Company”) is a clinical-stage biopharmaceutical company developing a novel therapeutic for the acute treatment of migraine. The Company’s product candidate, STS101, is a drug-device combination of a proprietary dry-powder formulation of dihydroergotamine mesylate, or DHE, which can be quickly and easily self-administered by a proprietary pre-filled, single-use, nasal delivery device. The Company, headquartered in South San Francisco, was incorporated in 2016 in the state of Delaware.

**Private Placement**

In February 2021, the Company entered into a Securities Purchase Agreement with certain purchasers, pursuant to which the Company agreed to sell and issue to certain purchasers an aggregate of 14,084,507 shares of its common stock at a per share purchase price of \$5.68, the closing price of its common stock on the Nasdaq Global Market on February 26, 2021, for gross proceeds of \$80.0 million (“Private Placement”). The Private Placement closed in March 2021 and the Company received \$75.2 million in net proceeds after deducting commissions and offering expenses.

**Liquidity**

The Company is subject to risks and uncertainties common to early-stage companies in the biopharmaceutical industry, including, but not limited to, risks of clinical delays or failure, development by competitors of new technological innovations, protection of proprietary technology, dependence on key personnel, reliance on contract manufacturing organizations (“CMOs”), contract research organizations (“CROs”), compliance with government regulations and the need to obtain additional financing to fund operations. STS101 is an investigational product candidate that will require additional clinical development prior to any submission for regulatory approval and commercialization, if approved. These efforts require significant amounts of additional capital, adequate personnel, infrastructure, and extensive compliance and reporting.

The Company has incurred significant losses and negative cash flows from operations in all periods since its inception and had an accumulated deficit of \$141.7 million as of December 31, 2021. The Company has historically financed its operations primarily through its initial public offering (“IPO”), and private placements of its equity securities and borrowings under its long-term debt facility. The Company has no products approved for sale, and the Company has not generated any revenue since its inception. The Company expects to incur significant additional operating losses over at least the next several years. There can be no assurance that in the event the Company requires additional financing, such financing will be available on terms which are favorable or at all. Failure to generate sufficient cash flows from operations or raise additional capital to support its operations would have a material adverse effect on the Company’s ability to achieve its intended business objectives.

As of December 31, 2021, the Company had cash, cash equivalents and marketable securities of \$95.8 million. The Company’s management believes that the Company’s current cash, cash equivalents and marketable securities will be sufficient to fund its planned operations for at least 12 months from the date of the issuance of these annual financial statements.

**Basis of Presentation**

The accompanying financial statements have been prepared in accordance with accounting principles generally accepted in the United States of America ("US GAAP"), as defined by the Financial Accounting Standards Board, or the FASB.

**Use of Estimates**

The preparation of financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the financial statements and the reported amounts of income and expenses during the reporting period. Such estimates include the accrual of research and development expenses, useful lives of property and equipment and the fair value of stock-based awards. The Company evaluates its estimates and assumptions on an ongoing basis using historical experience and other factors, including the impact of the COVID-19 pandemic which may delay the enrollment of subjects for our clinical trials and may disrupt our supply chain for development and manufacturing activities, and adjust those estimates and assumptions when facts and circumstances dictate. Actual results could differ materially from those estimates and assumptions.

**Segments**

The Company operates and manages its business as a single operating and reportable segment, which is the business of developing, seeking regulatory approval for and commercializing STS101 for the acute treatment of migraine. The Company's chief executive officer, who is the chief operating decision maker, reviews financial information on an aggregate basis for purposes of allocating resources and evaluating financial performance. No product revenue has been generated since its inception. As of December 31, 2021, the Company's long-lived assets of \$0.1 million were located in the United States and \$6.7 million in the United Kingdom and Europe. As of December 31, 2020, the Company's long-lived assets of \$1.5 million were located in the United States and \$5.0 million in the United Kingdom.

**Cash and Cash Equivalents**

The Company considers all highly liquid investments purchased with an original or remaining maturity of three months or less at the date of purchase to be cash equivalents.

**Marketable Debt Securities**

The Company determines the appropriate classification of its marketable debt securities at the time of purchase and reevaluates such designation at each balance sheet date. All marketable debt securities are considered available-for-sale and carried at estimated fair values and reported in cash equivalents, short-term marketable securities or long-term marketable securities. Unrealized gains and losses on available-for-sale debt securities are excluded from net income and reported in accumulated other comprehensive income (loss) as a separate component of stockholders' equity. Interest income includes amortization of purchase premiums and discounts, realized gains and losses on sales of securities and other-than-temporary declines in the fair value of securities, if any. The cost of securities sold is based on the specific identification method. The Company regularly reviews all its investments for other-than-temporary declines in fair value. The review includes the consideration of the cause of the impairment, including the creditworthiness of the security issuers, the number of securities in an unrealized loss position, the severity and duration of the unrealized losses, whether the Company has the intent to sell the securities and whether it is more likely than not that the Company will be required to sell the securities before the recovery of their amortized cost basis. When the Company determines that the decline in fair value of an investment is below its accounting basis and the decline is other-than-temporary, the Company reduces the carrying value of the security it holds and records a loss for the amount of such decline.

**Concentration of Credit Risk**

The Company has no significant off-balance sheet concentrations of credit risk. Financial instruments that potentially subject the Company to a concentration of credit risk consist of cash, cash equivalents and marketable

securities. Substantially all the Company's cash is held by one financial institution that management believes to be of high credit quality. Such deposits may, at times, exceed federally insured limits. The Company invests its cash equivalents in marketable securities and money market funds. The Company has not experienced any credit losses on its deposits of cash or cash equivalents.

### **Fair Value of Financial Instruments**

The carrying amounts of certain of the Company's financial instruments, including cash equivalents, accounts payable and accrued liabilities approximate fair value due to their relatively short maturities and market interest rates, if applicable. Refer to Note 2 for details on the fair value of marketable securities.

### **Deferred Offering Costs**

The Company capitalizes costs that are directly associated with in-process equity financings until such financings are consummated at which time such costs are recorded against the gross proceeds 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 statements of operations and comprehensive loss.

### **Property and Equipment, Net**

Property and equipment are stated at cost less accumulated depreciation. Depreciation is computed using the straight-line method over the estimated useful lives of the assets, which generally ranges from three to five years. Leasehold improvements are stated at cost and amortized over the shorter of the useful lives of the assets or the lease term. Maintenance and repairs are charged to expense as incurred. When assets are retired or otherwise disposed of, the cost and accumulated depreciation are removed from the balance sheet and any resulting gain or loss is reflected in the statements of operations and comprehensive loss in the period realized.

### **Impairment of Long-Lived Assets**

Long-lived assets consist of property and equipment. The Company reviews property and equipment for impairment whenever events or changes in circumstances indicate that the carrying amount of an asset or asset group may not be recoverable or that the useful life is shorter than the Company had originally estimated. Recoverability is measured by comparison of the carrying amount of the asset or asset group to the future undiscounted cash flows which the asset or asset group is expected to generate. If the asset or asset group is considered to be impaired, the impairment to be recognized is measured by the amount by which the carrying amount of the asset or asset group exceeds the fair value of the asset or asset group. If the useful life is shorter than originally estimated, the Company amortizes the remaining carrying value over the new shorter useful life. There have been no such impairments of long-lived assets during the years ended December 31, 2021 and 2020.

### **Research and Development Expenses**

The Company's research and development expenses consist primarily of payroll and personnel-related expenses, including salaries, employee benefit costs and stock-based compensation expenses for the Company's research and product development employees, fees paid to third parties to conduct preclinical and clinical studies and other research and development activities on behalf of the Company, including CROs, CMOs and other service providers, costs for licenses, and allocated overhead, including rent, equipment, depreciation, information technology costs and utilities. The Company charges all research and development costs, both internal and external, to research and development expenses within the statements of operations and comprehensive loss as incurred. Payments associated with licensing agreements to acquire exclusive licenses to develop, use, manufacture and commercialize products that have not reached technological feasibility and do not have alternate commercial use are also expensed as incurred.

## **Accrued Research and Development**

The Company monitors the activity under its various agreements with CROs, CMOs and other service providers to the extent possible through communication with each service provider, detailed invoice and task completion review, analysis of actual expenses against budget, pre-approval of any changes in scope, and review of contractual terms. The Company's research and development accruals are estimated based on the level of services performed, progress of the studies, including the phase or completion of events, and contracted costs. These estimates may or may not match the actual services performed by the service providers. The estimated costs of research and development provided, but not yet invoiced, are included accrued and other current liabilities on the balance sheet. If the actual timing of the performance of services or the level of effort varies from the original estimates, the Company will adjust the accrual accordingly. Payments made to service providers under these arrangements in advance of the performance of the related services are recorded as prepaid expenses and other current assets on the balance sheet until the services are rendered.

## **Stock-Based Compensation**

The Company maintains incentive plans under which incentive stock options and nonqualified stock options may be granted to employees and non-employee service providers. The Company accounts for all share-based awards granted to employees and non-employees based on the fair value on the date of grant and recognizes compensation expense for those awards over the requisite service period, which is generally the vesting period of the respective award. The Company accounts for forfeitures as they occur. Generally, the Company issues awards with only service-based vesting conditions. For share-based awards with service-based vesting conditions, the Company recognizes compensation expense using the straight-line method.

Estimating fair value of stock-based awards using an option pricing model requires input of subjective assumptions, including fair value of the Company's common stock, and, for stock options, expected term of options and stock price volatility. The Company uses the Black-Scholes option-pricing model to value its stock option awards. The assumptions used in calculating the fair value of stock-based awards represent management's estimates, involve inherent uncertainties and require application of management's judgment. As a result, if factors change and management uses different assumptions, stock-based compensation expense could be materially different for future awards.

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

## **Comprehensive Income (Loss)**

Comprehensive gain or loss is defined as a change in equity during a period from transactions and other events and circumstances from non-owner sources. In 2021 the Company recorded unrealized loss on marketable securities of \$0.1 million and in 2020 the company recorded an unrealized gain of less than \$0.1 million in other comprehensive income (loss).

## **Net Loss per Share Attributable to Common Stockholders**

Basic net loss per common share is calculated by dividing the net loss attributable to common stockholders by the weighted-average number of common stock outstanding during the period, without consideration of potentially dilutive securities. Diluted net loss per share is computed by dividing the net loss attributable to common stockholders by the weighted-average number of common stock and potentially dilutive securities outstanding for the period. For purposes of the diluted net loss per share calculation, outstanding stock options are considered to be potentially dilutive securities. Because the Company has reported a net loss for all periods presented, diluted net loss per common share is the same as basic net loss per common share for those periods.

## Income Taxes

Income taxes are recorded using an asset and liability approach. Deferred tax assets and liabilities are recognized for the future tax consequences attributable to differences between the financial statement carrying amounts of existing assets and liabilities and their respective tax bases using enacted tax rates in effect for the year in which the differences are expected to affect taxable income. Deferred tax assets are reduced by a valuation allowance if current evidence indicates that it is considered more likely than not that these benefits will not be realized. In making such a determination, management considers all available positive and negative evidence, including future reversals of existing taxable temporary differences, projected future taxable income, tax-planning strategies, and results of recent operations. If management determines that the Company would be able to realize its deferred tax assets in the future in excess of their net recorded amount, management would make an adjustment to the deferred tax asset valuation allowance, which would reduce the provision for income taxes.

The Company's tax positions are subject to income tax audits. The Company recognizes the tax benefit of an uncertain tax position only if it is more likely than not that the position is sustainable upon examination by the taxing authority, based on the technical merits. The tax benefit recognized is measured as the largest amount of benefit which is more likely than not to be realized upon settlement with the taxing authority. The Company recognizes interest accrued and penalties related to unrecognized tax benefits in its tax provision. The Company evaluates uncertain tax positions on a regular basis. The evaluations are based on a number of factors, including changes in facts and circumstances, changes in tax law, correspondence with tax authorities during the course of the audit, and effective settlement of audit issues. The provision for income taxes includes the effects of any accruals that the Company believes are appropriate, as well as the related net interest and penalties.

On June 29, 2020 California State Assembly Bill 85 (the "Trailer Bill") was enacted which suspends the use of California net operating loss ("NOL") deductions and certain tax credits, including research and development tax credits, for the 2020, 2021, and 2022 tax years.

## Recent Accounting Pronouncements

### *Recently Adopted Accounting Pronouncements*

In December 2019, the FASB issued ASU 2019-12, *Income Taxes (Topic 740): Simplifying the Accounting for Income Taxes*. ASU 2019-12 simplifies the accounting for income taxes by removing certain exceptions to the general principles in Topic 740 and improves consistent application of and simplifies GAAP for other areas of Topic 740 by clarifying existing guidance. For public business entities, this ASU is effective for fiscal years beginning after December 15, 2020, and interim periods within those fiscal years. Early adoption is permitted. The Company adopted this ASU effective January 1, 2021. The adoption of this ASU did not have a material effect on the Company's financial statements and related disclosures.

### *New Accounting Pronouncements Not Yet Adopted*

In February 2016, the FASB issued ASU No. 2016-02, *Leases (Topic 842)* ("ASC 842"), which sets out the principles for the recognition, measurement, presentation and disclosure of leases for both parties to a contract (i.e., lessees and lessors). The new standard requires lessees to apply a dual approach, classifying leases as either finance or operating leases based on the principle of whether or not the lease is effectively a financed purchase by the lessee. This classification will determine whether lease expense is recognized based on an effective interest method or on a straight-line basis over the term of the lease, respectively. A lessee is also required to record a right-of-use asset and a lease liability for all leases with a term of greater than 12 months regardless of their classification. ASC 842 provides a lessee with an option to not account for leases with a term of 12 month or less as leases in the scope of the new standard. ASC 842 supersedes the previous leases standard, ASC 840 *Leases*. This guidance is effective for the Company in fiscal years beginning after December 15, 2021, and for interim periods within fiscal years beginning after December 15, 2022. The Company is currently evaluating the impact the adoption of these ASUs will have on its financial statements and related disclosures. The Company expects to recognize a right-of-use asset and corresponding lease liability for its real estate operating leases upon adoption. See Note 6 for more information related to the Company's lease obligations, which are presented on an undiscounted basis therein.



In June 2016, the FASB issued ASU No. 2016-13, *Financial Instruments - Credit Losses (Topic 326)*, to provide financial statement users with more useful information about expected credit losses, which was subsequently updated by ASU 2019-04, *Codification Improvements to Topic 326, Financial Instrument - Credit Losses, Topic 815, Derivatives and Hedging, and Topic 825, Financial Instruments*, and ASU 2019-05, *Financial Instruments - Credit Losses (Topic 326): Targeted Transition Relief*. The amendment updates the guidance for measuring and recording credit losses on financial assets measured at amortized cost by replacing the “incurred loss” model with an “expected loss” model. Accordingly, these financial assets will be presented at the net amount expected to be collected. The amendment also requires that credit losses related to available-for-sale debt securities be recorded as an allowance through net income rather than reducing the carrying amount under the current, other-than-temporary-impairment model. In November 2019, the FASB issued ASU No. 2019-10, according to which, the new standard is effective for public business entities that meet the definition of an SEC filer, excluding entities eligible to be smaller reporting companies (“SRC”) as defined by the SEC, for fiscal years beginning after December 15, 2019, including interim periods within those fiscal years. For all other entities, the new standard is effective for fiscal years beginning after December 15, 2022, and interim periods within that fiscal year. Early adoption is permitted. The Company is a SRC for fiscal year 2020. The adoption of this standard is not expected to have a material impact on the Company’s financial statements and related disclosures.

## 2. Fair Value Measurements

The Company applies fair value accounting for all financial assets and liabilities and non-financial assets and liabilities that are recognized or disclosed at fair value in the financial statements on a recurring basis. Fair value is an 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 such, fair value is a market-based measurement that should be determined based on assumptions that market participants would use in pricing an asset or liability. As a basis for considering such assumptions, a three-tier fair value hierarchy has been established, which prioritizes the inputs used in measuring fair value as follows:

Level 1—Observable inputs, such as quoted prices in active markets for identical assets or liabilities at the measurement date.

Level 2—Observable inputs other than Level 1 prices such as quoted prices for similar assets or liabilities, quoted prices in markets that are not active, or other inputs that are observable or can be corroborated by observable market data for substantially the full term of the assets or liabilities.

Level 3—Unobservable inputs which reflect management’s best estimate of what market participants would use in pricing the asset or liability at the measurement date. Consideration is given to the risk inherent in the valuation technique and the risk inherent in the inputs to the model.

In determining fair value, the Company utilizes valuation techniques that maximize the use of observable inputs and minimize the use of unobservable inputs to the extent possible as well as considers counterparty credit risk in its assessment of fair value.

As of December 31, 2021, financial assets measured and recognized at fair value were as follows (in thousands):

	Fair Value Measurements at December 31, 2021			
	Quoted Price in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)	Total
<b>Assets</b>				
U.S. government bonds	\$ 4,667	\$ —	\$ —	\$ 4,667
Foreign government agency bonds (1)	—	6,526	—	6,526
Corporate bonds	—	49,989	—	49,989
Asset backed securities	—	18,753	—	18,753
Marketable securities	4,667	75,268	—	79,935
Money market funds (2)	15,809	—	—	15,809
Total fair value of assets	<u>\$ 20,476</u>	<u>\$ 75,268</u>	<u>\$ —</u>	<u>\$ 95,744</u>

(1) Consists of short-term agency bonds of Asian Development Bank and International Bank for Reconstruction and Development.

(2) Included in cash and cash equivalents on the balance sheet.

	Fair Value Measurements at December 31, 2021			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimate Fair Value
<b>Assets</b>				
U.S. government bonds	4,670	—	\$ (3)	4,667
Foreign government agency bonds (1)	6,530	—	(4)	6,526
Corporate bonds	50,008	—	(19)	49,989
Asset backed securities	18,769	—	(16)	18,753
Marketable securities	79,977	—	(42)	79,935
Money market funds (2)	15,809	—	—	15,809
Total fair value of assets	<u>\$ 95,786</u>	<u>\$ —</u>	<u>\$ (42)</u>	<u>\$ 95,744</u>

(1) Consists of short-term agency bonds of Asian Development Bank and International Bank for Reconstruction and Development.

(2) Included in cash and cash equivalents on the balance sheet.

As of December 31, 2020, financial assets measured and recognized at fair value were as follows (in thousands):

	Fair Value Measurements at December 31, 2020			
	Quoted Price in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)	Total
<b>Assets</b>				
Corporate bonds	\$ —	\$ 31,910	\$ —	\$ 31,910
Marketable securities	—	31,910	—	31,910
Money market funds (1)	36,304	—	—	36,304
Total fair value of assets	<u>\$ 36,304</u>	<u>\$ 31,910</u>	<u>\$ —</u>	<u>\$ 68,214</u>

(1) Included in cash and cash equivalents on the balance sheet.

	Fair Value Measurements at December 31, 2020			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimate Fair Value
<b>Assets</b>				
Corporate bonds	\$ 31,881	\$ 30	\$ (1)	\$ 31,910
Marketable securities	31,881	30	(1)	31,910
Money market funds (1)	36,304	—	—	36,304
Total fair value of assets	\$ 68,185	\$ 30	\$ (1)	\$ 68,214

(1) Included in cash and cash equivalents on the balance sheet.

There were no transfers of assets or liabilities between the fair value measurement levels during the years ended December 31, 2021 and 2020.

There were no financial liabilities measured and recognized at fair value as of December 31, 2021 and December 31, 2020. As of December 31, 2021, the fair value of the Term Loan (as defined in Note 4 below) approximated the carrying amount of the loan as the Term Loan bears floating interest rate that approximates the market rate.

### 3. Balance Sheet Components

#### Property and Equipment, Net

Property and equipment consisted of the following (in thousands, except years):

	Useful Life (In Years)	December 31,	
		2021	2020
Furniture and fixtures	3-5	\$ 75	\$ 63
Leasehold improvements	Shorter of useful life or lease term	62	62
Machinery and equipment	6	1,084	933
Tooling	6	974	840
Construction in progress	—	5,219	5,008
		7,414	6,906
Less: Accumulated depreciation		(622)	(433)
		\$ 6,792	\$ 6,473

Depreciation is computed using the straight-line method. Depreciation expense was \$0.4 million and \$0.2 million for the years ended December 31, 2021 and 2020, respectively.

#### Accrued and Other Current Liabilities

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

	December 31,	
	2021	2020
Accrued salaries and benefits	\$ 2,117	\$ 1,330
Accrued research and development expenses	3,396	910
Accrued professional services	361	232
Accrued interest	5	16
Other	64	187
	\$ 5,943	\$ 2,675

#### 4. Long-Term Debt

On October 26, 2018, the Company entered into a Loan and Security Agreement (the “Loan Agreement”) with Silicon Valley Bank. The Loan Agreement provided for loan advances of up to \$10.0 million. The first advance (the “Term A Loan”) of \$5.0 million was available for draw down by the Company as of the effective date of the Loan Agreement. The remaining \$5.0 million under the facility was never drawn down and is no longer available for draw. Interest on the loan advances is payable monthly at a floating per annum rate equal to the greater of 1.5% above the prime rate or 6.5%. Upon the occurrence of an event of default, interest will increase to 5.0% above the rate that is otherwise applicable. The maturity date of the loan advances is May 1, 2022. The effective interest rate of the Term Loan approximates its stated interest rates.

Principal on the Term A Loan is repayable commencing on December 1, 2019 in 30 monthly payments through maturity. In addition to regular monthly payments, a final payment equal to the original principal amount of the Term Loans multiplied by 5.0% is due on the earliest to occur of (a) May 1, 2022 or (b) the prepayment in full of the term loan advances. The Company has the option to prepay the term loan advances with a prepayment premium of 3.0% of the outstanding principal if prepayment is made prior to October 26, 2019, 2.0% of the outstanding principal if prepayment is made after October 26, 2019 but before October 26, 2020, and 1.0% of the outstanding principal if prepayment is made after October 26, 2020 but before May 1, 2022. The repayment of term loan advances will be accelerated upon occurrence of an event of default. The Loan Agreement contains customary affirmative and negative covenants and events of default, including covenants and restrictions that among other things, restrict the ability of the Company to incur liens, incur additional indebtedness, make loans and investments, engage in mergers and acquisitions, engage in asset sales or sale and leaseback transactions, and declare dividends or redeem or repurchase capital stock.

As of December 31, 2021, the Term A Loan advances, net of debt discount and debt issuance costs, were \$1.1 million and are included in current portion of long-term debt on the Company’s balance sheets.

As of December 31, 2021, the future contractual maturities of debt by fiscal year are as follows (in thousands):

2022	\$	833
Total future maturities of debt	\$	833

In accordance with the terms of the Loan Agreement, on October 26, 2018, the Company issued warrants to purchase 10,232 shares of the Company’s common stock at an exercise price of \$1.04 per share with a term of 10 years. The fair value of the warrants of less than \$0.1 million (estimated using the Option Pricing Model, or OPM) was accounted as a debt discount and accreted over the term of the Term A Loan using the effective interest rate method. The warrants were accounted for and classified as equity at the fair value and were not subject to subsequent remeasurement to fair value.

There were no common stock warrants outstanding as of December 31, 2021 and 2020.

The proceeds from the Term A Loan advance were allocated to the debt and the warrants based on their relative fair values. The resulting debt discount of less than \$0.1 million is being recognized as interest expense over the term of the loan of 3.6 years using the effective interest method.

The Company incurred debt issuance costs of \$0.1 million, which is presented as reduction of the Term A Loan advance, consistent with the presentation of debt discount. Debt issuance cost and final payment of \$0.3 million is recognized as additional interest expense using the effective interest method over the term of the loan.

The Company accreted the final payment due at maturity using the effective interest rate method. The accrued liabilities related to the accretion of the final payment were \$0.2 million and \$0.2 million as of December 31, 2021

and December 31, 2020, respectively, which was included in long-term debt and in the current portion of long-term debt on the Company's balance sheets, respectively.

## 5. Commitments and Contingencies

### Operating Leases

On January 9, 2018, the Company entered into an office lease agreement for office space in South San Francisco, California. The lease term was through April 30, 2021 and was amended in March 2021 to extend it through October 31, 2021. In October 2021, the Company entered into second amendment of the office lease agreement which extended the lease term through October 31, 2022.

In July 2019, the Company entered into a lease agreement to lease another office space in North Carolina. The lease term for this office space was three years and was schedule to expire in July 2022. The lease agreement was amended in February 2022 to extend the lease term through July 31, 2025.

Rent expense was \$0.3 million and \$0.3 million for the years ended December 31, 2021 and 2020, respectively. As of December 31, 2021, less than \$0.1 million of deferred rent representing future minimum rental payments for leases with scheduled rent escalations was included in accrued and other current liabilities on the Company's balance sheet.

Future minimum lease payments under non-cancelable operating leases as of December 31, 2021 were as follows (in thousands):

	Operating Leases	
2022	\$	201
Total minimum lease payments	\$	201

### Contingencies

From time to time, the Company may be involved in litigation related to claims that arise in the ordinary course of its business activities. The Company accrues for these matters when it is probable that future expenditures will be made, and these expenditures can be reasonably estimated. As of December 31, 2021 and 2020, the Company did not believe that any such matters, individually or in the aggregate, would have a material adverse effect on the Company's financial position, results of operations or cash flows.

### Indemnification

The Company enters into standard indemnification arrangements in the ordinary course of business. Pursuant to these arrangements, the Company indemnifies, holds harmless and agrees to reimburse the indemnified parties for losses suffered or incurred by the indemnified party, in connection with any trade secret, copyright, patent or other intellectual property infringement claim by any third party with respect to its technology. The term of these indemnification agreements is generally perpetual any time after the execution of the agreement. The maximum potential amount of future payments the Company could be required to make under these arrangements is not determinable. The Company has never incurred costs to defend lawsuits or settle claims related to these indemnification agreements. As a result, the Company believes the fair value of these agreements is minimal.

## 6. Preferred Stock

As of December 31, 2021 and 2020, the Company's certificate of incorporation, as amended and restated, authorized the Company to issue up to 10,000,000 shares of preferred stock at the par value of \$0.0001 per share. As of December 31, 2021 and 2020, there were no shares of preferred stock issued and outstanding.

## 7. Common Stock

The Company has authorized 300,000,000 shares of common stock, \$0.0001 par value per share.

Each holder of shares of common stock shall be entitled to one vote for each share thereof held.

The Company had reserved common stock, on an as-converted basis, for future issuance as follows:

	December 31,	
	2021	2020
Exercise of outstanding options	3,202,588	3,162,459
Shares of common stock available for grant under the 2019 Plan	1,493,893	844,475
Shares of common stock available for ESPP	477,276	319,054
Total	<u>5,173,757</u>	<u>4,325,988</u>

## 8. Stock-Based Compensation

### 2019 Incentive Award Plan

The Company's board of directors adopted and the Company's stockholders approved, effective on the day of effectiveness of the registration statement on Form S-1, the 2019 Incentive Award Plan (the "2019 Plan"). Awards granted under the 2019 Plan may be either incentive stock options ("ISOs"), nonqualified stock options ("NSOs"), stock appreciation rights ("SARs"), or restricted stock units ("RSUs"). ISOs may be granted only to Company employees (including officers and directors who are also employees). Following the effectiveness of the 2019 Plan, the Company will not make any further grants under the 2016 Equity Incentive Plan. However, the 2016 Plan will continue to govern the terms and conditions of the outstanding awards granted under it. Shares of common stock subject to awards granted under the 2016 Plan that are forfeited or lapse unexercised and which following the effective date of the 2019 Plan are not issued under the 2016 Plan will be available for issuance under the 2019 Plan.

### 2016 Incentive Award Plan

In 2016, the Company established its 2016 Equity Incentive Plan (the "2016 Plan") which provides for the granting of stock options to employees and consultants of the Company. Awards granted under the 2016 Plan may be either incentive stock options ("ISOs"), nonqualified stock options ("NSOs"), stock appreciation rights ("SARs"), or restricted stock units ("RSUs"). ISOs may be granted only to Company employees (including officers and directors who are also employees). NSOs may be granted to Company employees and consultants.

The exercise price of ISOs and NSOs shall not be less than 100% of the estimated fair value of the shares on the date of grant. The exercise price of ISOs granted to an employee who, at the time of grant, owns stock representing more than 10% ("10% stockholder") of the voting power of all classes of stock of the Company shall be no less than 110% of the estimated fair value of the shares on the date of grant. The options usually have a term of 10 years (or no more than five years if granted to a 10% stockholder). Vesting conditions determined by the plan administrator may apply to stock options and may include continued service, performance and/or other conditions. Generally, options and restricted stock awards vest over a four-year period.

In January 2022, the number of shares of common stock available for issuance under the 2019 Plan was increased by 1,261,822 shares as a result of the automatic increase provision in the 2019 Plan.

Activity under the 2019 Plan and 2016 Plan is set forth below:

	Shares Available for Grant	Outstanding Options		Weighted-Average Remaining Contractual Term (Years)
		Number of Shares	Weighted Average Exercise Price	
<b>Balance, January 1, 2020</b>	<u>1,778,044</u>	<u>1,568,874</u>	\$ 3.55	8.85
Additional shares authorized	695,281			
Options granted	(1,669,200)	1,669,200	\$ 14.56	9.63
Options exercised	—	(35,265)	\$ 2.34	
Options cancelled	40,350	(40,350)	\$ 8.83	
<b>Balance, December 31, 2020</b>	<u>844,475</u>	<u>3,162,459</u>	\$ 9.31	8.79
Additional shares authorized	697,479			
Options granted	(129,000)	129,000	\$ 4.85	9.65
Options exercised	—	(7,932)	\$ 1.04	
Options cancelled	80,939	(80,939)	\$ 9.77	
<b>Balance, December 31, 2021</b>	<u>1,493,893</u>	<u>3,202,588</u>	\$ 9.14	7.73
<b>Exercisable as of December 31, 2021</b>		1,678,549	\$ 8.27	7.04
<b>Vested and expected to vest, December 31, 2021</b>		3,202,588	\$ 9.14	7.73

The aggregate intrinsic value is calculated as the difference between the exercise price of the underlying stock options and the fair value of the Company's common stock for stock options that were in-the-money as of December 31, 2021 and December 31, 2020.

The aggregate intrinsic value of options vested and expected to vest as of December 31, 2021 and December 31, 2020 was \$2.2 million and \$1.9 million, respectively. The aggregate intrinsic value of stock options exercised during the years ended on December 31, 2021 and 2020 was less than \$0.1 million and \$0.8 million, respectively.

The weighted-average grant-date fair value of options granted during the years ended December 31, 2021 and December 2020 was \$3.66 and \$9.62 per share, respectively.

As of December 31, 2021, the total unrecognized stock-based compensation expense for stock options was \$9.6 million, which is expected to be recognized over a weighted-average period of 2.2 years.

The total fair value of options vested for the years ended December 31, 2021 and December 31, 2020 was \$5.3 and \$4.0 million, respectively.

The Company accounts for forfeitures as they occur.

### Stock-Based Compensation Associated with Awards to Employees and Non-employees

The Company estimated the fair value of stock options using the Black Scholes option-pricing model. The fair value of stock options was valued using the following assumptions:

	December 31,	
	2021	2020
Expected term (years)	5.8 - 6.1	5.5 - 6.1
Expected volatility	91.5%-98.6%	71.2% - 92.5%
Risk-free interest rate	0.6%-1.4%	0.3% - 1.7%
Dividend yield	0%	0%

*Expected Term.* The expected term is calculated using the simplified method, which is available where there is insufficient historical data about exercise patterns and post-vesting employment termination behavior. The simplified method is based on the vesting period and the contractual term for each grant, or for each vesting-tranche for awards with graded vesting. The mid-point between the vesting date and the maximum contractual expiration date is used as the expected term under this method. For awards with multiple vesting-tranches, the periods from grant until the mid-point for each of the tranches are averaged to provide an overall expected term.

*Expected Volatility.* The Company used an average historical stock price volatility of a peer group of publicly traded companies to be representative of its expected future stock price volatility, as the Company has limited trading history for its common stock. For purposes of identifying these peer companies, the Company considered the industry, stage of development, size and financial leverage of potential comparable companies. For each grant, the Company measured historical volatility over a period equivalent to the expected term.

*Risk-Free Interest Rate.* The risk-free interest rate is based on the implied yield currently available on U.S. Treasury zero-coupon issues with a remaining term equivalent to the expected term of a stock award.

*Expected Dividend Rate.* The Company has not paid any dividends and does not anticipate paying any dividends in the near future. Accordingly, the Company has estimated the dividend yield to be zero.

### **Fair Value of Common Stock**

Prior to the IPO the fair value of the Company's common stock underlying the stock options was determined by the Board of Directors with assistance from management and, in part, on input from an independent third-party valuation firm. The Board of Directors determined the fair value of common stock by considering a number of objective and subjective factors, including valuations of comparable companies, sales of convertible preferred stock, operating and financial performance, the lack of liquidity of the Company's common stock and the general and industry-specific economic outlook. Subsequent to the Company's IPO, the fair value of the Company's common stock is determined based on its closing market price.

### **2019 Employee Share Purchase Plan**

In September 2019, the Company adopted the 2019 Employee Share Purchase Plan ("ESPP"), which became effective on the business day prior to the effectiveness of the registration statement relating to the IPO. A total of 160,000 shares of common stock were initially reserved for issuance under the ESPP. The ESPP permits eligible employees to acquire shares of the Company's common stock through periodic payroll deductions of up to 15% of base compensation. No employee may purchase more than 50,000 shares during an offering period. In addition, no employee may purchase more than \$25,000 worth of stock, determined by the fair market value of the shares at the time such option is granted, in one calendar year. At the end of each purchase period, employees are able to purchase shares at 85% of the lower of the fair market value of the Company's common stock on the first trading day of the offering period or on the last trading day of the offering period.

The first offering period was for 6.5 months beginning from May 1, 2020 until November 15, 2020. The Company issued 14,766 shares under the ESPP for the year ended December 31, 2020. The second offering period was for 5.5 months beginning from July 1, 2021 until December 15, 2021. The Company issued 16,147 shares under the ESPP for the year ended December 31, 2021. Shares authorized for future purchase under the ESPP were 477,276 at December 31, 2021. In January 2022, the number of shares of common stock available for issuance under the ESPP was increased by 315,455 shares as a result of the automatic increase provision in the ESPP. The offering period and purchase period is determined by the board of directors. The Company entered into an additional offering period beginning December 16, 2021 and ending June 15, 2022.

Compensation expense is calculated using the fair value of the employees' purchase rights under the Black-Scholes option pricing model.



	December 31,	
	2021	2020
Expected term (years)	0.5	0.5
Expected volatility	58.8%	111.0%
Risk-free interest rate	0.50%	0.1%
Dividend yield	0%	0%

As of December 31, 2021, the Company had unrecognized employee stock-based compensation relating to ESPP awards of less than \$0.1 million, which is expected to be recognized over a weighted-average period of 0.5 years.

### Stock-Based Compensation Expense

Total stock-based compensation expense recorded was as follows (in thousands):

	Year Ended December 31,	
	2021	2020
Research and development	\$ 1,777	\$ 1,290
General and administrative	3,587	2,728
<b>Total</b>	<b>\$ 5,364</b>	<b>\$ 4,018</b>

The above stock-based compensation expense related to the following equity-based awards:

	Year Ended December 31,	
	2021	2020
Stock options	\$ 5,338	\$ 3,989
ESPP	26	29
<b>Total</b>	<b>\$ 5,364</b>	<b>\$ 4,018</b>

### 9. Net Loss Per Share Attributable to Common Stockholders

The following table sets forth the computation of basic and diluted net loss per share attributable to common stockholders (in thousands, except share and per share data):

	Year Ended December 31,	
	2021	2020
<b>Numerator:</b>		
Net loss attributable to common stockholders	\$ (51,172)	\$ (47,563)
<b>Denominator:</b>		
Weighted-average shares used in computing net loss per share attributable to common stockholders, basic and diluted	29,174,386	17,405,688
<b>Net loss per share attributable to common stockholders, basic and diluted</b>	<b>\$ (1.75)</b>	<b>\$ (2.73)</b>

The following outstanding shares of potentially dilutive securities were excluded from the computation of diluted net loss per share attributable to common stockholders for the period presented because including them would have been antidilutive:

	Year Ended December 31,	
	2021	2020
Options to purchase common stock	3,202,588	3,162,459
Shares committed under ESPP	33,203	—
<b>Total</b>	<b>3,235,791</b>	<b>3,162,459</b>

## 10. Income Taxes

No provision for income taxes was recorded for the years ended December 31, 2021 and 2020. The Company has incurred net operating losses only in the United States since its inception. The Company has not reflected any benefit of such net operating loss carryforwards in the financial statements.

The differences between the statutory tax expense (benefit) rate and the effective tax expense (benefit) rate, were as follows (in thousands):

	Year Ended December 31,	
	2021	2020
Tax at federal statutory income tax rate	\$ (10,746)	\$ (9,988)
Change in valuation allowance	12,877	9,950
Permanent differences	141	(20)
Prior year true ups	—	341
Research and development credits	(2,374)	(154)
State income taxes	(346)	(128)
Other	448	—
<b>Tax at effective income tax rate</b>	<b>\$ —</b>	<b>\$ 1</b>

Significant components of the Company's net deferred tax assets are summarized as follows (in thousands):

	December 31,	
	2021	2020
<b>Deferred tax assets:</b>		
Net operating loss carryforwards	\$ 27,511	\$ 17,915
Research and development credit carryforwards	3,514	847
Stock-based compensation	1,189	697
Accruals and other	432	286
Gross deferred tax assets	32,646	19,745
Less: Valuation allowance	(32,318)	(19,441)
Deferred tax assets, net of valuation allowance	328	304
<b>Deferred tax liabilities:</b>		
Property and equipment	(328)	(304)
<b>Net deferred tax assets</b>	<b>\$ —</b>	<b>\$ —</b>

As of December 31, 2021, the Company had federal and state net operating loss carryforwards ("NOLs") of \$130.4 million and \$2.9 million, respectively. The federal NOLs consist of: (1) \$4.7 million generated before January 1, 2018, which will begin to expire in 2036 but are able to offset 100% of taxable income; and (2) \$125.7 million generated after December 31, 2017 that will carryforward indefinitely, but are subject to an 80% taxable income limitation. The state NOLs will begin to expire in 2036 if unused.

The Company also has California state research and development ("R&D") credit carryforwards of \$0.8 million, which do not expire and Federal R&D credit carryforwards of \$3.3 million which will begin to expire in 2037.

The Company has not performed a formal study validating these credits claimed in the tax returns. Once a study is prepared, the amount of R&D tax credits available could vary from what was originally claimed on the tax returns.

As part of the Protecting Americans from Tax Hikes Act of 2015 (the “PATH Act”), certain eligible companies have the ability to convert a portion of their R&D tax credits to offset payroll tax liabilities. As of December 31, 2021, the Company had converted \$1.2 million of its federal R&D credits to be utilized as an offset against future payroll taxes.

The utilization of NOLs and tax credit carryforwards to offset future taxable income may be subject to an annual limitation as a result of ownership changes that have occurred previously or may occur in the future. Under Sections 382 and 383 of the Internal Revenue Code (“IRC”) a corporation that undergoes an ownership change may be subject to limitations on its ability to utilize its pre-change NOLs and other tax attributes otherwise available to offset future taxable income and/or tax liability. An ownership change is defined as a cumulative change of 50% or more in the ownership positions of certain stockholders during a rolling three-year period. The Company has not completed a formal study to determine if any ownership changes within the meaning of IRC Section 382 and 383 have occurred. If an ownership change has occurred, the Company’s ability to use its NOLs or tax credit carryforwards may be restricted, which could require the Company to pay federal or state income taxes earlier than would be required if such limitations were not in effect.

#### Uncertain Income Tax Positions

The total amount of unrecognized tax benefits as of December 31, 2021 was \$0.4 million. If recognized, none of the unrecognized tax benefits would affect the Company’s effective tax rate.

The following table summarizes the activity related to the Company’s unrecognized tax benefits:

Balance as of January 1, 2020	\$	238
Increase related to current year tax positions		80
Decrease related to prior year tax positions		(162)
Balance as of December 31, 2020	\$	156
Increase related to current year tax positions		213
Increase related to prior year tax positions		38
Balance as of December 31, 2021	\$	407

The Company’s policy is to account for interest and penalties as income tax expense. As of December 31, 2021, the Company had no interest related to unrecognized tax benefits. No amounts of penalties related to unrecognized tax benefits were recognized in the provision for income taxes. The Company does not anticipate any significant change within twelve months following the date of the filing of this Annual Report on Form 10-K.

The Company files income tax returns in the U.S. federal jurisdiction and various state jurisdictions. The Company is subject to U.S. federal and state income tax examination for calendar tax years beginning in 2016 due to net operating losses that are being carried forward for tax purposes.

#### 11. Related Party Transactions

The Company incurred expenses in connection with preclinical study services performed by SNBL of \$0 and less than \$0.1 million in the years ended December 31, 2021 and 2020, respectively, which are included in research and development expenses on the statements of operations and comprehensive loss. As of December 31, 2021 and 2020, the Company did not have any amounts due to SNBL.

Two existing stockholders of the Company that are affiliated with directors of the Company purchased a total of 2,464,788 shares of the Company’s common stock, with an aggregate purchase price of \$14.0 million, in the Private Placement.

## ITEM 9. CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURES

None.

## ITEM 9A. CONTROLS AND PROCEDURES

### Management's Evaluation of our Disclosure Controls and Procedures

We maintain "disclosure controls and procedures," as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended, or the Exchange Act, that are designed to ensure that information required to be disclosed in the reports that we file or submit under the Exchange Act is (1) recorded, processed, summarized and reported within the time periods specified in the Securities and Exchange Commission's rules and forms and (2) accumulated and communicated to our management, including our principal executive and principal financial and accounting officers, as appropriate to allow timely decisions regarding required disclosure. Our management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and our management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Our disclosure controls and procedures are designed to provide reasonable assurance of achieving their control objectives.

Our management, with the participation of our principal executive officer and principal financial and accounting officer, evaluated the effectiveness of our disclosure controls and procedures at the end of the period covered by this Annual Report on Form 10-K. Based upon such evaluation, our principal executive officer and principal financial and accounting officer have concluded that our disclosure controls and procedures were effective at the reasonable assurance level as of such date.

### Management's Annual Report on Internal Control over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting, as such term is defined in Rule 13a-15(f) under the Securities Exchange Act of 1934. Our internal control over financial reporting is designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles in the United States and includes those policies and procedures that:

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

Our management assessed the effectiveness of our internal control over financial reporting as of December 31, 2021. In making this assessment, management used the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission (COSO) in Internal Control-Integrated Framework (2013 framework). Based on our assessment, management concluded our internal control over financial reporting was effective as of December 31, 2021, based on the COSO criteria.

### Attestation Report of the Registered Public Accounting Firm

This Annual Report on Form 10-K does not include an attestation report of our registered public accounting firm due to an exemption established by the JOBS Act for "emerging growth companies."

**Inherent Limitations on Effectiveness of Controls and Procedures**

In designing and evaluating the disclosure controls and procedures, management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving the desired control objectives. In addition, the design of disclosure controls and procedures must reflect the fact that there are resource constraints and that management is required to apply judgment in evaluating the benefits of possible controls and procedures relative to their costs.

**Changes in Internal Control over Financial Reporting**

Management determined that, as of December 31, 2021, there were no changes in our internal control over financial reporting that occurred during the fiscal quarter then ended that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

**ITEM 9B. OTHER INFORMATION**

None.

**ITEM 9C. DISCLOSURE REGARDING FOREIGN JURISDICTIONS THAT PREVENT INSPECTIONS**

Not applicable.

## PART III

### **ITEM 10. DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE**

The information required by this item will be contained in our definitive proxy statement to be filed with the SEC in connection with the Annual Meeting of Stockholders within 120 days after December 31, 2021, or the Proxy Statement, and is incorporated in this Annual Report on Form 10-K by reference.

### **ITEM 11. EXECUTIVE COMPENSATION**

The information required by this item will be contained in the Proxy Statement and is incorporated in this Annual Report on Form 10-K by reference.

### **ITEM 12. SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT AND RELATED STOCKHOLDER MATTERS**

The information required by this item will be contained in the Proxy Statement and is incorporated in this Annual Report on Form 10-K by reference.

### **ITEM 13. CERTAIN RELATIONSHIPS AND RELATED PARTY TRANSACTIONS, AND DIRECTOR INDEPENDENCE**

The information required by this item will be contained in the Proxy Statement and is incorporated in this Annual Report on Form 10-K by reference.

### **ITEM 14. PRINCIPAL ACCOUNTING FEES AND SERVICES**

Our independent registered public accounting firm is KPMG LLP, San Diego, California, Auditor Firm ID: 185.

The information required by this item will be contained in the Proxy Statement and is incorporated in this Annual Report on Form 10-K by reference.

## PART IV

### ITEM 15. EXHIBITS AND FINANCIAL STATEMENT SCHEDULES

(a) The following documents are filed as part of this report:

(1) FINANCIAL STATEMENTS

The financial statements required by Item 15(a) are filed as part of this Annual Report on Form 10-K under Item 8 “Financial Statements and Supplementary Data.”

(2) FINANCIAL STATEMENT SCHEDULES

All schedules to the financial statements are omitted as the required information is either inapplicable or presented in the financial statements.

(3) EXHIBITS

### ITEM 16. FORM 10-K SUMMARY

None.

**EXHIBIT INDEX**

Exhibit Number	Exhibit Description	Incorporated by Reference			Filed Herewith
		Form	Date	Number	
3.1	<a href="#">Amended and Restated Certificate of Incorporation.</a>	8-K	9/17/2019	3.1	
3.2	<a href="#">Amended and Restated Bylaws.</a>	8-K	9/17/2019	3.2	
4.1	Reference is made to exhibits <a href="#">3.1</a> through <a href="#">3.2</a> .				
4.2	<a href="#">Form of Common Stock Certificate.</a>	S-1/A	9/3/2019	4.2	
4.3	<a href="#">Amended and Restated Investors' Rights Agreement, dated as of April 23, 2019, by and among Satsuma Pharmaceuticals, Inc. and the investors party thereto.</a>	S-1	8/16/2019	4.3	
4.4	<a href="#">Warrant by and between Satsuma Pharmaceuticals, Inc. and Silicon Valley Bank.</a>	S-1	8/16/2019	4.4	
4.5	<a href="#">Warrant by and between Satsuma Pharmaceuticals, Inc. and Life Science Loans II, LLC.</a>	S-1	8/16/2019	4.5	
4.6	<a href="#">Description of Capital Stock</a>				X
10.1	<a href="#">Lease Agreement, dated January 9, 2018, by and between Satsuma Pharmaceuticals, Inc. and Kashiwa Fudosan America, Inc.</a>	S-1	8/16/2019	10.1	
10.2(a)†	<a href="#">Amended and Restated Licensing and Assignment Agreement, dated December 16, 2016, by and between Satsuma Pharmaceuticals, Inc. and Shin Nippon Biomedical Laboratories, Ltd.</a>	S-1	8/16/2019	10.2(a)	
10.2(b)†	<a href="#">First Amendment to Amended and Restated Licensing and Assignment Agreement, dated January 13, 2017, by and between Satsuma Pharmaceuticals, Inc. and Shin Nippon Biomedical Laboratories, Ltd.</a>	S-1	8/16/2019	10.2(b)	
10.2(c)†	<a href="#">Second Amendment to Amended and Restated Licensing and Assignment Agreement, dated as of April 27, 2017, by and between Satsuma Pharmaceuticals, Inc. and Shin Nippon Biomedical Laboratories, Ltd.</a>	S-1	8/16/2019	10.2(c)	
10.2(d)†	<a href="#">Third Amendment to the Amended and Restated Licensing and Assignment Agreement, dated October 6, 2017, by and between Satsuma Pharmaceuticals, Inc. and Shin Nippon Biomedical Laboratories, Ltd.</a>	S-1	8/16/2019	10.2(d)	
10.3	<a href="#">Loan and Security Agreement, dated as of October 26, 2018, by and between Silicon Valley Bank and the Company.</a>	S-1	8/16/2019	10.3	
10.4(a)#	<a href="#">2016 Equity Incentive Plan.</a>	S-1	8/16/2019	10.4(a)#	
10.4(b)#	<a href="#">Form of Stock Option Agreement under 2016 Equity Incentive Plan.</a>	S-1	8/16/2019	10.4(b)#	
10.5(a)#	<a href="#">2019 Incentive Award Plan.</a>	S-1/A	9/3/2019	10.5(a)	
10.5(b)#	<a href="#">Form of Stock Option Grant Notice and Stock Option Agreement under the 2019 Incentive Award Plan.</a>	S-1	8/16/2019	10.5(b)	
10.5(c)#	<a href="#">Form of Restricted Stock Award Grant Notice and Restricted Stock Award Agreement under the 2019 Incentive Award Plan.</a>	S-1	8/16/2019	10.5(c)	



10.5(d)#	<a href="#">Form of Restricted Stock Unit Award Grant Notice and Restricted Stock Unit Award Agreement under the 2019 Incentive Award Plan.</a>	S-1	8/16/2019	10.5(d)	
10.6#	<a href="#">2019 Employee Stock Purchase Plan.</a>	S-1/A	9/3/2019	10.6	
10.7(a)#	<a href="#">Offer Letter, dated June 17, 2016, by and between Satsuma Pharmaceuticals, Inc. and John Kollins.</a>	S-1	8/16/2019	10.7(a)#	
10.7(b)#	<a href="#">First Amendment to Offer Letter, dated June 17, 2016, by and between Satsuma Pharmaceuticals, Inc. and John Kollins.</a>	S-1	8/16/2019	10.7(b)#	
10.8#	<a href="#">Offer Letter, dated June 12, 2017, by and between Satsuma Pharmaceuticals, Inc. and Detlef Albrecht.</a>	S-1	8/16/2019	10.8#	
10.9#	<a href="#">Offer Letter, dated December 21, 2018, by and between Satsuma Pharmaceuticals, Inc. and Tom O'Neil.</a>	S-1	8/16/2019	10.9#	
10.10#	<a href="#">Non-Employee Director Compensation Program.</a>	S-1/A	9/3/2019	10.10	
10.11	<a href="#">Form of Indemnification Agreement for Directors and Officers</a>	S-1	8/16/2019	10.11	
10.12#	<a href="#">Form Change in Control and Severance Agreement.</a>	S-1/A	9/3/2019	10.12	
23.1	<a href="#">Consent of Independent Registered Public Accounting Firm.</a>				X
24.1	<a href="#">Power of Attorney. Reference is made to the signature page to the Registration Statement.</a>				X
31.1	<a href="#">Certification of Principal Executive Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.</a>				X
31.2	<a href="#">Certification of Principal Financial Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.</a>				X
32.1*	<a href="#">Certification by the Principal Executive Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.</a>				X
32.2*	<a href="#">Certification by the Principal Financial Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.</a>				X
101.INS	XBRL Instance Document				X
101.SCH	XBRL Taxonomy Extension Schema Document				X
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document				X
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document				X

101.LAB	XBRL Taxonomy Extension Labels Linkbase Document	X
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document	X
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)	X

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# Indicates management contract or compensatory plan.

† Certain confidential portions (indicated by brackets and asterisks) have been omitted from this exhibit.

\* The certifications attached as Exhibit 32.1 and 32.2 that accompanies this Annual Report on Form 10-K is not deemed filed with the SEC and is not to be incorporated by reference into any filing of Satsuma Pharmaceuticals, Inc. under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended, whether made before or after the date of this Annual Report on Form 10-K, irrespective of any general incorporation language contained in such filing.



## POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints John Kollins and Tom O'Neil, jointly and severally, as his true and lawful attorneys-in-fact and agents, with full power of substitution and resubstitution, for him and in his name, place, and stead, in any and all capacities, to sign any and all amendments to this Annual Report on Form 10-K, and to file the same, with all exhibits thereto, and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents full power and authority to do and perform each and every act and thing requisite and necessary to be done in and about the premises, as fully to all intents and purposes as he might or could do in person, hereby ratifying and confirming that all said attorneys-in-fact and agents, or his or their substitute or substitutes, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Exchange Act of 1934, this Annual Report on Form 10-K has been signed below by the following persons on behalf of the Registrant and in the capacities and on the dates indicated:

Signature	Title	Date
/s/ John Kollins John Kollins	President and Chief Executive Officer (Principal Executive Officer)	March 15, 2022
/s/ Tom O'Neil Tom O'Neil	Chief Financial Officer (Principal Financial and Accounting Officer)	March 15, 2022
/s/ Elisabeth Sandoval Elisabeth Sandoval	Director	March 15, 2022
/s/ Heath Lukatch Heath Lukatch	Director	March 15, 2022
/s/ Ken Takanashi Ken Takanashi	Director	March 15, 2022
/s/ Michael Riebe Michael Riebe	Director	March 15, 2022
/s/ Mutya Harsch Mutya Harsch	Director	March 15, 2022
/s/ Rajeev Shah Rajeev Shah	Director	March 15, 2022
/s/ Thomas B. King Thomas B. King	Director	March 15, 2022
/s/ Tom Soloway Tom Soloway	Director	March 15, 2022

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

*The following summary describes our capital stock and the material provisions of our amended and restated certificate of incorporation and our amended and restated bylaws, the amended and restated investors' rights agreement to which we and certain of our stockholders are parties and of the Delaware General Corporation Law. Because the following is only a summary, it does not contain all of the information that may be important to you. For a complete description, you should refer to our amended and restated certificate of incorporation, amended and restated bylaws and amended and restated investors' rights agreement, copies of which are incorporated by reference as Exhibits 3.1, 3.2 and 4.3, respectively, to our Annual Report on Form 10-K.*

**Common Stock**

As of December 31, 2021, Satsuma Pharmaceuticals, Inc. ("Satsuma") had common stock, \$0.0001 par value per share, registered under Section 12 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), and listed on The Nasdaq Global Market under the trading symbol "STSA."

**Shares Outstanding**

We are authorized to issue up to 300,000,000 shares of Common Stock. As of December 31, 2021, there are 31,545,564 shares of Common Stock issued and outstanding and 3,202,588 shares are issuable upon the exercise of outstanding options to purchase common stock.

As of December 31, 2021, there were approximately 11 holders of record of our Common Stock. This number does not include beneficial owners whose shares are held by nominees in street name.

The actual number of stockholders is greater than the number of record holders and includes stockholders who are beneficial owners but whose shares are held in street name by brokers and other nominees. This number of holders of record also does not include stockholders whose shares may be held in trust by other entities.

**Voting Rights**

Each holder of our common stock is entitled to one vote for each share on all matters submitted to a vote of the stockholders, including the election of directors. Our stockholders do not have cumulative voting rights in the election of directors. Accordingly, holders of a majority of the voting shares are able to elect all of the directors. In addition, the affirmative vote of holders of 66 2/3% of the voting power of all of the then outstanding voting stock will be required to take certain actions, including amending certain provisions of our amended and restated certificate of incorporation, such as the provisions relating to amending our amended and restated bylaws, the classified board and director liability.

**Dividends**

Subject to preferences that may be applicable to any then outstanding preferred stock, holders of our common stock are entitled to receive dividends, if any, as may be declared from time to time by our board of directors out of legally available funds.

**Liquidation**

In the event of our liquidation, dissolution or winding up, holders of our common stock will be entitled to share ratably in the net assets legally available for distribution to stockholders after the payment of all of our debts and other liabilities and the satisfaction of any liquidation preference granted to the holders of any then outstanding shares of preferred stock.

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### ***Rights and Preferences***

Holders of our common stock have no preemptive, conversion, subscription or other rights, and there are no redemption or sinking fund provisions applicable to our common stock. The rights, preferences and privileges of the holders of our common stock are subject to and may be adversely affected by the rights of the holders of shares of any series of our preferred stock that we may designate in the future.

### ***Fully Paid and Nonassessable***

All of our outstanding shares of common stock are, and the shares of common stock to be issued in this offering will be, fully paid and nonassessable.

### ***Preferred Stock***

Our board of directors has the authority, without further action by our stockholders, to issue up to 10,000,000 shares of preferred stock in one or more series and to fix the rights, preferences, privileges and restrictions thereof. These rights, preferences and privileges could include dividend rights, conversion rights, voting rights, terms of redemption, liquidation preferences, sinking fund terms and the number of shares constituting, or the designation of, such series, any or all of which may be greater than the rights of our common stock. The issuance of our preferred stock could adversely affect the voting power of holders of common stock and the likelihood that such holders will receive dividend payments and payments upon our liquidation. In addition, the issuance of preferred stock could have the effect of delaying, deferring or preventing a change in control of our company or other corporate action. As of December 31, 2021, no shares of preferred stock were outstanding, and we have no present plan to issue any shares of preferred stock.

### ***Registration Rights***

Under our amended and restated investors' rights agreement, based on the number of shares outstanding as of December 31, 2021, the holders of approximately 4.7 million shares of common stock, or their transferees, have the right to require us to register their shares under the Securities Act so that those shares may be publicly resold, and to include their shares in any registration statement we file, in each case as described below.

#### ***Demand Registration Rights***

Based on the number of shares outstanding as of December 31, 2021, the holders of approximately 4.7 million shares of our common stock (on an as-converted basis), or their transferees, are entitled to certain demand registration rights. The holders of at least 20% of these shares can, on not more than two occasions, request that we register all or a portion of their shares if the aggregate price to the public of the shares offered is at least \$10.0 million (before deductions of underwriters' commissions and expenses).

#### ***Piggyback Registration Rights***

Based on the number of shares outstanding as of December 31, 2021, after the consummation of this offering, in the event that we determine to register any of our securities under the Securities Act (subject to certain exceptions), either for our own account or for the account of other security holders, the holders of approximately 4.7 million shares of our common stock (on an as-converted basis), or their transferees, are entitled to certain "piggyback" registration rights allowing the holders to include their shares in such registration, subject to certain marketing and other limitations. As a result, whenever we propose to file a registration statement under the Securities Act, other than with respect to a registration related to employee benefit plans, the offer and sale of debt securities, or corporate reorganizations or certain other transactions, the holders of these shares are entitled to notice of the registration and have the right, subject to limitations that the underwriters may impose on the number of shares included in the registration, to include their shares in the registration. In an underwritten offering, the managing underwriter, if any, has the right, subject to specified conditions, to exclude or limit the number of shares such holders may include.

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### ***Form S-3 Registration Rights***

Based on the number of shares outstanding as of December 31, 2021, the holders of approximately 4.7 million shares of our common stock (on an as-converted basis), or their transferees, are entitled to certain Form S-3 registration rights. The holders of at least 20% of these shares can make a written request that we register 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 (before deductions of underwriters' commissions and expenses). These stockholders may make an unlimited number of requests for registration on Form S-3, but in no event shall we be required to file more than two registrations on Form S-3 in any given twelve-month period.

### ***Expenses of Registration***

We will pay the registration expenses of the holders of the shares registered pursuant to the demand and Form S-3 registration rights described above.

### ***Expiration of Registration Rights***

The demand, piggyback and Form S-3 registration rights described above will expire, with respect to any particular stockholder, upon the earlier of five years after the consummation of our initial public offering or when that stockholder can sell all of its shares under Rule 144 of the Securities Act during any 90-day period (and without the requirement for the Company to be in compliance with the current public information required under Section c(1) of Rule 144 of the Securities Act).

### ***Anti-Takeover Effects of Provisions of our Amended and Restated Certificate of Incorporation, our Amended and Restated Bylaws and Delaware Law***

Certain provisions of Delaware law and our amended and restated certificate of incorporation and our amended and restated bylaws contain provisions that could make the following transactions more difficult: acquisition of us by means of a tender offer; acquisition of us by means of a proxy contest or otherwise; or removal of our incumbent officers and directors. It is possible that these provisions could make it more difficult to accomplish or could deter transactions that stockholders may otherwise consider to be in their best interest or in our best interests, including transactions that might result in a premium over the market price for our shares.

These provisions, summarized below, are expected to discourage coercive takeover practices and inadequate takeover bids. These provisions are also designed to encourage persons seeking to acquire control of us to first negotiate with our board of directors. We believe that the benefits of increased protection of our potential ability to negotiate with the proponent of an unfriendly or unsolicited proposal to acquire or restructure us outweigh the disadvantages of discouraging these proposals because negotiation of these proposals could result in an improvement of their terms.

### ***Delaware Anti-Takeover Statute***

We are subject to Section 203 of the Delaware General Corporation Law, which prohibits persons deemed "interested stockholders" from engaging in a "business combination" with a publicly-held Delaware corporation for three years following the date these persons become interested stockholders unless the business combination is, or the transaction in which the person became an interested stockholder was, approved in a prescribed manner or another prescribed exception applies. Generally, 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 voting stock. Generally, a "business combination" includes a merger, asset or stock sale, or other transaction resulting in a financial benefit to the interested stockholder. The existence of this provision may have an anti-takeover effect with respect to transactions not approved in advance by the board of directors, such as discouraging takeover attempts that might result in a premium over the market price of our common stock.

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### ***Undesignated Preferred Stock***

The ability to authorize undesignated preferred stock makes it possible for our board of directors to issue preferred stock with voting or other rights or preferences that could impede the success of any attempt to change control of us. These and other provisions may have the effect of deterring hostile takeovers or delaying changes in control or management of our company.

### ***Special Stockholder Meetings***

Our amended and restated bylaws provide that a special meeting of stockholders may be called at any time by our board of directors, or our President or Chief Executive Officer, but such special meetings may not be called by the stockholders or any other person or persons.

### ***Requirements for Advance Notification of Stockholder Nominations and Proposals***

Our amended and restated bylaws establish advance notice procedures with respect to stockholder proposals and the nomination of candidates for election as directors, other than nominations made by or at the direction of the board of directors or a committee of the board of directors.

### ***Elimination of Stockholder Action by Written Consent***

Our amended and restated certificate of incorporation and our amended and restated bylaws eliminate the right of stockholders to act by written consent without a meeting.

### ***Classified Board; Election and Removal of Directors; Filling Vacancies***

Our board of directors is divided into three classes. The directors in each class serve for a three-year term, with one class being elected each year by our stockholders, 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. Because our stockholders do not have cumulative voting rights, our stockholders holding a majority of the shares of common stock outstanding will be able to elect all of our directors. Our amended and restated certificate of incorporation will provide for the removal of any of our directors only for cause and requires a stockholder vote by the holders of at least a 66 2/3% of the voting power of the then outstanding voting stock. For more information on the classified board, see “Management—Board Composition.” Furthermore, any vacancy on our board of directors, however occurring, including a vacancy resulting from an increase in the size of the board, may only be filled by a resolution of the board of directors unless the board of directors determines that such vacancies shall be filled by the stockholders. This system of electing and removing directors and filling vacancies may tend to discourage a third party from making a tender offer or otherwise attempting to obtain control of us, because it generally makes it more difficult for stockholders to replace a majority of the directors.

### ***Choice of Forum***

Our amended and restated certificate of incorporation and our amended and restated bylaws provide that the Court of Chancery of the State of Delaware shall be the sole and exclusive forum for (i) any derivative action or proceeding brought on behalf of us, (ii) any action asserting a claim of breach of a fiduciary duty owed by any of our directors or officers to us or our stockholders, (iii) any action asserting a claim against us arising pursuant to any provision of the Delaware General Corporation Law or our amended and restated certificate of incorporation or amended and restated bylaws or (iv) any action asserting a claim against us governed by the internal affairs doctrine. As a result, any action brought by any of our stockholders with regard to any of these matters will need to be filed in the Court of Chancery of the State of Delaware and cannot be filed in any other jurisdiction; provided that, the exclusive forum provision will not apply to suits brought to enforce any liability or duty created by the Securities Act, the Exchange Act or any other claim for which the federal courts have exclusive jurisdiction; and provided further that, if and only if the Court of Chancery of the State of Delaware dismisses any such action for lack of subject matter jurisdiction, such action may be brought in another state or federal court sitting in the State of Delaware. Nothing in our amended and restated certificate of incorporation or amended and restated bylaws precludes stockholders that assert claims under the Securities Act or the Exchange Act from bringing such claims in state or federal court, subject to applicable law.

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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, other employees or stockholders, which may discourage lawsuits with respect to such claims, although our stockholders will not be deemed to have waived our compliance with federal securities laws and the rules and regulations thereunder.

### ***Amendment of Charter and Bylaws Provisions***

The amendment of any of the above provisions in our amended and restated certificate of incorporation, except for the provision making it possible for our board of directors to issue undesignated preferred stock would require approval by a stockholder vote by the holders of at least a 66 2/3% of the voting power of the then outstanding voting stock.

The provisions of the Delaware General Corporation Law, our amended and restated certificate of incorporation and our amended and restated bylaws could have the effect of discouraging others from attempting hostile takeovers and, as a consequence, they may also inhibit temporary fluctuations in the market price of our common stock that often result from actual or rumored hostile takeover attempts. These provisions may also have the effect of preventing changes in our management. It is possible that these provisions could make it more difficult to accomplish transactions that stockholders may otherwise deem to be in their best interests.

### **Limitations of Liability and Indemnification Matters**

Our amended and restated certificate of incorporation contains provisions that limit the liability of our directors for monetary damages to the fullest extent permitted by Delaware law. Consequently, our directors are not 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 Delaware General Corporation Law; or
- any transaction from which the director derived an improper personal benefit.

Each of our amended and restated certificate of incorporation and amended and restated bylaws provide that we are required to indemnify our directors and officers, in each case to the fullest extent permitted by Delaware law. Our amended and restated bylaws also obligates us to advance expenses incurred by a director or officer in advance of the final disposition of any action or proceeding, and permit us to secure insurance on behalf of any officer, director, employee or other agent for any liability arising out of his or her actions in that capacity regardless of whether we would otherwise be permitted to indemnify him or her under Delaware law. We have entered and expect to continue to enter into agreements to indemnify our directors, executive officers and other employees as determined by our board of directors. With specified exceptions, these agreements provide for indemnification for related expenses including, among other things, attorneys' fees, judgments, fines and settlement amounts incurred by any of these individuals in any action or proceeding. We believe that these bylaw provisions and indemnification agreements are necessary to attract and retain qualified persons as directors and officers. We also maintain directors' and officers' liability insurance.

The limitation of liability and indemnification provisions in our amended and restated certificate of incorporation and amended 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 our stockholders. Further, a stockholder's investment may be adversely affected to the extent that we pay the costs of settlement and damages.

### **Transfer Agent and Registrar**

The transfer agent and registrar for our common stock is American Stock Transfer and Trust Company, LLC. The transfer agent and registrar's address is 6201 15th Avenue, Brooklyn, New York 11219.

**Consent of Independent Registered Public Accounting Firm**

We consent to the incorporation by reference in the registration statements (Nos. 333-249645 and 333-255201) on Form S-3 and (Nos. 333-233808, 333-237058, and 333-254737) on Form S-8 of our report dated March 15, 2022, with respect to the financial statements of Satsuma Pharmaceuticals, Inc.

/s/ KPMG LLP

San Diego, California  
March 15, 2022

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

I, John Kollins, certify that:

1. I have reviewed this Annual Report on Form 10-K of Satsuma Pharmaceuticals, Inc. for the year ended December 31, 2021;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:
  - (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
  - (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;
  - (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
  - (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
  - (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
  - (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 15, 2022

By: \_\_\_\_\_ /s/ John Kollins  
John Kollins  
President and Chief Executive Officer and Director  
(Principal Executive Officer)

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

I, Tom O'Neil, certify that:

1. I have reviewed this Annual Report on Form 10-K of Satsuma Pharmaceuticals, Inc. for the year ended December 31, 2021;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:
  - (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
  - (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;
  - (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
  - (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
  - (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
  - (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 15, 2022

By: \_\_\_\_\_  
/s/ Tom O'Neil  
Tom O'Neil  
Chief Financial Officer  
(Principal Financial and Accounting Officer)

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

In connection with the Annual Report of Satsuma Pharmaceuticals, Inc. (the "Company") on Form 10-K for the year ended December 31, 2021 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I certify, pursuant to 18 U.S.C. § 1350, as adopted pursuant to § 906 of the Sarbanes-Oxley Act of 2002, that:

- (1) The Report fully complies with the requirements of section 13(a) or 15(d) of the Securities Exchange Act of 1934; and
- (2) The information contained in the Report fairly presents, in all material respects, the financial condition and result of operations of the Company for the period covered by the Report.

Date: March 15, 2022

By: \_\_\_\_\_ /s/ John Kollins  
John Kollins  
President and Chief Executive Officer and Director  
(Principal Executive Officer)

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

In connection with the Annual Report of Satsuma Pharmaceuticals, Inc. (the "Company") on Form 10-K for the year ended December 31, 2021 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I certify, pursuant to 18 U.S.C. § 1350, as adopted pursuant to § 906 of the Sarbanes-Oxley Act of 2002, that:

- (1) The Report fully complies with the requirements of section 13(a) or 15(d) of the Securities Exchange Act of 1934; and
- (2) The information contained in the Report fairly presents, in all material respects, the financial condition and result of operations of the Company for the period covered by the Report.

Date: March 15, 2022

By: \_\_\_\_\_ /s/ Tom O'Neil  
Tom O'Neil  
Chief Financial Officer  
(Principal Financial and Accounting Officer)