

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, 2024

OR

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

For the transition period from _____ to _____

Commission File Number: 001-39536

Taysha Gene Therapies, Inc.
(Exact Name of Registrant as Specified in its Charter)

Delaware
(State or other jurisdiction of
incorporation or organization)

3000 Pegasus Park Dr. Ste 1430
Dallas, Texas
(Address of principal executive offices)

84-3199512
(I.R.S. Employer
Identification No.)

75247
(Zip Code)

Registrant's telephone number, including area code: (214) 612-0000

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 \$0.00001 per share	TSHA	The Nasdaq Stock Market LLC

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 Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes No

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

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

Large accelerated filer	<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.

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

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

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

As of June 30, 2024, the aggregate market value of the common stock of the registrant held by non-affiliates was: \$370.7 million.

As of February 26, 2025, the registrant had 205,001,632 shares of common stock, \$0.00001 par value per share, outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's definitive Proxy Statement relating to the 2025 Annual Meeting of Stockholders are incorporated herein by reference in Part III of this Annual Report on Form 10-K. The Proxy Statement will be filed with the Securities and Exchange Commission within 120 days after the year ended December 31, 2024.

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SPECIAL CAUTIONARY NOTICE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K, or this Annual Report, contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act, that involve substantial risks and uncertainties. The forward-looking statements are contained principally in Part I, Item 1. “Business,” Part I, Item 1A. “Risk Factors,” and Part II, Item 7. “Management’s Discussion and Analysis of Financial Condition and Results of Operations,” but are also contained elsewhere in this Annual Report. In some cases, you can identify forward-looking statements by the words “may,” “might,” “will,” “could,” “would,” “should,” “expect,” “intend,” “plan,” “objective,” “anticipate,” “believe,” “estimate,” “predict,” “project,” “potential,” “continue” and “ongoing,” or the negative of these terms, or other comparable terminology intended to identify statements about the future. These statements involve known and unknown risks, uncertainties and other factors that may cause our actual results, levels of activity, performance or achievements to be materially different from the information expressed or implied by these forward-looking statements. Although we believe that we have a reasonable basis for each forward-looking statement contained in this Annual Report, we caution you that these statements are based on a combination of facts and factors currently known by us and our expectations of the future, about which we cannot be certain. Forward-looking statements include statements about:

- the timing, progress and results of our preclinical studies and clinical trials of our product candidates, including statements regarding the timing of initiation and completion of studies or trials and related preparatory work, the period during which the results of the trials will become available and our research and development programs;
 - the timing of our planned Investigational New Drug and Clinical Trial Agreement submissions, initiation of clinical trials and timing of expected clinical results for TSHA-102 for Rett syndrome and any other current and future product candidates that we advance;
 - the timing of any submission of filings for regulatory approval of, and our ability to obtain and maintain regulatory approvals for, our current and future product candidates;
 - our ability to identify patients with the diseases treated by our product candidates, and to enroll patients in trials;
 - our expectations regarding the size of the patient populations, market acceptance and opportunity for and clinical utility of our product candidates, if approved for commercial use;
 - our manufacturing process and strategy, including the scalability and commercial viability of our manufacturing methods and processes;
 - our expectations regarding the scope of any approved indication for TSHA-102 or any other current or future product candidate that we advance;
 - our ability to successfully commercialize our product candidates;
 - our ability to leverage our platform, including our next-generation technologies, to identify and develop future product candidates;
 - our estimates of our expenses, ongoing losses, future revenue, capital requirements and our need for or ability to obtain additional funding before we can expect to generate any revenue from product sales;
 - our ability to establish or maintain collaborations or strategic relationships;
 - the costs of litigation and our expectations regarding the outcome of lawsuits and other claims against us and any regulatory or legal proceedings;
 - our ability to identify, recruit and retain key personnel;
 - our reliance upon intellectual property licensed from third parties and our ability to obtain such licenses on commercially reasonable terms or at all;
 - our ability to protect and enforce our intellectual property position for our product candidates, and the scope of such protection;
 - our ability to comply with the terms of our term loan agreement;
 - our financial performance;
 - our competitive position and the development of and projections relating to our competitors or our industry;
 - our estimates regarding future revenue, expenses and needs for additional financing; and
-

- our expectations regarding the time during which we will be an emerging growth company under the JOBS Act.

You should refer to “Item 1A. Risk Factors” in this Annual Report for a discussion of important factors that may cause our actual results to differ materially from those expressed or implied by our forward-looking statements. As a result of these factors, we cannot assure you that the forward-looking statements in this Annual Report will prove to be accurate. Furthermore, if our forward-looking statements prove to be inaccurate, the inaccuracy may be material. In light of the significant uncertainties in these forward-looking statements, 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. The forward-looking statements in this Annual Report represent our views as of the date of this Annual Report. We anticipate that subsequent events and developments may cause our views to change. However, while we may elect to update these forward-looking statements at some point in the future, we undertake no obligation to publicly update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law. You should, therefore, not rely on these forward-looking statements as representing our views as of any date subsequent to the date of this Annual Report.

You should read this report and the documents that we reference in this report, completely and with the understanding that our actual future results may be materially different from what we expect. We qualify all of our forward-looking statements by these cautionary statements.

All brand names or trademarks appearing in this Annual Report are the property of their respective owners. Solely for convenience, the trademarks and trade names in this Annual Report are referred to without the symbols [®] and [™], but such references should not be construed as any indication that their respective owners will not assert, to the fullest extent under applicable law, their rights thereto.

Unless the context requires otherwise, references in this report to “Taysha,” the “Company,” “we,” “us,” and “our” refer to Taysha Gene Therapies, Inc. together with its consolidated subsidiaries.

PART I

Item 1. Business.

Overview

We are a clinical-stage biotechnology company focused on advancing AAV-based gene therapies for the treatment of severe monogenic diseases of the central nervous system, or CNS. Our lead clinical program TSHA-102 is in development for the treatment of Rett syndrome, a rare neurodevelopmental disorder with no approved disease-modifying therapies that address the genetic root cause of the disease. With a singular focus on developing transformative medicines, we aim to address severe unmet medical needs and dramatically improve the lives of patients and their caregivers. Our management team has proven experience in gene therapy development and commercialization. We leverage this experience, our manufacturing process and a clinically and commercially proven AAV9 capsid in an effort to rapidly translate treatments from bench to bedside.

We are evaluating TSHA-102 in the REVEAL Phase 1/2 adolescent and adult trial, which is a first-in-human, open-label, randomized, dose-escalation and dose-expansion study evaluating the safety and preliminary efficacy of TSHA-102 as a single lumbar intrathecal administration in adolescent and adult females aged 12 years and older with Rett syndrome due to MECP2 loss-of-function mutation. The trial is taking place in Canada and the United States. We are also evaluating TSHA-102 in the REVEAL Phase 1/2 pediatric trial, which is an open-label, randomized, dose-escalation and dose-expansion study evaluating the safety and preliminary efficacy of TSHA-102 as a single lumbar intrathecal administration in pediatric females with Rett syndrome due to MECP2 loss-of-function mutation. The trial is taking place in the United States, Canada and the United Kingdom.

We have completed dosing of the 10 patients in Part A of both REVEAL trials, which includes six patients in cohort two (high dose, 1×10^{15} total vg) and four patients in cohort one (low dose, 5.7×10^{14} total vg). As of the February 17, 2025 data cutoff, TSHA-102 was generally well tolerated, with no treatment-related serious adverse events, or SAEs, or dose-limiting toxicities, or DLTs, in the 10 patients dosed in Part A of the REVEAL trials. We believe this maturing dataset continues to support advancement toward the Part B registrational trial. We expect to report safety and efficacy data from cohort two of each of the REVEAL trials (high dose; $n=3$ for each trial) and an update on safety and efficacy data from cohort one of each of the REVEAL trials (low dose; $n=2$ for each trial), as well as an update on the anticipated pivotal trial design for TSHA-102, in the first half of 2025.

We have received orphan drug designation and rare pediatric disease designation from the United States Food and Drug Administration, or FDA, and orphan drug designation from the European Commission for TSHA-102 for the treatment of Rett syndrome. We also received Fast Track Designation from the FDA for TSHA-102 for the treatment of Rett syndrome. We also received CTA clearance from the United Kingdom's Medicines and Healthcare Products Regulatory Agency, or U.K. MHRA, in early 2024 for pediatric patients with Rett syndrome. In February 2024, we received Innovative Licensing and Access Pathway, or ILAP, designation for TSHA-102 from the U.K. MHRA. The ILAP aims to facilitate patient access to novel treatments by accelerating time to market through opportunities for enhanced engagements with U.K. regulatory authorities and other stakeholders. In April 2024, the FDA granted Regenerative Medicine Advanced Therapy, or RMAT, designation for TSHA-102 in Rett syndrome following the FDA's review of available safety and efficacy data from the first three patients with Rett syndrome dosed with the low dose of TSHA-102 (5.7×10^{14} total vg) across the REVEAL Phase 1/2 adolescent and adult trial and the REVEAL Phase 1/2 pediatric trial.

Our Pipeline

We are focused on discovering, developing and commercializing gene therapies for the treatment of monogenic diseases of the CNS, in both rare and large patient populations. Our primary focus is advancing our lead TSHA-102 clinical program in Rett syndrome, while our pipeline of CNS programs offers the potential for additional development opportunities in the future. The stage of development of our Rett syndrome program, including the progress in our ongoing clinical trials, is represented in the table below:



TSHA-102 for Rett Syndrome

TSHA-102 is a self-complementary intrathecally delivered AAV9 gene transfer therapy in clinical evaluation for Rett syndrome, a rare progressive neurodevelopmental disorder caused by mutations in the X-linked MECP2 gene encoding methyl CpG-binding protein 2, or MeCP2, which is essential for regulating neuronal and synaptic function in the brain. The disorder is characterized by loss of communication and hand function, slowing and/or regression of development, motor and respiratory impairment, seizures, intellectual disabilities and shortened life expectancy. Rett syndrome progression is divided into four key stages, beginning with early onset stagnation at 6 to 18 months of age followed by rapid regression, plateau and late motor deterioration. Rett syndrome primarily occurs in females and is one of the most common genetic causes of severe intellectual disability.

Designed as a one-time treatment, TSHA-102 aims to address the genetic root cause of the disease by delivering a functional form of MECP2 to cells in the CNS. The vector is delivered directly to the cerebrospinal fluid via intrathecal administration, which facilitates optimal biodistribution and cell transduction within key regions of the CNS. Because of the risks associated with both under- and over-expression of MeCP2, we have combined high-throughput microRNA, or miRNA, profiling and genome mining to create miRNA-Responsive Auto-Regulatory Element, or miRARE, our novel miRNA target panel. The miRARE element includes binding sites for endogenous miRNA, which are responsive to MeCP2 levels to prevent overexpression. By utilizing the miRARE technology, TSHA-102 is designed to mediate levels of MeCP2 in the CNS on a cell-by-cell basis to address risks associated with under- and over-expression. By increasing MECP2 levels in MECP2 deficient cells and maintaining healthy levels of MECP2 output of healthy cells, TSHA-102 has demonstrated the ability to produce and maintain safe transgene expression levels in the CNS.

Currently, there are no approved disease-modifying therapies that treat the genetic root cause of Rett syndrome, and there is a significant unmet medical need. According to the Rett Syndrome Research Trust, Rett syndrome affects more than 350,000 patients worldwide. The estimated addressable patient population with typical Rett syndrome caused by a pathogenic/likely pathogenic MECP2 mutation is between 15,000 and 20,000 patients in the United States, European Union and United Kingdom.

Phase 1/2 REVEAL Clinical Trials

We currently have two Phase 1/2 clinical trials ongoing for TSHA-102: an adolescent/adult study in the United States and Canada and a pediatric study in the United States, Canada and the United Kingdom, each as described below:

Study	Primary Study Objectives	Study Population	TSHA-102 Single IT Dosing Regimen	Active Geographies
REVEAL Phase 1/2 Adolescent and Adult Trial	To assess the safety, tolerability, and preliminary efficacy of TSHA-102 as a single lumbar IT administration	Adolescent and adult females with Rett syndrome, ≥ 12 years old	Part A: Cohort 1: 5.7×10^{14} vg IT Cohort 2: 1.0×10^{15} vg IT Part B: Dose Expansion with MTD or MAD	Canada, US
REVEAL Phase 1/2 Pediatric Trial	To assess the safety, tolerability, and preliminary efficacy of TSHA-102 as a single lumbar IT administration	Pediatric females with Rett syndrome Part A: 5-8 years old Part B: 3-8 years old	Part A: Cohort 1: 5.7×10^{14} vg IT Cohort 2: 1.0×10^{15} vg IT Part B: Dose Expansion with MTD or MAD in two age cohorts	US, UK, Canada

IT – Intrathecal; MTD – Maximum Tolerated Dose; MAD – Maximum Administered Dose.

The maximum tolerated dose or maximum administered dose established in Part A will be administered during dose expansion in Part B, which is the pivotal phase of the trials. Data from Part A is being assessed by regulatory agencies and the IDMC to determine key elements of Part B of the study, including efficacy endpoints, study duration and the MTD or MAD.

Efficacy endpoints for each trial include patient assessments performed by clinicians, including the use of the Clinical Global Impressions Scale – Improvement, or CGI-I, the Clinical Global Impressions Scale – Severity, or CGI-S, Rett Syndrome Hand Function Scale, or RSHFS, and Revised Motor Behavior Assessment, or R-MBA. Additional efficacy endpoints also include patient assessments by caregivers using Parental Global Impressions Improvement, or PGI-I, Seizure Diaries and other clinical assessment scales. Based on FDA feedback from our ongoing discussions, we intend to focus on objective measures that clinically capture functional gains in Part B of the trials; accordingly, the Rett Syndrome Behavior Questionnaire, or RSBQ, will not be included as a primary or secondary endpoint in Part B of the REVEAL trials, and we continue to advance discussions on the development plan for Part B as part of our conversations with the FDA.

Overview of Part A of the REVEAL Trials

We have completed dosing of the 10 patients in Part A of both REVEAL trials, which includes six patients in cohort two (high dose, 1×10^{15} total vg) and four patients in cohort one (low dose, 5.7×10^{14} total vg). As of the February 17, 2025 data cutoff, TSHA-102 was generally well tolerated, with no treatment-related SAEs or DLTs in the 10 patients dosed in Part A of the REVEAL trials. We believe this maturing dataset continues to support advancement toward the pivotal Part B trial.

June 2024 Clinical Update: Low-Dose Cohorts

In June 2024, we announced positive longer-term clinical data from the ongoing REVEAL Phase 1/2 adolescent and adult trial and preliminary clinical data from the ongoing REVEAL Phase 1/2 pediatric trial. In the adolescent and adult trial, we reported that both patients showed sustained and new clinical improvements and functional gains across multiple domains relative to baseline. In the pediatric trial, we reported data from both patients that showed initial clinical improvements and functional gains across multiple domains relative to baseline.

Adolescent and Adult Trial (n=2, low dose cohort)

TSHA-102 was generally well-tolerated in this cohort, with no treatment-related SAEs or DLTs as of the February 17, 2025 data cut.

The baseline characteristics of the two patients in the low-dose cohort of the adolescent and adult trial are shown below:

Adult Patient One	Adult Patient Two
<i>Diagnosed with stage four "late motor deterioration muscle wasting" Rett syndrome</i>	
20 year-old female	21 year-old female
Large <i>MECP2</i> deletion	Missense <i>MECP2</i> mutation
Severe phenotype	Milder phenotype
"Severely ill" – CGI-S baseline score of 6	"Moderately ill" – CGI-S baseline score of 4
Motor Skills: Complete loss of ambulation and ability to sit unassisted; wheelchair-bound by age 8 Loss of hand function by age 6 Communication/Socialization: Mostly non-verbal by age 6 Autonomic Function: Frequent apnea and hyperventilation by age 3 Seizures: Seizures at age 5 (2-4 per year at baseline)	Motor Skills: Partial loss of ambulation by age 2 Walks with impaired gait and balance by age 18 Hand stereotypies with weak grasping by age 3 Communication/Socialization: Mostly non-verbal by age 2 Autonomic Function: Frequent hyperventilation by age 3 Seizures: Seizures by age 10 (2-4 per week at baseline)

In the two adult patients with different clinical severity and genetic mutations, we observed improvements and functional gains as early as four weeks post-treatment across multiple domains, including motor skills, communication/socialization, autonomic function and seizures, that persisted and strengthened over time through week 52 (patient one) and week 25 (patient two) following completion of the steroid taper, as shown below:

Clinical Domain Improvements	Adult Patient One	Adult Patient Two
	52 weeks post-treatment <i>Completed steroid taper week 36 and sirolimus taper week 43</i>	25 weeks post-treatment <i>Completed steroid taper week 25 and sirolimus taper week 31</i>
Motor skills	<ul style="list-style-type: none"> Improved hand function and gained ability to sit unassisted and move legs for the first time in over a decade 	<ul style="list-style-type: none"> Improved hand stereotypies for the first time since regression at age three, and improved posture and stability
Communication / Socialization	<ul style="list-style-type: none"> Improved social interest, vocalization and use of eye-gaze driven communication device 	<ul style="list-style-type: none"> Improved social interest, including increased response to spoken words and eye contact
Autonomic function	<ul style="list-style-type: none"> Improved breathing patterns and circulation, and normalized sleep quality/duration with gained ability to sleep through night for the first time in 20 years 	<ul style="list-style-type: none"> Improved breathing patterns and circulation
Seizures	<ul style="list-style-type: none"> Stable seizure events with lower levels of anti-seizure medication relative to baseline 	<ul style="list-style-type: none"> Significantly reduced seizure events with 25% lower levels of anti-seizure medication relative to baseline Seizure free for 8.5 months post-TSHA-102*

Clinical observations made by the Principal Investigator are based on post-treatment assessments, pre-treatment observations, baseline assessments, pre-screening visits and patient's medical history. Video evidence was also obtained. Subject to change as the trial progresses.

*Seizure data for adult patient two is based on Seizure Diary and caregiver reports as of week 36 post-TSHA-102.

Further, we observed improvements across multiple efficacy measures as early as four weeks post-treatment, with sustained and new improvements across multiple efficacy measures at week 52 (patient one) and week 25 (patient two) following completion of the steroid taper, as shown below:

Scale Description	CGI-S		CGI-I, with Rett anchors		PGI-I		R-MBA		RSHFS	
	P1	P2	P1	P2	P1	P2	P1	P2	P1	P2
Clinician-reported 7-point assessment of illness severity 1=normal 7=among the most extremely ill	Clinician-reported 7-point assessment of overall improvement 1=very much improved 7=very much worse		Caregiver-reported 7-point assessment of overall improvement 1=considerably better 7=very much worse		Clinician-reported 24-question scale measuring disease behaviors of Rett syndrome Higher scores indicate greater severity		Clinician-reported assessment of hand function in Rett syndrome by an independent experienced physical therapist, being reported as best score for large objects 1=no active grasping 4=independent grasp			
Screening, Baseline	6 Severely ill	4 Moderately ill	-	-	-	-	43	38	DH: 3 NH: NA*	DH: NE* NH: 1
Week 4	5 Markedly ill	4 Moderately ill	2 Much improved	3 Minimally improved	3 A little better	3 A little better	48	31		DH: NE* NH: 1
Week 8	5 Markedly ill	4 Moderately ill	2 Much improved	3 Minimally improved	3 A little better	3 A little better	51	24	DH: 2 NH: 1	DH: 4 NH: 1
Week 12	5 Markedly ill	4 Moderately ill	2 Much improved	3 Minimally improved	2 Much better*	3 A little better	37	21	DH: 3 NH: 3*	DH: NE* NH: 1
Week 25	5 Markedly ill	4 Moderately ill	2 Much improved	3 Minimally improved	2 Much better	3 A little better	42	15	DH: 3 NH: 2	DH: 4 NH: 1
Week 52	5 Markedly ill		3 Minimally improved		1 Considerably better		26			
Overall Change	+	=	+	+	+	+	+	+	+	=

DH = dominant hand; NH = non-dominant hand; = not assessed; NE = not evaluable = improvement from baseline = no change from baseline = decline from baseline

*PGI-I week 12 assessment for patient one was captured at week 16; RSHFS week 12 assessment for patient one was captured on week 11; RSHFS assessment for patient one was not conducted at baseline; RSHFS assessment for patient two's DH was not conducted as defined in the guidelines at baseline, week 4 and week 12, therefore the data is not evaluable at these time points. Rett Syndrome Behavior Questionnaire (RSBQ) has been removed as it is no longer being considered as a primary/secondary endpoint in Part B of our TSHA-102 clinical studies based on discussions with the U.S. FDA and focus on objective endpoints.

Pediatric Trial (n=2, low dose cohort)

TSHA-102 was generally well-tolerated in this cohort, with no treatment-related SAEs or DLTs as of the February 17, 2025 data cutoff.

The baseline characteristics of the two patients in the low-dose cohort of the pediatric trial are shown below:

Pediatric Patient One	Pediatric Patient Two
<i>Diagnosed with stage three "pseudo stationary" Rett syndrome</i>	
6 year-old female	7 year-old female
MECP2 deletion	Missense MECP2 mutation
Moderate phenotype	Milder phenotype
"Markedly ill" – CGI-S baseline score of 5	"Moderately ill" – CGI-S baseline score of 4
Motor Skills: Non-ambulatory Sits unassisted for 30 seconds/stands with support by age 3 Impaired hand function by age 1.5 Communication/Socialization: Mostly non-verbal by age 1 Autonomic Function: Breath holding Seizures: Seizures by age 3 (1 seizure every 3 months at baseline)	Motor Skills: Partial loss of ambulation by age 1.5 Impaired hand function by age 1 Communication/Socialization: Non-verbal by age 1 Autonomic Function: Frequent hyperventilation by age 4 Seizures: Seizures by age 3 (2-4 seizures daily at baseline)

In the two pediatric patients with different clinical severity and genetic mutations, we observed improvements and functional gains as early as four weeks post-treatment across multiple domains, including motor skills, communication/socialization, autonomic function and seizures, through week 12 (patient one) and week 8 (patient two) as shown below:

Clinical Domain Improvements	Pediatric Patient One 12 weeks post-treatment	Pediatric Patient Two 8 weeks post-treatment
Motor skills	<ul style="list-style-type: none"> Improved hand function and grasping with ability to hold object up to 3 minutes vs 12 seconds at baseline Improved truncal stability and balance with gained ability to move her leg on her own to better take a step with assistance and sit unassisted for longer duration Improved swallowing and oral intake relative to gastrostomy tube feeding 	<ul style="list-style-type: none"> Improved hand function with ability to reach more quickly Improved gait, speed and stability when walking with new skills gained including the gained ability to stand up from a chair and walk up a stair
Communication / Socialization	<ul style="list-style-type: none"> Improved use of eye-gaze driven communication device with new words communicated and gained ability to string multiple words together and identify object functions through device New skills gained in visual reception and receptive language 	<ul style="list-style-type: none"> Improved social interest and eye contact
Autonomic function	<ul style="list-style-type: none"> Improved breathing patterns 	<ul style="list-style-type: none"> Improved breathing patterns
Seizures	<ul style="list-style-type: none"> Stable seizure events relative to baseline 	<ul style="list-style-type: none"> Increase in days reported seizure-free since dosing; a new anti-seizure medication was added to regimen week 4, which has been maintained through week 11

Clinical observations made by the Principal Investigator are based on post-treatment assessments, pre-treatment observations, baseline assessments, pre-screening visits and patient's medical history. Video evidence was also obtained. Subject to change as the trial progresses.

Further, we observed improvements across multiple efficacy measures as early as four weeks post-treatment, with sustained and new improvements across multiple efficacy measures week 12 (patient one) and week 8 (patient two) as shown below:

Scale Description	CGI-S		CGI-I, with Rett anchors		PGI-I		R-MBA		MSEL-A	
	P1	P2	P1	P2	P1	P2	P1	P2	P1	P2
Screening, Baseline	5 Markedly ill	4 Moderately ill	-	-	-	-	40	41	VR=25 mos RL=22 mos EL=7 mos FM=3 mos	VR=39 mos RL=13 mos EL=7 mos FM=6 mos
Week 4	5 Markedly ill	4 Moderately ill	3 Minimally improved	3 Minimally improved	3 A little better	3 A little better	35			
Week 8	5 Markedly ill	4 Moderately ill	3 Minimally improved	2 Much improved	3 A little better*	2 Much better	30	30		
Week 12	5 Markedly ill		3 Minimally improved		3 A little better		36		VR=26 mos RL=24 mos EL=7 mos FM=5 mos	
Overall Change	=	=	+	+	+	+	+	+	+	+

 = not assessed
 = improvement from baseline
 = no change from baseline
 = decline from baseline

*Patient one's RSBQ and R-MBA week 8 assessment was collected week 11. RSBQ has been removed as it is no longer being considered as a primary/secondary endpoint in Part B of our TSHA-102 clinical studies based on discussions with the U.S. FDA and focus on objective endpoints.

Clinical Development Plan for TSHA-102

We have completed dosing of the 10 patients in Part A of the REVEAL trials. We believe this maturing dataset continues to support advancement toward the pivotal Part B trial. We are in ongoing discussions with the FDA, including as part of our RMAT designation, with respect to the regulatory pathway for TSHA-102. We expect to report safety and efficacy data from cohort two of each of the REVEAL trials (high dose; n=6) and an update on safety and efficacy data from cohort one of each of the REVEAL trials (low dose; n=4), as well as an update on the anticipated pivotal trial design for TSHA-102, in the first half of 2025.

We completed a CMC-focused Type D with the FDA in the fourth quarter of 2024. The FDA endorsed our intended Good Manufacturing Practice, or GMP, commercial manufacturing process, proposed analytical methods, and corresponding qualification and validation plans, including key mechanism of action potency release assays. We also established analytical comparability between the clinical product and the product derived from the final commercial manufacturing process, and received FDA permission to use the GMP product in future clinical studies of TSHA-102.

Deprioritized Programs

We have previously deprioritized the evaluation of our clinical product candidates TSHA-105 for SLC13A5, TSHA-118 for CLN1 and TSHA-121 for CLN7. Although we are not currently evaluating the potential of TSHA-105, TSHA-118 and TSHA-121, we may again evaluate any of these in the future as a product candidate as a component of our pipeline expansion plans, or pursue partnerships to advance these programs.

TSHA-118 for CLN1 Disease

CLN1 disease (one of the forms of Batten disease), a lysosomal storage disorder, is a progressive, fatal neurodegenerative disease with early childhood onset that has an estimated incidence of approximately 1 in 138,000 live births worldwide. The estimated prevalence of CLN1 disease is 1,000 patients in the United States and European Union. CLN1 disease is caused by loss-of-function mutations in the CLN1 gene that encodes the enzyme palmitoyl-protein thioesterase-1, a small glycoprotein involved in the degradation of certain lipid-modified proteins. Loss of function mutations in the CLN1 gene causes accumulation of these lipid-modified proteins in cells, eventually leading to aggregation, neuronal cellular dysfunction and ultimately neuronal cell death.

In the infantile-onset form of CLN1 disease, clinical symptoms appear between six to 24 months and include rapid deterioration of speech and motor function, refractory epilepsy, ataxia and visual failure. Infantile-onset CLN1 patients are typically poorly responsive by five years of age and remain noncommunicative until their death, which usually occurs by seven years of age. Late-infantile-onset CLN1 disease begins between two to four years of age with initial visual and cognitive decline followed by the development of ataxia and myoclonus, or quick, involuntary muscle jerks. Juvenile-onset CLN1 disease patients present between the ages of five to ten years old, with vision loss as a first symptom followed by cognitive decline, seizures and motor decline. Approximately 60% of the children diagnosed with CLN1 disease in the United States present with early-onset infantile forms, with the remaining 40% experiencing later-onset childhood forms.

All currently available therapeutic approaches for patients with CLN1 disease are targeted towards the treatment of symptoms, and no disease-modifying therapies have been approved. Gene therapy has shown promise in correcting forms of neuronal ceroid lipofuscinoses diseases that involve mutations in soluble enzymes, in part, due to cross-correction of neighboring non-transduced cells.

We believe that the introduction of a functional *CLN1* gene using an AAV9 vector delivered intrathecally to the CNS offers the potential of a disease-modifying therapeutic approach for this disease. TSHA-118 is a self-complementary AAV9 viral vector that expresses human codon-optimized CLN1 complementary deoxyribonucleic acid under control of the chicken β -actin hybrid promoter. We acquired exclusive worldwide rights to certain intellectual property rights and know-how relating to the research, development and manufacture of TSHA-118 (formerly ABO-202) in August 2020 pursuant to a license agreement with Abeona Therapeutics Inc., or Abeona.

TSHA-118 has been granted orphan drug designation, rare pediatric disease designation and fast track designation from the FDA and orphan drug designation from the European Medicines Agency for the treatment of CLN1 disease.

There is currently an open IND for the CLN1 program. We submitted a CTA filing for TSHA-118 which was approved by Health Canada in 2021. Clinical trial material has been manufactured and released and is now ready for use in a clinical trial setting. We provided investigational clinical trial material for TSHA-118 in CLN1 to support an individual-patient investigator-initiated IND request from RUSH University Medical Center for the treatment of a patient with CLN1 disease.

TSHA-105 for SLC13A5 Deficiency

TSHA-105 is a gene replacement therapy in development for the treatment of SLC13A5 deficiency, a rare autosomal recessive epileptic encephalopathy characterized by the onset of seizures within the first few days of life. SLC13A5 deficiency is caused by bi-allelic loss-of function mutations in the SLC13A5 gene, which codes for a sodium dependent citrate transporter, or NaCT, that is largely expressed in the brain and liver. To date, all tested mutations result in no or a greatly reduced amount of the citrate in the cells. Diminished NaCT function leads to loss of neuronal uptake of citrate and other metabolites such as succinate that are critical to brain energy metabolism and function. Affected children have impairments in gross motor function and speech production with relative preservation of fine motor skills and receptive speech. Currently, there are no approved therapies for

SLC13A5 deficiency, and treatment is largely to address symptoms. The estimated prevalence of SLC13A5 deficiency is 1,900 patients in the United States and European Union.

TSHA-105 is constructed from a codon-optimized human SLC13A5 gene packaged in a self-complementary AAV9 capsid.

We have received orphan drug designation and rare pediatric disease designation from the FDA and orphan drug designation from the European Commission for TSHA-105 for the treatment of epilepsy caused by SLC13A5 deficiency. Clinical trial material has been manufactured and released and is now ready for use in a clinical trial setting.

Other Programs

We have a pipeline of early-stage gene therapy programs targeting CNS diseases that we may progress in the future or advance through potential partnerships.

TSHA-113 for Tauopathies

We are developing TSHA-113 for the treatment of tauopathies. Tauopathies comprise a large subset of neurodegenerative diseases involving the aggregation of microtubule associated protein tau, or MAPT, protein into neurofibrillary or gliofibrillary tangles in the human brain. These include MAPT-associated frontotemporal dementia, or FTD, progressive supranuclear palsy, or PSP, corticobasal degeneration, or CD, and Alzheimer's disease. There are an estimated 11,000 patients in United States and Europe affected by MAPT mediated FTD and 2,000 to 2,500 are affected with MAPT-mediated PSP. and CD, and Alzheimer's disease affects an estimated 6.2 million Americans and 7.8 million Europeans.

Intrathecal delivery of an antisense oligonucleotide, or ASO, targeting Tau mRNA by Biogen/Ionis in a Phase 1 study demonstrated durable, robust, time and dose dependent lowering of tau protein and phospho-tau in cerebrospinal fluid of Alzheimer's disease patients. Buoyed by these results, in August 2022, Biogen started a Phase 2 trial in people with mild cognitive impairment or mild dementia due to Alzheimer's disease. This ASO target validation paved the way for other approaches targeting intercellular tau mRNA (reduce tau protein production), for treating Tauopathies.

Unlike an ASO treatment, which would require repeat lifelong administration, we are developing a one-time treatment for Tauopathies. TSHA-113 is an AAV9 capsid that packages a tau-specific miRNA and is delivered in the cerebrospinal fluid for the treatment of tauopathies. This miRNA targets all six isoforms of tau mRNA.

We tested the efficacy of TSHA-113 in PS19 mice, a validated mouse model for tauopathies. These mice express human MAPT, and they exhibit significant tau pathology, neurodegeneration, loss of body weight and progressive hind-limb paralysis around nine to 12 months of age. We tested the efficacy of our treatment by delivering TSHA-113 to PS19 mice at three months, six months and nine months of age via intracisterna magna injection. We found that the tau mRNA and protein levels were significantly reduced by TSHA-113 treatment. Consistently, the tau seeding assay showed reduced levels of pathological tau in brains from PS19 mice treated with TSHA-113. In addition, TSHA-113 treatment was able to rescue the survival rate, loss in body weight, and the hind limb clasping phenotype in the PS19 mice when treated at three months, six months and nine months of age. Taken together, these results demonstrate that a one-time, vectorized delivery of a tau-specific miRNA is a promising approach for treatment for tauopathies. Ongoing and future work is focused on optimal dose determination for IND-enabling studies.

TSHA-106 for Angelman syndrome

We are developing TSHA-106 for the treatment of Angelman syndrome, a neurodevelopmental disorder caused by a maternal deficiency of the UBE3A gene. Angelman syndrome is characterized by profound developmental delay, ataxia and gait disturbance, sleep disorder, seizures, heightened anxiety, aggression and severe speech impairments. Angelman syndrome affects approximately one per 12,000 to 20,000 patients worldwide.

Angelman syndrome is an imprinting disorder in which the maternal gene is deficient and the paternal copy of UBE3A is intact but silenced by a long non-coding RNA, UBE3A antisense transcript, or UBE3A-ATS. Delivery of an ASO targeting UBE3A-ATS showed promising results in ameliorating Angelman syndrome symptoms in a transgenic mouse model.

We have in-licensed a novel gene replacement therapy from University of North Carolina. This novel construct is designed to express two isoforms of UBE3A mRNA from the same codon optimized transgene cassette and could potentially be a one-time treatment for the disease. The unique design feature allows short and long hUBE3A isoforms expression at a near-endogenous 3:1 (short/long) ratio, a feature that could help to support optimal therapeutic outcomes. Additionally, this construct uses human Synapsin 1 promoter, to limit UBE3A expression primarily in neurons, the primary therapeutic target for treating Angelman syndrome.

In a published study, this dual isoform expressing cassette was packaged into PHP.B capsids and administered by intracerebroventricular injections in neonatal mice models. This treatment significantly improved motor learning and innate behaviors in Angelman syndrome mice (PMID: 34676830). It rendered Angelman syndrome mice resilient to epileptogenesis and associated hippocampal neuropathologies induced by seizure kindling. These results demonstrated the feasibility, tolerability, and therapeutic potential for dual-isoform hUBE3A gene transfer in the treatment of AS in mice.

To advance these findings into translatable interventions, our collaborators packaged the dual isoform expressing cassette into AAV9 capsids and undertook animal proof of concept studies. Overall, these results are highly consistent with the published data describing neonatal ICV delivery of a similar dose of the PHP.B/hUBE3Aopt vector (PMID: 34676830) and support continued development. Ongoing and future work is focused on optimal dose and route of administration determination for IND enabling studies.

There are an estimated 55,000 patients with Angelman syndrome in the United States and Europe.

TSHA-114 for Fragile X Syndrome

We are developing TSHA-114 for the treatment of Fragile X syndrome, the most common single gene cause of autism and cognitive impairment, affecting about one in 6,000 individuals worldwide. Fragile X syndrome is diagnosed around three years of age and characterized by anxiety, aggression, hyperactivity, attention deficits and sleep and communication disruption.

Fragile X syndrome is caused by a pathological expansion of a CGG triplet repeat in the 5' untranslated region of the FMR1 gene. Expansion of the triplet above the normal 5–55 repeats to 200 or more causes hypermethylation of the gene promoter, and shutdown of transcription and translation of the encoded protein, fragile X mental retardation protein, or FMRP. The expanded repeat also induces formation of RNA: DNA heteroduplexes that induces epigenetic gene silencing. Although most patients with Fragile X syndrome do not express FMRP, some individuals with the full mutation produce low amounts of the protein (less than 10% of normal levels). FMRP expression in unaffected persons varies greatly from person to person. Current pharmacotherapeutic treatments for Fragile X syndrome are solely directed towards symptom relief.

We conducted proof of concept studies in animal models of Fragile X (Fmr1 KO) with TSHA-114. No significant adverse effects were observed in behavioral, serological or pathohistological markers up to 12 months after intrathecal administration of TSHA-114 in wild-type mice. TSHA-114 treated FMRKO showed widespread FMRP expression was observed throughout brain post administration. TSHA-114 treated FMRKO mice showed robust suppression of audiogenic seizures and normalization of fear conditioning behavior. In addition, assessment of circadian locomotor activity revealed restoration of hyperactivity and sleep. Assessment of transgene expression and behavioral responses in individual mice demonstrated correlations between the level of FMRP expression and potential drug efficacy.

The results from the study support continued development. Ongoing and future work is focused on optimal dose and route of administration determination for IND enabling studies.

There are an estimated 75,000 patients with Fragile X syndrome in the United States and Europe.

License Agreements

Research, Collaboration and License Agreement with The University of Texas Southwestern Medical Center

In November 2019, we entered into a research, collaboration and license agreement, or the UT Southwestern Agreement, with The Board of Regents of the University of Texas System on behalf of UT Southwestern, as amended in April 2020.

In connection with the UT Southwestern Agreement, we obtained an exclusive, worldwide, royalty-free license under certain patent rights of UT Southwestern and a non-exclusive, worldwide, royalty-free license under certain know-how of UT Southwestern, in each case to make, have made, use, sell, offer for sale and import licensed products for use in certain specified indications. Additionally, we obtained a non-exclusive, worldwide, royalty-free license under certain patents and know-how of UT Southwestern for use in all human uses, with a right of first refusal to obtain an exclusive license under certain of such patent rights and an option to negotiate an exclusive license under other of such patent rights. We are required to use commercially reasonable efforts to develop, obtain regulatory approval for, and commercialize at least one licensed product.

In connection with the UT Southwestern Agreement, we issued to UT Southwestern 2,179,000 shares of our common stock. We do not have any future milestone or royalty obligations to UT Southwestern under the UT Southwestern Agreement, other than costs related to the maintenance of patents.

The UT Southwestern Agreement expires on a country-by-country and licensed product-by-licensed product basis upon the expiration of the last valid claim of a licensed patent in such country for such licensed product. After the initial research term, we may terminate the agreement, on an indication-by-indication and licensed product-by-licensed product basis, at any time upon specified written notice to UT Southwestern. Either party may terminate the agreement upon an uncured material breach of the agreement or insolvency of the other party. In December 2023, we transferred rights to specific indications back to UT Southwestern.

License Agreement with Abeona (CLN1 Disease)

In August 2020, we entered into a license agreement, or the Abeona CLN1 Agreement, with Abeona Therapeutics Inc., or Abeona. In connection with the Abeona CLN1 Agreement, we obtained an exclusive, worldwide, royalty-bearing license, with the right to grant sublicenses under certain patents, know-how and materials originally developed by the University of North Carolina at Chapel Hill and Abeona to research, develop, manufacture, have manufactured, use, and commercialize licensed products for gene therapy for the prevention, treatment, or diagnosis of CLN1 Disease (one of the forms of Batten disease) in humans.

Subject to certain obligations of Abeona, we are obligated to use commercially reasonable efforts to develop at least one product and commercialize at least one product in the United States.

In connection with the license grant, we paid Abeona a one-time upfront license fee of \$3.0 million during fiscal year 2020. We are obligated to pay Abeona up to \$26.0 million in regulatory-related milestones and up to \$30.0 million in sales-related milestones per licensed product and high single-digit royalties on net sales of licensed products. Royalties are payable on a licensed product-by-licensed product and country-by-country basis until the latest of the expiration or revocation or complete rejection of the last licensed patent covering such licensed product in the country where the licensed product is sold, the loss of market exclusivity in such country where the product is sold, or, if no licensed product exists in such country and no market exclusivity exists in such country, ten years from first commercial sale of such licensed product in such country. In addition, concurrent with the Abeona CLN1 Agreement, we entered into a purchase and reimbursement agreement with Abeona, pursuant to which we purchased specified inventory from Abeona and reimbursed Abeona for certain research and development costs previously incurred for total consideration of \$4.0 million paid in fiscal year 2020.

In December 2021 our CTA filing for TSHA-118 for the treatment of CLN1 disease was approved by Health Canada and therefore triggered a regulatory milestone payment in connection with the Abeona CLN1 Agreement. We recorded \$3.0 million within research and development expenses in the consolidated statements of operations for the year ended December 31, 2021. The milestone fee was paid in January 2022 and has been classified as an investing outflow in the consolidated statements of cash flows for the year ended December 31, 2022. No additional milestone payments were made or triggered during the years ended December 31, 2023 and 2024.

The Abeona CLN1 Agreement expires on a country-by-country and licensed product-by-licensed product basis upon the expiration of the last royalty term of a licensed product in such country. Either party may terminate the agreement upon an uncured material breach of the agreement or insolvency of the other party. We may terminate the agreement for convenience upon specified prior written notice to Abeona.

License Agreement with Abeona (Rett Syndrome)

In October 2020, we entered into a license agreement, or the Abeona Rett Agreement, with Abeona pursuant to which we obtained an exclusive, worldwide, royalty-bearing license, with the right to grant sublicenses under certain patents, know-how and materials originally developed by the University of North Carolina at Chapel Hill, the University of Edinburgh and Abeona to research, develop, manufacture, have manufactured, use, and commercialize licensed products for gene therapy and the use of related transgenes for Rett syndrome.

Subject to certain obligations of Abeona, we are required to use commercially reasonable efforts to develop at least one licensed product and commercialize at least one licensed product in the United States.

In connection with the Abeona Rett Agreement, we paid Abeona a one-time upfront license fee of \$3.0 million during fiscal year 2020. We are obligated to pay Abeona up to \$26.5 million in regulatory-related milestones and up to \$30.0 million in sales-related milestones per licensed product and high single-digit royalties on net sales of licensed products. Royalties are payable on a licensed product-by-licensed product and country-by-country basis until the latest of the expiration or revocation or complete rejection of the last licensed patent covering such licensed product in the country where the licensed product is sold, the loss of market exclusivity in such country where the product is sold, or, if no licensed product exists in such country and no market exclusivity exists in such country, ten years from first commercial sale of such licensed product in such country.

In March 2022, our CTA filing for TSHA-102 for the treatment of Rett Syndrome was approved by Health Canada and therefore triggered a regulatory milestone payment in connection with the Rett Agreement. We recorded \$1.0 million within research and development expenses in the consolidated statements of operations for the year ended December 31, 2022. This milestone fee was paid in July 2022. In May 2023, we dosed the first patient with TSHA-102 in the Phase 1/2 REVEAL trial evaluating the safety and preliminary efficacy of TSHA-102 in adult patients with Rett syndrome and therefore triggered a milestone payment in connection with this agreement. We recorded \$3.5 million within research and development expenses in the consolidated statements of operations for the year ended December 31, 2023. This milestone fee was paid in August 2023 and has been classified as an investing cash outflow in the consolidated statements of cash flows for the year ended December 31, 2023. No additional milestone payments were made or triggered in connection with this agreement during the years ended December 31, 2023 and 2024.

The Abeona Rett Agreement expires on a country-by-country and licensed product-by-licensed product basis upon the expiration of the last royalty term of a licensed product in such country. Either party may terminate the agreement upon an uncured material breach of the agreement or insolvency of the other party. We may terminate the agreement for convenience upon specified prior written notice to Abeona.

Option Agreement with Astellas

On October 21, 2022, or the Effective Date, we entered into an Option Agreement, or the Option Agreement with Audentes Therapeutics, Inc. (d/b/a Astellas Gene Therapy), or Astellas.

TSHA-120 Giant Axonal Neuropathy

Under the Option Agreement, we granted to Astellas an exclusive option to obtain an exclusive, worldwide, royalty and milestone-bearing right and license (A) to research, develop, make, have made, use, sell, offer for sale, have sold, import, export and otherwise exploit, or, collectively, Exploit or the Exploitation, the product known, as of the Effective Date, as TSHA-120, or the 120 GAN Product, and any backup products with respect thereto for use in the treatment of GAN or any other gene therapy product for use in the treatment of GAN that is controlled by us or any of our affiliates or with respect to which we or any of our affiliates controls intellectual property rights covering the Exploitation thereof, or a GAN Product, and (B) under any intellectual property rights controlled by us or any of our affiliates with respect to such Exploitation, or the GAN Option. In January 2024, the Company initiated the return of the FDA Investigational New Drug application and transfer of the investigational clinical trial material for TSHA-120 in GAN to NINDS, enabling an opportunity for continued clinical evaluation of TSHA-120 in GAN after the Company discontinued development of TSHA-120 in GAN in September 2023. In January 2024, we gave notice of termination of the GAN License Agreement, and such termination became effective in July 2024 when all licensed rights under the GAN License Agreement reverted to HHF.

TSHA-102 Rett Syndrome

Under the Option Agreement, we also granted to Astellas an exclusive option to obtain an exclusive, worldwide, royalty and milestone-bearing right and license (A) to Exploit any Rett Product (as defined below), and (B) under any intellectual property rights controlled by us or any of our affiliates with respect to such Exploitation, or the Rett Option, and together with the GAN Option, each, an Option. Subject to certain extensions, the Rett Option is exercisable from the Effective Date through a specified period of time following Astellas' receipt of (1) certain clinical data from the female pediatric trial and (2) certain specified data with respect to TSHA-102, or the Rett Option Period related to (i) the product known, as of the Effective Date, as TSHA-102 and any backup products with respect thereto for use in the treatment of Rett syndrome, and (ii) any other gene therapy product for use in the treatment of Rett syndrome that is controlled by us or any of our affiliates or with respect to which we or any of our affiliates controls intellectual property rights covering the Exploitation thereof, or a Rett Product.

The parties have agreed that, if Astellas exercises an Option, the parties will, for a specified period, negotiate a license agreement in good faith on the terms and conditions outlined in the Option Agreement, including payments by Astellas of a to-be-determined upfront payment, certain to-be-determined milestone payments, and certain to-be-determined royalties on net sales of GAN Products and/or Rett Products, as applicable.

Intellectual Property

We actively seek to protect our proprietary technology, inventions, and other intellectual property that is commercially important to the development of our business by a variety of means, for example seeking, maintaining, and defending patent rights, whether developed internally or licensed from third parties. We also may rely on trade secrets and know-how relating to our proprietary technology platform, on continuing technological innovation and on in-licensing opportunities to develop, strengthen and maintain the strength of our position in the field of gene therapy that may be important for the development of our business. We also intend to seek patent protection or rely upon trade secret rights to protect other technologies that may be used to discover and validate

targets, and that may be used to manufacture and develop novel gene therapy products. We are a party to license agreements that give us rights to use specific technologies in our gene therapy products and in manufacturing our products. Additional regulatory protection may also be afforded through data exclusivity, market exclusivity and patent term extensions where available.

As of February 24, 2024, we in-license five U.S. patents, 14 foreign patents, 54 pending foreign patent applications and 13 pending United States utility patent applications. Our policy is to file patent applications to protect technology, inventions and improvements to inventions that may be commercially important to the development of our business. Patent applications and patents directed to specific product candidates are summarized below:

TSHA-102

We in-license from The Board of Regents of The University of Texas System five pending patent applications worldwide directed to a minigene encoding MECP2 packaged into an AAV vector, and methods of using that vector to treat Rett syndrome. Any patents based on these applications, if issued, are expected to expire in 2040, without taking into account any possible patent term adjustment, regulatory extensions, or terminal disclaimers, and assuming payment of all annuity and/or maintenance fees. We also in-license from The Board of Regents of The University of Texas System one issued U.S. patent with claims to an AAV vector comprising a MecP2 transgene and a regulatory region, as well as methods of using the same to treat Rett Syndrome. The issued U.S. Patent will expire on October 27, 2041, assuming all maintenance fees are timely paid.

We also in-license from the University of Edinburgh and the University of Glasgow 10 pending patent applications worldwide directed to MECP2 expression cassettes for gene therapy. Any patents based on these applications, if issued, are expected to expire in 2038, without taking into account any possible patent term adjustment, regulatory extensions, or terminal disclaimers, and assuming payment of all annuity and/or maintenance fees. We also in-license from the University of Edinburgh and the University of Glasgow two Japanese patents, one Australian patent, one Korean patent and one U.S. patent, each with claims to a MECP2 expression cassette and vector comprising the same, as well as their use for treating Rett Syndrome. The Japanese, Australian and Korean patents will expire in 2038 assuming all maintenance fees are timely paid. The U.S. patent expires on October 11, 2040, assuming all maintenance fees are timely paid.

We also in-license from the University of North Carolina at Chapel Hill 10 pending patent applications worldwide directed to feedback-enabled synthetic genes that inhibit MECP2 expression and use of these synthetic genes for treating Rett Syndrome. Any patents based on these applications, if issued, are expected to expire in 2039, without taking into account any possible patent term adjustment, regulatory extensions, or terminal disclaimers, and assuming payment of all annuity and/or maintenance fees. We also in-license from the University of North Carolina at Chapel Hill one Chinese patent with claims to feedback-enabled synthetic genes that inhibit MECP2 expression and use of these synthetic genes for treating Rett Syndrome. This patent will expire in 2039, assuming payment of all annuity and/or maintenance fees.

TSHA-118

We in-license certain patent rights directed to a palmitoyl-protein thioesterase 1-encoding transgene packaged into an AAV vector, and methods of using that vector to treat CLN1 disease (one of the forms of Batten disease). Specifically, pursuant to our license agreement with Abeona Therapeutics, Inc. we have in-licensed seven pending patent applications worldwide assigned to Abeona Therapeutics, Inc and University of North Carolina at Chapel Hill. Any patents based on these applications, if issued, are expected to expire in 2040, without taking into account any possible patent term adjustment, regulatory extensions, or terminal disclaimers, and assuming payment of all annuity and/or maintenance fees.

In addition, pursuant to the Abeona CLN1 agreement, we have sublicensed five pending patent applications worldwide assigned to the University of North Carolina at Chapel Hill. Any patents based on these patent applications, if issued, are expected to expire in 2037, without taking into account any possible patent term adjustment, regulatory extensions, or terminal disclaimers, and assuming payment of all annuity and/or maintenance fees. We have also licensed one Korean patent, one Israeli patent, one Indian patent and one Australian patent with claims to a CLN1 expression cassettes and vector comprising the same, which will expire in 2038 assuming all maintenance fees are timely paid. We have also licensed one U.S. patent with claims to a CLN1 expression cassettes and vector comprising the same, which will expire on January 12, 2039 assuming all maintenance fees are timely paid.

TSHA-105

We in-license from the University of North Carolina at Chapel Hill four pending patent applications worldwide directed to SLC13A5-encoding transgene packaged in an AAV vector and methods of using that vector to treat SLC13A5 deficiency. Any patents based on these applications, if issued, are expected to expire in 2041, without taking into account any possible patent term adjustment, regulatory extensions, or terminal disclaimers, and assuming payment of all annuity and/or maintenance fees.

We also in-license from The Board of Regents of The University of Texas System six pending patent applications worldwide directed to SLC13A5-encoding transgene packaged in an AAV vector and methods of using that vector to treat SLC13A5 deficiency. Any patents based on these applications, if issued, are expected to expire in 2042, without taking into account any possible patent term adjustment, regulatory extensions, or terminal disclaimers, and assuming payment of all annuity and/or maintenance fees.

TSHA-106

We in-license from The Board of Regents of The University of Texas System two pending patent applications worldwide directed to RNA interference (RNAi) constructs targeting UBE3A and methods of using these constructs for the treatment of Angelman Syndrome. Any patents based on these applications, if issued, are expected to expire in 2042, without taking into account any possible patent term adjustment, regulatory extensions, or terminal disclaimers, and assuming payment of all annuity and/or maintenance fees.

We also in-license from the University of North Carolina at Chapel Hill 8 pending patent applications worldwide directed to UBE3A-encoding transgene packaged in an AAV vector and methods of using that vector to Angelman Syndrome. Any patents based on these applications, if issued, are expected to expire in 2040, without taking into account any possible patent term adjustment, regulatory extensions, or terminal disclaimers, and assuming payment of all annuity and/or maintenance fees. We have also licensed one Chinese patent and one Japanese patent with claims to UBE3A-encoding transgene packaged in an AAV vector and methods of using that vector to Angelman Syndrome, which will expire in 2040 assuming all maintenance fees are timely paid.

TSHA-113

We in-license from The Board of Regents of The University of Texas System five pending patent applications worldwide directed to RNA interference (RNAi) constructs targeting MAPT and methods of using these constructs for the treatment of Tauopathies. Any patents based on these applications, if issued, are expected to expire in 2042, without taking into account any possible patent term adjustment, regulatory extensions, or terminal disclaimers, and assuming payment of all annuity and/or maintenance fees.

Fragile X Syndrome

We in-license from The Board of Regents of The University of Texas System three pending patent application worldwide directed to FMR1-encoding transgene packaged in an AAV vector and methods of using that vector to treat disorders associated with aberrant FMR1 expression (such as Fragile X Syndrome). Any patents based on these applications, if issued, are expected to expire in 2043, without taking into account any possible patent term adjustment, regulatory extensions, or terminal disclaimers, and assuming payment of all annuity and/or maintenance fees.

Adult Polyglucosan Body Disease and LaFora Disease

We in-license from The Board of Regents of The University of Texas System one pending U.S. patent application directed to RNA interference (RNAi) constructs targeting GYS1 and methods of using these constructs for the treatment of LaFora Disease and Adult Polyglucosan Body Disease. Any patents based on this application, if issued, is expected to expire in 2042, without taking into account any possible patent term adjustment, regulatory extensions, or terminal disclaimers, and assuming payment of all annuity and/or maintenance fees.

Government Regulation

The U.S. Food and Drug Administration, or 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, quality control, import, export, safety, effectiveness, labeling, packaging, storage, distribution, record keeping, approval, advertising, promotion, marketing, post-approval monitoring and post-approval reporting of biologics such as those we are developing.

Biological products are subject to regulation under the Food, Drug, and Cosmetic Act, or FDCA, and the Public Health Service Act, or PHSA, and other federal, state, local and foreign statutes and regulations. We, along with third-party contractors, will be required to navigate the various preclinical, clinical and commercial approval requirements of the governing regulatory agencies of the countries in which we wish to conduct studies or seek approval or licensure of our product candidates.

U.S. Biologics Regulation

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

- completion of extensive preclinical laboratory tests and animal studies performed in accordance with applicable regulations, including the good laboratory practice, or GLP, regulations;
- submission to the FDA of an IND application, which must become effective before clinical trials may begin;
- approval by an independent institutional review board, or IRB, or ethics committee at each clinical site before the trial is commenced;
- performance of adequate and well-controlled human clinical trials to establish the safety, purity and potency of the proposed biological product candidate for its intended purpose;
- preparation of and submission to the FDA of a biologics license application, or BLA after completion of all pivotal clinical trials;
- a determination by the FDA within 60 days of its receipt of a BLA to file the application for review;
- satisfactory completion of an FDA pre-approval inspection of the manufacturing facility or facilities at which the proposed product is produced to assess compliance with current Good Manufacturing Practice requirements, or cGMPs, and to assure that the facilities, methods and controls are adequate to preserve the biological product's continued safety, purity and potency, and of selected clinical investigation sites to assess compliance with the FDA's good clinical practices, or GCPs;
- satisfactory completion of an FDA Advisory Committee review, if applicable; and
- FDA review and approval, or licensure, of a BLA to permit commercial marketing of the product for particular indications for use in the United States.

Preclinical and Clinical Development

Prior to beginning the first clinical trial with a product candidate, we must submit an IND to the FDA. An IND is a request for authorization from the FDA to administer an investigational new drug product to humans. The central focus of an IND submission is on the general investigational plan and the protocol or protocols for preclinical studies and clinical trials. The IND also includes results of animal and *in vitro* studies assessing the toxicology, pharmacokinetics, pharmacology and pharmacodynamic characteristics of the product, chemistry, manufacturing and controls information, and any available human data or literature to support the use of the investigational product. An IND must become effective before human clinical trials may begin. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day period, raises safety concerns or questions about the proposed clinical trial. 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 the clinical trial can begin. Submission of an IND therefore may or may not result in FDA authorization to begin a clinical trial.

In addition to the submission of an IND to the FDA before initiation of a clinical trial in the United States, certain human clinical trials involving recombinant or synthetic nucleic acid molecules are subject to oversight at the local level as set forth in the National Institutes of Health, or NIH, Guidelines. Specifically, under the NIH Guidelines, supervision of human gene transfer trials includes evaluation and assessment by an Institutional Biosafety Committee, or IBC, a local institutional committee that reviews and oversees research utilizing recombinant or synthetic nucleic acid molecules at that institution. The IBC assesses the safety of the research and identifies any potential risk to public health or the environment, and such review may result in some delay before initiation of a clinical trial. While the NIH Guidelines are not mandatory unless the research in question is being conducted at or sponsored by institutions receiving NIH funding of recombinant or synthetic nucleic acid molecule research, many companies and other institutions not otherwise subject to the NIH Guidelines voluntarily follow them.

Clinical trials involve the administration of the investigational product 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 their participation in any clinical study. Clinical trials are conducted under protocols detailing, among other things, the objectives of the study, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated. A separate submission to the existing IND must be made for each successive clinical trial conducted during product development and for any subsequent protocol amendments. Furthermore, an independent IRB for each site proposing to conduct the clinical trial must review and approve the plan for any clinical trial and its informed consent form before the clinical trial begins at that site, and must monitor the study until completed. Regulatory authorities, the IRB or the sponsor may suspend a clinical trial at any time on various grounds, including a

finding that the subjects are being exposed to an unacceptable health risk or that the trial is unlikely to meet its stated objectives. Some studies also include oversight by an independent group of qualified experts organized by the clinical study sponsor, known as a data safety monitoring board, which provides authorization for whether or not a study may move forward at designated check points based on access to certain data from the study and may halt the clinical trial if it determines that there is an unacceptable safety risk for subjects or other grounds, such as no demonstration of efficacy. There are also requirements governing the reporting of ongoing preclinical studies and clinical trials and clinical study results to public registries.

For purposes of BLA approval of a product candidate, human clinical trials are typically conducted in three sequential phases that may overlap or be combined:

- Phase 1. For gene therapies, the investigational product is initially introduced into patients with the target disease or condition. These studies are designed to test the safety, dosage tolerance, absorption, metabolism and distribution of the investigational product in humans, the side effects associated with increasing doses, and, if possible, to gain early evidence on effectiveness.
- Phase 2. The investigational product is administered to a limited patient population to evaluate the preliminary efficacy, optimal dosages and dosing schedule and to identify possible adverse side effects and safety risks.
- Phase 3. The investigational product is administered to an expanded patient population to further evaluate dosage, to provide statistically significant evidence of clinical efficacy and to further test for safety, generally at multiple geographically dispersed clinical trial sites. These clinical trials are intended to establish the overall risk/benefit ratio of the investigational product and to provide an adequate basis for product approval.

In some cases, the FDA may require, or companies may voluntarily pursue, additional clinical trials after a product is approved to gain more information about the product. These so-called Phase 4 studies may be made a condition to approval of the BLA. 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 candidate and, among other things, must develop methods for testing the identity, strength, quality and purity of the final product, or for biologics, the safety, purity and potency. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the product candidate does not undergo unacceptable deterioration over its shelf life.

During all phases of clinical development, regulatory agencies require extensive monitoring and auditing of all clinical activities, clinical data, and clinical study investigators. The FDA or the sponsor or its data safety monitoring board may suspend a clinical study at any time on various grounds, including a finding that the research patients or patients are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical study at its institution if the clinical study is not being conducted in accordance with the IRB's requirements or if the biological product candidate has been associated with unexpected serious harm to patients. There are also requirements governing the reporting of ongoing clinical trials and completed clinical trial results to public registries. Sponsors of clinical trials of FDA-regulated products, including biologics, are required to register and disclose certain clinical trial information, which is publicly available at www.clinicaltrials.gov.

BLA Submission and Review

Assuming successful completion of all required testing in accordance with all applicable regulatory requirements, the results of product development, nonclinical studies and clinical trials are submitted to the FDA as part of a BLA requesting approval to market the product for one or more indications. The BLA must include all relevant data available from pertinent preclinical studies and clinical trials, 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. The submission of a BLA requires payment of a substantial application user fee to the FDA, unless a waiver or exemption applies. The FDA has sixty days from the applicant's submission of a BLA to either issue a refusal to file letter or accept the BLA for filing, indicating that it is sufficiently complete to permit substantive review.

Once a BLA has been accepted for filing, the FDA's goal is to review standard applications within ten months after it accepts the application for filing, or, if the application qualifies for priority review, six months after the FDA accepts the application for filing. In both standard and priority reviews, the review process is often significantly extended by FDA requests for additional information or clarification. The FDA reviews a BLA to determine, among other things, whether a product is safe, pure and potent for its intended use, and whether the facility in which it is manufactured, processed, packed or held meets standards designed to assure and preserve the product's identity, safety, strength, quality, potency and purity. The FDA may convene an advisory committee to provide clinical insight on application review questions. Before approving a BLA, the FDA will typically inspect the facility or facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities

are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving a BLA, the FDA will typically inspect one or more clinical sites to assure compliance with GCPs. If the FDA determines that the application, manufacturing process or manufacturing facilities are not acceptable, it will outline the deficiencies in the submission and often will request additional testing or information. Notwithstanding the submission of any requested additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval.

After the FDA evaluates a BLA and conducts inspections of manufacturing facilities where the investigational product and/or its drug substance will be manufactured, the FDA may issue an approval letter or a Complete Response letter. An approval letter authorizes commercial marketing of the product with specific prescribing information for specific indications. A Complete Response letter will describe all of the deficiencies that the FDA has identified in the BLA, except that where the FDA determines that the data supporting the application are inadequate to support approval, the FDA may issue the Complete Response letter without first conducting required inspections, testing submitted product lots and/or reviewing proposed labeling. In issuing the Complete Response letter, the FDA may recommend actions that the applicant might take to place the BLA in condition for approval, including requests for additional information or clarification, which may include the potential requirement for additional clinical studies. The FDA may delay or refuse approval of a BLA if applicable regulatory criteria are not satisfied, require additional testing or information and/or require post-marketing testing and surveillance to monitor safety or efficacy of a product.

If regulatory approval of a product is granted, such approval will be granted for particular indications and may entail limitations on the indicated uses for which such product may be marketed. For example, the FDA may approve the BLA with a Risk Evaluation and Mitigation Strategy, or REMS, to ensure the benefits of the product outweigh its risks. A REMS is a safety strategy to manage a known or potential serious risk associated with a product and to enable patients to have continued access to such medicines by managing their safe use, and could include medication guides, physician communication plans, or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. The FDA also may condition approval on, among other things, changes to proposed labeling or the development of adequate controls and specifications. Once approved, the FDA may withdraw the product approval if compliance with pre- and post-marketing requirements is not maintained or if problems occur after the product reaches the marketplace. The FDA may require one or more Phase 4 post-market studies and surveillance to further assess and monitor the product's safety and effectiveness after commercialization, and may limit further marketing of the product based on the results of these post-marketing studies.

Expedited Development and Review Programs

The FDA offers a number of expedited development and review programs for qualifying product candidates. The fast track program is intended to expedite or facilitate the process for reviewing new products that meet certain criteria. Specifically, new products are eligible for fast track designation if they are intended to treat a serious or life-threatening disease or condition and demonstrate the potential to address unmet medical needs for the disease or condition. Fast track designation applies to the combination of the product and the specific indication for which it is being studied. The sponsor of a fast track product has opportunities for frequent interactions with the review team during product development and, once a BLA is submitted, the product may be eligible for priority review. A fast track product may also be eligible for rolling review, where the FDA may consider for review sections of the BLA on a rolling basis before the complete application is submitted, if the sponsor provides a schedule for the submission of the sections of the BLA, the FDA agrees to accept sections of the BLA and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the BLA.

A product intended to treat a serious or life-threatening disease or condition may also be eligible for breakthrough therapy designation to expedite its development and review. A product can receive breakthrough therapy designation if preliminary clinical evidence indicates that the product, alone or in combination with one or more other drugs or biologics, may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. The designation includes all of the fast track program features, as well as more intensive FDA interaction and guidance beginning as early as Phase 1 and an organizational commitment to expedite the development and review of the product, including involvement of senior managers.

A regenerative medicine advanced therapy, or RMAT, is defined as cell therapies, therapeutic tissue engineering products, human cell and tissue products, and combination products using any such therapies or products. Gene therapies, including genetically modified cells that lead to a durable modification of cells or tissues may meet the definition of a Regenerative Medicine Therapy. The RMAT program is intended to facilitate efficient development and expedite review of RMATs, which are intended to treat, modify, reverse, or cure a serious or life-threatening disease or condition. A new drug application or a BLA for an RMAT may be eligible for priority review or accelerated approval through (1) surrogate or intermediate endpoints reasonably likely to predict long-term clinical benefit or (2) reliance upon data obtained from a meaningful number of sites. Benefits of such designation also include early interactions with FDA to discuss any potential surrogate or intermediate endpoint to be used to support accelerated approval. A

Regenerative Medicine Therapy that is granted accelerated approval and is subject to post-approval requirements may fulfill such requirements through the submission of clinical evidence, clinical studies, patient registries, or other sources of real-world evidence, such as electronic health records; the collection of larger confirmatory data sets; or post-approval monitoring of all patients treated with such therapy prior to its approval.

Any marketing application for a biologic submitted to the FDA for approval, including a product with a fast track designation and/or breakthrough therapy designation, may be eligible for other types of FDA programs intended to expedite the FDA review and approval process, such as priority review and accelerated approval. A product is eligible for priority review if it has the potential to provide a significant improvement in the treatment, diagnosis or prevention of a serious disease or condition. For original BLAs, priority review designation means the FDA's goal is to take action on the marketing application within six months of the 60-day filing date.

Additionally, products studied for their safety and effectiveness in treating serious or life-threatening diseases or conditions may receive accelerated approval upon a determination that the product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. As a condition of accelerated approval, the FDA will generally require the sponsor to perform adequate and well-controlled post-marketing clinical studies to verify and describe the anticipated effect on irreversible morbidity or mortality or other clinical benefit. In addition, the FDA currently requires as a condition for accelerated approval pre-approval of promotional materials, which could adversely impact the timing of the commercial launch of the product.

Fast track designation, breakthrough therapy designation, RMAT designation, priority review and accelerated approval do not change the standards for approval but may expedite the development or approval process. Even if a product qualifies for one or more of these programs, the FDA may later decide that the product no longer meets the conditions for qualification or decide that the time period for FDA review or approval will not be shortened.

Orphan Drug Designation

Under the Orphan Drug Act, the FDA may grant orphan designation to a drug or biologic intended to treat a rare disease or condition, which is a disease or condition that affects fewer than 200,000 individuals in the United States, or 200,000 or more than individuals in the United States for which there is no reasonable expectation that the cost of developing and making available in the United States a drug or biologic for this type of disease or condition will be recovered from sales in the United States for that drug or biologic. Orphan drug designation must be requested before submitting a BLA. After the FDA grants orphan drug designation, the generic identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. The orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review or approval process.

If a product that has orphan drug designation subsequently receives the first FDA approval for the disease for which it has such designation, the product is entitled to orphan drug exclusive approval (or exclusivity), which means that the FDA may not approve any other applications, including a full BLA, to market the same biologic for the same indication for seven years, except in limited circumstances, such as a showing of clinical superiority to the product with orphan drug exclusivity or if the holder of the orphan drug exclusivity cannot assure the availability of sufficient quantities of the orphan drug to meet the needs of patients with the disease or condition for which the drug was designated. Orphan drug exclusivity does not prevent the FDA from approving a different drug or biologic for the same disease or condition, or the same drug or biologic for a different disease or condition. Among the other benefits of orphan drug designation are tax credits for certain research and a waiver of the BLA application fee.

A designated orphan drug may not receive orphan drug exclusivity if it is approved for a use that is broader than the indication for which it received orphan designation. In addition, exclusive marketing rights in the United States may be lost if the FDA later determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantities of the product to meet the needs of patients with the rare disease or condition.

Rare Pediatric Disease Designation and Priority Review Vouchers

Under the FDCA, as amended, the FDA incentivizes the development of drugs and biologics that meet the definition of a "rare pediatric disease," defined to mean a serious or life-threatening disease in which the serious or life-threatening manifestations primarily affect individuals aged from birth to 18 years and the disease affects fewer than 200,000 individuals in the United States or affects 200,000 or more in the United States and for which there is no reasonable expectation that the cost of developing and making in the United States a drug for such disease or condition will be received from sales in the United States of such drug. The sponsor of a product candidate for a rare pediatric disease may be eligible for a voucher that can be used to obtain a priority review for a

subsequent human drug or biologic application after the date of approval of the rare pediatric disease drug product, referred to as a priority review voucher, or PRV. A sponsor may request rare pediatric disease designation from the FDA prior to the submission of its NDA or BLA. A rare pediatric disease designation does not guarantee that a sponsor will receive a PRV upon approval of its NDA or BLA. Moreover, a sponsor who chooses not to submit a rare pediatric disease designation request may nonetheless receive a PRV upon approval of their marketing application if they request such a voucher in their original marketing application and meet all of the eligibility criteria. If a PRV is received, it may be sold or transferred an unlimited number of times. Congress has extended the PRV program until December 20, 2024, with the potential for PRVs to be granted until September 30, 2026.

Post-Approval Requirements

Any products manufactured or distributed by us pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to record-keeping, reporting of adverse experiences, periodic reporting, product sampling and distribution, and advertising and promotion of the product. 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 the FDA assesses an annual program fee for each product identified in an approved BLA. Biologic manufacturers and their subcontractors are required to register their establishments with the FDA and certain state agencies and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMPs, which impose certain procedural and documentation requirements upon us and our third-party manufacturers. Changes to the manufacturing process are strictly regulated, and, depending on the significance of the change, may require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMPs 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 cGMPs and other aspects of regulatory compliance.

The FDA may withdraw approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical 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;
- consent decrees, corporate integrity agreements, debarment or exclusion from federal healthcare programs;
- mandated modification of promotional materials and labeling and the issuance of corrective information;
- the issuance of safety alerts, Dear Healthcare Provider letters, press releases and other communications containing warnings or other safety information about the product; or
- injunctions or the imposition of civil or criminal penalties.

The FDA closely regulates the marketing, labeling, advertising and promotion of biologics. A company can make only those claims relating to safety and efficacy, purity and potency that are approved by the FDA 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. Failure to comply with these requirements can result in, among other things, adverse publicity, warning letters, corrective advertising and potential civil and criminal penalties. Physicians may prescribe legally available products for uses that are not described in the product's labeling and that differ from those tested by us and approved by the FDA. Such off-label uses are common across medical specialties. Physicians may believe that such off-label uses are the best treatment for many patients in varied

circumstances. The FDA does not regulate the behavior of physicians in their choice of treatments. The FDA does, however, restrict manufacturer's communications on the subject of off-label use of their products.

Biosimilars and Reference Product Exclusivity

The Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or collectively the ACA, includes a subtitle called the Biologics Price Competition and Innovation Act, or BPCIA, which created an abbreviated approval pathway for biological products that are biosimilar to or interchangeable with an FDA-approved reference biological product. The FDA has issued several guidance documents outlining an approach to review and approval of biosimilars.

Biosimilarity, which requires that there be no clinically meaningful differences between the biological product and the reference product in terms of safety, purity, and potency, can be shown through analytical studies, animal studies, and a clinical study or studies. Interchangeability requires that a product is biosimilar to the reference product and the product must demonstrate that it can be expected to produce the same clinical results as the reference product in any given patient and, for products that are administered multiple times to an individual, the biologic and the reference biologic may be alternated or switched after one has been previously administered without increasing safety risks or risks of diminished efficacy relative to exclusive use of the reference biologic.

Under the BPCIA, an application for a biosimilar product may not be submitted to the FDA until four years following the date that the reference product was first licensed by the FDA. In addition, the approval of a biosimilar product may not be made effective by the FDA until 12 years from the date on which the reference product was first licensed. During this 12-year period of exclusivity, another company may still market a competing version of the reference product if the FDA approves a full BLA for the competing product containing that applicant's own preclinical data and data from adequate and well-controlled clinical trials to demonstrate the safety, purity and potency of its product. The BPCIA also created certain exclusivity periods for biosimilars approved as interchangeable products.

The BPCIA is complex and continues to be interpreted and implemented by the FDA. In addition, government proposals have sought to reduce the 12-year reference product exclusivity period. Other aspects of the BPCIA, some of which may impact the BPCIA exclusivity provisions, have also been the subject of litigation. As a result, the ultimate impact of the BPCIA is subject to significant uncertainty.

Foreign Regulation

In order to market any product outside of the United States, we would need to comply with numerous and varying regulatory requirements of other countries and jurisdictions regarding quality, safety, and efficacy and governing, among other things, clinical trials, marketing authorization, commercial sales and distribution of our products. Whether or not we obtain FDA approval for a product, we would need to obtain the necessary approvals by the comparable foreign regulatory authorities before we can commence clinical trials or marketing of the product in foreign countries and jurisdictions. Although many of the issues discussed above with respect to the United States apply similarly in the context of the European Union, the approval process varies between countries and jurisdictions and can involve additional product testing and additional administrative review periods. The time required to obtain approval in other countries and jurisdictions might differ from and be longer than that required to obtain FDA approval. Regulatory approval in one country or jurisdiction does not ensure regulatory approval in another, but a failure or delay in obtaining regulatory approval in one country or jurisdiction may negatively impact the regulatory process in others.

EU Regulation of medicinal products

Clinical Trials in the European Union

Similarly to the United States, the various phases of non-clinical and clinical research in the European Union are subject to significant regulatory controls. In the European Union, clinical trials are governed by the Clinical Trials Regulation (EU) No 536/2014, or CTR, which entered into application on January 31, 2022 repealing and replacing the former Clinical Trials Directive 2001/20, or CTD.

The CTR is intended to harmonize and streamline clinical trial authorizations, simplify adverse-event reporting procedures, improve the supervision of clinical trials and increase transparency. Specifically, the Regulation, which is directly applicable in all EU Member States, introduces a streamlined application procedure through a single-entry point, the "EU portal", the Clinical Trials Information System, or CTIS; a single set of documents to be prepared and submitted for the application; as well as simplified reporting procedures for clinical trial sponsors. A harmonized procedure for the assessment of applications for clinical trials has been introduced and is divided into two parts. Part I assessment is led by the competent authorities of a reference Member State selected by the trial sponsor and relates to clinical trial aspects that are considered to be scientifically harmonized across EU Member States. This

assessment is then submitted to the competent authorities of all concerned Member States in which the trial is to be conducted for their review. Part II is assessed separately by the competent authorities and Ethics Committees in each concerned EU Member State. Individual EU Member States retain the power to authorize the conduct of clinical trials on their territory. The CTR foresaw a three-year transition period that ended on January 31, 2025. Since this date, all new or ongoing trials are subject to the provisions of the CTR.

In all cases, clinical trials must be conducted in accordance with GCP and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki. Medicines used in clinical trials, including ATMPs, must be manufactured in accordance with the guidelines on cGMP and in a GMP licensed facility, which can be subject to GMP inspections.

EU Review and approval process

In the European Union, medicinal products can only be commercialized after a related marketing authorization, or MA, has been granted. To obtain an MA for a product in the European Union, an applicant must submit a Marketing Authorization Application, or MAA, either under a centralized procedure administered by the European Medicines Agency, or EMA, or one of the procedures administered by the competent authorities of EU Member States (decentralized procedure, national procedure or mutual recognition procedure). An MA may be granted only to an applicant established in the European Union.

The centralized procedure provides for the grant of a single MA by the European Commission that is valid throughout the EEA (which is comprised of the 27 EU Member States plus Norway, Iceland and Liechtenstein). Pursuant to Regulation (EC) No 726/2004, the centralized procedure is compulsory for specific products, including for (i) medicinal products derived from biotechnological processes, (ii) products designated as orphan medicinal products, (iii) advanced therapy medicinal products, or ATMPs, and (iv) products with a new active substance indicated for the treatment of HIV/AIDS, cancer, neurodegenerative diseases, diabetes, auto-immune and other immune dysfunctions and viral diseases. For products with a new active substance indicated for the treatment of other diseases and products that are highly innovative or for which a centralized process is in the interest of patients, authorization through the centralized procedure is optional on related approval.

Under the centralized procedure, the EMA's Committee for Medicinal Products for Human Use, or CHMP, conducts the initial assessment of a product. The CHMP is also responsible for several post-authorization and maintenance activities, such as the assessment of modifications or extensions to an existing MA. The maximum timeframe for the evaluation of an MAA under the centralized procedure is 210 days, excluding clock stops when additional information or written or oral explanation is to be provided by the applicant in response to questions of the CHMP. Accelerated assessment may be granted by the CHMP in exceptional cases, when a medicinal product targeting an unmet medical need is expected to be of major interest from the point of view of public health and, in particular, from the viewpoint of therapeutic innovation. If the CHMP accepts a request for accelerated assessment, the time limit of 210 days will be reduced to 150 days (excluding clock stops). The CHMP can, however, revert to the standard time limit for the centralized procedure if it considers that it is no longer appropriate to conduct an accelerated assessment.

Unlike the centralized authorization procedure, the decentralized MA procedure requires a separate application to, and leads to separate approval by, the competent authorities of each EU Member State in which the product is to be marketed. This application is identical to the application that would be submitted to the EMA for authorization through the centralized procedure. The reference EU Member State prepares a draft assessment and drafts of the related materials within 120 days after receipt of a valid application. The resulting assessment report is submitted to the concerned EU Member States who, within 90 days of receipt, must decide whether to approve the assessment report and related materials. If a concerned EU Member State cannot approve the assessment report and related materials due to concerns relating to a potential serious risk to public health, disputed elements may be referred to the Heads of Medicines Agencies' Coordination Group for Mutual Recognition and Decentralised Procedures – Human, or CMDh, for review. The subsequent decision of the European Commission is binding on all EU Member States.

The mutual recognition procedure allows companies that have a medicinal product already authorized in one EU Member State to apply for this authorization to be recognized by the competent authorities in other EU Member States. Like the decentralized procedure, the mutual recognition procedure is based on the acceptance by the competent authorities of the EU Member States of the MA of a medicinal product by the competent authorities of other EU Member States. The holder of a national MA may submit an application to the competent authority of an EU Member State requesting that this authority recognize the MA delivered by the competent authority of another EU Member State.

An MA has, in principle, an initial validity of five years. The MA may be renewed after five years on the basis of a re-evaluation of the risk-benefit balance by the EMA or by the competent authority of the EU Member State in which the original MA was granted. To support the application, the MA holder must provide the EMA or the competent authority with a consolidated version of the Common Technical Document providing up-to-date data concerning the quality, safety and efficacy of the product, including all variations introduced since the MA was granted, at least nine months before the MA ceases to be valid. The European Commission or

the competent authorities of the EU Member States may decide on justified grounds relating to pharmacovigilance, to proceed with one further five-year renewal period for the MA. Once subsequently definitively renewed, the MA shall be valid for an unlimited period. Any authorization which is not followed by the actual placing of the medicinal product on the EU market (for a centralized MA) or on the market of the authorizing EU Member State within three years after authorization ceases to be valid (the so-called sunset clause).

Innovative products that target an unmet medical need and are expected to be of major public health interest may be eligible for a number of expedited development and review programs, such as the Priority Medicines, or PRIME, scheme, which provides incentives similar to the breakthrough therapy designation in the U.S. PRIME is a voluntary scheme aimed at enhancing the EMA's support for the development of medicinal products that target unmet medical needs. Eligible products must target conditions for which there is an unmet medical need (there is no satisfactory method of diagnosis, prevention or treatment in the European Union or, if there is, the new medicinal product will bring a major therapeutic advantage) and they must demonstrate the potential to address the unmet medical need by introducing new methods of therapy or improving existing ones. Benefits accrue to sponsors of product candidates with PRIME designation, including but not limited to, early and proactive regulatory dialogue with the EMA, frequent discussions on clinical trial designs and other development program elements, and potentially accelerated MAA assessment once a dossier has been submitted.

In the European Union, a "conditional" MA may be granted in cases where all the required safety and efficacy data are not yet available. The European Commission may grant a conditional MA for a medicinal product if it is demonstrated that all of the following criteria are met: (i) the benefit-risk balance of the medicinal product is positive; (ii) it is likely that the applicant will be able to provide comprehensive data post-authorization; (iii) the medicinal product fulfils an unmet medical need; and (iv) the benefit of the immediate availability to patients of the medicinal product is greater than the risk inherent in the fact that additional data are still required. The conditional MA is subject to conditions to be fulfilled for generating the missing data or ensuring increased safety measures. It is valid for one year and must be renewed annually until all related conditions have been fulfilled. Once any pending studies are provided, the conditional MA can be converted into a traditional MA. However, if the conditions are not fulfilled within the timeframe set by the EMA and approved by the European Commission, the MA will cease to be renewed.

An MA may also be granted "under exceptional circumstances" where the applicant can show that it is unable to provide comprehensive data on efficacy and safety under normal conditions of use even after the product has been authorized and subject to specific procedures being introduced. These circumstances may arise in particular when the intended indications are very rare and, in the state of scientific knowledge at that time, it is not possible to provide comprehensive information, or when generating data may be contrary to generally accepted ethical principles. Like a conditional MA, an MA granted in exceptional circumstances is reserved to medicinal products intended to be authorized for treatment of rare diseases or unmet medical needs for which the applicant does not hold a complete data set that is required for the grant of a standard MA. However, unlike the conditional MA, an applicant for authorization in exceptional circumstances is not subsequently required to provide the missing data. Although the MA "under exceptional circumstances" is granted definitively, the risk-benefit balance of the medicinal product is reviewed annually, and the MA will be withdrawn if the risk-benefit ratio is no longer favorable.

Advanced Therapy Medicinal Products in the European Union

Advanced Therapy Medicinal Products, or ATMPs, include gene therapy products as well as somatic cell therapy products and tissue engineered products. The grant of marketing authorization in the European Union for products containing viable human tissues or cells such as gene therapy medicinal products is governed by Regulation (EC) No. 1394/2007 on ATMPs, read in combination with Directive (EC) No. 2001/83 of the European Parliament and of the Council, commonly known as the Community code on medicinal products. Regulation (EC) No. 1394/2007 establishes specific rules concerning the authorization, supervision and pharmacovigilance of gene therapy medicinal products, somatic cell therapy medicinal products and tissue engineered products. Manufacturers of advanced therapy medicinal products must demonstrate the quality, safety and efficacy of their products to the EMA which is required to provide an opinion regarding the application for marketing authorization. The European Commission grants or refuses marketing authorization in light of the opinion delivered by the EMA.

Products made from substances of human origin must also comply with Regulation (EU) 2024/1938 on standards of quality and safety for substances of human origin intended for human application. This Regulation describes the conditions and quality requirements which must be applied when sourcing the substances of human origin intended for manufacturing of such medicinal products and removed divergences between EU Member States that were present under the (now repealed) Directive (EC) No. 2004/23.

Pediatric Development

In the European Union, Regulation (EC) No 1901/2006 provides that all MAAs for new medicinal products have to include the results of trials conducted in the pediatric population, in compliance with a pediatric investigation plan, or PIP, agreed with the

EMA's Pediatric Committee, or PDCO. The PIP sets out the timing and measures proposed to generate data to support a pediatric indication of the medicinal product for which MA is being sought. The PDCO can grant a deferral of the obligation to implement some or all of the measures provided in the PIP until there are sufficient data to demonstrate the efficacy and safety of the product in adults. Further, the obligation to provide pediatric clinical trial data can be waived by the PDCO when these data are not needed or appropriate because the product is likely to be ineffective or unsafe in children, the disease or condition for which the product is intended occurs only in adult populations, or when the product does not represent a significant therapeutic benefit over existing treatments for pediatric patients. Once the MA is obtained in all EU Member States and study results are included in the product information, even when negative, the product is eligible for a six-month extension to the Supplementary Protection Certificate, or SPC, if any is in effect at the time of authorization or, in the case of orphan medicinal products, a two-year extension of orphan market exclusivity.

Manufacturing Regulation in the European Union

In addition to an MA, various other requirements apply to the manufacturing and placing on the EU market of medicinal products. The manufacturing of medicinal products in the European Union requires a manufacturing authorization and import of medicinal products into the European Union requires a manufacturing authorization allowing for import. The manufacturing authorization holder must comply with various requirements set out in the applicable EU laws, regulations and guidance, including EU cGMP standards. Similarly, the distribution of medicinal products within the European Union is subject to compliance with the applicable EU laws, regulations and guidelines, including the requirement to hold appropriate authorizations for distribution granted by the competent authorities of EU Member States. Marketing authorization holders and/or manufacturing and import authorization, or MA holders and/or distribution authorization holders may be subject to civil, criminal or administrative sanctions, including suspension of manufacturing authorization, in case of non-compliance with the EU or EU Member States' requirements applicable to the manufacturing of medicinal products.

Data and Market Exclusivity in the European Union

The European Union provides opportunities for data and market exclusivity related to MAs. Upon receiving an MA, innovative medicinal products are generally entitled to receive eight years of data exclusivity and 10 years of market exclusivity. Data exclusivity, if granted, prevents regulatory authorities in the European Union from referencing the innovator's data to assess a generic application or biosimilar application for eight years from the date of authorization of the innovative product, after which a generic or biosimilar MAA can be submitted, and the innovator's data may be referenced. The market exclusivity period prevents a successful generic or biosimilar applicant from commercializing its product in the European Union until 10 years have elapsed from the initial MA of the reference product in the European Union. The overall ten-year period may, occasionally, be extended for a further year to a maximum of 11 years if, during the first eight years of those ten years, the MA holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to their authorization, are held to bring a significant clinical benefit in comparison with existing therapies. However, there is no guarantee that a product will be considered by the European Union's regulatory authorities to be a new chemical/biological entity, and products may not qualify for data exclusivity.

In the European Union, there is a special regime for biosimilars, or biological medicinal products that are similar to a reference medicinal product but that do not meet the definition of a generic medicinal product. For such products, the results of appropriate preclinical or clinical trials must be provided in support of an application for MA. Guidelines from the EMA detail the type of quantity of supplementary data to be provided for different types of biological product.

Orphan Designation in the European Union

In the European Union, Regulation (EC) No. 141/2000, as implemented by Regulation (EC) No. 847/2000 provides that a medicinal product can be designated as an orphan medicinal product by the European Commission if its sponsor can establish that: (i) the product is intended for the diagnosis, prevention or treatment of life-threatening or chronically debilitating conditions; (ii) either (a) such conditions affect not more than 5 in 10,000 persons in the European Union when the application is made, or (b) the product without the benefits derived from orphan status, would not generate sufficient return in the European Union to justify the necessary investment in developing the medicinal product; and (iii) there exists no satisfactory authorized method of diagnosis, prevention, or treatment of the condition that has been authorized in the European Union, or even if such method exists, the product will be of significant benefit to those affected by that condition.

Regulation (EC) No 847/2000 sets out further provisions for implementation of the criteria for designation of a medicinal product as an orphan medicinal product. An application for the designation of a medicinal product as an orphan medicinal product must be submitted at any stage of development of the medicinal product but before filing of an MAA. An MA for an orphan medicinal product may only include indications designated as orphan. For non-orphan indications treated with the same active pharmaceutical ingredient, a separate marketing authorization has to be sought.

Orphan medicinal product designation entitles an applicant to incentives such as fee reductions or fee waivers, protocol assistance, and access to the centralized marketing authorization procedure. Upon grant of a marketing authorization, orphan medicinal products are entitled to a ten-year period of market exclusivity for the approved therapeutic indication, which means that the EMA cannot accept another marketing authorization application or accept an application to extend for a similar product and the European Commission cannot grant a marketing authorization for the same indication for a period of ten years. The period of market exclusivity is extended by two years for orphan medicinal products that have also complied with an agreed PIP. No extension to any supplementary protection certificate can be granted on the basis of pediatric studies for orphan indications. Orphan medicinal product designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process.

The period of market exclusivity may, however, be reduced to six years if, at the end of the fifth year, it is established that the product no longer meets the criteria on the basis of which it received orphan medicinal product designation, including where it can be demonstrated on the basis of available evidence that the original orphan medicinal product is sufficiently profitable not to justify maintenance of market exclusivity or where the prevalence of the condition has increased above the threshold. Additionally, an MA may be granted to a similar medicinal product with the same orphan indication during the 10 year period if: (i) if the applicant consents to a second original orphan medicinal product application, (ii) if the manufacturer of the original orphan medicinal product is unable to supply sufficient quantities; or (iii) if the second applicant can establish that its product, although similar, is safer, more effective or otherwise clinically superior to the original orphan medicinal product. A company may voluntarily remove a product from the register of orphan products.

Post-authorization Requirements

Where an MA is granted in relation to a medicinal product in the European Union, the holder of the MA is required to comply with a range of regulatory requirements applicable to the manufacturing, marketing, promotion and sale of medicinal products. Similar to the United States, both MA holders and manufacturers of medicinal products are subject to comprehensive regulatory oversight by the EMA, the European Commission and/or the competent regulatory authorities of the individual EU Member States. The holder of an MA must establish and maintain a pharmacovigilance system and appoint an individual qualified person for pharmacovigilance who is responsible for oversight of that system. Key obligations include expedited reporting of suspected serious adverse reactions and submission of periodic safety update reports, or PSURs.

All new MAAs must include a risk management plan, or RMP, describing the risk management system that the company will put in place and documenting measures to prevent or minimize the risks associated with the product. The regulatory authorities may also impose specific obligations as a condition of the MA. Such risk-minimization measures or post-authorization obligations may include additional safety monitoring, more frequent submission of PSURs, or the conduct of additional clinical trials or post-authorization safety studies.

In the European Union, the advertising and promotion of medicinal products are subject to both European Union and EU Member States' laws governing promotion of medicinal products, interactions with physicians and other healthcare professionals, misleading and comparative advertising and unfair commercial practices. General requirements for advertising and promotion of medicinal products, such as direct-to-consumer advertising of prescription medicinal products are established in EU law. However, the details are governed by regulations in individual EU Member States and can differ from one country to another. For example, applicable laws require that promotional materials and advertising in relation to medicinal products comply with the product's Summary of Product Characteristics, or SmPC, which may require approval by the competent national authorities in connection with an MA. The SmPC is the document that provides information to physicians concerning the safe and effective use of the product. Promotional activity that does not comply with the SmPC is considered off-label and is prohibited in the European Union.

Other Healthcare Laws and Compliance Requirements

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: the U.S. federal Anti-Kickback Statute, the civil False Claims Act, the Health Insurance Portability and Accountability Act of 1996, or HIPAA, and similar foreign, federal and state fraud and abuse, transparency and privacy laws.

The U.S. federal Anti-Kickback Statute prohibits, among other things, persons and entities from knowingly and willfully soliciting, receiving, offering or paying remuneration, to induce, or in return for, either the referral of an individual, or the purchase or recommendation of an item or service for which payment may be made under any federal healthcare program. The term remuneration has been interpreted broadly to include anything of value, including stock options. The U.S. federal Anti-Kickback Statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on one hand and prescribers, purchasers, and others on the other hand. There are a number of statutory exceptions and regulatory safe harbors protecting some common activities from prosecution, but they are drawn narrowly, and practices that involve remuneration, such as consulting agreements, that may be alleged

to be intended to induce prescribing, purchasing or recommending may be subject to scrutiny if they do not qualify for an exception or safe harbor. Failure to meet all of the requirements of a particular applicable statutory exception or regulatory safe harbor does not make the conduct per se illegal under the U.S. federal Anti-Kickback Statute. Instead, the legality of the arrangement will be evaluated on a case-by-case basis based on a cumulative review of all of its facts and circumstances. Our practices may not in all cases meet all of the criteria for protection under a statutory exception or regulatory safe harbor. 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. In addition, a claim including items or 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.

Civil and criminal false claims laws, and civil monetary penalty laws, including the civil False Claims Act, which can be enforced through civil whistleblower or qui tam actions, prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment to the federal government, including federal healthcare programs, that are false or fraudulent. For example, the civil False Claims Act prohibits any person 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. A claim includes “any request or demand” for money or property presented to the U.S. government. Several pharmaceutical and other healthcare companies have been prosecuted under these laws for allegedly providing free product to customers with the expectation that the customers would bill federal programs for the product.

HIPAA created additional federal civil and criminal liability for, among other things, knowingly and willfully executing a scheme to defraud any healthcare benefit program, or obtain, by means of false or fraudulent pretenses, representations, or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program, regardless of the payor (e.g., public or private) and knowingly and willfully falsifying, concealing, or covering up by any trick or device a material fact or making any materially false statements in connection with the delivery of, or payment for, healthcare benefits, items or services relating to healthcare matters. Similar to the federal Anti-Kickback Statute, a person or entity can be found guilty of violating HIPAA without actual knowledge of the statute or specific intent to violate it. In addition, HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, or HITECH, and their respective implementing regulations, impose certain requirements on HIPAA covered entities, which include certain healthcare providers, healthcare clearing houses and health plans, and individuals and entities that provide services on their behalf that involve individually identifiable health information, known as business associates, relating to the privacy, security and transmission of individually identifiable health information, as well as their covered subcontractors. HITECH also created new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorneys’ fees and costs associated with pursuing federal civil actions.

The U.S. 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 annually report to the Centers for Medicare & Medicaid Services, or CMS, information related to payments or other transfers of value made to physicians (currently defined to include doctors, dentists, optometrists, podiatrists and chiropractors), other health care professionals (such as physician assistants and nurse practitioners) and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members.

We are also subject to additional similar U.S. state and foreign law equivalents of each of the above federal laws, such as anti-kickback and false claims laws which may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third party payors, including private insurers, or that apply regardless of payor, state and foreign laws which require pharmaceutical companies to comply with the pharmaceutical industry’s voluntary compliance guidelines and the relevant compliance guidance promulgated by the government, state, local and foreign laws which require pharmaceutical companies to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures, state and foreign laws which require the reporting of information related to drug pricing, state, local and foreign laws requiring the registration of pharmaceutical sales representatives, and state and foreign laws governing the privacy and security of health information which, in some cases, differ from each other in significant ways, and may not have the same effect, thus complicating compliance efforts. If our operations are found to be in violation of any of such laws or any other governmental regulations that apply, we may be subject to penalties, including, without limitation, significant civil, criminal and administrative penalties, imprisonment 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.

Coverage and Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of any pharmaceutical or biological product for which we obtain regulatory approval. Sales of any product, if approved, 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, if any, for such product by third-party payors. Decisions regarding whether to cover any of our product candidates, if approved, the extent of coverage and amount of reimbursement to be provided are made on a plan-by-plan basis. Further, no uniform policy for coverage and reimbursement exists in the United States, and coverage and reimbursement can differ significantly from payor to payor.

Nonetheless, product candidates may not be considered medically necessary or cost effective. A decision by a third-party payor not to cover any product candidates we may develop could reduce physician utilization of such product candidates once approved and have a material adverse effect on our sales, results of operations and financial condition. Third-party payors often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement rates, but also have their own methods and approval process apart from Medicare determinations. As a result, the coverage determination process is often a time-consuming and costly process that will require us to provide scientific and clinical support for the use of our product candidates to each payor separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance.

For products administered under the supervision of a physician, obtaining coverage and adequate reimbursement may be particularly difficult because of the higher prices often associated with such drugs. Additionally, separate reimbursement for the product itself or the treatment or procedure in which the product is used may not be available, which may impact physician utilization.

In addition, the U.S. government, state legislatures and foreign governments have continued implementing cost-containment programs, including price controls, restrictions on coverage and reimbursement and requirements for substitution of generic products. Third-party payors are increasingly challenging the prices charged for medical products and services, examining the medical necessity and reviewing the cost effectiveness of pharmaceutical or biological products, medical devices and medical services, in addition to questioning safety and efficacy. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit sales of any product that receives approval. Decreases in third-party reimbursement for any product or a decision by a third-party not to cover a product could reduce physician usage and patient demand for the product.

Outside the United States, ensuring adequate coverage and payment for any biological candidates we may develop will face challenges. Pricing of prescription pharmaceuticals is subject to governmental control in many countries. Pricing negotiations with governmental authorities can extend well beyond the receipt of regulatory marketing approval for a product and may require us to conduct a clinical study that compares the cost effectiveness of any product candidates we may develop to other available therapies. The conduct of such a clinical study could be expensive and result in delays in our commercialization efforts. In the European Union, pricing and reimbursement schemes vary widely from country to country. Some countries provide that products may be marketed only after a reimbursement price has been agreed. Some countries may require the completion of additional studies that compare the cost-effectiveness of a particular product candidate to currently available therapies (so called health technology assessments) in order to obtain reimbursement or pricing approval. This HTA process is the procedure according to which the assessment of the public health impact, therapeutic impact and the economic and societal impact of use of a given medicinal product in the national healthcare systems of the individual country is conducted. The outcome of HTA regarding specific medicinal products will often influence the pricing and reimbursement status granted to these medicinal products by the competent authorities of individual EU Member States. For example, the European Union provides options for its member states to restrict the range of products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. European Union member states may approve a specific price for a product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the product on the market. Other member states allow companies to fix their own prices for products but monitor and control prescription volumes and issue guidance to physicians to limit prescriptions. Recently, many countries in the European Union have increased the amount of discounts required on pharmaceuticals and these efforts could continue as countries attempt to manage healthcare expenditures, especially in light of the severe fiscal and debt crises experienced by many countries in the European Union. The downward pressure on healthcare costs in general, particularly prescription products, has become intense. As a result, increasingly high barriers are being erected to the entry of new products. Political, economic, and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after reimbursement has been obtained. Reference pricing used by various European Union member states, and parallel trade (arbitrage between low-priced and high-priced member states), can further reduce prices. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any of our products, if approved in those countries.

Healthcare Reform

The United States and some foreign jurisdictions are considering or have enacted a number of reform proposals to change the healthcare system. There is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality or expanding access. In the United States, the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by federal and state legislative initiatives, including those designed to limit the pricing, coverage, and reimbursement of pharmaceutical and biopharmaceutical products, especially under government-funded healthcare programs, and increased governmental control of drug pricing.

The ACA, which was enacted in March 2010, substantially changed the way healthcare is financed by both governmental and private insurers in the United States, and significantly affected the pharmaceutical industry. The ACA contains a number of provisions of particular import to the pharmaceutical and biotechnology industries, including, but not limited to, those governing enrollment in federal healthcare programs, 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, and annual fees based on pharmaceutical companies' share of sales to federal healthcare programs. Since its enactment, there have been judicial, Congressional and executive branch challenges to certain aspects of the ACA, and we expect there will be additional challenges and amendments to the ACA in the future. For example, on August 16, 2022, the Inflation Reduction Act of 2022, or IRA, was signed into law, which among other things, extends enhanced subsidies for individuals purchasing health insurance coverage in ACA marketplaces through plan year 2025. The IRA also eliminates the "donut hole" under the Medicare Part D program beginning in 2025 by significantly lowering the beneficiary maximum out-of-pocket cost and creating a new manufacturer discount program. It is possible that the ACA will be subject to judicial or Congressional challenges in the future. It is also unclear how such challenges and the healthcare reform measures of the second Trump administration will impact the ACA and our business.

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. These reductions went into effect in April 2013 and, due to subsequent legislative amendments to the statute, will remain in effect through 2032 unless additional action is taken by Congress. Additionally, on March 11, 2021, the American Rescue Plan Act of 2021 was signed into law, which eliminates the statutory Medicaid drug rebate cap, currently set at 100% of a drug's average manufacturer price, for single source and innovator multiple source drugs, effective January 1, 2024.

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 federal and state legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drug products. For example, the IRA, among other things, (i) directs the U.S. Department of Health and Human Services, or HHS, to negotiate the price of certain high-expenditure, single-source biologics that have been on the market for at least 11 years covered under Medicare, or the Medicare Drug Price Negotiation and subject drug manufacturers to civil monetary penalties and a potential excise tax by offering a price that is not equal to or less than the negotiated "maximum fair price" for such drugs and biologics under the law, and (ii) imposes rebates with respect to certain drugs and biologics covered under Medicare Part B or Medicare Part D to penalize price increases that outpace inflation. The IRA permits HHS to implement many of these provisions through guidance, as opposed to regulation, for the initial years. These provisions began to take effect progressively starting in fiscal year 2023. On August 15, 2024, HHS announced the agreed-upon price of the first ten drugs that were subject to price negotiations, although the Medicare Drug Price Negotiation Program is currently subject to legal challenges. On January 17, 2025, HHS selected fifteen additional products covered under Part D for price negotiation in 2025. Each year thereafter more Part B and Part D products will become subject to the Medicare Drug Price Negotiation Program. Further, on December 7, 2023, an initiative to control the price of prescription drugs through the use of march-in rights under the Bayh-Dole Act was announced. On December 8, 2023, the National Institute of Standards and Technology published for comment a Draft Interagency Guidance Framework for Considering the Exercise of March-In Rights which for the first time includes the price of a product as one factor an agency can use when deciding to exercise march-in rights. While march-in rights have not previously been exercised, it is uncertain if that will continue under the new framework.

In December 2021, Regulation No 2021/2282 on Health Technology Assessment, or HTA Regulation, was adopted. The HTA Regulation is intended to boost cooperation among EU Member States in assessing health technologies, including new medicinal products, and providing the basis for cooperation at EU level for joint clinical assessments in these areas. The HTA Regulation entered into application on January 12, 2025 through a phased implementation and is intended to harmonize the clinical benefit assessment of HTA across the European Union.

Additional state, federal and foreign healthcare reform measures may be adopted in the future. At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical product pricing, including price

or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing.

Data privacy and security

In the ordinary course of our business, we may process personal or sensitive data. Accordingly, we are subject to numerous data privacy and security obligations, including federal, state, local, and foreign laws, regulations, guidance, and industry standards related to data privacy, security, and protection. Such obligations may include, without limitation, the Federal Trade Commission Act, the Telephone Consumer Protection Act of 1991, the Controlling the Assault of Non-Solicited Pornography And Marketing Act of 2003, the California Consumer Privacy Act of 2018, or the CCPA, the Canadian Personal Information Protection and Electronic Documents Act, Canada’s Anti-Spam Legislation, the European Union’s General Data Protection Regulation 2016/679, or the EU GDPR, the EU GDPR as it forms part of UK law by virtue of section 3 of the European Union (Withdrawal) Act 2018, or the UK GDPR, and the ePrivacy Directive. Several states within the United States have enacted or proposed data privacy laws.

The CCPA and EU GDPR are examples of the increasingly stringent and evolving regulatory frameworks related to personal data processing that may increase our compliance obligations and exposure for any noncompliance. For example, the CCPA imposes obligations on covered businesses to provide specific disclosures related to a business’s collecting, using, and disclosing personal data and to respond to certain requests from California residents related to their personal data (for example, requests to know of the business’s personal data processing activities, to delete the individual’s personal data, and to opt out of certain personal data disclosures). Also, the CCPA provides for civil penalties and a private right of action for data breaches which may include an award of statutory damages.

Foreign data privacy and security laws (including but not limited to the EU GDPR and UK GDPR) impose significant and complex compliance obligations on entities that are subject to those laws. As one example, the EU GDPR applies to any company established in the EEA and to companies established outside the EEA that process personal data in connection with the offering of goods or services to data subjects in the EEA or the monitoring of the behavior of data subjects in the EEA. These obligations may include limiting personal data processing to only what is necessary for specified, explicit, and legitimate purposes; requiring a legal basis for personal data processing; requiring the appointment of a data protection officer in certain circumstances; increasing transparency obligations to data subjects; requiring data protection impact assessments in certain circumstances; limiting the collection and retention of personal data; increasing rights for data subjects; formalizing a heightened and codified standard of data subject consents; requiring the implementation and maintenance of technical and organizational safeguards for personal data; mandating notice of certain personal data breaches to the relevant supervisory authority(ies) and affected individuals; and mandating the appointment of representatives in the UK and/or the EU in certain circumstances.

See the section titled “Risk Factors – General Risks” for additional information about the laws and regulations to which we may become subject and about the risks to our business associated with such laws and regulation.

Human Capital Resources

Our human capital is integral to helping us achieve our mission of eradicating monogenic diseases of the CNS. We have built a culture of high performance based on our core values:

- Developing cutting-edge technologies and medicines;
- Being an ally to the rare disease community;
- Uncovering never-before-seen scientific discoveries;
- Having a true sense for the term “partnership”; and
- Exploring uncharted territory.

Our human capital 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.

As of December 31, 2024, we had 73 employees, all of whom were full-time. All of our employees are located in the United States. None of our employees are represented by a labor union or covered by a collective bargaining agreement. We consider our relationship with our employees to be good.

Corporate Information

We were incorporated under the laws of the State of Texas in September 2019. In February 2020, we converted to a Delaware corporation. Our principal executive offices are located at 3000 Pegasus Park Drive Ste 1430, Dallas, Texas 75247 and our telephone number is (214) 612-0000.

Available Information

Our internet website address is www.tayshagtx.com. In addition to the information about us and our subsidiaries contained in this Annual Report, information about us can be found on our website. Our website and information included in or linked to our website are not part of this Annual Report.

Our annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended, are available free of charge through our website as soon as reasonably practicable after they are electronically filed with or furnished to the Securities and Exchange Commission, or SEC. Additionally the SEC maintains an internet site that contains reports, proxy and information statements and other information. The address of the SEC's website is www.sec.gov.

Item 1A. Risk Factors.

The following information sets forth risk factors that could cause our actual results to differ materially from those contained in forward-looking statements we have made in this Annual Report on Form 10-K and those we may make from time to time. You should carefully consider the risks described below, in addition to the other information contained in this Annual Report on Form 10-K and our other public filings. Our business, financial condition or results of operations could be harmed by any of these risks. The risks and uncertainties described below are not the only ones we face. Additional risks not presently known to us or other factors not perceived by us to present significant risks to our business at this time also may impair our business operations.

Selected Risks Affecting Our Business

Our business is subject to a number of risks of which you should be aware before making a decision to invest in our common stock. These risks are more fully described in this “Risk Factors” section, including the following:

- We have incurred significant losses since our inception. We expect to incur losses over the next several years and may never achieve or maintain profitability.
- We will need substantial additional funding to meet our financial obligations and to pursue our business objectives. If we are unable to raise capital when needed, we could be forced to curtail our planned operations and the pursuit of our growth strategy.
- We have a limited operating history and no history of commercializing products, which may make it difficult for an investor to evaluate the success of our business to date and to assess our future viability.
- All of our product candidates are in preclinical or clinical development. If we are unable to successfully develop, receive regulatory approval for and commercialize our product candidates for these or any other indications, or successfully develop any other product candidates, or experience significant delays in doing so, our business will be harmed.
- Because gene therapy is novel and the regulatory landscape that governs any product candidates we may develop is rigorous, complex, uncertain and subject to change, we cannot predict the time and cost of obtaining regulatory approval, if we receive it at all, for any product candidates we may develop.
- We intend to identify and develop novel gene therapy product candidates, which makes it difficult to predict the time, cost and potential success of product candidate development.
- The regulatory approval processes of the U.S. Food and Drug Administration, or FDA, the European Commission and comparable foreign authorities are lengthy, time consuming and inherently unpredictable. If we are not able to obtain required regulatory approval for our product candidates, our business will be substantially harmed.
- We have not yet completed testing of any product candidates in clinical trials. Success in preclinical studies or earlier clinical trials may not be indicative of results in future clinical trials.
- We may not be successful in our efforts to build a pipeline of additional product candidates or our next-generation platform technologies.
- Unfavorable conditions in our industry or the global economy could limit our ability to grow our business and negatively affect our results of operations.
- Gene therapies are novel, complex and difficult to manufacture. We could experience manufacturing problems that result in delays in the development or commercialization of our product candidates or otherwise harm our business.
- We and our contract manufacturers for AAV9 are subject to significant regulation with respect to manufacturing our products. The third-party manufacturing facilities on which we rely, and any manufacturing facility that we may have in the future, may have limited capacity or fail to meet the applicable stringent regulatory requirements.
- We currently rely exclusively on our collaboration with UT Southwestern for our preclinical research and development programs, including for discovering, preclinically developing and conducting all IND-enabling studies for our lead product candidates and our near-term future pipeline. Failure or delay of UT Southwestern to fulfill all or part of its obligations to us under the agreement, a breakdown in collaboration between the parties or a complete or partial loss of this relationship would materially harm our business.
- UT Southwestern has entered into collaborations with third parties, including certain of our competitors, addressing targets and disease indications outside the scope of our collaboration. As a result, UT Southwestern may have competing interests with respect to their priorities and resources.

- Negative public opinion of gene therapy and increased regulatory scrutiny of gene therapy and genetic research may adversely impact the development or commercial success of our current and future product candidates.
- We face significant competition from other biotechnology and pharmaceutical companies, and our operating results will suffer if we fail to compete effectively.
- Third parties may initiate legal proceedings alleging that we are infringing their intellectual property rights, the outcome of which would be uncertain.
- We may be subject to legal proceedings from time to time which seek material damages.
- Our term loan agreement contains restrictions that potentially limit our flexibility in operating our business, and we may be required to make a prepayment or repay our outstanding indebtedness earlier than we expect.
- If we are unable to obtain or protect intellectual property rights related to any of our product candidates, we may not be able to compete effectively in our market.

Risks Related to our Financial Position and Capital Needs

We have incurred significant losses since our inception. We expect to incur losses over the next several years and may never achieve or maintain profitability.

Since our inception, we have incurred significant net losses, and we expect to continue to incur significant expenses and operating losses for the foreseeable future. Our net losses were \$89.3 million and \$111.6 million for the years ended December 31, 2024 and 2023, respectively. As of December 31, 2024, we had an accumulated deficit of \$602.3 million. We have financed our operations with \$671.0 million in gross proceeds from equity financings, including from pre-IPO private placements of convertible preferred stock, our initial public offering, or the IPO, and subsequent sales of common stock in public and private securities offerings, from our previous loan agreement with Silicon Valley Bank and our current loan agreement with Trinity Capital and from the option agreement dated October 21, 2022, or the Option Agreement, with Audentes Therapeutics, Inc. (d/b/a Astellas Gene Therapy), or Astellas, and the securities purchase agreement dated October 21, 2022, or the Securities Purchase Agreement (and together with the Option Agreement, the Astellas Transactions), with Astellas. We have no products approved for commercialization and have never generated any revenue from product sales.

All of our product candidates are still in the clinical or preclinical development stage. We expect to continue to incur significant expenses and operating losses over the next several years. We expect that it could be several years, if ever, before we have a commercialized product. Our net losses may fluctuate significantly from quarter to quarter and year to year. We anticipate that our expenses will increase substantially as we:

- continue to advance the preclinical and clinical development of our product candidates and preclinical and discovery programs;
- conduct our ongoing clinical trials of TSHA-102 and any other current and future product candidates that we advance;
- seek regulatory approval for any product candidates that successfully complete clinical trials;
- continue to develop our gene therapy product candidate pipeline and next-generation platforms;
- scale up our clinical and regulatory capabilities;
- manufacture current good manufacturing practice, or cGMP, material for clinical trials or potential commercial sales;
- establish a commercialization infrastructure and scale up internal and external manufacturing and distribution capabilities to commercialize any product candidates for which we may obtain regulatory approval;
- adapt our regulatory compliance efforts to incorporate requirements applicable to marketed products;
- maintain, expand and protect our intellectual property portfolio;
- hire additional clinical, manufacturing quality control, regulatory, manufacturing and scientific and administrative personnel;
- add operational, financial and management information systems and personnel, including personnel to support our product development and planned future commercialization efforts; and
- incur additional legal, accounting and other expenses in operating as a public company.

In 2023, we generated revenue from the Astellas Transactions; however, to date we have not generated any revenue from product sales. To become and remain profitable, we must succeed in developing and eventually commercializing product candidates that generate significant revenue. This will require us to be successful in a range of challenging activities, including completing preclinical testing and clinical trials of our product candidates, obtaining regulatory approval, and manufacturing, marketing and selling any product candidates for which we may obtain regulatory approval, as well as discovering and developing additional product candidates. We are only in the preliminary stages of most of these activities and all of our product candidates are in clinical or preclinical development. We may never succeed in these activities and, even if we do, may never generate any revenue or revenue that is significant enough to achieve profitability.

Even if we achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would depress the value of our company and could impair our ability to raise capital, expand our business, maintain our development efforts, obtain product approvals, diversify our offerings or continue our operations. A decline in the value of our company could also cause you to lose all or part of your investment.

We have a limited operating history and no history of commercializing products, which may make it difficult for an investor to evaluate the success of our business to date and to assess our future viability.

We are a clinical-stage gene therapy company with a limited operating history. We commenced operations in 2019, and our operations to date have been largely focused on organizing and staffing our company, business planning, raising capital and entering into collaboration and license agreements for conducting preclinical research and development activities for our product candidates and gene therapy pipeline. To date, we have not yet demonstrated our ability to successfully complete clinical trials, including pivotal clinical trials, obtain regulatory approvals, manufacture a product on a commercial scale, or arrange for a third party to do so on our behalf, or conduct sales and marketing activities necessary for successful commercialization. Consequently, any predictions you make about our future success or viability may not be as accurate as they could be if we had a longer operating history or a history of successfully developing and commercializing products.

We may encounter unforeseen expenses, difficulties, complications, delays and other known or unknown factors in achieving our business objectives. We will need to develop commercial capabilities, and we may not be successful in doing so.

We will need substantial additional funding to meet our financial obligations and to pursue our business objectives. If we are unable to raise capital when needed, we could be forced to curtail our planned operations and the pursuit of our growth strategy.

Our operations have consumed substantial amounts of cash since inception. Identifying potential product candidates and conducting preclinical testing and clinical trials is a time-consuming, expensive and uncertain process that takes years to complete, and we may never generate the necessary data or results required to obtain regulatory approval and achieve product sales. We expect to continue to incur significant expenses and operating losses over the next several years as we conduct clinical trials of our product candidates, initiate future clinical trials of our product candidates, advance our preclinical programs, seek marketing approval for any product candidates that successfully complete clinical trials and advance any of our other product candidates we may develop or otherwise acquire. In addition, our product candidates, if approved, may not achieve commercial success. Our revenue, if any, primarily will be derived from sales of products that we do not expect to be commercially available for a number of years, if at all. If we obtain marketing approval for any product candidates that we develop or otherwise acquire, we expect to incur significant commercialization expenses related to product sales, marketing, distribution and manufacturing. We also expect an increase in our expenses associated with creating additional infrastructure to support operations as a public company.

As of December 31, 2024, we had cash and cash equivalents of \$139.0 million. We believe that our existing cash and cash equivalents will be sufficient to fund our operating expenses and capital requirements into the fourth quarter of 2026. This estimate is based on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we expect. Changes may occur beyond our control that would cause us to consume our available capital before that time, including changes in and progress of our development activities, acquisitions of additional product candidates, and changes in regulation. Our future capital requirements will depend on many factors, including:

- the scope, progress, costs and results of discovery, preclinical development, laboratory testing and clinical trials for TSHA-102 and any current and future product candidates that we advance;
- our ability to access sufficient additional capital on a timely basis and on favorable terms, including with respect to our term loan facility with Trinity Capital;
- the extent to which we develop, in-license or acquire other product candidates and technologies in our gene therapy product candidate pipeline;

- the costs and timing of process development and manufacturing scale-up activities associated with our product candidates and other programs as we advance them through preclinical and clinical development;
- the number and development requirements of product candidates that we may pursue;
- the costs, timing and outcome of regulatory review of our product candidates;
- our headcount growth and associated costs as we expand our research and development capabilities and establish a commercial infrastructure;
- the costs and timing of future commercialization activities, including product manufacturing, marketing, sales, and distribution, for any of our product candidates for which we receive marketing approval;
- the costs and timing of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending any intellectual property-related claims;
- the costs incurred in defending ourselves in any legal proceedings that we may be subject to;
- the revenue, if any, received from commercial sales of our product candidates for which we receive marketing approval; and
- the costs of operating as a public company.

We will require additional capital to achieve our business objectives, including to conduct our ongoing and planned clinical trials of our product candidates. Additional funds may not be available on a timely basis, on favorable terms, or at all, and such funds, if raised, may not be sufficient to enable us to continue to implement our long-term business strategy. Further, our ability to raise additional capital may be adversely impacted by potential worsening global economic conditions, including fluctuations in inflation rates and concerns of a recession in the United States or other major markets, potential tariffs and disruptions to and volatility in the credit and financial markets in the United States and worldwide. Weakness and volatility in the capital markets and the economy in general could also increase our costs of borrowing. If we are unable to raise sufficient additional capital, we could be forced to curtail our planned operations and the pursuit of our growth strategy.

Our existing indebtedness contains restrictions that potentially limit our flexibility in operating our business. In addition, we may be required to make a prepayment or repay our outstanding indebtedness earlier than we expect under our Trinity Term Loan Agreement if we are unable to satisfy certain conditions.

On November 13, 2023, we entered into a Loan and Security Agreement, or the Trinity Term Loan Agreement, with the lenders party thereto from time to time, or the Trinity Lenders, and Trinity Capital Inc., as administrative agent and collateral agent for the Trinity Lenders, or Trinity, which provides for term loans of up to \$40.0 million in the aggregate available in a single tranche. The Trinity Term Loan Agreement contains various covenants that limit our ability to engage in specified types of transactions. These covenants limit our ability to, among other things:

- incur or assume certain debt;
- merge or consolidate or acquire all or substantially all of the capital stock or property of another entity;
- change the nature of our business;
- change our organizational structure or type;
- license, transfer, or dispose of certain assets;
- grant certain types of liens on our assets;
- make certain investments;
- pay cash dividends; and
- enter into material transactions with affiliates.

A breach of any of these covenants could result in an event of default under the Trinity Term Loan Agreement. An event of default will also occur if, among other things, a material adverse change in our business, operations, or condition occurs, which could potentially include a material impairment of the prospect of our repayment of any portion of the amounts we owe under the Trinity Term Loan Agreement. In the case of a continuing event of default under the Trinity Term Loan Agreement, the Trinity Lenders could elect to declare all amounts outstanding to be immediately due and payable, proceed against the collateral in which we granted the

Trinity Lenders a security interest under the Trinity Term Loan Agreement, or otherwise exercise the rights of a secured creditor. Amounts outstanding under the Trinity Term Loan Agreement are secured by all of our existing and future assets, including intellectual property.

At closing, we drew the full \$40.0 million.

We may not have enough available cash to repay or refinance our indebtedness at the time any such repayment is required. In such an event, we may be required to delay, limit, reduce, or terminate our preclinical and clinical product development or commercialization efforts or grant others rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves. Our business, financial condition, and results of operations could be materially adversely affected as a result.

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

Until such time, if ever, as we can generate substantial revenue, we may finance our cash needs through a combination of equity offerings, government or private party grants, debt financings and license and collaboration agreements. We do not currently have any other committed external source of funds. To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect your rights as a common stockholder. Debt financing and equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends.

If we raise additional funds through collaborations, strategic alliances or marketing, distribution or licensing arrangements with third parties, we may be required to relinquish valuable rights to our technologies, future revenue streams or product candidates, grant licenses on terms that may not be favorable to us or commit to future payment streams. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Unfavorable global economic 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. Unfavorable conditions in the economy both in the United States and abroad, including conditions resulting from changes in gross domestic product growth in the United States or abroad, financial and credit market fluctuations, inflation, fluctuating interest rates, potential tariffs and other concerns regarding international trade relations, political turmoil, natural catastrophes, outbreaks of contagious diseases, warfare and terrorist attacks on the United States, Europe, the Asia Pacific region or elsewhere, such as the conflict in the Middle East, could cause a decrease in business investments, disrupt the timing and cadence of key industry events, and negatively affect the growth of our business and our results of operations. For example, the COVID-19 pandemic adversely affected workforces, economies and financial markets globally, leading to a reduction in the ability of, or the inability of, partners, suppliers, vendors or other parties to meet their contractual obligations, and for a period of time, a reduction in customer spending on technology, and such conditions may reoccur in the future. The war in Ukraine and the related political and economic responses imposed on Russia such as sanctions, may also exacerbate these issues and trends especially in Europe. A severe or prolonged economic downturn could result in a variety of risks to our business, including weakened demand for our product candidates and our ability to raise additional capital when needed on acceptable terms, if at all. A weak or declining economy could also strain our suppliers, possibly resulting in supply disruption, or cause delays in payments for our services by third-party payors or our collaborators. Any of the foregoing could harm our business and we cannot anticipate all of the ways in which the current economic climate and financial market conditions could adversely impact our business, financial condition, results of operations and prospects.

Risks Related to the Development of our Product Candidates

TSHA-102 is currently our lead product candidate and there is no guarantee that we will be able to successfully develop and commercialize TSHA-102.

We are currently focused on the potential development of our lead product candidate, TSHA-102. We are still developing TSHA-102 and it cannot be marketed or sold in the United States or in foreign markets until regulatory approval has been obtained from the FDA or applicable foreign regulatory agencies. The process of obtaining regulatory approval is expensive and time consuming. The FDA and foreign regulatory authorities may never approve TSHA-102 for sale and marketing, and even if TSHA-102 is ultimately approved, regulatory approval may be delayed or limited in the United States or in other jurisdictions. Even if we are authorized to sell and market TSHA-102 in one or more markets, there is no assurance that we will be able to successfully market

TSHA-102 or that TSHA-102 will achieve market acceptance sufficient to generate profits. If we are unable to successfully develop and commercialize TSHA-102 due to failure to obtain regulatory approval for TSHA-102, to successfully market TSHA-102, to generate profits from the sale of TSHA-102, or due to other risk factors outlined in this report, it would have material adverse effects on our business, financial condition, and results of operations as TSHA-102 is currently our sole product candidate in clinical development.

All of our product candidates are in clinical or preclinical development. If we are unable to successfully develop, receive regulatory approval for and commercialize our product candidates for these or any other indications, or successfully develop any other product candidates, or experience significant delays in doing so, our business will be harmed.

All of our product candidates are still in clinical or preclinical development. Each of our programs and product candidates will require additional preclinical and/or clinical development, regulatory approval, obtaining manufacturing supply, capacity and expertise, building a commercial organization or successfully outsourcing commercialization, substantial investment and significant marketing efforts before we generate any revenue from product sales. We do not have any products that are approved for commercial sale, and we may never be able to develop or commercialize marketable products.

Our ability to generate revenue from our product candidates, which we do not expect will occur for several years, if ever, will depend heavily on the successful development, regulatory approval and eventual commercialization of our product candidates. The success of TSHA-102 or any other product candidates that we develop or otherwise may acquire will depend on several factors, including:

- effective INDs from the FDA or comparable foreign applications that allow commencement of our planned clinical trials or future clinical trials for our product candidates;
- successful enrollment and completion of clinical trials, including under the FDA's and comparable foreign regulatory authorities' current good clinical practices, or GCPs, and current Good Laboratory Practices;
- timely and successful completion of preclinical studies, including toxicology studies, biodistribution studies and minimally efficacious dose studies in animals, where applicable, and clinical trials;
- sufficiency of our financial and other resources to complete the necessary preclinical studies and clinical trials;
- successful development of, or making arrangements with third-party manufacturers for, our commercial manufacturing processes for any of our product candidates that receive regulatory approval;
- receipt of timely marketing approvals from applicable regulatory authorities;
- launching commercial sales of products, if approved, whether alone or in collaboration with others;
- acceptance of the benefits and use of our products, including method of administration, if approved, by patients, the medical community and third-party payors, for their approved indications;
- the prevalence and severity of adverse events experienced with TSHA-102 or any other product candidates;
- the availability, perceived advantages, cost, safety and efficacy of alternative therapies for any product candidate, and any indications for such product candidate, that we develop;
- our ability to produce TSHA-102 or any other product candidates we develop on a commercial scale;
- obtaining and maintaining patent, trademark and trade secret protection and regulatory exclusivity for our product candidates and otherwise protecting our rights in our intellectual property portfolio;
- maintaining compliance with regulatory requirements, including cGMPs, and complying effectively with other procedures;
- obtaining and maintaining third-party coverage and adequate reimbursement and patients' willingness to pay out-of-pocket in the absence of such coverage and adequate reimbursement; and
- maintaining a continued acceptable safety, tolerability and efficacy profile of the products following approval.

If we are not successful with respect to one or more of these factors in a timely manner or at all, we could experience significant delays or an inability to successfully commercialize the product candidates we develop, which would materially harm our business. If we do not receive marketing approvals for any product candidate we develop, we may not be able to continue our operations.

We intend to identify and develop novel gene therapy product candidates, which makes it difficult to predict the time, cost and potential success of product candidate development.

Our strategy is to identify, develop and commercialize gene therapy product candidates using an AAV9 capsid for intrathecal delivery of therapeutic transgenes to certain kinds of cells. Our future success depends on the successful development of these novel therapeutic approaches. To date, very few products that utilize gene transfer have been approved in the United States, the European Union or other European countries and no gene transfer therapy products that utilize an intrathecal method of administration have been approved. There have been a limited number of clinical trials of gene transduction technologies.

Although AAV9 has been tested in numerous clinical trials and is used in two currently approved products, we cannot be certain that our AAV9 product candidates will successfully complete preclinical studies and clinical trials, or that they will not cause significant adverse events or toxicities. We also cannot be certain that we will be able to avoid triggering toxicities in our future preclinical studies or clinical trials or that our intrathecal method of administration will not cause unforeseen side effects or other challenges. Any such results could impact our ability to develop a product candidate, including our ability to enroll patients in our clinical trials. As a result of these factors, it is more difficult for us to predict the time and cost of product candidate development, and we cannot predict whether the application of our approach to gene therapy, or any similar or competitive programs, will result in the identification, development, and regulatory approval of any product candidates, or that other gene therapy programs will not be considered better or more attractive. There can be no assurance that any development problems we experience in the future related to our current gene therapy product candidates or any of our research programs will not cause significant delays or unanticipated costs, or that such development problems can be solved. We may also experience delays and challenges in achieving sustainable, reproducible, and scalable production. Any of these factors may prevent us from completing our preclinical studies or clinical trials or commercializing any product candidates we may develop on a timely or profitable basis, if at all.

Because gene therapy is novel and the regulatory landscape that governs any product candidates we may develop is rigorous, complex, uncertain and subject to change, we cannot predict the time and cost of obtaining regulatory approval, if we receive it at all, for any product candidates we may develop.

The regulatory requirements that will govern any novel gene therapy product candidates we develop are not entirely clear and are subject to change. Within the broader genetic medicine field, very few therapeutic products have received marketing authorization from the FDA or the European Commission. Even with respect to more established products that fit into the categories of gene therapies or cell therapies, the regulatory landscape is still developing. Regulatory requirements governing gene therapy products and cell therapy products have changed frequently and will likely continue to change in the future. Moreover, there is substantial overlap in those responsible for regulation of existing gene therapy products and cell therapy products. For example, in the United States, the FDA has established the Office of Tissues and Advanced Therapies within its Center for Biologics Evaluation and Research, or CBER, to consolidate the review of gene therapy and related products, and the Cellular, Tissue and Gene Therapies Advisory Committee to advise CBER on its review.

Our product candidates will need to meet safety and efficacy standards applicable to any new biologic under the regulatory framework administered by the FDA. In addition to FDA oversight and oversight by institutional review boards, or IRBs, under guidelines promulgated by the National Institutes of Health, or NIH, gene therapy clinical trials are also subject to review and oversight by an institutional biosafety committee, or IBC, a local institutional committee that reviews and oversees research utilizing recombinant or synthetic nucleic acid molecules at that institution. The IBC assesses the safety of the research and identifies any potential risk to public health or the environment. While the NIH guidelines are not mandatory unless the research in question is being conducted at or sponsored by institutions receiving NIH funding of recombinant or synthetic nucleic acid molecule research, many companies and other institutions not otherwise subject to the NIH Guidelines voluntarily follow them. Although the FDA decides whether individual gene therapy protocols may proceed, the review process and determinations of other reviewing bodies can impede or delay the initiation of a clinical trial, even if the FDA has reviewed the trial and approved its initiation.

Similar considerations apply in the European Union. The EMA's Committee for Advanced Therapies, or CAT, is responsible for assessing the quality, safety, and efficacy of advanced-therapy medicinal products. Advanced-therapy medicinal products include gene therapy medicines, somatic-cell therapy medicines and tissue-engineered medicines. The role of the CAT is to prepare a draft opinion on an application for marketing authorization for a gene therapy medicinal candidate that is submitted to the EMA. In the European Union, the development and evaluation of a gene therapy product must be considered in the context of the relevant EU legislation and guidelines. The EMA may issue new guidelines concerning the development and marketing authorization for gene therapy products and require that we comply with these new guidelines. As a result, the procedures and standards applied to gene therapy products and cell therapy products may be applied to any gene therapy product candidate we may develop, but that remains uncertain at this point.

Adverse developments in preclinical studies or clinical trials conducted by others in the field of gene therapy and gene regulation products may cause the FDA, the European Union, and other regulatory authorities to revise the requirements for approval of any product candidates we may develop or limit the use of products utilizing gene regulation technologies, either of which could harm our business. In addition, the clinical trial requirements of the FDA, the European Union, national competent authorities of EU Member States and other regulatory authorities and the criteria these regulators use to determine the safety and efficacy of a product candidate vary substantially according to the type, complexity, novelty, and intended use and market of the potential products. The regulatory approval process for product candidates such as ours can be more expensive and take longer than for other, better known, or more extensively studied pharmaceutical or other product candidates. Further, as we are developing novel potential treatments for diseases in which, in some cases, there is little clinical experience with potential new endpoints and methodologies, there is heightened risk that the FDA, the EMA or the European Commission or other regulatory authorities may not consider the clinical trial endpoints to provide clinically meaningful results, and the resulting clinical data and results may be more difficult to analyze. In addition, we may not be able to identify or develop appropriate animal disease models to enable or support planned clinical development. Any natural history studies that we may conduct or rely upon in our clinical development may not be accepted by the FDA, EMA or the European Commission or other regulatory authorities. Regulatory authorities administering existing or future regulations or legislation may not allow production and marketing of products utilizing gene regulation technology in a timely manner or under technically or commercially feasible conditions. In addition, regulatory action or private litigation could result in expenses, delays, or other impediments to our research programs or the commercialization of resulting products. Further, approvals by one regulatory authority may not be indicative of what other regulatory authorities may require for approval.

The regulatory review committees and advisory groups described above and the new guidelines they promulgate may lengthen the regulatory review process, require us to perform additional preclinical studies or clinical trials, increase our development costs, lead to changes in regulatory positions and interpretations, delay or prevent approval and commercialization of these treatment candidates, or lead to significant post-approval limitations or restrictions. As we advance our research programs and develop future product candidates, we will be required to consult with these regulatory and advisory groups and to comply with applicable guidelines. If we fail to do so, we may be required to delay or discontinue development of any product candidates we identify and develop. These additional processes may result in a review and approval process that is longer than we otherwise would have expected. Delays as a result of an increased or lengthier regulatory approval process or further restrictions on the development of our product candidates can be costly and could negatively impact our ability to complete clinical trials and commercialize our current and future product candidates in a timely manner, if at all.

Preclinical studies and clinical trials are expensive, time-consuming, difficult to design and implement and involve an uncertain outcome. Further, we may encounter substantial delays in completing the development of our product candidates.

All of our product candidates are in clinical or preclinical development and their risk of failure is high. The clinical trials and manufacturing of our product candidates are, and the manufacturing and marketing of our products, if approved, will be, subject to extensive and rigorous review and regulation by numerous government and regulatory authorities in the United States and in other countries where we intend to test and market our product candidates. Before obtaining regulatory approvals for the commercial sale of any of our product candidates, we must demonstrate through lengthy, complex and expensive preclinical testing and clinical trials that our product candidates are both safe and effective for use in each target indication. In particular, because our product candidates are subject to regulation as biological products, we will need to demonstrate that they are safe, pure and potent for use in their target indications. Each product candidate must demonstrate an adequate risk versus benefit profile in its intended patient population and for its intended use.

Clinical testing is expensive and can take many years to complete and is subject to uncertainty. We cannot guarantee that any clinical trials will be conducted as planned or completed on schedule, if at all. Failure can occur at any time during the clinical trial process. Even if our future clinical trials are completed as planned, we cannot be certain that their results will support the safety and effectiveness of our product candidates for their targeted indications or support continued clinical development of such product candidates. Our future clinical trial results may not be successful.

In addition, even if such trials are successfully completed, we cannot guarantee that the FDA or foreign regulatory authorities will interpret the results as we do, and more trials could be required before we submit our product candidates for approval. This is particularly true for clinical trials in very rare diseases, such as with TSHA-102 for the treatment of Rett syndrome, where the very small patient population makes it difficult or impossible to conduct two traditional, adequate and well-controlled studies, and therefore the FDA or comparable foreign regulatory authorities are required to exercise flexibility in approving therapies for such diseases. Moreover, results acceptable to support approval in one jurisdiction may be deemed inadequate by another regulatory authority to support regulatory approval in that other jurisdiction. To the extent that the results of the trials are not satisfactory to the FDA or

foreign regulatory authorities for support of a marketing application, we may be required to expend significant resources, which may not be available to us, to conduct additional trials in support of potential approval of our product candidates.

To date, we have not completed any clinical trials required for the approval of our product candidates. We may experience delays in conducting any clinical trials and we do not know whether our clinical trials will begin on time, need to be redesigned, recruit and enroll patients on time or be completed on schedule, or at all. Events that may prevent successful or timely completion of clinical development include:

- inability to generate sufficient preclinical, toxicology, or other *in vivo* or *in vitro* data to support the initiation of clinical trials;
- delays in sufficiently developing, characterizing or controlling a manufacturing process suitable for advanced clinical trials, including our natural history studies;
- delays in developing suitable assays for screening patients for eligibility for trials with respect to certain product candidates;
- delays in reaching agreement with the FDA, EMA or other regulatory authorities as to the design or implementation of our clinical trials;
- obtaining regulatory approval to commence a clinical trial;
- reaching an agreement on acceptable terms with clinical trial sites or prospective contract research organizations, or CROs, the terms of which can be subject to extensive negotiation and may vary significantly among different clinical trial sites;
- obtaining IRB approval and positive Ethics Committee opinions at each trial site;
- recruiting suitable patients to participate in a clinical trial;
- having patients complete a clinical trial or return for post-treatment follow-up;
- clinical sites, CROs or other third parties deviating from trial protocol or dropping out of a trial;
- failure to perform in accordance with the FDA's GCP requirements, or applicable regulatory guidelines in other countries;
- addressing patient safety concerns that arise during the course of a trial, including occurrence of adverse events associated with the product candidate that are viewed to outweigh its potential benefits;
- adding a sufficient number of clinical trial sites; or
- manufacturing sufficient quantities of product candidate for use in clinical trials.

We may experience numerous unforeseen events during, or as a result of, clinical trials that could delay or prevent our ability to receive marketing approval or commercialize our product candidates or significantly increase the cost of such trials, including:

- we may experience changes in regulatory requirements or guidance, or receive feedback from regulatory authorities that requires us to modify the design of our clinical trials;
- clinical trials of our product candidates may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional clinical trials or abandon development programs;
- the number of patients required for clinical trials of our product candidates 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;
- our third-party contractors may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all;
- we or our investigators might have to suspend or terminate clinical trials of our product candidates for various reasons, including non-compliance with regulatory requirements, a finding that our product candidates have 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 our product candidates may be greater than we anticipate and we may not have funds to cover the costs;

- the supply or quality of our product candidates or other materials necessary to conduct clinical trials of our product candidates may be insufficient or inadequate;
- regulators may revise the requirements for approving our product candidates, or such requirements may not be as we anticipate; and
- any future collaborators that conduct clinical trials may face any of the above issues, and may conduct clinical trials in ways they view as advantageous to them but that are suboptimal for us.

If we are required to conduct additional clinical trials or other testing of our product candidates beyond those that we currently contemplate, if we are unable to successfully complete clinical trials of our product candidates or other testing, if the results of these trials or tests are not positive or are only modestly positive or if there are safety concerns, we may:

- incur unplanned costs;
- be delayed in obtaining marketing approval for our product candidates 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 or Risk Evaluation and Mitigation Strategies, or REMS, or comparable foreign strategies;
- be subject to additional post-marketing testing requirements; or
- have the product removed from the market after obtaining marketing approval.

We could encounter delays if a clinical trial is suspended or terminated by us, by the IRBs or Ethics Committees of the institutions in which such trials are being conducted, by the Data Safety Monitoring Board for such trial or by the FDA, the competent authorities of EU Member States or other regulatory authorities. Such authorities may impose such a suspension or termination 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, the competent authorities of EU Member States 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 drug, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial.

All of our product candidates will require extensive clinical testing before we are prepared to submit a BLA or marketing authorization application, or MAA, for regulatory approval. We cannot predict with any certainty if or when we might complete the clinical development for our product candidates and submit a BLA or MAA for regulatory approval of any of our product candidates or whether any such BLA or MAA will be approved. We may also seek feedback from the FDA, EMA or other regulatory authorities on our clinical development program, and the FDA, EMA or such regulatory authorities may not provide such feedback on a timely basis, or such feedback may not be favorable, which could further delay our development programs.

We cannot predict with any certainty whether or when we might complete a given clinical trial. If we experience delays in the commencement or completion of our clinical trials, or if we terminate a clinical trial prior to completion, the commercial prospects of our product candidates could be harmed, and our ability to generate revenues from our product candidates may be delayed or lost. In addition, any delays in our clinical trials could increase our costs, slow down the development and approval process and jeopardize our ability to commence product sales and generate revenues. Any of these occurrences may harm our business, financial condition and results of operations. 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 our product candidates.

The regulatory approval processes of the FDA, European Commission and comparable foreign authorities are lengthy, time consuming and inherently unpredictable. If we are not able to obtain required regulatory approval for our product candidates, our business will be substantially harmed.

The time required to obtain approval or other marketing authorizations by the FDA, European Commission and comparable foreign authorities is unpredictable, and it typically takes many years following the commencement of clinical trials and depends upon numerous factors, including the substantial discretion of the regulatory authorities. In addition, approval policies, regulations, and the type and amount of clinical data necessary to gain approval may change during the course of a product candidate's clinical development and may vary among jurisdictions. We have not obtained regulatory approval for any product candidate, and it is possible that we may never obtain regulatory approval for any product candidates we may seek to develop in the future. Neither we

nor any current or future collaborator is permitted to market any drug product candidates in the United States until we receive regulatory approval of a BLA from the FDA, and we cannot market it in the European Union until we receive approval for a MAA from the European Commission, or other required regulatory approval in other countries. To date, we have had only limited discussions with the FDA regarding clinical development programs or regulatory approval for any product candidate within the United States. In addition, we have only had limited discussions with Health Canada, and no discussions with the EMA and other comparable foreign authorities, regarding clinical development programs or regulatory approval for any product candidate outside of the United States.

Prior to obtaining approval to commercialize any drug product candidate in the United States or abroad, we must demonstrate with substantial evidence from well-controlled clinical trials, and to the satisfaction of the FDA or foreign regulatory authorities, that such product candidates are safe, pure and effective for their intended uses. Results from preclinical studies and clinical trials can be interpreted in different ways. Even if we believe the preclinical or clinical data for our product candidates are promising, such data may not be sufficient to support approval by the FDA and other regulatory authorities. The FDA or comparable foreign regulatory authorities may also require us to conduct additional preclinical studies or clinical trials for our product candidates either prior to or after approval, or it may object to elements of our clinical development programs.

Of the large number of products in development, only a small percentage successfully complete the FDA or foreign regulatory approval processes and are commercialized. The lengthy approval and marketing authorization process as well as the unpredictability of future clinical trial results may result in our failing to obtain regulatory approval and marketing authorization to market our product candidates, which would significantly harm our business, financial condition, results of operations and prospects.

We have invested a significant portion of our time and financial resources in the development of our preclinical product candidates. Our business is dependent on our ability to successfully complete preclinical and clinical development of, obtain regulatory approval for, and, if approved, successfully commercialize TSHA-102 and any future product candidates in a timely manner.

Even if we eventually complete clinical testing and receive approval of a BLA or foreign marketing application for TSHA-102 or any future product candidates, the FDA, European Commission or the applicable foreign regulatory authority may grant approval or other marketing authorization contingent on the performance of costly additional clinical trials, including post-marketing clinical trials. The FDA, European Commission or the applicable foreign regulatory authority also may approve or authorize for marketing a product candidate for a more limited indication or patient population than we originally request, and the FDA, European Commission or applicable foreign regulatory authority may not approve or authorize the labeling that we believe is necessary or desirable for the successful commercialization of a product candidate. Any delay in obtaining, or inability to obtain, applicable regulatory approval or other marketing authorization would delay or prevent commercialization of that product candidate and would materially adversely impact our business and prospects.

In addition, the FDA, EU and related regulatory authorities and other regulatory authorities may change their policies, issue additional regulations or revise existing regulations, or take other actions, which may prevent or delay approval of our future products under development on a timely basis. Such policy or regulatory changes could impose additional requirements upon us that could delay our ability to obtain approvals, increase the costs of compliance or restrict our ability to maintain any marketing authorizations we may have obtained.

We have not yet completed testing of any product candidate in clinical trials. Success in preclinical studies or earlier clinical trials may not be indicative of results in future clinical trials.

Success in preclinical testing and early clinical trials does not ensure that later clinical trials will generate the same results or otherwise provide adequate data to demonstrate the efficacy and safety of a product candidate. Preclinical tests and Phase 1 and Phase 2 clinical trials are primarily designed to test safety, to study pharmacokinetics and pharmacodynamics and to understand the side effects of product candidates at various doses and schedules. Success in preclinical or animal studies and early clinical trials does not ensure that later large-scale efficacy trials will be successful nor does it predict final results. For example, we may be unable to identify suitable animal disease models for our product candidates, which could delay or frustrate our ability to proceed into clinical trials or obtain marketing approval. Our product candidates may fail to show the desired safety and efficacy in clinical development despite positive results in preclinical studies or having successfully advanced through initial clinical trials. Our Phase 1/2 clinical trials of TSHA-102 involve small patient populations. Because of the small sample sizes, the results of these trials may not be indicative of results of future clinical trials. Further, although other gene therapy clinical trials conducted by others also utilized AAV9 vectors, these trials should not be relied upon as evidence that our planned clinical trials will succeed.

Many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late-stage clinical trials even after achieving promising results in preclinical testing and earlier-stage clinical trials. Data obtained from preclinical and

clinical activities are subject to varying interpretations, which may delay, limit or prevent regulatory approval. In addition, we may experience regulatory delays or rejections as a result of many factors, including changes in regulatory policy during the period of our product candidate development. Any such delays could negatively impact our business, financial condition, results of operations and prospects.

Interim “top-line” and preliminary results 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 publish interim top-line or preliminary results from our clinical trials. Interim results 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. Preliminary or top-line results 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, interim and preliminary data should be viewed with caution until the final data are available. For example, in June 2024, we announced initial clinical data from the first two pediatric patients and interim clinical data from the first two adult patients treated in the Phase 1/2 REVEAL trials of TSHA-102. However, those observations may not endure or be repeated in subsequently dosed patients or any age or disease severity, including patients receiving higher doses of TSHA-102 in either the adolescent/adult or pediatric trial. Initial clinical observations also may not translate into success on primary endpoints of the REVEAL trial. Differences between preliminary or interim data and final data could significantly harm our business prospects and may cause the trading price of our common stock to fluctuate significantly.

Further, others, including regulatory authorities, 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 approvability or commercialization of the particular product candidate or product and our business 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 the material or otherwise appropriate information to include in our disclosure, and any information we determine not to disclose may ultimately be deemed significant with respect to future decisions, conclusions, views, activities or otherwise regarding a particular drug, product candidate or our business. If the top-line 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 any of our product candidates, our business, operating results, prospects or financial condition may be harmed.

Our preclinical studies and clinical trials may fail to demonstrate the safety and efficacy of our product candidates, or serious adverse or unacceptable side effects may be identified during the development of our product candidates, which could prevent or delay regulatory approval and commercialization, increase our costs or necessitate the abandonment or limitation of the development of some of our product candidates.

Before obtaining regulatory approvals for the commercial sale of our product candidates, we must demonstrate through lengthy, complex and expensive preclinical testing and clinical trials that our product candidates are safe, pure and effective for use in each target indication, and failures can occur at any stage of testing. Preclinical studies and clinical trials often fail to demonstrate safety or efficacy of the product candidate studied for the target indication. Further, the patients evaluated in our clinical trials are often seriously ill. Any side effects or patient deaths could affect the development of our product candidates, even if deemed to not be drug related. Among the risks in any gene therapy product based on viral vectors are the risks of immunogenicity, elevated liver enzymes and insertional oncogenesis, which is the process whereby the insertion of a functional gene near a gene that is important in cell growth or division results in uncontrolled cell division, which could potentially enhance the risk of malignant transformation.

While new AAV vectors have been developed to reduce side effects previously reported in third-party gene therapy treatments, and AAV9 has been generally well tolerated in clinical trials and in approved products, gene therapy is still a relatively new approach to disease treatment and additional adverse side effects could develop. There also is the potential risk of delayed adverse events following exposure to gene therapy products due to persistent biologic activity of the genetic material or other components of products used to carry the genetic material.

Possible adverse side effects that could occur with treatment with gene therapy products include an immunologic reaction early after administration, which, while not necessarily adverse to the patient’s health, could substantially limit the effectiveness of the treatment. For example, in previous third-party clinical trials involving other AAV vectors for gene therapy, some subjects experienced the development of a T-cell antibody response, whereby after the vector is within the target cells, the cellular immune response system triggers the removal of transduced cells by activated T-cells. Other preclinical studies have suggested that high dosages of AAV administration may result in toxicity due to degeneration of the DRG. If our vectors demonstrate a similar effect in other programs, we may decide or be required to perform additional preclinical studies or to halt or delay further clinical development of our product candidates.

In addition to side effects caused by the product candidate, the administration process or related procedures also can cause adverse side effects. Each of our lead product candidates are expected to be administered by intrathecal injection. While this method of administration has been available for decades, its use for therapies is relatively new, no gene therapy is currently approved for intrathecal administration, and it may be perceived as having greater risk than more common methods of administration, such as intravenous injection. If any such adverse events occur, our clinical trials could be suspended or terminated. If we cannot demonstrate that any adverse events were not caused by the drug or administration process or related procedures, the FDA or foreign regulatory authorities could order us to cease further development of, or deny approval of, our product candidates for any or all targeted indications. Even if we are able to demonstrate that all future serious adverse events are not product-related, such occurrences could affect patient recruitment or the ability of enrolled patients to complete the trial. Moreover, if we elect, or are required, to not initiate, delay, suspend or terminate any future clinical trial of any of our product candidates, the commercial prospects of such product candidates may be harmed and our ability to generate product revenues from any of these product candidates may be delayed or eliminated. Any of these occurrences may harm our ability to develop other product candidates, and may harm our business, financial condition and prospects significantly.

If our product candidates are associated with side effects in clinical trials or have characteristics that are unexpected, we may need to abandon their development or limit development to more narrow uses in which the side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective. The FDA, comparable foreign regulatory authorities, or an IRB or Ethics Committee may also require that we suspend, discontinue, or limit our clinical trials based on safety information, or that we conduct additional animal or human studies regarding the safety and efficacy of our product candidates which we have not planned or anticipated. Such findings could further result in regulatory authorities failing to provide marketing authorization for our product candidates or limiting the scope of the approved indication, if approved. Many product candidates that initially showed promise in early-stage testing have later been found to cause side effects that prevented further development of the product candidate.

Additionally, if one or more of our product candidates receives marketing approval, and we or others identify undesirable side effects caused by such products, a number of potentially significant negative consequences could result, including:

- regulatory authorities may withdraw, vary or suspend approvals of such product;
- regulatory authorities may require additional warnings on the labels;
- we may be required to create a medication guide outlining the risks of such side effects for distribution to patients or other requirements subject to a REMS or comparable foreign strategies;
- we could be sued and held liable for harm caused to patients;
- we may not be able to achieve or maintain third-party payor coverage and adequate reimbursement; and
- our reputation and physician or patient acceptance of our products may suffer.

There can be no assurance that we will resolve any issues related to any product-related adverse events to the satisfaction of the FDA or foreign regulatory authority in a timely manner or at all. Moreover, any of these events could prevent us from achieving or maintaining market acceptance of the particular product candidate, if approved, and could significantly harm our business, results of operations and prospects.

As an organization, we have never conducted pivotal clinical trials, and may be unable to do so for any product candidates we may develop, including TSHA-102.

We will need to successfully complete our ongoing and planned clinical trials, including pivotal clinical trials, in order to obtain FDA and comparable foreign regulatory approval to market our product candidates. Carrying out later-stage clinical trials and the submission of a successful BLA and comparable foreign application is a complicated process. As an organization, we have initiated Phase 1/2 clinical trials, have not previously conducted any later stage or pivotal clinical trials, but have limited experience in preparing, submitting and prosecuting regulatory filings and have not previously submitted a BLA or comparable foreign application for any product candidate. In addition, we have had limited interactions with the FDA and comparable foreign regulatory authorities and cannot be certain how many additional clinical trials of our product candidates will be required or how such trials should be designed. Consequently, we may be unable to successfully and efficiently execute and complete necessary clinical trials in a way that leads to BLA submission or comparable foreign application and approval of any product candidate. We may require more time and incur greater costs than our competitors and may not succeed in obtaining regulatory approvals of product candidates that we develop. Failure to commence or complete, or delays in, our planned clinical trials, could prevent us from or delay us in commercializing our product candidates.

The disorders we seek to treat have low prevalence and it may be difficult to identify and enroll patients with these disorders. If we experience delays or difficulties in the enrollment and/or maintenance of patients in clinical trials, our receipt of necessary regulatory approvals could be delayed or prevented.

Successful and timely completion of clinical trials will require that we enroll a sufficient number of patients. Patient enrollment, a significant factor in the timing of clinical trials, is affected by many factors, including the size and nature of the patient population and competition for patients with other trials. Genetic diseases generally, and especially the rare diseases for which some of our current product candidates are targeted, have low incidence and prevalence. For example, the estimated addressable patient population with typical Rett syndrome caused by a pathogenic/likely pathogenic MECP2 mutation is between 15,000 and 20,000 patients in the United States, European Union and United Kingdom, and accordingly it may be difficult for us to identify and timely recruit a sufficient number of eligible patients to conduct our clinical trials. Further, any natural history studies that we or our collaborators may conduct may fail to provide us with patients for our clinical trials because patients enrolled in the natural history studies may not be good candidates for our clinical trials, or may choose to not enroll in our clinical trials.

Trials may be subject to delays as a result of patient enrollment taking longer than anticipated or patient withdrawal. We may not be able to initiate or continue clinical trials for our product candidates if we are unable to locate and enroll a sufficient number of eligible patients to participate in these trials as required by the FDA, EMA or foreign regulatory authorities. We cannot predict how successful we will be at enrolling subjects in future clinical trials. Subject enrollment is affected by other factors including:

- the eligibility criteria for the trial in question;
- the size of the patient population and process for identifying patients;
- the perceived risks and benefits of the product candidate in the trial, including relating to AAV9-based gene therapy approaches and intrathecal delivery systems;
- the availability of competing commercially available therapies and other competing therapeutic candidates' clinical trials;
- the willingness of patients to be enrolled in our clinical trials;
- the efforts to facilitate timely enrollment in clinical trials;
- potential disruptions caused by public health crises, such as pandemics or similar outbreaks, including difficulties in initiating clinical sites, enrolling and retaining participants, diversion of healthcare resources away from clinical trials, travel or quarantine policies that may be implemented, and other factors;
- the patient referral practices of physicians;
- the ability to monitor patients adequately during and after treatment; and
- the proximity and availability of clinical trial sites for prospective patients.

Our inability to enroll a sufficient number of patients for clinical trials would result in significant delays and could require us to abandon one or more clinical trials altogether. Enrollment delays in these clinical trials may result in increased development costs for our product candidates, which would cause the value of our company to decline and limit our ability to obtain additional financing. Furthermore, we expect to rely on CROs and clinical trial sites to ensure the proper and timely conduct of our clinical trials and we will have limited influence over their performance.

Furthermore, even if we are able to enroll a sufficient number of patients for our clinical trials, we may have difficulty maintaining enrollment of such patients in our clinical trials.

We may seek orphan drug designation for some of our product candidates and we may be unsuccessful, or may be unable to maintain the benefits associated with orphan drug designation, including the potential for market exclusivity, for product candidates for which we obtain orphan drug designation.

Regulatory authorities in some jurisdictions, including the United States, may designate drugs or biologics intended to treat relatively small patient populations as orphan drug products. Under the Orphan Drug Act, the FDA may designate a drug or biologic as an orphan drug if it is intended to treat a rare disease or condition, which is generally defined as a patient population of fewer than 200,000 individuals in the United States, or a patient population of 200,000 or more in the United States where there is no reasonable expectation that the cost of developing the drug will be recovered from sales in the United States.

In the United States, orphan drug designation entitled a party to financial incentives such as tax advantages and user fee waivers. Opportunities for grant funding toward clinical trial costs may also be available for clinical trials of drugs or biologics for rare diseases, regardless of whether the drugs or biologics are designated for the orphan use. In addition, if a drug or biologic with an orphan drug designation subsequently receives the first marketing approval for the indication for which it has such designation, the product is entitled to a seven year period of marketing exclusivity, which precludes the FDA from approving another marketing application for the same drug and indication for that time period, except in limited circumstances. If our competitors are able to obtain orphan drug exclusivity prior to us, for products that constitute the “same drug” and treat the same indications as our product candidates, we may not be able to have competing products approved by the applicable regulatory authority for a significant period of time.

In the European Union, a medicinal product can be designated as an orphan medicinal product by the European Commission if its sponsor can establish that: (i) the product is intended for the diagnosis, prevention or treatment of life-threatening or chronically debilitating conditions; (ii) either (a) such conditions affect not more than 5 in 10,000 persons in the European Union when the application is made, or (b) the product without the benefits derived from orphan status, would not generate sufficient return in the European Union to justify the necessary investment in developing the medicinal product; and (iii) there exists no satisfactory authorized method of diagnosis, prevention, or treatment of the condition that has been authorized in the European Union, or even if such method exists, the product will be of significant benefit to those affected by that condition.

Orphan medicinal product designation entitles an applicant to incentives such as fee reductions or fee waivers, protocol assistance, and access to the centralized marketing authorization procedure. Upon grant of a marketing authorization, orphan medicinal products are entitled to a ten-year period of market exclusivity for the approved therapeutic indication, which means that the EMA cannot accept another marketing authorization application or accept an application to extend for a similar product and the European Commission cannot grant a marketing authorization for the same indication for a period of ten years. The period of market exclusivity is extended by two years for orphan medicinal products that have also complied with an agreed PIP. The period of market exclusivity may, however, be reduced to six years if, at the end of the fifth year, it is established that the product no longer meets the criteria on the basis of which it received orphan medicinal product designation, including where it can be demonstrated on the basis of available evidence that the original orphan medicinal product is sufficiently profitable not to justify maintenance of market exclusivity or where the prevalence of the condition has increased above the threshold. Additionally, an MA may be granted to a similar medicinal product with the same orphan indication during the 10 year period if: (i) if the applicant consents to a second original orphan medicinal product application, (ii) if the manufacturer of the original orphan medicinal product is unable to supply sufficient quantities; or (iii) if the second applicant can establish that its product, although similar, is safer, more effective or otherwise clinically superior to the original orphan medicinal product. A company may voluntarily remove a product from the register of orphan products. Orphan medicinal product designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process. We have obtained orphan drug designation from the FDA for TSHA-102 for the treatment of Rett syndrome and TSHA-105 for the treatment of SLC13A5 deficiency. In addition, TSHA-118 has received orphan drug designation for the treatment of CLN1 disease from the FDA and EMA.

We may seek orphan designation for certain of our other current and future product candidates. However, we may be unsuccessful in obtaining orphan drug designation for these or other product candidates and may be unable to maintain the benefits associated with orphan drug designation. Even if we obtain orphan drug exclusivity for any of our product candidates, that exclusivity may not effectively protect those product candidates from competition because different drugs can be approved for the same condition, and orphan drug exclusivity does not prevent the FDA or comparable foreign regulatory authorities from approving the same or a different drug in another indication. Even after an orphan drug is granted orphan exclusivity and approved, the FDA can subsequently approve a later application for the same drug for the same condition before the expiration of the seven-year exclusivity period if the FDA concludes that the later drug is clinically superior in that it is shown to be safer in a substantial portion of the target populations, more effective or makes a major contribution to patient care. In addition, a designated orphan drug may not receive orphan drug exclusivity if it is approved for a use that is broader than the indication for which it received orphan designation. Moreover, orphan-drug-exclusive marketing rights in the United States may be lost if the FDA later determines that the request for designation was materially defective or if we are unable to manufacture sufficient quantities of the product to meet the needs of patients with the rare disease or condition. Orphan drug designation neither shortens the development time or regulatory review time of a drug nor gives the drug any advantage in the regulatory review or approval process.

We have received rare pediatric disease designation for TSHA-102 for the treatment of Rett syndrome. However, a marketing application for TSHA-102, if approved, may not meet the eligibility criteria for a PRV or the rare pediatric disease designation program may sunset before FDA is able to consider us for a voucher.

We have received rare pediatric disease designation for TSHA-102 for the treatment of Rett syndrome. Designation of a drug or biologic as a product for a rare pediatric disease does not guarantee that a BLA for such drug or biologic will meet the eligibility criteria for a rare pediatric disease PRV at the time the application is approved. Under the FDCA, we will need to request a rare

pediatric disease PRV in our original BLA for TSHA-102, and any other candidates for which we submit a marketing application. The FDA may determine that such BLA, if approved, does not meet the eligibility criteria for a PRV, including for the following reasons:

- Rett syndrome no longer meets the definition of a rare pediatric disease;
- the BLA contains an active ingredient that has been previously approved in a BLA;
- the BLA is not deemed eligible for priority review;
- the BLA does not rely on clinical data derived from studies examining a pediatric population and dosages of the drug intended for that population (that is, if the BLA does not contain sufficient clinical data to allow for adequate labeling for use by the full range of affected pediatric patients); or
- the BLA is approved for a different adult indication than the rare pediatric disease for which TSHA-102 is designated.

The authority for the FDA to award rare pediatric disease PRVs for drugs that have received rare pediatric disease designation currently expires on September 30, 2026. Absent any extension through federal legislation, if the BLA for TSHA-102 is not approved prior to September 30, 2026 for any reason, regardless of whether it meets the criteria for a rare pediatric disease PRV, it will not be eligible for a PRVs.

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

Because we have limited financial and management resources, we must focus on development programs and product candidates that we identify for specific indications. As such, we are currently primarily focused on the development of TSHA-102 (Rett syndrome). As a result, we may forego or delay pursuit of opportunities with other product candidates, including TSHA-101 (GM2 gangliosidosis), TSHA-103 (SLC6A1), TSHA-105 (SLC13A5 deficiency), TSHA-118 (CLN1 disease), and TSHA-121 (CLN7) or for other indications for these product candidates that later prove to have greater commercial potential. Our resource allocation decisions, for example, our strategic prioritization in March 2022, may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future development programs and product candidates for specific indications may not yield any commercially viable products. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate.

We are currently conducting our Phase 1/2 adolescent and adult trial of TSHA-102 in Canada and our Phase 1/2 pediatric trial of TSHA-102 in the United Kingdom and Canada and plan to conduct in the future additional clinical trials for our product candidates outside the United States, and the FDA and similar foreign regulatory authorities may not accept data from such trials.

We are conducting our Phase 1/2 adolescent and adult clinical trial of TSHA-102 in Canada and our Phase 1/2 pediatric clinical trial of TSHA-102 in the United Kingdom and Canada and may in the future choose to conduct additional clinical trials outside the United States, including in the United Kingdom, European Union or other foreign jurisdictions. The acceptance of trial data from clinical trials conducted outside the United States by the FDA may be subject to certain conditions. In cases where data from clinical trials conducted outside the United States are intended to serve as the sole basis for marketing approval in the United States, the FDA will generally not approve the application on the basis of foreign data alone unless (i) the data are applicable to the U.S. population and U.S. medical practice; (ii) the trials were performed by clinical investigators of recognized competence and (iii) the data may be considered valid without the need for an on-site inspection by the FDA or, if the FDA considers such an inspection to be necessary, the FDA is able to validate the data through an on-site inspection or other appropriate means. Additionally, the FDA's clinical trial requirements, including sufficient size of patient populations and statistical powering, must be met. Many foreign regulatory bodies have similar approval requirements. In addition, such foreign trials would be subject to the applicable local laws of the foreign jurisdictions where the trials are conducted. There can be no assurance that the FDA or any similar foreign regulatory authority will accept data from trials conducted outside of the United States or the applicable jurisdiction. If the FDA or any similar foreign regulatory authority does not accept such data, it would result in the need for additional trials, which would be costly and time-consuming and delay aspects of our business plan, and which may result in our product candidates not receiving approval or clearance for commercialization in the applicable jurisdiction.

We may not be successful in our efforts to build a pipeline of additional product candidates.

Our business model is centered on developing therapies for patients with rare, monogenic central nervous system, or CNS, disorders by establishing focused selection criteria to select, develop and advance product candidates that we believe will have a high probability of technical and regulatory success through development into commercialization. We may not be able to continue to

identify and develop new product candidates, including from our next-generation platform technologies, in addition to the pipeline of product candidates that we have established through our collaboration with UT Southwestern. Even if we are successful in continuing to build our pipeline, the potential product candidates that we identify may not be suitable for clinical development. For example, they may be shown to have harmful side effects or other characteristics that indicate that they are unlikely to be drugs that will receive marketing approval and achieve market acceptance. If we do not successfully develop and commercialize product candidates based upon our approach, we will not be able to obtain product revenue in future periods, which likely would result in significant harm to our financial position and adversely affect our stock price.

If we do not achieve our projected development goals in the time frames we announce and expect, the commercialization of our products may be delayed.

From time to time, we may estimate the timing of the accomplishment of various scientific, clinical, regulatory, manufacturing and other product development goals, which we sometimes refer to as milestones. These milestones may include the commencement or completion of preclinical studies and clinical trials and the submission of regulatory filings, including IND/CTA submissions. From time to time, we may publicly announce the expected timing of some of these milestones. All of these milestones are, and will be, based on a variety of assumptions. The actual timing of these milestones can vary significantly compared to our estimates, in some cases for reasons beyond our control. We may experience numerous unforeseen events during, or as a result of, any future clinical trials that we conduct that could delay or prevent our ability to receive marketing approval or commercialize our product candidates.

The United Kingdom's withdrawal from the European Union may adversely impact our ability to obtain regulatory approvals of our product candidates in the European Union, result in restrictions or imposition of taxes and duties for importing our product candidates into the European Union and require us to incur additional expenses in order to develop, manufacture and commercialize our product candidates in the European Union.

The United Kingdom's withdrawal from the European Union on January 31, 2020, commonly referred to as Brexit, has changed the regulatory relationship between the United Kingdom and the European Union. The Medicines and Healthcare products Regulatory Agency, or MHRA, is now the United Kingdom's standalone regulator for medicinal products and medical devices. Great Britain (England, Scotland and Wales) is now a third country to the European Union. Northern Ireland will, with regard to EU regulations, continue to follow the EU regulatory rules for now.

The UK regulatory framework in relation to clinical trials is governed by the Medicines for Human Use (Clinical Trials) Regulations 2004, as amended, which is derived from the CTD, as implemented into the UK national law through secondary legislation. On January 17, 2022, the MHRA launched an eight-week consultation on reframing the UK legislation for clinical trials. The UK Government published its response to the consultation on March 21, 2023 confirming that it would bring forward changes to the legislation. These resulting legislative amendments will, if implemented in their current form, bring the UK into closer alignment with the CTR. In October 2023, the MHRA announced a new Notification Scheme for clinical trials which enables a more streamlined and risk-proportionate approach to initial clinical trial applications for Phase 4 and low-risk Phase 3 clinical trial applications.

All existing EU marketing authorizations for centrally authorized products were automatically converted or grandfathered into UK marketing authorizations, effective in the United Kingdom only, free of charge on January 1, 2021, unless the marketing authorization holder opted-out of this possibility. Northern Ireland remained within the scope of EU authorizations in relation to centrally authorized medicinal products until January 1, 2025. However, on January 1, 2025, a new arrangement as part of the so-called "Windsor Framework" came into effect and reintegrated Northern Ireland under the regulatory authority of the MHRA with respect to medicinal products. The Windsor Framework removes EU licensing processes and EU labelling and serialization requirements in relation to Northern Ireland and introduces a UK-wide licensing process for medicines.

The MHRA has also introduced changes to national marketing authorization procedures. This includes introduction of procedures to prioritize access to new medicines that will benefit patients, including a 150-day assessment route, a rolling review procedure and the International Recognition Procedure. Since January 1, 2024, the MHRA may rely on the International Recognition Procedure, or IRP, when reviewing certain types of marketing authorization applications. This procedure is available for applicants for marketing authorization who have already received an authorization for the same product from a reference regulator. These include the FDA, the EMA, and national competent authorities of individual European Economic Area, or EEA, countries. A positive opinion from the EMA and CHMP, or a positive end of procedure outcome from the mutual recognition or decentralized procedures are considered to be authorizations for the purposes of the IRP.

There is no pre-marketing authorization orphan designation for medicinal products in the United Kingdom. Instead, the MHRA reviews applications for orphan designation in parallel to the corresponding marketing authorization application. The criteria are essentially the same as those in the European Union, but have been tailored for the market. This includes the criterion that

prevalence of the condition in the United Kingdom, rather than the European Union, must not be more than five in 10,000. Upon the grant of a marketing authorization with orphan status, the medicinal product will benefit from up to 10 years of market exclusivity from similar products in the approved orphan indication. The start of this market exclusivity period will be set from the date of first approval of the product in the United Kingdom.

Since a significant proportion of the regulatory framework in the United Kingdom applicable to our business and our product candidates is derived from European Union directives and regulations, Brexit has materially impacted and could continue to further impact, the regulatory regime with respect to the development, manufacture, importation, approval and commercialization of our product candidates in the United Kingdom or the European Union. Any delay in obtaining, or an inability to obtain, any marketing approvals, as a result of Brexit or otherwise, would limit our ability to generate revenue and achieve and sustain profitability. In addition, while the Trade and Cooperation Agreement provides for the tariff-free trade of medicinal products between the United Kingdom and the European Union there are additional non-tariff costs to such trade which did not exist prior to Brexit. Furthermore, Brexit has reduced trade between the European Union and the United Kingdom and there are frequent delays in the transit of goods between the European Union and the United Kingdom. The ongoing impact of Brexit may force us to restrict or delay efforts to seek regulatory approval in the United Kingdom or the European Union for our product candidates, or incur significant additional expenses to operate our business, which could significantly and materially harm or delay our ability to generate revenues or achieve profitability of our business. Any further changes in international trade, tariff and import/export regulations as a result of Brexit or otherwise may impose unexpected duty costs or other non-tariff barriers on us.

Risks Related to the Manufacturing of our Product Candidates

Gene therapies are novel, complex and difficult to manufacture. We could experience manufacturing problems that result in delays in the development or commercialization of our product candidates or otherwise harm our business.

The manufacture of gene therapy products is technically complex and necessitates substantial expertise and capital investment. Production difficulties caused by unforeseen events may delay the availability of material for our clinical studies.

We currently rely on third-party contract manufacturing organizations, or CMOs, including Catalent, to manufacture our product candidates. We expect to rely on CMOs for our manufacturing needs for the foreseeable future. To date, our manufacturing partners have met our manufacturing requirements and quality standards for our program materials, and we expect that these organizations, primarily Catalent, will be capable of providing sufficient quantities of our program materials to meet anticipated clinical trial scale demands. While we believe that there are alternative sources of supply for our program materials that can satisfy our clinical and commercial requirements, identifying and establishing relationships with such sources, if necessary, would result in delays and additional costs, both of which could be significant.

The manufacturers of pharmaceutical products must comply with strictly enforced cGMP requirements, state and federal regulations, as well as foreign requirements when applicable. Any failure of us or our CMOs to adhere to or document compliance to such regulatory requirements could lead to a delay or interruption in the availability of our program materials for clinical trials or enforcement action from the FDA, competent authorities of EU Member States or foreign regulatory authorities. If we or our manufacturers were to fail to comply with the FDA, European Union or other regulatory authority requirements, it could result in sanctions being imposed on us, including clinical holds, fines, injunctions, civil penalties, delays, suspension, variation or withdrawal of approvals, license revocation, seizures or recalls of product candidates or products, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our product candidates. Our potential future dependence upon others for the manufacture of our product candidates may also adversely affect our future profit margins and our ability to commercialize any product candidates that receive regulatory approval on a timely and competitive basis.

Biological products are inherently difficult to manufacture. Although we believe that the manufacture of our product candidates may be simplified due to their shared raw materials and other similarities, we cannot be certain that this will be the case and we may be required to develop manufacturing methods that ultimately differ significantly between product candidates, which would require that we invest substantial time and capital to develop suitable manufacturing methods. Our program materials are manufactured using technically complex processes requiring specialized equipment and facilities, highly specific raw materials, cells, and reagents, and other production constraints. Our production process requires a number of highly specific raw materials, cells and reagents with limited suppliers. Even though we aim to have backup supplies of raw materials, cells and reagents whenever possible, we cannot be certain they will be sufficient if our primary sources are unavailable. A shortage of a critical raw material, cell line, or reagent, or a technical issue during manufacturing may lead to delays in clinical development or commercialization plans. We are particularly susceptible to any shortages, delays or our inability to obtain suitable AAV9 raw materials, given that all of our current and planned product candidates require this starting material. Any changes in the manufacturing of components of the raw materials we use could result in unanticipated or unfavorable effects in our manufacturing processes, resulting in delays.

We and our contract manufacturers for AAV9 are subject to significant regulation with respect to manufacturing our products. The third-party manufacturing facilities on which we rely may have limited capacity or fail to meet the applicable stringent regulatory requirements.

We currently have relationships with a limited number of suppliers for the manufacturing of plasmids and viruses, components of our product candidates. However, if we experience slowdowns or problems with our facility or those of our manufacturing partners and are unable to establish or scale our internal manufacturing capabilities, we will need to continue to contract with manufacturers that can produce the preclinical, clinical and commercial supply of our products. Each supplier may require licenses to manufacture such components if such processes are not owned by the supplier or in the public domain and we may be unable to license such intellectual property rights on reasonable commercial terms or to transfer or sublicense the intellectual property rights we may have with respect to such activities.

All entities involved in the preparation of therapeutics for clinical trials or commercial sale, including our existing CMOs for components of our product candidates, are subject to extensive regulation. Components of a finished therapeutic product approved for commercial sale or used in late-stage clinical trials in the European Union must be manufactured in accordance with cGMP. These regulations govern manufacturing processes and procedures (including record keeping) and the implementation and operation of quality systems to control and assure the quality of investigational products and products approved for sale. Poor control of production processes can lead to the introduction of adventitious agents or other contaminants, or to inadvertent changes in the properties or stability of our product candidates that may not be detectable in final product testing. We are at an increased risk given that our product candidates have been and for the foreseeable future will be produced on the same manufacturing lines, which could, for example, lead to issues with cross-contamination. We or our CMOs must supply all necessary documentation in support of a BLA or MAA on a timely basis. Our facilities and quality systems and the facilities and quality systems of some or all of our third-party contractors must pass a pre-approval inspection for compliance with the applicable regulations as a condition of regulatory approval of our product candidates or any of our other potential products. In addition, the regulatory authorities may, at any time, audit or inspect a manufacturing facility involved with the preparation of our product candidates or our other potential products or the associated quality systems for compliance with the regulations applicable to the activities being conducted, and they could put a hold on one or more of our clinical trials if the facilities of our contract development and manufacturing organizations, or CDMOs, do not pass such audit or inspections. If these facilities do not pass a pre-approval plant inspection, FDA approval of the products will not be granted.

The regulatory authorities also may, at any time following approval of a product for sale, inspect or audit our manufacturing facilities or those of our third-party contractors, including periodic unannounced inspections by the FDA, competent authorities of EU Member States or other comparable foreign regulatory authorities, to monitor and ensure compliance with cGMP. If any such inspection or audit identifies a failure to comply with applicable regulations or if a violation of our product specifications or applicable regulations occurs independent of such an inspection or audit, we or the relevant regulatory authority may require remedial measures that may be costly and/or time-consuming for us or a third party to implement and that may include the temporary or permanent suspension of a clinical trial or commercial sales or the temporary or permanent closure of a facility. Any such remedial measures imposed upon us or third parties with whom we contract could harm our business. If we or any of our third-party manufacturers fail to maintain regulatory compliance, the FDA or comparable foreign regulatory authority can impose regulatory sanctions including, among other things, shutdown of the third-party vendor or invalidation of drug product lots or processes, fines, injunctions, civil penalties, delays, refusal to approve a pending application for a new drug product or biologic product, or revocation, suspension or variation of a pre-existing approval, license revocation, seizures or recalls of product candidates or drugs, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our products, if approved, and significantly harm our business, financial condition, results of operations and prospects. Additionally, if supply from one approved manufacturer is interrupted, there could be a significant disruption in commercial supply. An alternative manufacturer would need to be qualified through a BLA and/or MAA supplement which could result in further delay. The regulatory authorities may also require additional studies if a new manufacturer is relied upon for commercial production. Switching manufacturers may involve substantial costs and is likely to result in a delay in our desired clinical and commercial timelines.

These factors could cause the delay of clinical trials, regulatory submissions, required approvals or commercialization of our product candidates, cause us to incur higher costs and prevent us from commercializing our products successfully, if approved. Furthermore, if our suppliers fail to meet contractual requirements, and we are unable to secure one or more replacement suppliers capable of production at a substantially equivalent cost, our clinical trials may be delayed or we could lose potential revenue.

We depend on third-party suppliers for materials used in the manufacture of our product candidates, and the loss of these third-party suppliers or their inability to supply us with adequate materials could harm our business.

We rely on third-party suppliers for certain materials and components required for the production of our product candidates. Our dependence on these third-party suppliers and the challenges we may face in obtaining adequate supplies of materials involve several risks, including limited control over pricing, availability, and quality and delivery schedules. There is substantial demand and limited supply for certain of the raw materials used to manufacture gene therapy products. As a small company, our negotiation leverage is limited and we are likely to get lower priority than our competitors that are larger than we are. We cannot be certain that our suppliers will continue to provide us with the quantities of these raw materials that we require or satisfy our anticipated specifications and quality requirements. Any supply interruption in limited or sole sourced raw materials could materially harm our ability to manufacture our product candidates until a new source of supply, if any, could be identified and qualified. We may be unable to find a sufficient alternative supply channel 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 our product candidates, including limiting supplies necessary for clinical trials and regulatory approvals, which would have a material adverse effect on our business.

Any contamination or interruption in our manufacturing process, shortages of raw materials or failure of our suppliers of plasmids and viruses to deliver necessary components could result in delays in our clinical development or marketing schedules.

Given the nature of gene therapy manufacturing, there is a risk of contamination. Any contamination could adversely affect our ability to produce product candidates on schedule and could, therefore, harm our results of operations and cause reputational damage. Some of the raw materials required in our manufacturing process are derived from biologic sources. Such raw materials are difficult to procure and may be subject to contamination or recall. A material shortage, contamination, recall or restriction on the use of biologically derived substances in the manufacture of our product candidates could adversely impact or disrupt the commercial manufacturing or the production of clinical material, which could adversely affect our development timelines and our business, financial condition, results of operations and prospects.

Changes in methods of product candidate manufacturing or formulation may result in additional costs or delay.

As product candidates proceed through preclinical studies to late-stage clinical trials towards potential approval and commercialization, it is common that various aspects of the development program, such as manufacturing methods and formulation, are altered along the way in an effort to optimize processes and product characteristics. Such changes carry the risk that they will not achieve our intended objectives. Any such changes could cause our product candidates to perform differently and affect the results of planned clinical trials or other future clinical trials conducted with the materials manufactured using altered processes. Such changes may also require additional testing, FDA notification or FDA approval, or comparable foreign regulatory requirements. This could delay completion of clinical trials, require the conduct of bridging clinical trials or the repetition of one or more clinical trials, increase clinical trial costs, delay approval of our product candidates and jeopardize our ability to commence sales and generate revenue. In addition, we may be required to make significant changes to our upstream and downstream processes across our pipeline, which could delay the development of our future product candidates.

Risks Related to the Commercialization of our Product Candidates

Even if any of our product candidates receive marketing approval, they may fail to achieve the degree of market acceptance by physicians, patients, third-party payors and others in the medical community necessary for commercial success.

If any of our product candidates receive marketing approval, they may nonetheless fail to gain sufficient market acceptance by physicians, patients, third-party payors and others in the medical community. If our product candidates do not achieve an adequate level of acceptance, we may not generate significant revenue and we may not become profitable. The degree of market acceptance of our product candidates, if approved for commercial sale, will depend on a number of factors, including:

- the efficacy, safety and potential advantages compared to alternative treatments;
- our ability to offer our products for sale at competitive prices;
- the convenience and ease of administration compared to alternative treatments;
- product labeling or product insert requirements of the FDA or foreign regulatory authorities, including any limitations or warnings contained in a product's approved labeling, including any black box warning or REMS or comparable foreign strategy;
- the willingness of the target patient population to try new treatments and of physicians to prescribe these treatments;
- our ability to hire and retain a sales force in the United States;

- the strength of marketing and distribution support;
- the availability of third-party coverage and adequate reimbursement for TSHA-102 and any other product candidates, once approved;
- the prevalence and severity of any side effects; and
- any restrictions on the use of our products together with other medications.

Negative public opinion of gene therapy and increased regulatory scrutiny of gene therapy and genetic research may adversely impact the development or commercial success of our current and future product candidates.

Our potential therapeutic products involve introducing genetic material into a patient's cells via intrathecal administration. The clinical and commercial success of our potential products will depend in part on public acceptance of the use of gene therapy and gene regulation for the prevention or treatment of human diseases. Public attitudes may be influenced by claims that gene therapy and gene regulation are unsafe, unethical or immoral, and consequently, our products may not gain the acceptance of the public or the medical community. Adverse public attitudes may adversely impact our ability to enroll clinical trials. Moreover, our success will depend upon physicians prescribing, and their patients being willing to receive, treatments that involve the use of product candidates we may develop in lieu of, or in addition to, existing treatments with which they are already familiar and for which greater clinical data may be available.

More restrictive government regulations or negative public opinion would have a negative effect on our business or financial condition and may delay or impair the development and commercialization of our product candidates or demand for any products once approved. For example, in 2003, trials using early versions of murine gamma-retroviral vectors, which integrate with, and thereby alter, the host cell's DNA, led to several well-publicized adverse events, including reported cases of leukemia. Although none of our current product candidates utilize murine gamma-retroviral vectors, our product candidates use AAV9 viral vectors. Among the risks in any gene therapy product based on viral vectors are the risks of immunogenicity, elevated liver enzymes, and insertional oncogenesis. If any of our vectors demonstrate a similar effect we may decide or be required to halt or delay further clinical development of any product candidates that utilize that vector. Adverse events in our or others' clinical trials, even if not ultimately attributable to our product candidates, and the resulting publicity could result in increased governmental regulation, unfavorable public perception, potential regulatory delays in the testing or approval of our product candidates, stricter labeling requirements for those product candidates that are approved and a decrease in demand for any such product candidates. The risk of cancer remains a concern for gene therapy and we cannot assure that it will not occur in any of our planned or future clinical trials or in any clinical trials conducted by other companies. In addition, there is the potential risk of delayed adverse events following exposure to gene therapy products due to persistent biological activity of the genetic material or other components of products used to carry the genetic material. In addition, for our regulated gene replacement therapy candidates that require that the expression of a therapeutic transgene be tightly regulated, such as TSHA-102, we may inadvertently cause overexpression, which could lead to numerous issues, including safety and toxicity concerns. Furthermore, these regulatory gene replacement therapy candidates require the insertion of miRNA targets into the viral genome, which is a technology that to our knowledge is not present in any approved gene therapy products. If any such adverse events occur, commercialization of our product candidates or further advancement of our clinical trials could be halted or delayed, which would have a negative impact on our business and operations.

If we are unable to establish sales, marketing and distribution capabilities for TSHA-102 or any other product candidate that may receive regulatory approval, we may not be successful in commercializing those product candidates if and when they are approved.

We do not have sales or marketing infrastructure. To achieve commercial success for TSHA-102 or any other product candidate for which we may obtain marketing approval, we will need to establish a sales and marketing organization. In the future, we expect to build a focused sales and marketing infrastructure to market some of our product candidates in the United States, if and when they are approved. There are risks involved with establishing our own sales, marketing and distribution capabilities. For example, recruiting and training a sales force is expensive and time-consuming and could delay any product launch. If the commercial launch of a product candidate for which we recruit a sales force and establish marketing capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. This may be costly, and our investment would be lost if we cannot retain or reposition our sales and marketing personnel.

Factors that may inhibit our efforts to market our products on our own include:

- our inability to recruit, train and retain adequate numbers of effective sales and marketing personnel;
- the inability of sales personnel to obtain access to physicians in order to educate physicians about our product candidates, once approved;

- the lack of complementary products to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines; and
- unforeseen costs and expenses associated with creating an independent sales and marketing organization.

If we are unable to establish our own sales, marketing and distribution capabilities and are forced to enter into arrangements with, and rely on, third parties to perform these services, our revenue and our profitability, if any, are likely to be lower than if we had developed such capabilities ourselves. In addition, we may not be successful in entering into arrangements with third parties to sell, market and distribute our product candidates or may be unable to do so on terms that are favorable to us. We likely will have little control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our products effectively. If we do not establish sales, marketing and distribution capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing our product candidates.

The affected populations for our other product candidates may be smaller than we or third parties currently project, which may affect the addressable markets for our product candidates.

We currently focus our research and product development on several indications that are orphan diseases. However, our projections of the number of people who have the diseases we are seeking to treat, as well as the subset of people with these diseases who have the potential to benefit from treatment with our product candidates, are estimates based on our knowledge and understanding of these diseases. These estimates may prove to be incorrect and new studies may further reduce the estimated incidence or prevalence of this disease. The number of patients in the United States, the European Union and elsewhere may turn out to be lower than expected, may not be otherwise amenable to treatment with our product candidate or patients may become increasingly difficult to identify and access, all of which would adversely affect our business, financial condition, results of operations and prospects.

The total addressable market opportunity for our product candidates will ultimately depend upon a number of factors including the diagnosis and treatment criteria included in the final label, if approved for sale in specified indications, acceptance by the medical community, patient access and product pricing and reimbursement. Incidence and prevalence estimates are frequently based on information and assumptions that are not exact and may not be appropriate, and the methodology is forward-looking and speculative. The process we have used in developing an estimated incidence and prevalence range for the indications we are targeting has involved collating limited data from multiple sources. Accordingly, the incidence and prevalence estimates included in this Annual Report on Form 10-K should be viewed with caution. Further, the data and statistical information used in this Annual Report on Form 10-K, including estimates derived from them, may differ from information and estimates made by our competitors or from current or future studies conducted by independent sources.

We face significant competition from other biotechnology and pharmaceutical companies, and our operating results will suffer if we fail to compete effectively.

Drug development, particularly in the gene therapy field, is highly competitive and subject to rapid and significant technological advancements. As a significant unmet medical need exists in the neurology field, particularly for the treatment of neurodegenerative diseases, neurodevelopmental disorders and genetic epilepsies, there are several large and small pharmaceutical companies focused on delivering therapeutics for the treatment of these diseases. Further, it is likely that additional drugs will become available in the future for the treatment of our target indications.

Trofinetide was approved by the FDA in March 2023 for the treatment of Rett Syndrome. We are aware that our competitors are developing product candidates for the treatment of diseases that our product candidates will target. With respect to TSHA-102, we are aware that Neurogene has a clinical stage gene therapy program for the treatment of Rett syndrome.

Many of our existing or potential competitors have substantially greater financial, technical and human resources than we do and significantly greater experience in the discovery and development of product candidates, as well as in obtaining regulatory approvals of those product candidates in the United States and in foreign countries. Our current and potential future competitors may also have significantly more experience commercializing drugs, particularly gene therapy and other biological products, that have been approved for marketing. Mergers and acquisitions in the pharmaceutical and biotechnology industries could result in even more resources being concentrated among a small number of our competitors.

We will face competition from other drugs or from other non-drug products currently approved or that will be approved in the future in the neurology field, including for the treatment of diseases and disorders in the therapeutic categories we intend to target. Therefore, our ability to compete successfully will depend largely on our ability to:

- develop and commercialize drugs that are superior to other products in the market;
- demonstrate through our clinical trials that our product candidates are differentiated from existing and future therapies;
- attract qualified scientific, product development and commercial personnel;
- obtain patent or other proprietary protection for our medicines;
- obtain required regulatory approvals;
- obtain coverage and adequate reimbursement from, and negotiate competitive pricing with, third-party payors; and
- successfully collaborate with pharmaceutical companies in the discovery, development and commercialization of new medicines.

The availability of our competitors' products could limit the demand, and the price we are able to charge, for any product candidate we develop. The inability to compete with existing or subsequently introduced drugs would have an adverse impact on our business, financial condition and prospects. In addition, the reimbursement structure of approved gene therapies by other companies could impact the anticipated reimbursement structure of our gene therapies, if approved, and our business, financial condition, results of operations and prospects.

Established pharmaceutical companies may invest heavily to accelerate discovery and development of novel compounds or to in-license novel compounds that could make our product candidates less competitive. In addition, any new product that competes with an approved product must demonstrate compelling advantages in efficacy, convenience, tolerability and safety in order to overcome price competition and to be commercially successful. Accordingly, our competitors may succeed in obtaining patent protection, discovering, developing, receiving regulatory and marketing approval for, or commercializing, drugs before we do, which would have an adverse impact on our business and results of operations.

Biologic products may face competition sooner than anticipated.

The Biologics Price Competition and Innovation Act, or BPCIA, created an abbreviated approval pathway for biological products that are biosimilar to or interchangeable with an FDA-licensed reference biological product. Under the BPCIA, an application for a biosimilar product may not be submitted to the FDA until four years following the date that the reference product was first licensed by the FDA. In addition, the approval of a biosimilar product may not be made effective by the FDA until 12 years from the date on which the reference product was first licensed. During this 12-year period of exclusivity, another company may still market a competing version of the reference product if the FDA approves a full BLA for the competing product containing the sponsor's own preclinical data and data from adequate and well-controlled clinical trials to demonstrate the safety, purity and potency of their product.

There is a risk that any of our product candidates approved as a biological product under a BLA would not qualify for the 12-year period of exclusivity or that this exclusivity could be shortened due to congressional action or otherwise, or that the FDA will not consider our product candidates to be reference products for competing products, potentially creating the opportunity for generic competition sooner than anticipated. If competitors are able to obtain marketing approval for biosimilars referencing our candidates, if approved, our products may become subject to competition from such biosimilars, with the attendant competitive pressure and potential adverse consequences.

The success of our product candidates will depend significantly on coverage and adequate reimbursement or the willingness of patients to pay for these procedures.

We believe our success depends on obtaining and maintaining coverage and adequate reimbursement for our product candidates, including TSHA-102 for the treatment of Rett syndrome and the extent to which patients will be willing to pay out-of-pocket for such products, in the absence of reimbursement for all or part of the cost. In the United States and in other countries, patients who are provided medical treatment for their conditions generally rely on third-party payors to reimburse all or part of the costs associated with their treatment. The availability of coverage and adequacy of reimbursement for our products by third-party payors, including government health care programs (e.g., Medicare, Medicaid, TRICARE), managed care providers, private health insurers, health maintenance organizations, and other organizations is essential for most patients to be able to afford medical services and pharmaceutical products such as our product candidates. Third-party payors often rely upon Medicare coverage policy and payment limitations in setting their own coverage and reimbursement policies. However, decisions regarding the extent of coverage

and amount of reimbursement to be provided are made on a payor-by-payor basis. One payor's determination to provide coverage for a drug product does not assure that other payors will also provide coverage, and adequate reimbursement. The principal decisions about reimbursement for new medicines are typically made by the Centers for Medicare & Medicaid Services, or CMS, an agency within the U.S. Department of Health and Human Services, or HHS. CMS decides whether and to what extent products will be covered and reimbursed under Medicare and private payors tend to follow CMS to a substantial degree.

Third-party payors determine which products and procedures they will cover and establish reimbursement levels. Even if a third-party payor covers a particular product or procedure, the resulting reimbursement payment rates may not be adequate. Patients who are treated in-office for a medical condition generally rely on third-party payors to reimburse all or part of the costs associated with the procedure, including costs associated with products used during the procedure, and may be unwilling to undergo such procedures in the absence of such coverage and adequate reimbursement. Physicians may be unlikely to offer procedures for such treatment if they are not covered by insurance and may be unlikely to purchase and use our product candidates, if approved, for our stated indications unless coverage is provided and reimbursement is adequate. In addition, for products administered under the supervision of a physician, obtaining coverage and adequate reimbursement may be particularly difficult because of the higher prices often associated with such drugs.

Reimbursement by a third-party payor may depend upon a number of factors, including the third-party payor's determination that a procedure is safe, effective and medically necessary; appropriate for the specific patient; cost-effective; supported by peer-reviewed medical journals; included in clinical practice guidelines; and neither cosmetic, experimental, nor investigational. Further, increasing efforts by third-party payors in the United States and abroad to cap or reduce healthcare costs may cause such organizations to limit both coverage and the level of reimbursement for newly approved products and, as a result, they may not cover or provide adequate payment for our product candidates. In order to secure coverage and reimbursement for any product that might be approved for sale, we may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of our products, in addition to the costs required to obtain FDA or comparable regulatory approvals. Additionally, we may also need to provide discounts to purchasers, private health plans or government healthcare programs. Our product candidates may nonetheless not be considered medically necessary or cost-effective. If third-party payors do not consider a product to be cost-effective compared to other available therapies, they may not cover the product after approval as a benefit under their plans or, if they do, the level of payment may not be sufficient to allow a company to sell its products at a profit. We expect to experience pricing pressures from third-party payors in connection with the potential sale of any of our product candidates.

Foreign governments also have their own healthcare reimbursement systems, which vary significantly by country and region, and we cannot be sure that coverage and adequate reimbursement will be made available with respect to the treatments in which our products are used under any foreign reimbursement system. The European Union provides options for EU 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. An EU Member State may approve a specific price for the medicinal product, it may refuse to reimburse a product at the price set by the manufacturer 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. Many EU Member States also periodically review their reimbursement procedures for medicinal products, which could have an adverse impact on reimbursement status. Moreover, in order to obtain reimbursement for our products in some European countries, including some EU Member States, we may be required to compile additional data comparing the cost-effectiveness of our products to other available therapies. This Health Technology Assessment, or HTA, of medicinal products is becoming an increasingly common part of the pricing and reimbursement procedures in some EU Member States, including those representing the larger markets. The HTA process is the procedure to assess therapeutic, economic and societal impact of a given medicinal product in the national healthcare systems of the individual country. The outcome of an HTA will often influence the pricing and reimbursement status granted to these medicinal products by the competent authorities of individual EU Member States. The extent to which pricing and reimbursement decisions are influenced by the HTA of the specific medicinal product currently varies between EU Member States.

Legislators, policymakers and healthcare insurance funds in the European Union and the United Kingdom may continue to propose and implement cost-containing measures to keep healthcare costs down, particularly due to the financial strain that the COVID-19 pandemic has placed on national healthcare systems of European countries. These measures could include limitations on the prices we would be able to charge for product candidates that we may successfully develop and for which we may obtain regulatory approval or the level of reimbursement available for these products from governmental authorities or third-party payors. Further, an increasing number of EU and other foreign countries use prices for medicinal products established in other countries as "reference prices" to help determine the price of the product in their own territory. Consequently, a downward trend in prices of medicinal products in some countries could contribute to similar downward trends elsewhere.

There can be no assurance that TSHA-102 or any other product candidate, if approved for sale in the United States or in other countries, will be considered medically reasonable and necessary, that it will be considered cost-effective by third-party payors, that coverage or an adequate level of reimbursement will be available or that reimbursement policies and practices in the United States and

in foreign countries where our products are sold will not adversely affect our ability to sell our product candidates profitably, if they are approved for sale.

Product liability lawsuits against us could cause us to incur substantial liabilities and to limit commercialization of any products that we may develop.

We face an inherent risk of product liability exposure related to the testing of our product candidates in human clinical trials and will face an even greater risk if we commercially sell any products that we may develop. If we cannot successfully defend ourselves against claims that our product candidates or drugs caused injuries, we will incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

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

Although we maintain product liability insurance coverage, such insurance may not be adequate to cover all liabilities that we may incur. We may need to increase our insurance coverage as we expand our clinical trials or if we commence commercialization of our product candidates. Insurance coverage is increasingly expensive. We may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise.

Risks Related to Our Dependence on Third Parties

We currently rely on our collaboration with UT Southwestern for our preclinical research and development programs, including for discovering, preclinically developing and conducting all IND-enabling studies for our lead product candidates and our near-term future pipeline. Failure or delay of UT Southwestern to fulfill all or part of its obligations to us under the agreement, a breakdown in collaboration between the parties or a complete or partial loss of this relationship would materially harm our business.

Our collaboration with UT Southwestern is critical to our business. We entered into the UT Southwestern Agreement with UT Southwestern to discover and develop certain AAV vector-based therapeutics, and the product candidates developed under such collaboration currently represent all of our pipeline and discovery programs. We currently rely on UT Southwestern for much of our preclinical research and development capabilities, and in particular the UT Southwestern Gene Therapy Program under the direction of Drs. Steven Gray and Berge Minassian. Pursuant to the UT Southwestern Agreement, UT Southwestern is primarily responsible for discovery, preclinical development activities, including all IND-enabling non-clinical studies and research grade manufacturing, and other collaborative activities set forth in the plan for the funded research including leading interactions with FDA and other regulatory authorities. Either party has the right in certain circumstances to terminate the collaboration pursuant to the terms of the UT Southwestern Agreement. If UT Southwestern delays or fails to perform its obligations under the UT Southwestern Agreement, disagrees with our interpretation of the terms of the collaboration or our discovery plan or terminates our existing agreement, our pipeline of product candidates would be significantly adversely affected and our prospects will be materially harmed.

The term of the research funding portion of the UT Southwestern Agreement, under which we have the ability to acquire exclusive rights to additional gene therapy products for rare, monogenic CNS indications, has been extended to expand research funding pursuant to sponsored research agreements on a program-by-program basis. UT Southwestern has also entered into collaborations with third parties, including certain of our competitors, addressing targets and disease indications outside the scope of our collaboration. As a result, UT Southwestern may have competing interests with respect to their priorities and resources. We may have disagreements with UT Southwestern with respect to the interpretation of the UT Southwestern Agreement, use of resources or otherwise that could cause our relationship with UT Southwestern to deteriorate. As a result, UT Southwestern may reduce their focus on, and resources allocated to, our programs, potentially delaying or terminating our ability to advance product candidates through preclinical studies. Additionally, if either of Dr. Gray or Dr. Minassian were to leave UT Southwestern or to otherwise no longer be meaningfully involved with us, our preclinical research and development capabilities may be substantially reduced.

Further, under the UT Southwestern Agreement, UT Southwestern is primarily responsible for prosecuting and maintaining our licensed intellectual property, and it may fail to properly prosecute, maintain or defend such intellectual property. In such event, if we are unable to otherwise maintain or defend such intellectual property, we could face the potential invalidation of the intellectual property or be subjected to litigation or arbitration, any of which would be time-consuming and expensive. To enforce the licensed intellectual property rights under the UT Southwestern Agreement, we will need to coordinate with UT Southwestern, which could slow down or hamper our ability to enforce our licensed intellectual property rights. In such event, we could face increased competition that could materially and adversely affect our business.

We intend to rely on third parties to conduct a significant portion of our existing clinical trials and potential future clinical trials for product candidates, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such trials.

We have engaged CROs for our ongoing and planned clinical trials for TSHA-102. We expect to continue to rely on third parties, including clinical data management organizations, medical institutions and clinical investigators, to conduct those clinical trials. Any of these third parties may terminate their engagements with us, some in the event of an uncured material breach and some at any time for convenience. If any of our relationships with these third parties terminate, we may not be able to timely enter into arrangements with alternative third parties or to do so on commercially reasonable terms, if at all. Switching or adding CROs involves substantial cost and requires management time and focus. In addition, there is a natural transition period when a new CRO commences work. As a result, delays occur, which can materially impact our ability to meet our desired clinical development timelines. Though we intend to carefully manage our relationships with our CROs, there can be no assurance that we will not encounter challenges or delays in the future or that these delays or challenges will not have a material adverse impact on our business, financial condition and prospects. Further, the performance of our CROs may also be interrupted by health epidemics, including due to travel restrictions, quarantine policies, heightened exposure of CRO staff who are healthcare providers to health epidemics or prioritization of resources toward a health epidemic.

In addition, any third parties conducting our clinical trials will not be our employees, and except for remedies available to us under our agreements with such third parties, we cannot control whether or not they devote sufficient time and resources to our clinical programs. If these third parties do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols, regulatory requirements or for other reasons, our clinical trials may be extended, delayed or terminated and we may not be able to obtain regulatory approval for or successfully commercialize our product candidates. Consequently, our results of operations and the commercial prospects for our product candidates would be harmed, our costs could increase substantially and our ability to generate revenue could be delayed significantly.

We rely on these parties for execution of our preclinical studies and clinical trials, and generally do not control their activities. Our reliance on these third parties for research and development activities will reduce our control over these activities but will not relieve us of our responsibilities. For example, we will remain responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols for the trial. Moreover, the FDA and comparable foreign regulatory authorities require us to comply with standards, commonly referred to as GCPs, for conducting, recording and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of trial participants are protected. We also are required to register ongoing clinical trials and post the results of completed clinical trials on government-sponsored databases, such as ClinicalTrials.gov, within specified timeframes. Failure to do so can result in fines, adverse publicity and civil and criminal sanctions. If we or any of our CROs or other third parties, including trial sites, fail to comply with applicable GCPs, the clinical data generated in our clinical trials may be deemed unreliable and the FDA, European Commission or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our clinical trials complies with GCP regulations. In addition, our clinical trials must be conducted with product produced under cGMP conditions. Our failure to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process.

In addition, principal investigators for our clinical trials may serve as scientific advisors or consultants to us from time to time and receive compensation in connection with such services. Under certain circumstances, we may be required to report some of these relationships to the FDA and comparable foreign regulatory authorities. The FDA or comparable foreign regulatory authority may conclude that a financial relationship between us and a principal investigator has created a conflict of interest or otherwise affected interpretation of the trial. The FDA or comparable foreign regulatory authority may therefore question the integrity of the data generated at the applicable clinical trial site and the utility of the clinical trial itself may be jeopardized. This could result in a delay in approval, or rejection, of our marketing applications by the FDA or comparable foreign regulatory authority and may ultimately lead to the denial of marketing approval of TSHA-102 or any other product candidates.

We also expect to rely on other third parties to store and distribute product supplies for our clinical trials. Any performance failure on the part of our distributors could delay clinical development or marketing approval of our product candidates or commercialization of our products, producing additional losses and depriving us of potential revenue.

We may seek collaborations with third parties for the development or commercialization of our product candidates. If those collaborations are not successful, we may not be able to capitalize on the market potential of these product candidates.

We may seek third-party collaborators for the development and commercialization of our product candidates, including for the commercialization of any of our product candidates that are approved for marketing outside the United States. Our likely collaborators for any such arrangements include regional and national pharmaceutical companies and biotechnology companies. If we enter into any additional such arrangements with any third parties, we will likely have limited control over the amount and timing of resources that our collaborators dedicate to the development or commercialization of our product candidates. Our ability to generate revenue from these arrangements will depend on our collaborators' abilities to successfully perform the functions assigned to them in these arrangements.

Collaborations involving our product candidates would pose the following risks to us:

- collaborators have significant discretion in determining the efforts and resources that they will apply to these collaborations;
- collaborators may not perform their obligations as expected;
- collaborators may not pursue development and commercialization of any product candidates that achieve regulatory approval or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in the collaborators' strategic focus or available funding, or external factors, such as an acquisition, that divert resources or create competing priorities;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our product candidates if the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours;
- we could grant exclusive rights to our collaborators that would prevent us from collaborating with others;
- product candidates discovered in collaboration with us may be viewed by our collaborators as competitive with their own product candidates or drugs, which may cause collaborators to cease to devote resources to the commercialization of our product candidates;
- a collaborator with marketing and distribution rights to one or more of our product candidates that achieve regulatory approval may not commit sufficient resources to the marketing and distribution of such products;
- disagreements with collaborators, including disagreements over proprietary rights, contract interpretation or the preferred course of development, might cause delays or termination of the research, development or commercialization of product candidates, might lead to additional responsibilities for us with respect to product candidates, or might result in litigation or arbitration, any of which would be time-consuming and expensive;
- collaborators may not properly maintain or defend our or their intellectual property rights or may use our or their proprietary information in such a way as to invite litigation that could jeopardize or invalidate such intellectual property or proprietary information or expose us to potential litigation;
- collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability; and
- collaborations may be terminated for the convenience of the collaborator and, if terminated, we could be required to raise additional capital to pursue further development or commercialization of the applicable product candidates.

Collaboration agreements may not lead to development or commercialization of product candidates in the most efficient manner or at all. If any future collaborator of ours were to be involved in a business combination, the continued pursuit and emphasis on our product development or commercialization program could be delayed, diminished or terminated.

We face significant competition in seeking appropriate collaborators. Whether we reach a definitive agreement for any collaboration will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator's evaluation of a number of factors. Those factors may include the design or results of clinical trials, the likelihood of approval by the FDA or similar regulatory authorities outside the United States, the potential market for the subject product candidate, the costs and complexities of manufacturing and delivering such product candidate to patients, the potential of competing products, the existence of uncertainty with respect to our ownership of technology, which can exist if there is a challenge to such ownership without regard to the merits of the challenge and industry and market conditions generally. The collaborator may also consider alternative product candidates or technologies for similar indications that may be available to collaborate on and whether such a collaboration could be more attractive than the one with us for our product candidate. Collaborations are complex and time-consuming to negotiate and document. In addition, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators.

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

Risks Related to our Intellectual Property

If we are unable to obtain or protect intellectual property rights related to any of our product candidates, we may not be able to compete effectively in our market.

We rely upon a combination of patents, trade secret protection and confidentiality agreements to protect the intellectual property related to our product candidates. Our success depends in large part on our ability to obtain and maintain patent and other intellectual property protection in the United States and in other countries with respect to our proprietary technology and product candidates.

We cannot offer any assurances about which of our patent applications will issue, the breadth of any resulting patent or whether any of the issued patents will be found invalid and unenforceable or will be threatened by third parties. We cannot offer any assurances that the breadth of our granted patents will be sufficient to stop a competitor from developing and commercializing a product, including a biosimilar product that would be competitive with one or more of our product candidates. Furthermore, any successful challenge to these patents or any other patents owned by or licensed to us after patent issuance could deprive us of rights necessary for the successful commercialization of any of our product candidates. Further, if we encounter delays in regulatory approvals, the period of time during which we could market a product candidate under patent protection could be reduced.

The patent prosecution process is expensive and time-consuming. We may not be able to prepare, file and prosecute all necessary or desirable patent applications at a commercially reasonable cost or in a timely manner or in all jurisdictions. It is also possible that we may fail to identify patentable aspects of inventions made in the course of development and commercialization activities before it is too late to obtain patent protection on them. Moreover, depending on the terms of any future in-licenses to which we may become a party, we may not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the patents, covering technology in-licensed from third parties. Therefore, these patents and patent applications may not be prosecuted and enforced in a manner consistent with the best interests of our business.

In addition to the protection provided by our patent estate, we rely on trade secret protection and confidentiality agreements to protect proprietary know-how that is not amenable to patent protection. Although we generally require all of our employees to assign their inventions to us, and all of our employees, consultants, advisors and any third parties who have access to our proprietary know-how, information, or technology to enter into confidentiality agreements, we cannot provide any assurances that all such agreements have been duly executed, or that our trade secrets and other confidential proprietary information will not be disclosed. Moreover, our competitors may independently develop knowledge, methods and know-how equivalent to our trade secrets. Competitors could purchase our products, if approved, and replicate some or all of the competitive advantages we derive from our development efforts for technologies on which we do not have patent protection. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent them, or those to whom they communicate it, from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor, our competitive position would be harmed.

We also seek to preserve the integrity and confidentiality of our data and trade secrets by maintaining physical security of our premises and physical and electronic security of our information technology systems. While we have confidence in these individuals, organizations and systems, our agreements or security measures may be breached, and we may not have adequate remedies for any breach. Also, if the steps taken to maintain our trade secrets are deemed inadequate, we may have insufficient recourse against third parties for misappropriating the trade secret. In addition, others may independently discover our trade secrets and proprietary information. For example, the FDA is considering whether to make additional information publicly available on a routine basis, including information that we may consider to be trade secrets or other proprietary information, and it is not clear at the present time how the FDA's disclosure policies may change in the future. If we are unable to prevent material disclosure of the non-patented intellectual property related to our technologies to third parties, and there is no guarantee that we will have any such enforceable trade secret protection, we may not be able to establish or maintain a competitive advantage in our market, which could materially adversely affect our business, results of operations and financial condition.

Patent terms may be inadequate to protect our competitive position on our products for an adequate amount of time, and if we do not obtain protection under the Hatch-Waxman Amendments and similar non-U.S. legislation for extending the term of patents covering each of our product candidates, our business may be materially harmed.

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. Depending upon the timing, duration and conditions of FDA marketing approval of our product candidates, one or more of our U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, referred to as the Hatch-Waxman Amendments, and similar legislation in the European Union. The Hatch-Waxman Amendments permit a patent term extension of up to five years for a patent covering an approved product as compensation for effective patent term lost during product development and the FDA regulatory review process. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval. Only one patent may be extended, and only those claims covering the approved drug, a method for using it, or a method for manufacturing it may be extended. However, we may not receive an extension if we fail to apply within applicable deadlines, fail to apply prior to expiration of relevant patents or otherwise fail to satisfy applicable requirements. Moreover, the length of the extension could be less than we request. If we are unable to obtain patent term extension or the term of any such extension is less than we request, the period during which we can enforce our patent rights for that product will be shortened and our competitors may obtain approval to market competing products sooner. As a result, our revenue from applicable products could be reduced and could have a material adverse effect on our business.

If we fail to comply with our obligations in our current and future intellectual property licenses with third parties, we could lose rights that are important to our business.

We are heavily reliant upon licenses to certain patent rights and proprietary technology for the development of our product candidates, in particular the UT Southwestern Agreement and our license agreement with Abeona. These license agreements impose diligence, development and commercialization timelines and milestone payment, royalty, insurance and other obligations on us. If we fail to comply with our obligations, our licensors may have the right to terminate our licenses, in which event we might not be able to develop, manufacture or market any product that is covered by the intellectual property we in-license from such licensor and may face other penalties. Such an occurrence would materially adversely affect our business prospects.

Licenses to additional third-party technology and materials that may be required for our development programs may not be available in the future or may not be available on commercially reasonable terms, or at all, which could have a material adverse effect on our business and financial condition. Although we control the prosecution, maintenance and enforcement of the licensed and sublicensed intellectual property relating to our product candidates, we may require the cooperation of our licensors and any upstream licensor, which may not be forthcoming. Therefore, we cannot be certain that the prosecution, maintenance and enforcement of these patent rights will be in a manner consistent with the best interests of our business. If we or our licensor fail to maintain such patents, or if we or our licensor lose rights to those patents or patent applications, the rights we have licensed may be reduced or eliminated and our right to develop and commercialize any of our product candidates that are the subject of such licensed rights could be adversely affected. In addition to the foregoing, the risks associated with patent rights that we license from third parties will also apply to patent rights we may own in the future. Further, if we fail to comply with our development obligations under our license agreements, we may lose our patent rights with respect to such agreement on a territory-by-territory basis, which would affect our patent rights worldwide.

Termination of our current or any future license agreements would reduce or eliminate our rights under these agreements and may result in our having to negotiate new or reinstated agreements with less favorable terms or cause us to lose our rights under these agreements, including our rights to important intellectual property or technology. Any of the foregoing could prevent us from commercializing our other product candidates, which could have a material adverse effect on our operating results and overall financial condition.

In addition, intellectual property rights that we in-license in the future may be sublicenses under intellectual property owned by third parties, in some cases through multiple tiers. The actions of our licensors may therefore affect our rights to use our sublicensed intellectual property, even if we are in compliance with all of the obligations under our license agreements. Should our licensors or any of the upstream licensors fail to comply with their obligations under the agreements pursuant to which they obtain the rights that are sublicensed to us, or should such agreements be terminated or amended, our ability to develop and commercialize our product candidates may be materially harmed.

Patent reform legislation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our future patents.

Our ability to obtain patents is highly uncertain because, to date, some legal principles remain unresolved, and there has not been a consistent policy regarding the breadth or interpretation of claims allowed in patents in the United States. Furthermore, the specific content of patents and patent applications that are necessary to support and interpret patent claims is highly uncertain due to the complex nature of the relevant legal, scientific, and factual issues. Changes in either patent laws or interpretations of patent laws in the United States and other countries may diminish the value of our intellectual property or narrow the scope of our patent protection.

For example, on September 16, 2011, the Leahy-Smith America Invents Act, or the Leahy-Smith Act, was signed into law. The Leahy-Smith Act included a number of significant changes to U.S. patent law. These included provisions that affect the way patent applications will be prosecuted and may also affect patent litigation. The United States Patent and Trademark Office, or USPTO, has developed new and untested regulations and procedures to govern the full implementation of the Leahy-Smith Act, and many of the substantive changes to patent law associated with the Leahy-Smith Act, and in particular, the first to file provisions, became effective in March 2013. The Leahy-Smith Act has also introduced procedures making it easier for third parties to challenge issued patents, as well as to intervene in the prosecution of patent applications. Finally, the Leahy-Smith Act contained new statutory provisions that require the USPTO to issue new regulations for their implementation, and it may take the courts years to interpret the provisions of the new statute. It is too early to tell what, if any, impact the Leahy-Smith Act will have on the operation of our business and the protection and enforcement of our intellectual property. However, the Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our future patents. Further, the United States 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 actions by the United States 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 patents that we have owned or licensed or that we might obtain in the future. An inability to obtain, enforce, and defend patents covering our proprietary technologies would materially and adversely affect our business prospects and financial condition.

Similarly, changes in patent laws and regulations in other countries or jurisdictions, changes in the governmental bodies that enforce them or changes in how the relevant governmental authority enforces patent laws or regulations may weaken our ability to obtain new patents or to enforce patents that we may obtain in the future. Further, the laws of some foreign countries do not protect proprietary rights to the same extent or in the same manner as the laws of the United States. As a result, we may encounter significant problems in protecting and defending our intellectual property both in the United States and abroad. For example, if the issuance in a given country of a patent covering an invention is not followed by the issuance in other countries of patents covering the same invention, or if any judicial interpretation of the validity, enforceability or scope of the claims or the written description or enablement, in a patent issued in one country is not similar to the interpretation given to the corresponding patent issued in another country, our ability to protect our intellectual property in those countries may be limited. Changes in either patent laws or in interpretations of patent laws in the United States and other countries may materially diminish the value of our intellectual property or narrow the scope of our patent protection.

We may be involved in lawsuits to protect or enforce our patents, which could be expensive, time-consuming and unsuccessful.

Competitors may infringe the patents for which we have applied. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time-consuming. If we initiate legal proceedings against a third party to enforce a patent covering one of our product candidates, the defendant could counterclaim that the patent covering our product or product candidate is invalid and/or unenforceable. In patent litigation in the United States, counterclaims alleging invalidity and/or unenforceability are common, and there are numerous grounds upon which a third party can assert invalidity or unenforceability of a patent. In an infringement proceeding, a court may decide that the patent claims we are asserting are invalid and/or unenforceable, or may refuse to stop the other party from using the technology at issue on the grounds that our patent claims do not cover the technology in question. Third parties may also raise similar claims before administrative bodies in the United States or abroad, even outside the context of litigation. Such mechanisms include re-examination, post grant review, inter partes review and equivalent proceedings in foreign jurisdictions (for example, opposition proceedings). Such proceedings could result in revocation of or amendment to our

patents in such a way that they no longer cover our product candidates. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to the validity question, for example, we cannot be certain that there is no invalidating prior art, of which we, our patent counsel, and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity and/or unenforceability, we would lose at least part, and perhaps all, of the patent protection on our product candidates. An adverse result in any litigation or defense proceedings could put one or more of our patents at risk of being invalidated or interpreted narrowly, could put our patent applications at risk of not issuing and could have a material adverse impact on our business.

Interference proceedings provoked by third parties or brought by us may be necessary to determine the priority of inventions with respect to our patent applications. An unfavorable outcome could require us to cease using the related technology or force us to take a license under the patent rights of the prevailing party, if available. Furthermore, our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms. 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. We may not be able to prevent misappropriation of our intellectual property rights, particularly in countries where the laws may not protect those rights as fully as in the United States.

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 be unsuccessful in licensing or acquiring intellectual property from third parties that may be required to develop and commercialize our product candidates.

A third party may hold intellectual property, including patent rights that are important or necessary to the development and commercialization of our product candidates. It may be necessary for us to use the patented or proprietary technology of third parties to commercialize our product candidates, in which case we would be required to acquire or obtain a license to such intellectual property from these third parties, and we may be unable to do so on commercially reasonable terms or at all. The licensing or acquisition of third-party intellectual property rights is a competitive area, and several more established companies may pursue strategies to license or acquire third-party intellectual property rights that we may consider attractive or necessary. These established companies may have a competitive advantage over us due to their size, capital resources and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We also may be unable to license or acquire third-party intellectual property rights on terms that would allow us to make an appropriate return on our investment or at all. If we are unable to successfully obtain rights to required third-party intellectual property rights or maintain the existing intellectual property rights we have, we may have to abandon development of the relevant program or product candidate, which could have a material adverse effect on our business.

Third parties may initiate legal proceedings alleging that we are infringing their intellectual property rights, the outcome of which would be uncertain.

As our current and future product candidates progress toward commercialization, the possibility of a patent infringement claim against us increases. We cannot provide any assurance that our current and future product candidates do not infringe other parties' patents or other proprietary rights, and competitors or other parties may assert that we infringe their proprietary rights in any event. We may become party to, or threatened with, adversarial proceedings or litigation regarding intellectual property rights with respect to our current and future product candidates, including interference or derivation proceedings before the USPTO. Even if we believe such claims are without merit, a court of competent jurisdiction could hold that these third-party patents are valid, enforceable and infringed, which could have a negative impact on our ability to commercialize TSHA-102 or any future product candidates. In order to successfully challenge the validity of any such U.S. patent in federal court, we would need to overcome a presumption of validity. As this burden is high and requires us to present clear and convincing evidence as to the invalidity of any such U.S. patent claim, there is no assurance that a court of competent jurisdiction would agree with us and invalidate the claims of any such U.S. patent. Moreover, given the vast number of patents in our field of technology, we cannot be certain that we do not infringe existing patents or that we will not infringe patents that may be granted in the future.

While we may decide to initiate proceedings to challenge the validity of these or other patents in the future, we may be unsuccessful, and courts or patent offices in the United States and abroad could uphold the validity of any such patent. Furthermore, because patent applications can take many years to issue and may be confidential for 18 months or more after filing, and because pending patent claims can be revised before issuance, there may be applications now pending which may later result in issued patents that may be infringed by the manufacture, use or sale of our product candidates. Regardless of when filed, we may fail to identify relevant third-party patents or patent applications, or we may incorrectly conclude that a third-party patent is invalid or not infringed by our product candidates or activities. If a patent holder believes that one of our product candidates infringes its patent, the patent

holder may sue us even if we have received patent protection for our technology. Moreover, we may face patent infringement claims from non-practicing entities that have no relevant drug revenue and against whom our own patent portfolio may thus have no deterrent effect. If a patent infringement suit were threatened or brought against us, we could be forced to stop or delay research, development, manufacturing or sales of the drug or product candidate that is the subject of the actual or threatened suit.

We are aware of issued patent or patents issued to REGENX that claim AAV vectors that have an AAV9 capsid serotype. If we commercialize any of our product candidates prior to the expiry of those patents in 2026 without a license, the patent owner could bring an action claiming infringement. If we are found to infringe a third party's valid intellectual property rights, we could be required to obtain a license from such third party to continue commercializing our product candidates. However, we may not be able to obtain any required license on commercially reasonable terms or at all. Even if a license can be obtained on acceptable terms, the rights may be non-exclusive, which could give our competitors access to the same technology or intellectual property rights licensed to us. If we fail to obtain a required license, we may be unable to effectively market product candidates based on our technology, which could limit our ability to generate revenue or achieve profitability and possibly prevent us from generating revenue sufficient to sustain our operations. Alternatively, we may need to redesign our infringing products, which may be impossible or require substantial time and monetary expenditure. Under certain circumstances, we could be forced, including by court orders, to cease commercializing our product candidates. In addition, in any such proceeding or litigation, we could be found liable for substantial monetary damages, potentially including treble damages and attorneys' fees, if we are found to have willfully infringed the patent at issue. A finding of infringement could prevent us from commercializing our product candidates or force us to cease some of our business operations, which could harm our business. Any claims by third parties that we have misappropriated their confidential information or trade secrets could have a similar negative impact on our business.

The cost to us in defending or initiating any litigation or other proceeding relating to patent or other proprietary rights, even if resolved in our favor, could be substantial, and litigation would divert our management's attention. Some of our competitors may be able to sustain the costs of complex patent litigation more effectively than we can because they have substantially greater resources. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could delay our research and development efforts and limit our ability to continue our operations.

We may be subject to claims that our employees, consultants, or independent contractors have wrongfully used or disclosed confidential information of third parties.

We employ individuals who were previously employed at other biotechnology or biopharmaceutical companies. Although we try to ensure that our employees, consultants and advisors do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that we or our employees, consultants, or independent contractors have inadvertently or otherwise used or disclosed confidential information of our employees' former employers or other third parties. We may also be subject to claims that former employers or other third parties have an ownership interest in our future patents. Litigation may be necessary to defend against these claims. There is no guarantee of success in defending these claims, and even if we are successful, litigation could result in substantial cost and be a distraction to our management and other employees.

We may be subject to claims challenging the inventorship or ownership of our future 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 patent applications, our future patents, or other intellectual property. We may be subject to ownership disputes in the future arising, for example, from conflicting obligations of consultants or others who are involved in developing our product candidates. Although it is our policy to require our employees and contractors who may be involved in the conception or development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who, in fact, conceives or develops intellectual property that we regard as our own, and we cannot be certain that our agreements with such parties will be upheld in the face of a potential challenge, or that they will not be breached, for which we may not have an adequate remedy. The assignment of intellectual property rights may not be self-executing or the assignment agreements may be breached, and 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 as exclusive ownership of, or right to use, valuable intellectual property. 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 be a distraction to management and other employees.

Reliance on third parties requires us to share our trade secrets, which increases the possibility that a competitor will discover them or that our trade secrets will be misappropriated or disclosed.

If we rely on third parties to manufacture or commercialize our product candidates, or if we collaborate with additional third parties for the development of such product candidates, we must, at times, share trade secrets with them. We may also conduct joint research and development programs that may require us to share trade secrets under the terms of our research and development

partnerships or similar agreements. We seek to protect our proprietary technology in part by entering into confidentiality agreements and, if applicable, material transfer agreements, consulting agreements or other similar agreements with our advisors, employees, third-party contractors and consultants prior to beginning research or disclosing proprietary information. These agreements typically limit the rights of the third parties to use or disclose our confidential information, including our trade secrets. Despite the contractual provisions employed when working with third parties, the need to share trade secrets and other confidential information 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. Given that our proprietary position is based, in part, on our know-how and trade secrets, a competitor's discovery of our trade secrets or other unauthorized use or disclosure could have an adverse effect on our business and results of operations.

In addition, these agreements typically restrict the ability of our advisors, employees, third-party contractors and consultants to publish data potentially relating to our trade secrets. Despite our efforts to protect our trade secrets, we may not be able to prevent the unauthorized disclosure or use of our technical know-how or other trade secrets by the parties to these agreements. Moreover, we cannot guarantee that we have entered into such agreements with each party that may have or have had access to our confidential information or proprietary technology and processes. 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. If any of the collaborators, scientific advisors, employees, contractors and consultants who are parties to these agreements breaches or violates the terms of any of these agreements, we may not have adequate remedies for any such breach or violation, and we could lose our trade secrets as a result. Moreover, if confidential information that is licensed or disclosed to us by our partners, collaborators, or others is inadvertently disclosed or subject to a breach or violation, we may be exposed to liability to the owner of that confidential information. Enforcing a claim that a third party illegally obtained and is using our trade secrets, like patent litigation, is expensive and time consuming, and the outcome is unpredictable. In addition, courts outside the United States are sometimes less willing to protect trade secrets.

We may enjoy only limited geographical protection with respect to certain patents and we may not be able to protect our intellectual property rights throughout the world.

Filing and prosecuting patent applications and defending patents covering our product candidates in all countries throughout the world would be prohibitively expensive. 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 rights are not as strong as that in the United States or Europe. These products may compete with our product candidates, and our future patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

In addition, we may decide to abandon national and regional patent applications before they are granted. The examination of each national or regional patent application is an independent proceeding. As a result, patent applications in the same family may issue as patents in some jurisdictions, such as in the United States, but may issue as patents with claims of different scope or may even be refused in other jurisdictions. It is also quite common that depending on the country, the scope of patent protection may vary for the same product candidate or technology.

While we intend to protect our intellectual property rights in our expected significant markets, we cannot ensure that we will be able to initiate or maintain similar efforts in all jurisdictions in which we may wish to market our product candidates. Accordingly, our efforts to protect our intellectual property rights in such countries may be inadequate, which may have an adverse effect on our ability to successfully commercialize our product candidates in all of our expected significant foreign markets. If we encounter difficulties in protecting, or are otherwise precluded from effectively protecting, the intellectual property rights important for our business in such jurisdictions, the value of these rights may be diminished, and we may face additional competition from others in those jurisdictions.

The laws of some jurisdictions do not protect intellectual property rights to the same extent as the laws or rules and regulations in the United States and Europe and many companies have encountered significant difficulties in protecting and defending such rights in such jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets, and other intellectual property rights, which could make it difficult for us to stop the infringement of our future patents or marketing of competing products in violation of our proprietary rights generally. Proceedings to enforce our patent rights in other jurisdictions, whether or not successful, could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our future patents at risk of being invalidated or interpreted narrowly and our patent applications at risk of not issuing as patents, 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.

Some countries also have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In addition, some countries limit the enforceability of patents against government agencies or government contractors. In those countries, the patent owner may have limited remedies, which could materially diminish the value of such patents. If we are forced to grant a license to third parties with respect to any patents relevant to our business, our competitive position may be impaired.

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

Periodic maintenance fees, renewal fees, annuity fees and various other government fees on patents and/or applications will be due to be paid to the USPTO and various government patent agencies outside of the United States over the lifetime of our patents and/or applications and any patent rights we may obtain in the future. Furthermore, the USPTO and various non-United States government patent agencies require compliance with several procedural, documentary, fee payment and other similar provisions during the patent application process. In many cases, an inadvertent lapse of a patent or patent application can be cured by payment of a late fee or by other means in accordance with the applicable rules. There are situations, however, in which non-compliance can result in abandonment or lapse of the patents or patent applications, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, potential competitors might be able to enter the market, which could have a material adverse effect on our business.

Any trademarks we have obtained or may obtain may be infringed or otherwise violated, or successfully challenged, resulting in harm to our business.

We expect to rely on trademarks as one means to distinguish our product candidates, if approved for marketing, from the drugs of our competitors. Once we select new trademarks and apply to register them, our trademark applications may not be approved. Third parties may oppose or attempt to cancel our trademark applications or trademarks, or otherwise challenge our use of the trademarks. In the event that our trademarks are successfully challenged, we could be forced to rebrand our drugs, which could result in loss of brand recognition and could require us to devote resources to advertising and marketing new brands. Our competitors may infringe or otherwise violate our trademarks and we may not have adequate resources to enforce our trademarks. Any of the foregoing events may have a material adverse effect on our business.

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. The following examples are illustrative:

- others may be able to make products that are similar to or otherwise competitive with our product candidates but that are not covered by the claims of our current or future patents;
- an in-license necessary for the manufacture, use, sale, offer for sale or importation of one or more of our product candidates may be terminated by the licensor;
- we or future collaborators might not have been the first to make the inventions covered by our issued or future issued patents or our pending patent applications;
- we 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 in-license may be held invalid or unenforceable as a result of legal challenges by our competitors;
- issued patents that we own or in-license may not provide coverage for all aspects of our product candidates in all countries;
- 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.

Risks Related to Legal and Regulatory Compliance Matters

Our relationships with customers, healthcare providers, including physicians, and third-party payors are subject, directly or indirectly, to federal, state and foreign healthcare fraud and abuse laws, false claims laws, health information privacy and security laws, and other healthcare laws and regulations. If we are unable to comply, or have not fully complied, with such laws, we could face substantial penalties.

Healthcare providers, including physicians, and third-party payors in the United States and elsewhere will play a primary role in the recommendation and prescription of any product candidates for which we obtain marketing approval. Our current and future arrangements with healthcare professionals, principal investigators, consultants, customers and third-party payors subject us to various federal, state and foreign fraud and abuse laws and other healthcare laws, including, without limitation in the United States, the federal Anti-Kickback Statute, the federal civil and criminal false claims laws and the law commonly referred to as the Physician Payments Sunshine Act and regulations promulgated under such laws. These laws will impact, among other things, our clinical research, proposed sales, marketing and educational programs, and other interactions with healthcare professionals. In addition, we may be subject to patient privacy laws by both the federal government, the states and foreign countries in which we conduct or may conduct our business. The laws that will affect our operations include, but are not limited to:

- the federal Anti-Kickback Statute, which prohibits, among other things, individuals or entities from knowingly and willfully soliciting, receiving, offering or paying any remuneration (including any kickback, bribe or rebate), directly or indirectly, overtly or covertly, in cash or in kind in return for, or to induce, either the referral of an individual, or the purchase, lease, order or arrangement for or recommendation of the purchase, lease, order or arrangement for any good, facility, item or service for which payment may be made, in whole or in part, under a federal healthcare program, such as the Medicare and Medicaid programs. The term “remuneration” has been broadly interpreted to include anything of value. Although there are a number of statutory exceptions and regulatory safe harbors protecting some common activities from prosecution, the exceptions and safe harbors are drawn narrowly. Practices that involve remuneration that may be alleged to be intended to induce prescribing, purchases or recommendations may be subject to scrutiny if they do not qualify for an exception or safe harbor. A person does not need to have actual knowledge of this statute or specific intent to violate it in order to have committed a violation. In addition, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or collectively, the ACA, signed into law in 2010, provides that the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal False Claims Act;
- the federal civil and criminal false claims laws, including, without limitation, the federal False Claims Act, which can be enforced by private citizens through civil whistleblower or qui tam actions, and civil monetary penalty laws which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment or approval from the federal government, including Medicare, Medicaid and other government payors, that are false or fraudulent or knowingly making, using or causing to be made or used a false record or statement material to a false or fraudulent claim or to avoid, decrease or conceal an obligation to pay money to the federal government. A claim includes “any request or demand” for money or property presented to the United States federal government. Several pharmaceutical and other healthcare companies have been prosecuted under these laws for allegedly providing free product to customers with the expectation that the customers would bill federal programs for the product. Other companies have been prosecuted for causing false claims to be submitted because of the companies’ marketing of products for unapproved, and thus non-reimbursable, uses;
- the Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created additional federal criminal statutes which prohibit, among other things, a person from knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, including private third-party payors and knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services. Similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, and their implementing regulations, which imposes certain requirements relating to the privacy, security and transmission of individually identifiable health information on health plans, healthcare clearinghouses and certain healthcare providers, known as “covered entities”, and their respective HIPAA “business associates”, which are independent contractors that perform certain services for or on behalf of covered entities involving the use or disclosure of individually identifiable

health information, as well as their covered subcontractors. HITECH also created new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce HIPAA and seek attorneys' fees and costs associated with pursuing federal civil actions;

- the federal transparency laws, including the federal Physician Payments Sunshine Act, which requires certain manufacturers of drugs, medical devices, biologicals and medical supplies for which payment is available under Medicare, Medicaid or the State Children's Health Insurance Program, with specific exceptions, to report annually to CMS information related to: (i) payments or other "transfers of value" made to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), other health care professionals (such as physician assistants and nurse practitioners), and teaching hospitals, and (ii) ownership and investment interests held by physicians and their immediate family members; and
- analogous state and foreign laws and regulations; state and foreign laws that require manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers, marketing expenditures or drug pricing; state and foreign 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 that otherwise restrict payments that may be made to healthcare providers; state and local laws that require the registration of pharmaceutical sales representatives; and state and foreign laws that govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.
- Outside the United States, interactions between pharmaceutical companies and health care professionals are also governed by strict laws, such as national anti-bribery laws of European countries, national sunshine rules, regulations, industry self-regulation codes of conduct and physicians' codes of professional conduct. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines or imprisonment.

Because of the breadth of these laws and the narrowness of the statutory exceptions and regulatory safe harbors available, it is possible that some of our business activities could be subject to challenge under one or more of such laws. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant penalties, including, without limitation, civil, criminal and administrative penalties, damages, fines, disgorgement, imprisonment, exclusion from participating in federal and state funded healthcare programs, such as Medicare and Medicaid, or comparable foreign programs, additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, contractual damages, diminished profits and future earnings, reputational harm and the curtailment or restructuring of our operations, any of which could harm our business.

The risk of our being found in violation of these laws is increased by the fact that many of them have not been fully interpreted by the regulatory authorities or the courts, and their provisions are open to a variety of interpretations. Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. Any action against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management's attention from the operation of our business. The shifting compliance environment and the need to build and maintain robust and expandable systems to comply with multiple jurisdictions with different compliance and/or reporting requirements increases the possibility that a healthcare company may run afoul of one or more of the requirements.

Even if we obtain regulatory approval for TSHA-102 or any future product candidates, they will remain subject to ongoing regulatory oversight.

Even if we obtain any regulatory approval for TSHA-102, or any future product candidates, such product candidates, once approved, will be subject to ongoing regulatory requirements applicable to manufacturing, labeling, packaging, storage, advertising, promoting, sampling, record-keeping and submitting of safety and other post-market information, among other things. Any regulatory approvals that we receive for TSHA-102, or any future product candidates may also be subject to a REMS, comparable foreign strategies, limitations on the approved indicated uses for which the drug may be marketed or to the conditions of approval, or requirements that we conduct potentially costly post-marketing testing, including Phase 4 trials and surveillance to monitor the quality, safety and efficacy of the drug. An unsuccessful post-marketing study or failure to complete such a study could result in the

withdrawal of marketing approval. We will further be required to immediately report any serious and unexpected adverse events and certain quality or production problems with our products to regulatory authorities along with other periodic reports.

Any new legislation addressing drug safety issues could result in delays in product development or commercialization, or increased costs to assure compliance. We will also have to comply with requirements concerning advertising and promotion for our products. Promotional communications with respect to prescription drug products 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 will not be allowed to promote our products for indications or uses for which they do not have approval, commonly known as off-label promotion. The holder of an approved BLA or comparable foreign approval must submit new or supplemental applications and obtain prior approval for certain changes to the approved product, product labeling, or manufacturing process. A company that is found to have improperly promoted off-label uses of their products may be subject to significant civil, criminal and administrative penalties.

In addition, drug manufacturers are subject to payment of user fees and continual review and periodic inspections by the FDA and other regulatory authorities for compliance with cGMP requirements and adherence to commitments made in the BLA or foreign marketing application. If we, or a regulatory authority, discover previously unknown problems with a drug, such as adverse events of unanticipated severity or frequency, or problems with the facility where the drug is manufactured or if a regulatory authority disagrees with the promotion, marketing or labeling of that drug, a regulatory authority may impose restrictions relative to that drug, the manufacturing facility or us, including requesting a recall or requiring withdrawal of the drug from the market or suspension of manufacturing.

If we fail to comply with applicable regulatory requirements following approval of TSHA-102 or any future product candidates, a regulatory authority may:

- issue an untitled letter or warning letter asserting that we are in violation of the law;
- seek an injunction or impose administrative, civil or criminal penalties or monetary fines;
- suspend, vary or withdraw regulatory approval;
- suspend any ongoing clinical trials;
- refuse to approve a pending BLA or comparable foreign marketing application (or any supplements thereto) submitted by us or our strategic partners;
- restrict the marketing or manufacturing of the drug;
- seize or detain the drug or otherwise require the withdrawal of the drug from the market;
- refuse to permit the import or export of product candidates; or
- refuse to allow us to enter into supply contracts, including government contracts.

Any government investigation of alleged violations of law could require us to expend significant time and resources in response and could generate negative publicity. The occurrence of any event or penalty described above may inhibit our ability to commercialize TSHA-102 or any future product candidates and harm our business, financial condition, results of operations and prospects.

Even if we obtain FDA or EMA approval any of our product candidates in the United States or European Union, we may never obtain approval for or commercialize any of them in any other jurisdiction, which would limit our ability to realize their full market potential.

In order to market any products in any particular jurisdiction, we must establish and comply with numerous and varying regulatory requirements on a country-by-country basis regarding safety and efficacy.

Approval by the FDA in the United States or the European Commission in the European Union does not ensure approval by regulatory authorities in other countries or jurisdictions. However, the failure to obtain approval in one jurisdiction may negatively impact our ability to obtain approval elsewhere. In addition, clinical trials conducted in one country may not be accepted by regulatory authorities in other countries, and regulatory approval in one country does not guarantee regulatory approval in any other country.

Approval processes vary among countries and can involve additional product testing and validation and additional administrative review periods. Seeking foreign regulatory approval could result in difficulties and increased costs for us and require additional preclinical studies or clinical trials which could be costly and time consuming. Regulatory requirements can vary widely

from country to country and could delay or prevent the introduction of our products in those countries. We do not have any product candidates approved for sale in any jurisdiction, including in international markets, and we do not have experience in obtaining regulatory approval in international markets. If we fail to comply with regulatory requirements in international markets or to obtain and maintain required approvals, or if regulatory approvals in international markets are delayed, our target market will be reduced and our ability to realize the full market potential of any product we develop will be unrealized.

Healthcare legislative or regulatory reform measures may have a negative impact on our business and results of operations.

In the United States and some foreign jurisdictions, there have been, and continue to be, several legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of product candidates, restrict or regulate post-approval activities, and affect our ability to profitably sell any product candidates for which we obtain marketing approval.

Among policy makers and payors in the United States and elsewhere, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality and/or expanding access. In the United States, the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major legislative initiatives. For example, in March 2010, the ACA was passed, which substantially changed the way healthcare is financed by both the government and private insurers, and significantly impacts the U.S. pharmaceutical industry.

There have been judicial, congressional, and executive branch challenges to certain aspects of the ACA, including efforts to repeal or replace certain aspects of the ACA. For example, on August 16, 2022, the Inflation Reduction Act of 2022, or the IRA, was signed into law, which among other things, extends enhanced subsidies for individuals purchasing health insurance coverage in ACA marketplaces through plan year 2025. The IRA also eliminates the “donut hole” under the Medicare Part D program beginning in 2025 by significantly lowering the beneficiary maximum out-of-pocket cost and creating a new manufacturer discount program. It is possible that the ACA will be subject to judicial or Congressional challenges in the future. It is also unclear how any additional healthcare reform measures of the second Trump administration will impact the ACA and our business.

Other legislative changes have been proposed and adopted since the ACA was enacted. These changes include aggregate reductions to Medicare payments to providers of 2% per fiscal year pursuant to the Budget Control Act of 2011, which began in 2013, and due to subsequent legislative amendments to the statute, will remain in effect until 2032, unless additional congressional action is taken. These laws may result in additional reductions in Medicare and other healthcare funding, which could have an adverse effect on customers for our product candidates, if approved, and, accordingly, our financial operations. Additionally, on March 11, 2021, the American Rescue Plan Act of 2021 was signed into law, which eliminates the statutory Medicaid drug rebate cap, currently set at 100% of a drug’s average manufacturer price, for single source and innovator multiple source drugs, effective January 1, 2024.

Additionally, there has been heightened governmental scrutiny in the United States of pharmaceutical pricing practices in light of the rising cost of prescription drugs and biologics. Such scrutiny has resulted in several recent Presidential executive orders, congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for products. At the federal level, the IRA, among other things, (i) directs HHS to negotiate the price of certain high-expenditure, single-source biologics that have been on the market for at least 11 years covered under Medicare, or the Medicare Drug Price Negotiation Program, and subject drug manufacturers to civil monetary penalties and a potential excise tax by offering a price that is not equal to or less than the negotiated “maximum fair price” for such drugs and biologics under the law, and (ii) imposes rebates with respect to certain drugs and biologics covered under Medicare Part B or Medicare Part D to penalize price increases that outpace inflation. The IRA permits HHS to implement many of these provisions through guidance, as opposed to regulation, for the initial years. These provisions began to take effect progressively starting in fiscal year 2023. On August 15, 2024, HHS announced the agreed-upon price of the first ten drugs that were subject to price negotiations, although the Medicare Drug Price Negotiation Program is currently subject to legal challenges. On January 17, 2025, HHS selected fifteen additional products covered under Part D for price negotiation in 2025. Each year thereafter more Part B and Part D products will become subject to the Medicare Drug Price Negotiation Program. Further, on December 7, 2023, an initiative to control the price of prescription drugs through the use of march-in rights under the Bayh-Dole Act was announced. On December 8, 2023, the National Institute of Standards and Technology published for comment a Draft Interagency Guidance Framework for Considering the Exercise of March-In Rights which for the first time includes the price of a product as one factor an agency can use when deciding to exercise march-in rights. While march-in rights have not previously been exercised, it is uncertain if that will continue under the new framework. At the state level, legislatures have 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.

We expect that these and other healthcare reform measures that may be adopted in the future may result in more rigorous coverage criteria and in additional downward pressure on the price that we receive for any approved drug. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our drugs.

In addition, FDA and comparable foreign regulatory regulations and guidance may be revised or reinterpreted by the FDA or the comparable foreign regulatory in ways that may significantly affect our business and our products. Any new regulations or guidance, or revisions or reinterpretations of existing regulations or guidance, may impose additional costs or lengthen FDA review times for TSHA-102 or any future product candidates. We cannot determine how changes in regulations, statutes, policies, or interpretations when and if issued, enacted or adopted, may affect our business in the future. Such changes could, among other things, require:

- additional clinical trials to be conducted prior to obtaining approval;
- changes to manufacturing methods;
- recalls, replacements, or discontinuance of one or more of our products; and
- additional recordkeeping.

For instance, the regulatory landscape related to clinical trials in the European Union recently evolved. The EU Clinical Trials Regulation, or CTR, which was adopted in April 2014 and repeals the EU Clinical Trials Directive, became applicable on January 31, 2022. The CTR allows sponsors to make a single submission to both the competent authority and an ethics committee in each EU Member State, leading to a single decision for each EU Member State. The assessment procedure for the authorization of clinical trials has been harmonized as well, including a joint assessment by all EU Member States concerned, and a separate assessment by each EU Member State with respect to specific requirements related to its own territory, including ethics rules. Each EU Member State's decision is communicated to the sponsor via the centralized EU portal. Once the clinical trial is approved, clinical study development may proceed. The CTR foresees a three-year transition period. The extent to which ongoing and new clinical trials will be governed by the CTR varies. For clinical trials in relation to which application for approval was made on the basis of the Clinical Trials Directive before January 31, 2023, the Clinical Trials Directive continued to apply on a transitional basis until January 31, 2025, by which date all ongoing trials under the Clinical Trials Directive became subject to the provisions of the CTR and all new trials since January 31, 2023 have been subject to the CTR. Compliance with the CTR requirements by us and our third-party service providers, such as CROs, may impact our developments plans.

In addition, on April 26, 2023, the European Commission adopted a proposal for a new Directive and Regulation to revise the existing pharmaceutical legislation. The proposed revisions remain to be agreed and adopted by the European Council. Moreover, on December 1, 2024, a new European Commission took office. The proposal could, therefore, still be subject to revisions. If adopted in the form proposed, the recent European Commission proposals to revise the existing EU laws governing authorization of medicinal products may result in a decrease in data and market exclusivity opportunities for our product candidates in the European Union and make them open to generic or biosimilar competition earlier than is currently the case with a related reduction in reimbursement status.

If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, our development plans may be impacted.

Such changes would likely require substantial time and impose significant costs, or could reduce the potential commercial value of TSHA-102 or other product candidates, and could materially harm our business and our financial results. In addition, delays in receipt of or failure to receive regulatory clearances or approvals for any other products would harm our business, financial condition, and results of operations.

Disruptions at the FDA, the SEC and other government agencies and regulatory authorities caused by funding shortages or global health concerns could hinder their ability to hire and retain key leadership and other personnel, prevent new products and services from being developed or commercialized in a timely manner or otherwise prevent those agencies from performing normal business functions on which the operation of our business may rely, which could negatively impact our business.

The ability of the FDA and comparable foreign regulatory authorities to review and approve new products can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel and accept the payment of user fees, and statutory, regulatory, and policy changes. Average review times at the agency have fluctuated in recent years as a

result. In addition, government funding of the U.S. Securities and Exchange Commission, or SEC, and other government agencies on which our operations may rely, including those that fund research and development activities, is subject to the political process, which is inherently fluid and unpredictable.

Disruptions at the FDA and other agencies and comparable regulatory authorities may also slow the time necessary for new drugs or biologics to be reviewed and/or approved by necessary government agencies and regulatory authorities, which would adversely affect our business. For example, over the last several years, including most recently from December 22, 2018 to January 25, 2019, the U.S. government has shut down several times and certain regulatory agencies, such as the FDA and the SEC, have had to furlough critical FDA, SEC and other government employees and stop critical activities. If a prolonged government shutdown occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business.

We are subject to legal proceedings and claims from time to time that may seek material damages or otherwise may have a material adverse effect on our business. The costs we incur in defending ourselves or associated with settling any of these proceedings, as well as a material final judgment or decree against us, could materially adversely affect our financial condition.

We are subject to legal proceedings and claims from time to time that may seek material damages or otherwise may have a material adverse effect on our business. For example, in January 2024 and April 2024, we were named a nominal defendant in stockholder derivative lawsuits asserting claims against certain of our current and former directors, among others, in the Court of Chancery of the State of Delaware. These lawsuits, which have since been consolidated, seek unspecified monetary damages, disgorgement of profits, and reasonable costs and expenses, including attorneys' fees, and other relief. See "Item 3-Legal Proceedings" and "Part II, Item 8, Note 13-Commitments and Contingencies" in this Annual Report for more information. Due to the inherent uncertainties in legal proceedings, we cannot accurately predict the ultimate outcome of any such proceedings. This or any future litigation, regardless of the merits of any such proceeding, could harm our reputation and result in substantial costs and diversion of management's attention and resources, which could adversely impact our business. Although we have directors' and officers' liability insurance, it provides for a substantial retention of liability and is subject to limitations and may not cover a significant portion, or any, of the expenses or liabilities we may incur or be subject to in connection with these lawsuits or other litigation to which we are party. The costs we incur in defending ourselves or associated with settling such proceedings, as well as a material final judgment or decree against us, that are not covered by our directors' and officers' liability insurance could materially adversely affect our financial condition. In addition, additional lawsuits may be filed, the conclusion of which in a manner adverse to us and for which we incur substantial costs or damages not covered by our directors' and officers' liability insurance could have a material adverse effect on our financial condition and business.

Risks Related to Employee Matters and Managing our Growth

Our future success depends on our ability to retain key executives and to attract, retain and motivate qualified personnel, and recent changes to our team might harm future operating results.

We are highly dependent on the management, development, clinical, financial and business development expertise of our executive officers. Each of our executive officers may currently terminate their employment with us at any time. We do not maintain "key person" insurance for any of our executives or employees.

In March 2022, as part of our strategic prioritization initiatives to improve operating efficiency, we reduced our headcount by approximately 35%, and throughout 2022 and early 2023 we further reduced headcount, including the separations of our former Chief Executive Officer, Chief Medical Officer and Chief Development Officer. These reductions resulted in a year-over-year reduction in headcount of 63% at December 31, 2022 as compared to December 31, 2021. As of December 31, 2023, we had 52 employees. As a result of our headcount reductions, we have engaged various outside consultants, principally in the areas of clinical development and clinical operations. Although we believe these employee transitions are in the best interest of our company and our stockholders, these transitions may result in the loss of personnel with deep institutional or technical knowledge. Further, the transition could potentially disrupt our operations and relationships with employees, suppliers and partners and due to added costs, operational inefficiencies, decreased employee morale and productivity and increased turnover. In addition, our competitors may seek to use these transitions and the related potential disruptions to gain a competitive advantage over us. Furthermore, these changes increase our dependency on the other members of our leadership team and clinical and preclinical operations teams that remain with us, who are not contractually obligated to remain employed with us and may leave at any time. Any such departure could be particularly disruptive and, to the extent we experience additional turnover, competition for top talent is high such that it may take some time to find a candidate that meets our requirements. Our future operating results depend substantially upon the continued service of our key personnel and in significant part upon our ability to attract and retain qualified management personnel. If we are unable to mitigate these or other similar risks, our business, results of operation and financial condition may be adversely affected.

Recruiting and retaining qualified scientific and clinical personnel and, if we progress the development of our product pipeline toward scaling up for commercialization, manufacturing and sales and marketing personnel, will also be critical to our success. The loss of the services of our executive officers or other key employees could impede the achievement of our development and commercialization objectives and seriously harm our ability to successfully implement our business strategy. Furthermore, replacing executive officers and key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to successfully develop, gain regulatory approval of and commercialize products. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate these key personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. Such competition may increase due to the recent move by companies to offer a remote or hybrid work environment. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our development and commercialization strategy. Our consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us. Further, we may experience employee turnover, consistent with high numbers of employee resignations across the broader American economy, that would have an adverse impact on our business strategy. New hires require significant training and, in most cases, take significant time before they achieve full productivity. New employees may not become as productive as we expect, and we may be unable to hire or retain sufficient numbers of qualified individuals. If we are unable to continue to attract and retain high quality personnel, motivate existing employees or maintain our corporate culture in a hybrid or remote work environment, particularly if we experience increased turnover, our ability to pursue our growth strategy will be limited.

Our employees, independent contractors, consultants, collaborators, principal investigators, CROs, suppliers and vendors may engage in misconduct or other improper activities, including non-compliance with regulatory standards and requirements.

We are exposed to the risk that our employees, independent contractors, consultants, collaborators, principal investigators, CROs, suppliers and vendors may engage in fraudulent conduct or other illegal activity. Misconduct by these parties could include intentional, reckless and/or negligent conduct that violates FDA or comparable foreign regulations, including those laws requiring the reporting of true, complete and accurate information to the FDA or comparable foreign regulatory authority, manufacturing standards, federal and state healthcare laws and regulations, and laws that require the true, complete and accurate reporting of financial information or data. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Misconduct by these parties could also involve the improper use of individually identifiable information, including, without limitation, information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. We have adopted a code of business conduct and ethics, but it is not always possible to identify and deter misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant civil, criminal and administrative penalties, including, without limitation, damages, fines, disgorgement, imprisonment, exclusion from participation in government healthcare programs, such as Medicare and Medicaid, additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, and the curtailment or restructuring of our operations.

Risks Related to Ownership of our Common Stock

The trading price of the shares of our common stock may be volatile, and purchasers of our common stock could incur substantial losses.

Our stock price may be volatile. The stock market in general and the market for biopharmaceutical companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. Specifically, from September 24, 2020, the date our stock began trading on Nasdaq, through February 25, 2025 our stock price fluctuated from a low of \$0.50 to a high of \$33.35 per share. As a result of this volatility, investors may not be able to sell their common stock at or above the price paid for the shares. The market price for our common stock may be influenced by many factors, including:

- the reporting of unfavorable preclinical results;
- the commencement, enrollment or results of our clinical trials of TSHA-102 or any future clinical trials we may conduct, or changes in the development status of our product candidates;
- any delay in our regulatory filings for TSHA-102 or any other product candidate we may develop, and any adverse development or perceived adverse development with respect to the applicable regulatory authority's review of such

filings, including without limitation the FDA's issuance of a "refusal to file" letter or a request for additional information;

- an inability to obtain additional funding;
- failure by us to comply with the terms of the Trinity Term Loan Agreement;
- adverse results from, delays in or termination of clinical trials;
- adverse regulatory decisions, including failure to receive regulatory approval of our product candidates;
- unanticipated serious safety concerns related to the use of TSHA-102 or any other product candidate;
- changes in financial estimates by us or by any equity research analysts who might cover our stock;
- conditions or trends in our industry;
- changes in the market valuations of similar companies;
- reports of adverse events in other gene therapy products or clinical studies of such products;
- stock market price and volume fluctuations of comparable companies and, in particular, those that operate in the biopharmaceutical industry;
- publication of research reports about us or our industry or positive or negative recommendations or withdrawal of research coverage by securities analysts;
- announcements by us or our competitors of significant acquisitions, strategic partnerships or divestitures;
- our relationships with our collaborators;
- announcements of investigations or regulatory scrutiny of our operations or lawsuits filed against us;
- investors' general perception of our company and our business;
- recruitment or departure of key personnel;
- overall performance of the equity markets;
- trading volume of our common stock;
- disputes or other developments relating to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our technologies;
- significant lawsuits, including patent or stockholder litigation;
- changes in the structure of healthcare payment systems;
- general political and economic conditions; and
- other events or factors, many of which are beyond our control.

The stock market in general, and the Nasdaq Global Market and biotechnology companies in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies, which has resulted in decreased stock prices for many companies notwithstanding the lack of a fundamental change in their underlying business models or prospects. Broad market and industry factors, including potentially worsening economic conditions, inflation and other adverse effects or developments, may negatively affect the market price of our common stock, regardless of our actual operating performance. The realization of any of the above risks or any of a broad range of other risks, including those described in this section, could have a significant and material adverse impact on the market price of our common stock.

In addition, in the past, stockholders have initiated class action lawsuits against pharmaceutical and biotechnology companies following periods of volatility in the market prices of these companies' stock. Such litigation, if instituted against us, could cause us to incur substantial costs and divert management's attention and resources from our business.

If equity research analysts do not publish research or reports, or publish unfavorable research or reports, about us, our business or our market, our stock price and trading volume could decline.

The trading market for our common stock will be influenced by the research and reports that equity research analysts publish about us and our business. Equity research analysts may elect not to provide research coverage of our common stock, and such lack of research coverage may adversely affect the market price of our common stock. In the event we do have equity research analyst coverage, we will not have any control over the analysts or the content and opinions included in their reports. The price of our stock could decline if one or more equity research analysts downgrade our stock or issue other unfavorable commentary or research. If one or more equity research analysts ceases coverage of our company or fails to publish reports on us regularly, demand for our stock could decrease, which in turn could cause our stock price or trading volume to decline.

Sales of a substantial number of shares of our common stock in the public market could cause the market price of our common stock to drop significantly, even if our business is doing well.

Sales of a substantial number of shares of our common stock in the public market could occur at any time, subject to the restrictions and limitations described below. If our stockholders sell, or the market perceives that our stockholders intend to sell, substantial amounts of our common stock in the public market, the market price of our common stock could decline significantly. All of our outstanding shares of common stock are available for sale in the public market, subject only to the restrictions of Rule 144 under the Securities Act in the case of our affiliates.

In addition, we have filed registration statements on Form S-8 under the Securities Act of 1933, as amended, or the Securities Act, registering the issuance of shares of common stock subject to options or other equity awards issued or reserved for future issuance under our equity incentive plans. Shares registered under these registration statements on Form S-8 are available for sale in the public market subject to vesting arrangements and exercise of options and the restrictions of Rule 144 in the case of our affiliates.

An active trading market for our common stock may not continue to be developed or sustained.

Prior to our initial public offering, there was no public market for our common stock. Although our common stock is listed on The Nasdaq Global Market, an active trading market for our shares may never develop or be sustained. If an active market for our common stock does not develop or is not sustained, it may be difficult for you to sell shares of our common stock at an attractive price or at all.

Provisions in our corporate charter documents and under Delaware law may prevent or frustrate attempts by our stockholders to change our management and hinder efforts to acquire a controlling interest in us, and the market price of our common stock may be lower as a result.

There are provisions in our certificate of incorporation and bylaws that may make it difficult for a third party to acquire, or attempt to acquire, control of our company, even if a change of control was considered favorable by you and other stockholders. For example, our board of directors has the authority to issue up to 10,000,000 shares of preferred stock. The board of directors can fix the price, rights, preferences, privileges, and restrictions of the preferred stock without any further vote or action by our stockholders. The issuance of shares of preferred stock may delay or prevent a change of control transaction. As a result, the market price of our common stock and the voting and other rights of our stockholders may be adversely affected. An issuance of shares of preferred stock may result in the loss of voting control to other stockholders.

Our charter documents also contain other provisions that could have an anti-takeover effect, including:

- only one of our three classes of directors will be elected each year;
- stockholders will not be entitled to remove directors other than by a 66 2/3% vote and only for cause;
- stockholders will not be permitted to take actions by written consent;
- stockholders cannot call a special meeting of stockholders; and
- stockholders must give advance notice to nominate directors or submit proposals for consideration at stockholder meetings.

In addition, we are subject to the anti-takeover provisions of Section 203 of the Delaware General Corporation Law, which regulates corporate acquisitions by prohibiting Delaware corporations from engaging in specified business combinations with particular stockholders of those companies. These provisions could discourage potential acquisition proposals and could delay or

prevent a change of control transaction. They could also have the effect of discouraging others from making tender offers for our common stock, including transactions that may be in your best interests. These provisions may also prevent changes in our management or limit the price that investors are willing to pay for our stock.

Concentration of ownership of our common stock among our principal stockholders may prevent new investors from influencing significant corporate decisions.

Our current beneficial owners of 5% or more of our common stock and their respective affiliates beneficially own a large percentage of our common stock. As a result, these persons, acting together, would be able to significantly influence all matters requiring stockholder approval, including the election and removal of directors, any merger, consolidation, sale of all or substantially all of our assets, or other significant corporate transactions.

Some of these persons or entities may have interests different than yours. For example, because many of these stockholders purchased their shares at prices substantially below the current market price of our common stock and have held their shares for a longer period, they may be more interested in selling our company to an acquirer than other investors, or they may want us to pursue strategies that deviate from the interests of other stockholders.

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

We are an “emerging growth company” as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act, and we intend to take advantage of some of the exemptions from reporting requirements that are applicable to other public companies that are not emerging growth companies, including:

- not being required to comply with the auditor attestation requirements in the assessment of our internal control over financial reporting;
- not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor’s report providing additional information about the audit and the financial statements;
- reduced disclosure obligations regarding executive compensation in our periodic reports, proxy statements and registration statements; and
- not being required to hold a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved.

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 expect that our eligibility to qualify as an “emerging growth company” will end on December 31, 2025, the last day of our fiscal year following the fifth anniversary of the date of our initial public offering.

Even after we no longer qualify as an emerging growth company, we may, under certain circumstances, still qualify as a “smaller reporting company,” which would allow us to take advantage of many of the same exemptions from disclosure requirements, including reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements.

We have broad discretion in the use our cash and cash equivalents.

We have broad discretion over the use of our cash and cash equivalents. You may not agree with our decisions, and our use of the proceeds may not yield any return on your investment. Our failure to apply our cash and cash equivalents effectively could compromise our ability to pursue our growth strategy and we might not be able to yield a significant return, if any, on our investment of these net proceeds. You will not have the opportunity to influence our decisions on how to use our cash and cash equivalents.

Because we do not anticipate paying any cash dividends on our common stock in the foreseeable future, capital appreciation, if any, will be your sole source of gains and you may never receive a return on your investment.

You should not rely on an investment in our common stock to provide dividend income. We have not declared or paid cash dividends on our common stock to date. We currently intend to retain our future earnings, if any, to fund the development and growth

of our business. In addition, the terms of the Trinity Term Loan Agreement restricts our ability to pay dividends. As a result, capital appreciation, if any, of our common stock will be your sole source of gain for the foreseeable future. Investors seeking cash dividends should not purchase our common stock.

Our amended and restated certificate of incorporation provides that the Court of Chancery of the State of Delaware and the federal district courts of the United States of America will be the exclusive forums for substantially all 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 provides that the Court of Chancery of the State of Delaware is the exclusive forum for the following types of actions or proceedings under Delaware statutory or common law:

- 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 under the Delaware General Corporation Law, our amended and restated certificate of incorporation, or our amended and restated bylaws;
- any claim or cause of action seeking to interpret, apply, enforce or determine the validity of our restated certificate or our amended and restated bylaws;
- any claim or cause of action as to which the Delaware General Corporation Law confers jurisdiction on the Court of Chancery of the state of Delaware; and
- any action asserting a claim against us that is governed by the internal-affairs doctrine.

This provision would not apply to suits brought to enforce a duty or liability created by the Exchange Act. Furthermore, Section 22 of the Securities Act creates concurrent jurisdiction for federal and state courts over all such Securities Act actions. Accordingly, both state and federal courts have jurisdiction to entertain such claims. To prevent having to litigate claims in multiple jurisdictions and the threat of inconsistent or contrary rulings by different courts, among other considerations, our amended and restated certificate of incorporation further provides that the federal district courts of the United States of America will be the exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act. While the Delaware courts have determined that such choice of forum provisions are facially valid, a stockholder may nevertheless seek to bring a claim in a venue other than those designated in the exclusive forum provisions. In such instance, we would expect to vigorously assert the validity and enforceability of the exclusive forum provisions of our amended and restated certificate of incorporation. This may require significant additional costs associated with resolving such action in other jurisdictions and there can be no assurance that the provisions will be enforced by a court in those other jurisdictions.

These exclusive forum provisions may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers, or other employees, which may discourage lawsuits against us and our directors, officers and other employees. If a court were to find either exclusive-forum provision in our amended and restated certificate of incorporation to be inapplicable or unenforceable in an action, we may incur further significant additional costs associated with resolving the dispute in other jurisdictions, all of which could seriously harm our business.

We have a limited number of unreserved, authorized shares.

If we seek equity financing we may need to use a significant percentage of our unreserved authorized shares of common stock in such an offering, and would therefore need stockholder approval to implement an increase in our authorized shares of common stock or a reverse stock split in order to issue additional shares of common stock in the future. Our amended and restated certificate of incorporation and the Delaware General Corporation Law currently require the approval of not less than a majority of votes cast by the stockholders entitled to vote on the matter in order to approve an increase in our authorized shares of common stock or a reverse stock split. There are no assurances that stockholder approval will be obtained, in which event we will be unable to raise additional capital through the issuance of shares of common stock to fund our future operations.

General Risks

We and the third parties with whom we work are subject to stringent and evolving U.S. and foreign laws, regulations, and rules, contractual obligations, industry standards, policies and other obligations related to data privacy and security. Our (or the third parties with whom we work) actual or perceived failure to comply with such obligations could lead to regulatory investigations or

actions; litigation (including class claims) and mass arbitration demands; fines and penalties; disruptions of our business operations; reputational harm; loss of revenue or profits; and other adverse business consequences.

In the ordinary course of business, we collect, receive, store, process, use, generate, transfer, disclose, make accessible, protect, secure, dispose of, transmit, and share (collectively, Process) personal data and sensitive information, and other information necessary to operate our business, for legal and marketing purposes, and for other business-related purposes, such as information we collect about patients and healthcare providers in connection with clinical trials in the U.S. and abroad, proprietary and confidential business data, trade secrets, and intellectual property.

Our data Processing activities subject us to numerous data privacy and security obligations, such as various federal, state, local, and foreign laws, regulations, and guidance industry standards, external and internal data privacy and security policies, contractual requirements, and other obligations relating to data privacy and security. The number and scope of which is changing, subject to differing applications and interpretations, and which may be inconsistent among jurisdictions, or in conflict with other rules, laws or Data Protection Obligations (as defined below).

In the United States, federal, state, and local governments have enacted numerous data privacy and security laws, including data breach notification laws, personal data privacy laws, and consumer protection laws. For example, the HIPAA, as amended by HITECH, imposes specific requirements relating to the privacy, security, and transmission of individually identifiable health information.

Numerous U.S. states have enacted comprehensive data privacy and security laws that impose certain obligations on covered businesses, including providing specific disclosures in privacy notices and affording residents with certain rights concerning their personal data. As applicable, such rights may include the right to access, correct, or delete certain personal data, and to opt-out of certain data Processing activities, such as targeted advertising, profiling, and automated decision-making. The exercise of these rights may impact our business and ability to provide our products and services. Certain states also impose stricter requirements for Processing certain personal data, including sensitive information, such as conducting data privacy impact assessments. These state laws allow for statutory fines for noncompliance. For example, the California Consumer Privacy Act of 2018, as amended by the California Privacy Rights Act of 2020, or, collectively, the CCPA, applies to personal data of consumers, business representatives, and employees who are California residents, and requires businesses to provide specific disclosure in privacy notices and honor requests of California residents certain rights. The CCPA allows for up to \$7,988 per intentional violation and allows private litigants affected by certain data breaches to recover significant statutory damages. The CCPA and other comprehensive U.S. state privacy laws exempt some data Processed in the context of clinical trials, these developments further complicate compliance efforts, and increase legal risk and compliance costs for us and the third parties with whom we work.

Outside the United States, an increasing number of laws, regulations, and industry standards govern data privacy and security. Our operations may be subject to increased scrutiny or attention from foreign data privacy and security authorities. Our clinical trial programs and research collaborations outside the United States may implicate foreign data privacy and security laws, including in Canada, the United Kingdom and Europe. The European Union's General Data Protection Regulation, or EU GDPR, the United Kingdom's General Data Protection Regulation, or UK GDPR, and Canada's Personal Information Protection and Electronic Documents and various related provincial laws, as well as Canada's Anti-Spam Legislation, may apply to our operations. The EU GDPR, and the UK GDPR, impose strict requirements for Processing the personal data of individuals located, respectively, within the EEA, and the United Kingdom.

Under the GDPR, companies may face temporary or definitive bans on data Processing and other corrective actions, as well as fines of up to 20 million Euros under the EU GDPR, 17.5 million pounds sterling under the UK GDPR or, in each case, 4% of the annual global revenue, whichever is greater. Further, the law allows for private litigation related to Processing of personal data brought by classes of data subjects or consumer protection groups authorized by law to represent their interests.

Our employees and personnel use generative artificial intelligence, or AI, technologies to perform their work, and the disclosure and use of personal data in generative AI technologies is subject to various privacy laws and other privacy obligations. Governments have passed and are likely to pass additional laws regulating generative AI. Our use of this technology could result in additional compliance costs, regulatory investigations and actions, and lawsuits. If we are unable to use generative AI, it could make our business less efficient and result in competitive disadvantages.

In the ordinary course of business, we transfer personal data from Europe and other jurisdictions to the United States or other countries. Certain jurisdictions, including Europe and the United Kingdom, have enacted data localization laws and cross-border personal data transfers laws. For example, absent appropriate safeguards or other circumstances, the EU GDPR and UK GDPR generally restricts the transfer of personal data to countries outside of the EEA and United Kingdom respectively, such as the United

States. Other jurisdictions have enacted or are considering similar cross-border personal data transfer laws and local personal data residency laws, any of which could increase the cost and complexity of doing business.

Although there are currently various mechanisms that may be used to transfer personal data from the EEA and United Kingdom to the United States in compliance with law, such as the EEA standard contractual clauses, the UK's International Data Transfer Agreement/Addendum, and the EU-U.S. Data Privacy Framework and the UK extension thereto (which allows for transfers to relevant U.S.-based organizations who self-certify compliance and participate in the Framework), these mechanisms are subject to legal challenges, and there is no assurance that we can satisfy or rely on these measures to lawfully transfer personal data to the United States.

If there is no lawful manner for us to transfer personal data from the EEA, the United Kingdom or other jurisdictions to the United States, or if the requirements for a legally-compliant transfer are too onerous, we may face significant adverse consequences, including interruption or degradation of our operations, the need to relocate part of or all of our business or data processing activities to other jurisdictions (such as Europe) at significant expense, increased exposure to regulatory actions, substantial fines, and penalties, the inability to transfer data and work with partners, vendors and other third parties, and injunctions against Processing or transferring personal data from Europe or elsewhere.

Inability to import personal data to the United States may significantly and negatively impact our business operations, including by limiting our ability to conduct clinical trial activities in Europe and elsewhere; limiting our ability to collaborate with parties subject to European and other data protection laws or requiring us to increase our personal data Processing capabilities in Europe and/or elsewhere at significant expense. Additionally, companies that transfer personal data out of the EEA and United Kingdom to other jurisdictions, particularly to the United States, are subject to increased scrutiny from regulators, individual litigants, and activist groups. Some European regulators have ordered certain companies to suspend or permanently cease certain transfers out of Europe for allegedly violating the EU GDPR's cross-border data transfer limitations.

We are also subject to the terms of our data privacy and security policies, representations, certifications, standards, publications and frameworks, and contractual obligations to third parties related to data privacy, security and the Processing of personal data (collectively, "Data Protection Obligations"), including without limitation, operating rules and standards imposed by industry organizations. Data privacy and security issues worldwide are, and are likely to remain, uncertain for the foreseeable future. We strive to comply with applicable data privacy and security laws and Data Protection Obligations to the extent possible, but we may at times fail to do so, or may be perceived to have failed to do so. Moreover, despite our efforts, we may not be successful in achieving compliance if our personnel, partners or vendors do not comply with applicable data privacy and security laws and Data Protection Obligations.

We publish privacy policies, whitepapers, marketing materials and other statements, such as compliance with certain certifications or self-regulatory principles, regarding data privacy and security. Regulators in the United States are increasingly scrutinizing these statements, and if these policies, materials or statements are found to be deficient, lacking in transparency, deceptive, unfair, misleading, or misrepresentative of our practices, we may be subject to investigation, enforcement actions by regulators or other adverse consequences.

If we or the third parties with whom we work fail, or are perceived to have failed, to address or comply with applicable data privacy and security laws and Data Protection Obligations, such failure or perceived failure could: increase our compliance and operational costs; expose us to regulatory scrutiny, actions, fines and penalties; result in reputational harm; interrupt or stop clinical trials; result in litigation and liability; result in an inability to Process personal data or to operate in certain jurisdictions; cause a material adverse impact to business operations or financial results; result in imprisonment of company officials; and otherwise result in other material harm to our business.

With applicable data privacy and security laws, and Data Protection Obligations imposing complex and burdensome obligations, and with substantial uncertainty over the interpretation and application of these requirements, we have faced and may face additional challenges in addressing and complying with them, and making necessary changes to our privacy policies and practices, and may incur material costs and expenses in an effort to do so, any of which could materially adversely affect our business operations and financial results, and may limit the adoption and use of, and reduce the overall demand for, our products, which could have an adverse impact on our business.

If our information technology systems or those third parties with whom we work or our data are or were compromised, we could experience adverse consequences resulting from such compromise, including, but not limited to regulatory investigations or

actions; litigation; fines and penalties; disruptions to our operations such as our clinical trials; claims that we breached our data privacy and security laws; reputational harm; a loss of customers or sales; and other adverse consequences.

In the ordinary course of our business, we, and the third parties with whom we work, Process proprietary, confidential and sensitive information, including personal data (including health-related data), intellectual property, trade secrets, and proprietary business information owned or controlled by ourselves or other parties.

We rely on third parties to help us operate critical business systems and to Process sensitive information in a variety of context, including, without limitation, cloud-based infrastructure, data center facilities, encryption and authentication technology, employee email, and other functions. We also share sensitive information with third parties in conjunction with our business. Our ability to monitor these third parties' information security practices is limited, and these third parties may not have adequate information security measures in place. If we, or the third parties with whom we work, experience, or in the future experience, any security incident(s) that result in any data loss, deletion or destruction, unauthorized access to, loss of, unauthorized acquisition or disclosure of, or inadvertent exposure or disclosure of, personal data or sensitive information, or compromise related to the security, confidentiality, integrity or availability of our information technology, software, services, communications or data (or those of the third parties with whom we work), it may have a material adverse effect on our business, including without limitation, regulatory investigations or enforcement actions, litigation, indemnity obligations, negative publicity and financial loss, additional reporting requirements and/or oversight and restrictions on Processing sensitive information (including personal data).

While we may be entitled to damages if our third-party service providers fail to satisfy their data privacy or security-related obligations to us, any award may be insufficient to cover our damages, or we may be unable to recover such award. 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 could require us to incur substantial cost to recover or reproduce such data. Security breaches and attendant consequences may prevent or cause customers to stop using our products, deter new customers for using our products, and otherwise negatively impact our ability to grow and operate our business.

Cyber-attacks, malicious internet-based activity and online and offline fraud and other similar activities are prevalent and continue to increase and threaten the confidentiality, integrity, and availability of our sensitive information and information technology systems, and those of the third parties with whom we work. These threats are prevalent, continue to rise, are increasingly difficult to detect, and come from a variety of sources from a variety of sources, including traditional computer "hackers," threat actors, personnel misconduct or error (employee theft or misuse), sophisticated nation-state and nation-state supported actors, "hacktivists," organized criminal threat actors, and personnel (such as through theft or misuse). We and the third-parties we rely are subject to a variety of evolving threats, including but not limited to social engineering attacks (including through deep fakes, which are increasingly more difficult to identify as fake, and phishing attacks), malicious code (such as viruses and worms), malware (including as a result of advanced persistent threat intrusions), denial-of-service attacks, credential stuffing, credential harvesting, personnel misconduct or error, ransomware attacks, supply-chain attacks, software bugs, server malfunction, software or hardware failures, loss of data or other information technology assets, adware, telecommunications failures, earthquakes, fire, flood, attacks enhanced or facilitated by AI, and other similar threats.

Ransomware attacks, including those perpetrated by organized criminal threat actors, nation-states, and nation-state supported actors, are becoming increasingly prevalent and severe and can lead to significant interruptions in our operations, loss of data and income, reputational harm, and diversion of funds. Extortion payments may alleviate the negative impact of a ransomware attack, but we may be unwilling or unable to make such payments due to, for example, applicable laws or regulations prohibiting payments.

Similarly, supply-chain attacks have increased in frequency and severity, and we cannot guarantee that third parties and infrastructure in our supply chain have not been compromised or that they do not contain exploitable defects or bugs that could result in a breach of or disruption to our information technology systems or the third-party information technology systems that support us and our services. Some actors now engage and are expected to continue to engage in cyber-attacks, including without limitation nation-state actors for geopolitical reasons and in conjunction with military conflicts and defense activities. During times of war and other major conflicts, we, the third parties with whom we work, and our customers may be vulnerable to a heightened risk of these attacks, including retaliatory cyber-attacks, that could materially disrupt our systems and operations, supply chain, and ability to produce, sell and distribute our goods and services.

Remote work has increased risks to our information technology systems and data, as more of our employees utilize network connections, computers and devices outside our premises or network, including working at home, while in transit and in public locations. Future or past business transactions (such as acquisitions or integrations) could expose us to additional cybersecurity risks and vulnerabilities, as our systems could be negatively affected by vulnerabilities present in acquired or integrated entities' systems

and technologies. Furthermore, we may discover security issues that were not found during due diligence of such acquired or integrated entities, and it may be difficult to integrate companies into our information technology environment and security program.

We have been in the past, and may in the future, be required to expend significant resources, fundamentally change our business activities (including our clinical trial activities) and practices, and/or modify our operations, including our clinical trial activities or information technology, in an effort to protect against security breaches and to mitigate, detect, and remediate actual and potential vulnerabilities. Applicable data privacy and security laws and Data Protection Obligations may require us to implement specific security measures or use industry-standard or reasonable measures to protect against security breaches. While we have implemented security measures designed to protect against security breaches, there can be no assurance that our security measures or those of our service providers, partners and other third parties will be effective in protecting against all security breaches and material adverse impacts that may arise from such breaches. The recovery systems, security protocols, network protection mechanisms and other security measures that we (and our third parties) have integrated into our platform, systems, networks and physical facilities, which are designed to protect against, detect and minimize security breaches, may not be adequate to prevent or detect service interruption, system failure or data loss.

We have not always been able in the past and may be unable in the future to detect, anticipate, measure or prevent threats or techniques used to detect or exploit vulnerabilities in our (or our third parties') information technology, services, communications or software, or cause security breaches, because such threats and techniques change frequently, are often sophisticated in nature, and may not be detected until after an incident has occurred. In addition, security researchers and other individuals have in the past and will continue in the future to actively search for and exploit actual and potential vulnerabilities in our (or our third parties') information technology and communications. While we take steps designed to detect and remediate vulnerabilities, we may not be able to detect and remediate vulnerabilities on a timely basis. Therefore, such vulnerabilities could be exploited but may not be detected until after a security breach has occurred. These vulnerabilities pose material risks to our business. We cannot be certain that we will be able to address any such vulnerabilities, in whole or part, and there may be delays in developing and deploying patches and other remedial measures to adequately address vulnerabilities. Any of the previously identified or similar threats could cause a security breach or other interruption that could result in unauthorized, unlawful, or accidental acquisition, modification, destruction, loss, alteration, encryption, disclosure of, or access to our sensitive information or our information technology systems, or those of the third parties with whom we work.

Applicable data privacy and security laws and Data Protection Obligations may require us, or we may voluntarily choose, to notify relevant stakeholders of security breaches, including affected individuals, regulators and investors, of security incidents, or to take other actions, such as providing credit monitoring and identity theft protection services. Such disclosures and related actions can be costly, and the disclosures or the failure to comply with such applicable requirements, could lead to adverse consequences.

Our contracts may not contain limitations of liability and even where they do, there can be no assurance the limitations of liability in our contracts are sufficient to protect us from liabilities, damages, or claims related to our data privacy and security obligations. We may not have adequate insurance coverage in the event of a security breach. We cannot assure that our existing coverage will be adequate or otherwise protect us from or adequately mitigate liabilities or damages with respect to claims, costs, expenses, litigation, fines, penalties, business loss, data loss, regulatory actions or material adverse impacts arising out of our data privacy and security practices, Processing or security breaches we may experience, or that such coverage will continue to be available on acceptable terms or at all. The successful assertion of one or more large claims against us that exceeds our available insurance coverage, or results in changes to our insurance policies (including premium increases or the imposition of large deductible or co-insurance requirements), could have an adverse effect on our business. In addition, we cannot be sure that our existing insurance coverage and coverage for errors and omissions will continue to be available on acceptable terms or that our insurers will not deny coverage as to any future claim.

In addition to experiencing a security breach, third parties may gather, collect, or infer sensitive information about us from public sources, data brokers, or other means that reveals competitively sensitive details about our organization and could be used to undermine our competitive advantage or market position. Additionally, sensitive information could be leaked, disclosed, or revealed as a result of or in connection with our employees', personnel's, or vendors' use of generative AI technologies.

If we fail, or are perceived to have failed, to address or comply with these data privacy and security laws and Data Protection Obligations, we could face significant consequences. These consequences may include, but are not limited to, government enforcement actions (e.g., investigations, fines, penalties, audits, inspections and similar); litigation (including class-related claims); additional reporting requirements and/or oversight; bans on Processing personal data; and orders to destroy or not use personal data.

Our business activities will be subject to the Foreign Corrupt Practices Act, or FCPA, and similar anti-bribery and anti-corruption laws.

As we expand our business activities outside of the United States, including our clinical trial efforts, we will be subject to the FCPA and similar anti-bribery or anti-corruption laws, regulations or rules of other countries in which we operate. The FCPA generally prohibits offering, promising, giving, or authorizing others to give anything of value, either directly or indirectly, to a non-U.S. government official in order to influence official action, or otherwise obtain or retain business. The FCPA also requires public companies to make and keep books and records that accurately and fairly reflect the transactions of the corporation and to devise and maintain an adequate system of internal accounting controls. Our business is heavily regulated and therefore involves significant interaction with public officials, including officials of non-U.S. governments. Additionally, in many other countries, the healthcare providers who prescribe pharmaceuticals are employed by their government, and the purchasers of pharmaceuticals are government entities; therefore, our dealings with these prescribers and purchasers will be subject to regulation under the FCPA. We may engage third parties to sell our products outside the United States, to conduct clinical trials, and/or to obtain necessary permits, licenses, patent registrations, and other regulatory approvals. We have direct or indirect interactions with officials and employees of government agencies or government-affiliated hospitals, universities, and other organizations. There is no certainty that all of our employees, agents, suppliers, manufacturers, contractors, or collaborators, or those of our affiliates, will comply with all applicable laws and regulations, particularly given the high level of complexity of these laws. We can be held liable for the corrupt or other illegal activities of our employees, agents, contractors, and other collaborators, even if we do not explicitly authorize or have actual knowledge of such activities. Violations of these laws and regulations could result in fines, criminal sanctions against us, our officers, or our employees, the closing down of facilities, including those of our suppliers and manufacturers, requirements to obtain export licenses, cessation of business activities in sanctioned countries, implementation of compliance programs, and prohibitions on the conduct of our business. Any such violations could include prohibitions on our ability to offer our products in one or more countries as well as difficulties in manufacturing or continuing to develop our products, and could materially damage our reputation, our brand, our international expansion efforts, our ability to attract and retain employees, and our business, prospects, operating results, and financial condition.

We are subject to governmental export and import controls that could impair our ability to compete in international markets due to licensing requirements and subject us to liability if we are not in compliance with applicable laws. Compliance with these legal requirements could limit our ability to compete in foreign markets and subject us to liability if we violate them.

We are subject to export control and import laws and regulations, including the U.S. Export Administration Regulations, U.S. Customs regulations and various economic and trade sanctions regulations administered by the U.S. Treasury Department's Office of Foreign Assets Controls. Exports of our product candidates outside of the United States must be made in compliance with these laws and regulations. If we fail to comply with these laws and regulations, we and certain of our employees could be subject to substantial civil or criminal penalties, including the possible loss of export or import privileges; fines, which may be imposed on us and responsible employees or managers; and, in extreme cases, the incarceration of responsible employees or managers.

In addition, changes in our product candidates or changes in applicable export or import laws and regulations may create delays in the introduction, provision or sale of our product candidates in international markets, prevent customers from using our product candidates or, in some cases, prevent the export or import of our product candidates to certain countries, governments or persons altogether. Any limitation on our ability to export, provide or sell our product candidates could adversely affect our business, financial condition and results of operations.

We are obligated to maintain proper and effective internal controls over financial reporting, and any failure to maintain the adequacy of these internal controls may adversely affect investor confidence in our company and, as a result, the value of our common stock.

We are required, pursuant to Section 404 of the Sarbanes-Oxley Act, or Section 404, to furnish a report by management on, among other things, the effectiveness of our internal control over financial reporting on an annual basis. This assessment includes disclosure of any material weaknesses identified by our management in our internal control over financial reporting. We are also required to disclose significant changes made in our internal control procedures on a quarterly basis. In addition, our independent registered public accounting firm will be required to attest to the effectiveness of our internal control over financial reporting in our first annual report required to be filed with the SEC following the date we are no longer an emerging growth company.

During the evaluation and testing process of our internal controls, if we identify one or more material weaknesses in our internal control over financial reporting, we will be unable to assert that our internal control over financial reporting is effective. We cannot assure you that there will not be material weaknesses or significant deficiencies in our internal control over financial reporting in the future. Any failure to maintain internal control over financial reporting could severely inhibit our ability to accurately report our financial condition or results of operations. If we are unable to conclude that our internal control over financial reporting is effective,

or if our independent registered public accounting firm determines we have a material weakness or significant deficiency in our internal control over financial reporting, we could lose investor confidence in the accuracy and completeness of our financial reports, the market price of our common stock could decline, and we could be subject to sanctions or investigations by the Nasdaq, the SEC or other regulatory authorities. Failure to remedy any material weakness in our internal control over financial reporting, or to maintain other effective control systems required of public companies, could also restrict our future access to the capital markets.

Our effective tax rate may fluctuate, and we may incur obligations in tax jurisdictions in excess of accrued amounts.

We are subject to taxation in more than one tax jurisdiction. As a result, our effective tax rate is derived from a combination of applicable tax rates in the various places that we operate. In preparing our financial statements, we estimate the amount of tax that will become payable in each such jurisdiction. Nevertheless, our effective tax rate may be different than experienced in the past due to numerous factors, including passage of newly enacted tax legislation, changes in the mix of our profitability from jurisdiction to jurisdiction, the results of examinations and audits of our tax filings, our inability to secure or sustain acceptable agreements with tax authorities, changes in accounting for income taxes and changes in existing tax laws. Any of these factors could cause us to experience an effective tax rate significantly different from previous periods or our current expectations and may result in tax obligations in excess of amounts accrued in our financial statements.

We might not be able to utilize a significant portion of our net operating loss carryforwards.

We have generated and expect to continue to generate significant federal and state net operating loss, or NOL, carryforwards in the future. As of December 31, 2024, there were federal and state NOLs of \$268.3 million and \$11.7 million respectively. A portion of these NOL carryforwards could expire unused and be unavailable to offset future income tax liabilities. Under the Tax Cuts and Jobs, or the Tax Act, as modified by the Coronavirus Aid, Relief, and Economic Security Act, or the CARES Act, federal NOLs incurred in taxable years beginning after December 31, 2017 may be carried forward indefinitely, but the deductibility of such federal NOLs is limited. It is uncertain if and to what extent various states will conform to the Tax Act and CARES Act. In addition, under Section 382 of the Internal Revenue Code of 1986, as amended, and corresponding provisions of state law, if a corporation undergoes an “ownership change,” which is generally defined as a greater than 50% change, by value, in its equity ownership over a three-year period, the corporation’s ability to use its pre-change NOL carryforwards and other pre-change tax attributes to offset its post-change income or taxes may be limited. During 2023, we performed a detailed analysis of historical and current Section 382 ownership shifts that may limit the utilization of NOL carryforwards. None of our gross federal NOLs are permanently limited. However, as a result of the ownership shift that occurred in August 2023, \$27.1 million of our research credits will expire and \$217.9 million of our gross Federal NOLs are subject to an annual utilization limitation of \$3.1 million. However, sales of our common stock by our existing stockholders, or additional sales of our common stock by us, could trigger additional limitations under Section 382 which could have a material adverse effect on our results of operations in future years. At the state level, there may be periods during which the use of NOLs is suspended or otherwise limited, which could accelerate or permanently increase state taxes owed.

New tax laws or regulations, changes to existing tax laws or regulations or changes in their application to us or our customers may have a material adverse effect on our business, cash flows, financial condition or results of operations.

New tax laws, statutes, rules, regulations, directives, decrees or ordinances could be enacted at any time. Further, existing tax laws, statutes, rules, regulations, directives, decrees or ordinances could be interpreted, changed or modified. Any such enactment, interpretation, change or modification could adversely affect us, possibly with retroactive effect. For example, the IRA imposes, among other rules, a 15% minimum tax on the book income of certain large corporations and a 1% excise tax on certain corporate stock repurchases. In addition, for certain research and experimental, or R&E, expenses incurred in tax years beginning after December 31, 2021, the Tax Act requires the capitalization and amortization of such expenses over five years if incurred in the United States and fifteen years if incurred outside the United States, rather than deducting such expenses currently. Although there have been legislative proposals to repeal or defer the capitalization requirement, there can be no assurance that such requirement will be repealed, deferred or otherwise modified. Changes in corporate tax rates, the realization of net deferred tax assets relating to our operations, the taxation of foreign earnings and the deductibility of expenses under the Tax Act, as amended by the CARES Act or any future tax reform legislation, could have a material impact on the value of our deferred tax assets, result in significant one-time charges and increase our future U.S. tax expense.

We have incurred and will continue to incur increased costs and demands upon management as a result of being a public company.

As a public company listed in the United States, we have incurred and will continue to incur significant additional legal, accounting and other costs including the cost of director and officer liability insurance. These additional costs could negatively affect our financial results. In addition, changing laws, regulations and standards relating to corporate governance and public disclosure,

including regulations implemented by the SEC and the Nasdaq Stock Market, may increase legal and financial compliance costs and make some activities more time-consuming. These laws, regulations and standards are subject to varying interpretations and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. We intend to invest resources to comply with evolving laws, regulations and standards, and this investment may result in increased general and administrative expenses and a diversion of management's time and attention from revenue-generating activities to compliance activities. If notwithstanding our efforts to comply with new laws, regulations and standards, we fail to comply, regulatory authorities may initiate legal proceedings against us and our business may be harmed.

Failure to comply with these rules might also make it more difficult for us to obtain some types of insurance, including director and officer liability insurance, and we might be forced to accept reduced policy limits and coverage or incur substantially higher costs to obtain the same or similar coverage. The impact of these events could also make it more difficult for us to attract and retain qualified persons to serve on our board of directors, on committees of our board of directors or as members of senior management.

Item 1B. Unresolved Staff Comments.

None.

Item 1C. Cybersecurity.

Risk management and strategy

We have implemented and maintain various information security processes designed to identify, assess and manage material risks from cybersecurity threats to our critical computer networks, third party hosted services, communications systems, hardware and software, and our critical data, including intellectual property, confidential information that is proprietary, strategic or competitive in nature, and clinical trial data, or Information Systems and Data.

Our information technology team, led by our Vice President of Information Technology, helps identify, assess, and manage our cybersecurity threats and risks. Our information technology team assesses risks from cybersecurity threats by monitoring and evaluating our threat environment using various methods including, for example analyzing threat reports, conducting audits, and using intelligence feeds.

Depending on the environment, systems, and data, we implement and maintain various technical, physical, and organizational measures, processes, standards, and policies designed to manage and mitigate material risks from cybersecurity threats to our Information Systems and Data, including, for example: incident detection and response, employee training, access controls, cyber insurance, and systems monitoring.

Our assessment and management of material risks from cybersecurity threats are integrated into our overall risk management processes. For example, our senior management along with our information technology team evaluates material risks from cybersecurity threats against our overall business objectives and reports to the Audit Committee of the board of directors, which evaluates our overall enterprise risk.

We use third-party service providers to assist us from time to time to identify, assess, and manage material risks from cybersecurity threats, including for example cybersecurity software providers, managed cybersecurity service providers, and dark web monitoring services.

We use third-party service providers to perform a variety of functions throughout our business, such as contract research organizations, contract manufacturing organizations, and hosting companies. We have a vendor management process to manage cybersecurity risks associated with our use of these providers which includes risk assessments and audits. Depending on the nature of the services provided, the sensitivity of the Information Systems and Data at issue, and the identity of the provider, our vendor management process may involve different levels of assessment designed to help identify cybersecurity risks associated with a provider.

For a description of the risks from cybersecurity threats that may materially affect us and how they may do so, see our risk factors under Part 1. Item 1A. Risk Factors in this Annual Report on Form 10-K, including "If our information technology systems or those third parties with whom we work or our data are or were compromised, we could experience adverse consequences resulting from such compromise, including, but not limited to regulatory investigations or actions; litigation; fines and penalties; disruptions to

our operations such as our clinical trials; claims that we breached our data privacy and security laws; reputational harm; a loss of customers or sales; and other adverse consequences.”

Governance

Our board of directors addresses our cybersecurity risk management as part of its general oversight function. The board of directors’ Audit Committee is responsible for overseeing our cybersecurity risk management processes, including oversight of mitigation of risks from cybersecurity threats.

Our cybersecurity risk assessment and management processes are implemented and maintained by certain Company management, including our Compliance Officer and Vice President of Information Technology, both of whom have previously served in management roles at other public biotechnology companies.

Company management is responsible for hiring appropriate personnel, helping to integrate cybersecurity risk considerations into our overall risk management strategy, and communicating key priorities to relevant personnel. Company management is responsible for approving budgets, helping prepare for cybersecurity incidents, approving cybersecurity processes, and reviewing security assessments and other security-related reports.

Our cybersecurity incident response plan is designed to escalate certain cybersecurity incidents to members of our legal team depending on the circumstances. Our information technology team works with our incident response team to help the Company mitigate and remediate cybersecurity incidents of which they are notified. In addition, the Company’s incident response plan includes reporting to the Audit Committee of the board of directors for certain cybersecurity incidents.

Item 2. Properties.

In January 2021, we entered into a lease agreement for 15,000 square feet of administrative space in Dallas, Texas, pursuant to a lease agreement that expires approximately ten years after the lease commenced in May 2021. This lease was amended in December 2021 to lease an additional 18,000 square feet of administrative space in Dallas, TX, pursuant to a lease amendment that expires approximately ten years after the lease commencement date. In December 2020, we entered into a lease agreement for approximately 187,500 square feet of a manufacturing facility in Durham, North Carolina, pursuant to a lease agreement that expires in September 2036. We have two options to extend the term of that lease, each for a period of an additional five years. In August 2021 we entered into a lease agreement for 9,400 square feet of laboratory space in Research Triangle Park, North Carolina, pursuant to a lease agreement that expires approximately four years after the lease commenced in September 2021. This lease was amended in December 2021 to rent approximately 3,600 square feet of additional laboratory space.

We believe that our facilities are suitable and adequate to meet our needs. We intend to add new facilities or expand existing facilities as we add employees, and we believe that suitable additional or substitute space will be available as needed to accommodate any such expansion of our operations.

Item 3. Legal Proceedings.

In January 2024 and April 2024, the Company was named a nominal defendant in two putative stockholder derivative actions filed by stockholders of the Company in the Court of Chancery of the State of Delaware. The lawsuits have since been consolidated and a lead plaintiff has been appointed. In October 2024, the lead plaintiff filed an amended complaint asserting claims relating to the Company’s August 2023 Private Placement against (i) certain of the Company’s current and former directors and officers for breach of fiduciary duty and unjust enrichment; and (ii) certain participants in the Company’s August 2023 Private Placement for aiding and abetting breach of fiduciary duty and unjust enrichment. The complaints seek an unspecified award of damages in the Company’s favor, plus pre-judgment and post-judgment interest, and an award to the plaintiffs for the costs and disbursement of the action, including fees for their attorneys and experts. The board of directors of the Company has formed a special litigation committee to investigate the claims and allegations in the amended complaint. On January 27, 2025, the court entered an order staying the litigation until June 30, 2025, while the special litigation committee conducts its investigation. The Company has not recorded a liability related to these lawsuits because, at this time, the Company is unable to reasonably estimate possible losses or gains or determine whether an unfavorable outcome is either probable or remote.

From time to time, we may be involved in additional legal or regulatory proceedings. Regardless of 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.

Not applicable.

PART II

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

Market Information for Common Stock

Our common stock is listed on The Nasdaq Global Market under the symbol “TSHA.”

Holders of Record

As of February 24, 2025, we had 38 holders of record of our common stock, which excludes stockholders whose shares were held in nominee or street name by brokers. The actual number of common 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.

Dividend Policy

We have never paid cash dividends on any of our capital stock and currently intend to retain our future earnings, if any, to fund the development and growth of our business.

Issuer Purchases of Equity Securities

None.

Item 6. [Reserved].

Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations.

The following discussion and analysis of our financial condition and results of operations should be read in conjunction with our consolidated financial statements and related notes.

Overview

We are a clinical-stage biotechnology company focused on advancing AAV-based gene therapies for the treatment of severe monogenic diseases of the central nervous system, or CNS. Our lead clinical program TSHA-102 is in development for the treatment of Rett syndrome, a rare neurodevelopmental disorder with no approved disease-modifying therapies that address the genetic root cause of the disease. With a singular focus on developing transformative medicines, we aim to address severe unmet medical needs and dramatically improve the lives of patients and their caregivers. Our management team has proven experience in gene therapy development and commercialization. We leverage this experience, our manufacturing process and a clinically and commercially proven AAV9 capsid in an effort to rapidly translate treatments from bench to bedside.

We currently are conducting two Phase 1/2 clinical trials for TSHA-102: an adolescent/adult study in the United States and Canada and a pediatric study in the United States. In addition, we received approval to expand the pediatric study into the United Kingdom in 2024 following clearance of the CTA by the U.K. MHRA and received approval to expand the pediatric study into Canada in 2024 following clearance of the CTA by Health Canada.

In early 2025, we announced the completion of dosing of the 10 patients in Part A, the dose escalation portion of both REVEAL Phase 1/2 trials, that is expected to serve as primary dataset to support advancement toward the Part B registrational trial. Cohort one (low dose cohort of 5.7×10^{14} total vg) consists of four patients and cohort two (high dose cohort of 1×10^{15} total vg) consists of six patients across both REVEAL trials. In early 2025, we announced TSHA-102 was generally well-tolerated with no serious adverse events (SAEs) or dose-limiting toxicities (DLTs) related to TSHA-102 in the 10 pediatric, adolescent and adult patients dosed across the two REVEAL Phase 1/2 trials as of the February 17, 2025, data cutoff.

We have received orphan drug designation and rare pediatric disease designation from the United States Food and Drug Administration, or FDA, and orphan drug designation from the European Commission for TSHA-102 for the treatment of Rett syndrome. We also received Fast Track Designation from the FDA for TSHA-102 for the treatment of Rett syndrome. We also received CTA clearance from the United Kingdom's Medicines and Healthcare Products Regulatory Agency, or U.K. MHRA, in early 2024 for pediatric patients with Rett syndrome. In February 2024, we received Innovative Licensing and Access Pathway, or ILAP, designation for TSHA-102 from the U.K. MHRA. The ILAP aims to facilitate patient access to novel treatments by accelerating time to market through opportunities for enhanced engagements with U.K. regulatory authorities and other stakeholders. In April 2024, the FDA granted Regenerative Medicine Advanced Therapy, or RMAT, designation for TSHA-102 in Rett syndrome. Sponsor companies receiving RMAT designation can benefit from increased interactions with the FDA involving senior managers, with the goal of expediting drug development.

We completed a CMC-focused Type D with the FDA in the fourth quarter of 2024. The FDA endorsed our intended Good Manufacturing Practice, or GMP, commercial manufacturing process, proposed analytical methods, and corresponding qualification and validation plans, including key mechanism of action potency release assays. We also established analytical comparability between the clinical product and the product derived from the final commercial manufacturing process, and received FDA permission to use the GMP product in future clinical studies of TSHA-102.

We have a limited operating history. Since our inception, our operations have focused on organizing and staffing our company, business planning, raising capital and entering into collaboration agreements for conducting preclinical and clinical development activities for our product candidates. Our lead product candidate is still in the clinical stage. We do not have any product candidates approved for sale and have not generated any revenue from product sales. Through December 31, 2024, we have funded our operations primarily through: (i) the sale of equity, raising an aggregate of \$671.0 million of gross proceeds from our initial public offering, or the IPO, sales of common stock pursuant to our Sales Agreement (as defined below), our October 2022 follow-on offering, our 2023 private placement and our June 2024 Offering (as defined below); (ii) pre-IPO private placements of our convertible preferred stock; (iii) our Term Loan Agreement (as defined below) and subsequently the Trinity Term Loan Agreement (as defined below); and (iv) the Astellas Transactions.

On November 13, 2023, or the Trinity Closing Date, we entered into a Loan and Security Agreement, or the Trinity Term Loan Agreement, by and among us, the lenders party thereto from time to time, or the Trinity Lenders, and Trinity Capital Inc., as administrative agent and collateral agent for the Trinity Lenders, or Trinity. The Trinity Term Loan Agreement provided for, on the Trinity Closing Date, \$40.0 million aggregate principal amount of term loans, or, collectively, the Trinity Term Loans. We drew the Trinity Term Loans in full on the Trinity Closing Date. The proceeds of the Trinity Term Loans were used to repay our obligations

under the Loan and Security Agreement, or the Term Loan Agreement, with the lenders party thereto from time to time, or the Lenders and Silicon Valley Bank, as administrative agent and collateral agent for the Lenders, or the Agent, in full. The Term Loan Agreement with Silicon Valley Bank was terminated concurrently with entry into the Trinity Term Loan Agreement.

Since our inception, we have incurred significant operating losses. Our net losses were \$89.3 million for the year ended December 31, 2024 and \$111.6 million for the year ended December 31, 2023. As of December 31, 2024, we had an accumulated deficit of \$602.3 million. We expect to continue to incur significant expenses and operating losses for the foreseeable future. We anticipate that our expenses will increase significantly in connection with our ongoing activities, as we:

- continue to advance the clinical development of our product candidates and, if we determine to do so in the future, reprioritize the advancement of our preclinical and discovery programs;
- conduct our ongoing clinical trials of TSHA-102 and any other current and future product candidates that we advance;
- seek regulatory approval for any product candidates that successfully complete clinical trials;
- continue to develop our gene therapy product candidate pipeline;
- scale up our clinical and regulatory capabilities;
- work with CMOs for the manufacture current Good Manufacturing Practice, or cGMP material for clinical trials or potential commercial sales;
- establish a commercialization infrastructure and scale up internal and external manufacturing and distribution capabilities to commercialize any product candidates for which we may obtain regulatory approval;
- adapt our regulatory compliance efforts to incorporate requirements applicable to marketed products;
- maintain, expand and protect our intellectual property portfolio;
- hire additional clinical, manufacturing quality control, regulatory, manufacturing and scientific and administrative personnel;
- add operational, financial and management information systems and personnel, including personnel to support our product development and planned future commercialization efforts; and
- incur additional legal, accounting and other expenses in operating as a public company.

License Agreements

Research, Collaboration and License Agreement with The University of Texas Southwestern Medical Center

In November 2019, we entered into the UT Southwestern Agreement with The Board of Regents of the University of Texas System on behalf of UT Southwestern, as amended in April 2020.

In connection with the UT Southwestern Agreement, we obtained an exclusive, worldwide, royalty-free license under certain patent rights of UT Southwestern and a non-exclusive, worldwide, royalty-free license under certain know-how of UT Southwestern, in each case to make, have made, use, sell, offer for sale and import licensed products for use in certain specified indications. We are required to use commercially reasonable efforts to develop, obtain regulatory approval for, and commercialize at least one licensed product. Additionally, we obtained a right of first refusal to negotiate for an exclusive license under certain additional patent rights and know-how of UT Southwestern.

In connection with the UT Southwestern Agreement, we issued to UT Southwestern 2,179,000 shares of our common stock. We do not have any future milestone or royalty obligations to UT Southwestern under the UT Southwestern Agreement, other than costs related to the maintenance of patents.

License Agreement with Abeona (CLN1 Disease)

In August 2020, we entered into the Abeona CLN1 Agreement with Abeona. In connection with the Abeona CLN1 Agreement, we obtained an exclusive, worldwide, royalty-bearing license, with the right to grant sublicenses under certain patents, know-how and materials originally developed by the University of North Carolina at Chapel Hill and Abeona to research, develop, manufacture, have manufactured, use, and commercialize licensed products for gene therapy for the prevention, treatment, or diagnosis of CLN1 Disease (one of the forms of Batten disease) in humans.

Subject to certain obligations of Abeona, we are obligated to use commercially reasonable efforts to develop at least one product and commercialize at least one product in the United States.

In connection with the license grant, we paid Abeona a one-time upfront license fee of \$3.0 million during fiscal year 2020. We are obligated to pay Abeona up to \$26.0 million in regulatory-related milestones and up to \$30.0 million in sales-related milestones per licensed product and high single-digit royalties on net sales of licensed products. Royalties are payable on a licensed product-by-licensed product and country-by-country basis until the latest of the expiration or revocation or complete rejection of the last licensed patent covering such licensed product in the country where the licensed product is sold, the loss of market exclusivity in such country where the product is sold, or, if no licensed product exists in such country and no market exclusivity exists in such country, ten years from first commercial sale of such licensed product in such country. In addition, concurrent with the Abeona CLN1 Agreement we entered into a purchase and reimbursement agreement with Abeona, pursuant to which we purchased specified inventory from Abeona and reimbursed Abeona for certain research and development costs previously incurred for total consideration of \$4.0 million paid in fiscal year 2020. In December 2021 a regulatory milestone was triggered in connection with the Abeona CLN1 Agreement. No additional milestone payments were made or triggered during the years ended December 31, 2023 and 2024.

The Abeona CLN1 Agreement expires on a country-by-country and licensed product-by-licensed product basis upon the expiration of the royalty term of a licensed product in such country. Either party may terminate the agreement upon an uncured material breach of the agreement or insolvency of the other party. We may terminate the agreement for convenience upon specified prior written notice to Abeona.

License Agreement with Abeona (Rett Syndrome)

In October 2020, we entered into the Abeona Rett Agreement with Abeona pursuant to which we obtained an exclusive, worldwide, royalty-bearing license, with the right to grant sublicenses under certain patents, know-how and materials originally developed by the University of North Carolina at Chapel Hill, the University of Edinburgh and Abeona to research, develop, manufacture, have manufactured, use, and commercialize licensed products for gene therapy and the use of related transgenes for Rett syndrome.

Subject to certain obligations of Abeona, we are required to use commercially reasonable efforts to develop at least one licensed product and commercialize at least one licensed product in the United States.

In connection with the Abeona Rett Agreement, we paid Abeona a one-time upfront license fee of \$3.0 million during fiscal year 2020. We are obligated to pay Abeona up to \$26.5 million in regulatory-related milestones and up to \$30.0 million in sales-related milestones per licensed product and high single-digit royalties on net sales of licensed products. Royalties are payable on a licensed product-by-licensed product and country-by-country basis until the latest of the expiration or revocation or complete rejection of the last licensed patent covering such licensed product in the country where the licensed product is sold, the loss of market exclusivity in such country where the product is sold, or, if no licensed product exists in such country and no market exclusivity exists in such country, ten years from first commercial sale of such licensed product in such country.

In March 2022, our CTA filing for TSHA-102 for the treatment of Rett Syndrome was approved by Health Canada and therefore triggered a regulatory milestone payment in connection with the Rett Agreement. We recorded a \$1.0 million charge within research and development expenses in the consolidated statements of operations for the year ended December 31, 2022. This milestone fee was paid in July 2022 and has been classified as an investing outflow in the consolidated statements of cash flows for the year ended December 31, 2022. In May 2023, we dosed the first patient with TSHA-102 in the Phase 1/2 REVEAL trial evaluating the safety and preliminary efficacy of TSHA-102 in adult patients with Rett syndrome and therefore triggered a milestone payment in connection with this agreement. We recorded \$3.5 million within research and development expenses in the consolidated statements of operations for the year ended December 31, 2023. This milestone fee was paid in August 2023 and has been classified as an investing cash outflow in the consolidated statements of cash flows for the year ended December 31, 2023. No additional milestone payments were made or triggered in connection with this agreement during the years ended December 31, 2023 and 2024.

The Abeona Rett Agreement expires on a country-by-country and licensed product-by-licensed product basis upon the expiration of the royalty term of a licensed product in such country. Either party may terminate the agreement upon an uncured material breach of the agreement or insolvency of the other party. We may terminate the agreement for convenience upon specified prior written notice to Abeona.

Option Agreement with Astellas

On the Effective Date we entered into the Option Agreement with Astellas.

TSHA-120 Giant Axonal Neuropathy

Under the Option Agreement, we granted to Astellas the GAN Option. Subject to certain extensions, the GAN Option was exercisable from the Effective Date through a specified period of time following Astellas' receipt of (i) the formal minutes from the Type B end-of-Phase 2 meeting between us and the FDA in response to our meeting request sent to the FDA on September 19, 2022 for the 120 GAN Product, (ii) all written feedback from the FDA with respect to the Type B end-of-Phase 2 Meeting, and (iii) all briefing documents sent by us to the FDA with respect to the Type B end-of-Phase 2 Meeting. Following the receipt of Type C meeting feedback from the FDA regarding a registrational path for TSHA-120 in September 2023, Astellas elected not to exercise the GAN Option.

TSHA-102 Rett Syndrome

Under the Option Agreement, we also granted to Astellas the Rett Option. Subject to certain extensions, the Rett Option is exercisable for the Rett Option Period related to the Rett Product.

The parties have agreed that, if Astellas exercises an Option, the parties will, for a specified period, negotiate a license agreement in good faith on the terms and conditions outlined in the Option Agreement, including payments by Astellas of a to-be-determined upfront payment, certain to-be-determined milestone payments, and certain to-be-determined royalties on net sales of GAN Products and/or Rett Products, as applicable.

Components of Results of Operations

Revenue

Revenue for the years ended December 31, 2024 and 2023 was derived from the Astellas Transactions. We recognize revenue as research and development activities related to our Rett program are performed. Revenue related to the material rights associated with the Rett Option and the GAN Option must be recognized at a point in time when the options are exercised or the option period expires. In September 2023, Astellas elected not to exercise the GAN Option, therefore we recognized revenue related to the GAN Option during the year ended December 31, 2023.

To date, we have not recognized any revenue from product sales, and we do not expect to generate any revenue from the sale of products, if approved, in the foreseeable future. If our development efforts for our product candidates are successful and result in regulatory approval, or license agreements with third parties, we may generate revenue in the future from product sales. However, there can be no assurance as to when we will generate such revenue, if at all.

Operating Expenses

Research and Development Expenses

Research and development expenses primarily consist of preclinical development of our product candidates and discovery efforts, including conducting preclinical studies, manufacturing development efforts, preparing for clinical trials and activities related to regulatory filings for our product candidates. Research and development expenses are recognized as incurred and payments made prior to the receipt of goods or services to be used in research and development are capitalized until the goods or services are received. Costs incurred in obtaining technology licenses through asset acquisitions are charged to research and development expense if the licensed technology has not reached technological feasibility and has no alternative future use. Research and development expenses include or could include:

- employee-related expenses, including salaries, bonuses, benefits, stock-based compensation, other related costs for those employees involved in research and development efforts;
- license maintenance fees and milestone fees incurred in connection with various license agreements;
- external research and development expenses incurred under agreements with consultants, contract research organizations, or CROs, investigative sites and consultants to conduct our preclinical studies;
- costs related to manufacturing material for our preclinical studies and clinical trials, including fees paid to contract manufacturing organizations, or CMOs;
- laboratory supplies and research materials;

- costs related to compliance with regulatory requirements; and
- facilities, depreciation and other allocated expenses, which include direct and allocated expenses for rent, maintenance of facilities, insurance and equipment.

Research and development activities are central to our business model. Product candidates in later stages of clinical development generally have higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of later-stage clinical trials. We have increased, and expect to continue to increase for the foreseeable future, our research and development spend with respect to the Rett clinical trials as we continue the development of TSHA-102 and manufacturing processes and conduct discovery and research activities for our preclinical programs. We cannot determine with certainty the timing of initiation, the duration or the completion costs of current or future preclinical studies and clinical trials of our product candidates due to the inherently unpredictable nature of preclinical and clinical development. Clinical and preclinical development timelines, the probability of success and development costs can differ materially from expectations. We anticipate that we will make determinations as to which product candidates to pursue and how much funding to direct to each product candidate on an ongoing basis in response to the results of ongoing and future preclinical studies and clinical trials, regulatory developments and our ongoing assessments as to each product candidate's commercial potential. We will need to raise substantial additional capital in the future. Our clinical development costs are expected to increase significantly as we commence clinical trials. Our future expenses may vary significantly each period based on factors such as:

- expenses incurred to conduct preclinical studies required to advance our product candidates into clinical development;
- per patient trial costs, including based on the number of doses that patients received;
- the number of patients who enroll in each trial;
- the number of trials required for approval;
- the number of sites included in the trials;
- the countries in which the trials are conducted;
- the length of time required to enroll eligible patients;
- the drop-out or discontinuation rates of patients;
- potential additional safety monitoring requested by regulatory agencies;
- the duration of patient participation in the trials and follow-up;
- the phase of development of the product candidate;
- third-party contractors failing to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all;
- the cost to manufacture our product candidates;
- the ability of our CMOs to manufacture our product candidates;
- regulators or institutional review boards requiring that we or our investigators suspend or terminate clinical development for various reasons, including noncompliance with regulatory requirements or a finding that the participants are being exposed to unacceptable health risks; and
- the efficacy and safety profile of our product candidates.

General and Administrative Expenses

General and administrative expenses consist or will consist principally of salaries and related costs for personnel in executive and administrative functions, including stock-based compensation, travel expenses and recruiting expenses. Other general and administrative expenses include professional fees for legal, consulting, accounting and audit and tax-related services and insurance costs.

We anticipate that our general and administrative expenses as a result of payments for accounting, audit, legal, consulting services, as well as costs associated with maintaining compliance with Nasdaq listing rules and SEC requirements, director and officer liability insurance, investor and public relations activities and other expenses associated with operating as a public company may increase in the near future. In addition, we expect to incur legal fees in connection with the shareholder derivative lawsuit against

certain of our current and former directors in the Court of Chancery of the State of Delaware. See “Part II, Item 8, Note 13—Commitments and Contingencies” in this Annual Report.

Impairment of Long-lived Assets

Impairment of long-lived assets are the result of an asset group's carrying value exceeding the fair value. In November 2022, we decided not to continue building out our manufacturing facility in North Carolina. We recorded a non-cash impairment charge related to the construction in progress and right-of-use lease assets at the manufacturing facility. We recorded additional impairment charges related to the construction in progress and assets held for sale at the manufacturing facility in the years ended December 31, 2023 and 2024.

Other Income (Expense)

Other income (expense) consists primarily of dividends earned from our money market fund and interest income on our cash and cash equivalents, interest expense on borrowings under the Trinity Term Loan, and non-cash changes in the fair value of our outstanding warrant liability and the Trinity Term Loan.

Results of Operations

Results of Operations for the Year Ended December 31, 2024 and 2023

The following table summarizes our results of operations for the years ended December 31, 2024 and 2023 (in thousands):

	For the Year Ended December 31,	
	2024	2023
Revenue	\$ 8,333	\$ 15,451
Operating expenses:		
Research and development	66,001	56,778
General and administrative	28,953	30,047
Impairment of long-lived assets	4,838	1,065
Total operating expenses	<u>99,792</u>	<u>87,890</u>
Loss from operations	<u>(91,459)</u>	<u>(72,439)</u>
Other income (expense):		
Change in fair value of warrant liability	16	(34,718)
Change in fair value of term loan	(4,583)	(1,538)
Loss on debt extinguishment	—	(1,398)
Interest income	6,940	3,572
Interest expense	(102)	(4,998)
Other expense	(110)	(47)
Total other income (expense), net	<u>2,161</u>	<u>(39,127)</u>
Net loss	<u>\$ (89,298)</u>	<u>\$ (111,566)</u>

Revenue

Revenue was \$8.3 million for the year ended December 31, 2024, compared to \$15.5 million for the year ended December 31, 2023. Revenue for the years ended December 31, 2024 and 2023 was derived entirely from the Astellas Transactions. The revenue recorded for the year ended December 31, 2024 is the result of Rett syndrome research and development activities performed during the year of \$8.3 million. The revenue recorded for the year ended December 31, 2023 is the result of Rett syndrome research and development activities performed during the year of \$13.2 million and the expiration of the material right associated with the GAN Option of \$2.3 million.

Research and Development Expenses

Research and development expenses were \$66.0 million for the year ended December 31, 2024, compared to \$56.8 million for the year ended December 31, 2023. The \$9.2 million increase was primarily driven by higher GMP batch activities during the year ended December 31, 2024, which is representative of the intended commercial manufacturing process for TSHA-102 in Rett syndrome and additional clinical trial activities in the TSHA-102 Phase 1/2 REVEAL clinical trials for the year ended December 31, 2024.

General and Administrative Expenses

General and administrative expenses were \$29.0 million for the year ended December 31, 2024, compared to \$30.0 million for the year ended December 31, 2023. The decrease of \$1.0 million was primarily due to the issuance costs allocated to the liability-classified 2023 Pre-Funded Warrants (as defined below) during the year ended December 31, 2023 as a result of the August 2023 Private Placement, which did not occur in 2024.

Impairment of Long-lived Assets

We recorded a non-cash impairment charge of \$4.8 million related to our manufacturing facility and assets previously classified as held for sale which were marketed for sale or sublease for the year ended December 31, 2024. We recorded non-cash impairment charges of \$1.1 million related to assets held for sale and construction in progress for the year ended December 31, 2023.

Other Income (Expense)

Change in fair value of warrant liability

Change in fair value of warrant liability was a non-cash gain totaling less than \$0.1 million for the year ended December 31, 2024 related to the SSI Warrants (as defined below) compared to a non-cash expense totaling \$34.7 million for the year ended December 31, 2023 related to the 2023 Pre-Funded Warrants and the SSI Warrants. The expense for the year ended December 31, 2023 is primarily due to the substantial increase in the fair value of the common stock underlying the Pre-Funded Warrants from the date of issuance through the date the warrants were reclassified into equity, which resulted in a non-recurring expense of \$34.5 million. As the Pre-Funded Warrants were classified into equity during the year ended December 31, 2023, there will be no additional fair value adjustments related to these warrants. The change in fair value related to the SSI Warrants was \$0.2 million for the year ended December 31, 2023.

Change in fair value of term loan

We elected the fair value option for the Trinity Term Loan and changes to fair value, other than changes that are directly attributed to instrument-specific credit risk, were recorded as a component of other income (expense). The change in fair value was \$4.6 million for the year ended December 31, 2024.

Loss on debt extinguishment

Loss on debt extinguishment was a non-recurring expense totaling \$1.4 million for the year ended December 31, 2023 due to the early payoff of the Term Loan with Silicon Valley Bank in November 2023.

Interest income

Interest income was \$6.9 million for the year ended December 31, 2024 compared to \$3.6 million for the year ended December 31, 2023. The increase in income is primarily attributable to dividends earned from our money market fund and interest earned on our savings account following the investment of proceeds raised in our August 2023 Private Placement and our June 2024 Offering.

Interest expense

Interest expense was \$0.1 million for the year ended December 31, 2024, compared to \$5.0 million for the year ended December 31, 2023. The decrease of \$4.9 million was primarily attributable to interest expense incurred under the Term Loan Agreement with Silicon Valley Bank during the year ended December 31, 2023. No interest expense was recorded on the Trinity Term Loan for the period ended December 31, 2024 due to the election of the fair value option.

Liquidity and Capital Resources

Overview

Since our inception, we have not generated any revenue from product sales and have incurred significant operating losses. As of December 31, 2024, we had cash and cash equivalents of \$139.0 million. Through December 31, 2024, we have funded our operations primarily through equity financings, raising an aggregate of \$671.0 million in gross proceeds from equity financings, including from pre-IPO private placements of convertible preferred stock, our IPO, and subsequent sales of common stock in public and private securities offerings, our term loans and the Astellas Transactions.

On August 12, 2021, or the Closing Date, we entered into a Loan and Security Agreement, or the Term Loan Agreement, with the lenders party thereto from time to time, or the Lenders and Silicon Valley Bank, as administrative agent and collateral agent

for the Lenders, or the Agent. We drew \$30.0 million in term loans on the Closing Date and an additional \$10.0 million in term loans on December 29, 2021. We did not draw on any of the additional \$20.0 million tranches prior to their expiration on September 30, 2022 and March 31, 2023. The loan repayment schedule provided for interest only payments until August 31, 2024, followed by consecutive monthly payments of principal and interest. All unpaid principal and accrued and unpaid interest with respect to each term loan was due and payable in full on August 1, 2026.

On the Trinity Closing Date, we entered the Trinity Term Loan Agreement. The Trinity Term Loan Agreement provides for, on the Trinity Closing Date, \$40.0 million aggregate principal amount of the Trinity Term Loans. We drew the Trinity Term Loans in full on the Trinity Closing Date. The interest rate applicable to the Trinity Term Loans is the greater of (a) the WSJ Prime Rate plus 4.50% or (b) 12.75% per annum. The Trinity Term Loans are interest only from the Trinity Closing Date through 36 months from the Trinity Closing Date, which may be extended to 48 months from the Trinity Closing Date upon the satisfaction of certain milestones set forth in the Trinity Term Loan Agreement, after which we are required to pay equal monthly installments of principal through November 13, 2028, or the Maturity Date. The Trinity Term Loans may be prepaid in full (i) from the Trinity Closing Date through November 13, 2024, with payment of a 3.00% prepayment premium, (ii) from November 13, 2024 through November 13, 2025, with payment of a 2% prepayment premium, and (iii) from November 13, 2025 through, but excluding, the Maturity Date, with payment of a 1% prepayment premium. On the Trinity Closing Date, we paid to Trinity a commitment fee of 1.00% of the original principal amount of the Trinity Term Loans. Upon repayment in full of the Trinity Term Loans, we will pay to Trinity an end of term payment equal to 5.00% of the original principal amount of the Trinity Term Loans.

The obligations under the Trinity Term Loan Agreement are secured by a perfected security interest in all of our assets except for certain customarily excluded property pursuant to the terms of the Trinity Term Loan Agreement. There are no financial covenants and no warrants associated with the Trinity Term Loan Agreement. The Trinity Term Loan Agreement contains various covenants that limit our ability to engage in specified types of transactions without the consent of Trinity and the Trinity Lenders which include, among others, incurring or assuming certain debt; merging, consolidating or acquiring all or substantially all of the capital stock or property of another entity; changing the nature of our business; changing our organizational structure or type; licensing, transferring or disposing of certain assets; granting certain types of liens on our assets; making certain investments; and paying cash dividends. The Trinity Term Loan Agreement also contains customary representations and warranties, and also includes customary events of default, including payment default, breach of covenants, change of control, and material adverse effects. Upon the occurrence of an event of default, a default interest rate of an additional 5% per annum may be applied to the outstanding loan balances, and the Trinity Lenders may declare all outstanding obligations immediately due and payable and exercise all of its rights and remedies as set forth in the Trinity Term Loan Agreement and under applicable law. The proceeds of the Trinity Term Loans were used to repay our obligations under the Term Loan Agreement (as defined below) with Silicon Valley Bank in full. The Term Loan Agreement with Silicon Valley Bank was terminated concurrently with entry into the Trinity Term Loan Agreement.

On October 5, 2021, we filed a shelf registration statement on Form S-3 with the SEC in relation to the registration of common stock, preferred stock, debt securities, warrants and units or any combination thereof up to a total aggregate offering price of \$350.0 million. We also simultaneously entered into a Sales Agreement, or the Sales Agreement with SVB Leerink LLC and Wells Fargo Securities, LLC, or the Sales Agents, pursuant to which we may issue and sell, from time to time at our discretion, shares of our common stock having an aggregate offering price of up to \$150.0 million through the Sales Agents. In March 2022, we amended the Sales Agreement to, among other things, include Goldman Sachs & Co. LLC as an additional Sales Agent. In April 2022, we sold 2,000,000 shares of common stock pursuant to the Sales Agreement and received net proceeds of \$11.6 million. On December 13, 2024, we filed a new shelf registration statement on Form S-3 following the expiration of our prior registration statement, in relation to the registration of common stock, preferred stock, debt securities, warrants and units or any combination thereof up to a total aggregate offering price of \$300.0 million, including up to \$100.0 million shares of common stock that may be offered and sold pursuant to the Sales Agreement. No other shares of common stock have been issued and sold pursuant to the Sales Agreement as of December 31, 2024.

On October 21, 2022, we entered into the Option Agreement with Astellas granting Astellas an exclusive option to obtain exclusive, worldwide, royalty and milestone-bearing rights and licenses related to TSHA-120 and TSHA-102. As partial consideration for the rights granted to Astellas under the Option Agreement, Astellas paid us a one-time payment in the amount of \$20.0 million, or the Upfront Payment, in November 2022.

Also on October 21, 2022, we entered into the Securities Purchase Agreement with Astellas, pursuant to which we agreed to issue and sell to Astellas in a private placement, or the Private Placement, an aggregate of 7,266,342 shares of our common stock, or the Private Placement Shares, for aggregate proceeds of \$30.0 million. The Private Placement closed on October 24, 2022. Pursuant to the Securities Purchase Agreement, in connection with the Private Placement, Astellas has the right to designate one individual to attend all meetings of the Board in a non-voting observer capacity. We also granted Astellas certain registration rights with respect to the Private Placement Shares.

On October 26, 2022, we entered into the Underwriting Agreement, to issue and sell 14,000,000 shares of our common stock, par value \$0.00001 per share, in an underwritten public offering pursuant to effective registration statement on Form S-3 and a related prospectus and prospectus supplement. The offering price to the public was \$2.00 per share and the Underwriter purchased the shares from us pursuant to the Underwriting Agreement at a price of \$1.88 per share. In addition, we granted the Underwriter an option to purchase, for a period of 30 days, up to an additional 2,100,000 shares of our common stock. The Follow-on Offering closed on October 31, 2022 and we received net proceeds of \$26.0 million after deducting underwriting discounts, commissions and offering expenses. On November 10, 2022, the Underwriter exercised their option to purchase an additional 765,226 shares of our common stock and we received net proceeds of \$1.4 million after deducting underwriting discounts and commissions.

In April 2023, we entered into a securities purchase agreement, or the SSI Securities Purchase Agreement, with two affiliates of SSI Strategy Holdings LLC, or SSI, named therein, or the SSI Investors, pursuant to which we agreed to issue and sell to the SSI Investors in a private placement, or the SSI Private Placement, 705,218 shares of our common stock, or the SSI Shares, and warrants, or the SSI Warrants, to purchase an aggregate of 525,000 shares of our common stock, or the Warrant Shares. SSI provides certain consulting services to us. Each SSI Warrant has an exercise price of \$0.7090 per Warrant Share, which was the closing price of our common stock on the Nasdaq Global Market on April 4, 2023. The SSI Warrants issued in the SSI Private Placement provide that the holder of the SSI Warrants will not have the right to exercise any portion of its SSI Warrants until the achievement of certain clinical and regulatory milestones related to our clinical programs. The SSI Private Placement closed on April 5, 2023. Gross proceeds of the SSI Private Placement were \$0.5 million.

On August 14, 2023, we entered into a Securities Purchase Agreement, or the August 2023 Securities Purchase Agreement, with certain institutional and other accredited investors, or the Purchasers, pursuant to which we agreed to sell and issue to the Purchasers in a private placement transaction, or the August 2023 Private Placement, that closed on August 16, 2023: (i) 122,412,376 shares of our common stock and (ii) with respect to certain Purchasers, pre-funded warrants, or the 2023 Pre-Funded Warrants, to purchase 44,250,978 shares of common stock in lieu of shares of common stock. The closing of the August 2023 Private Placement, or the Closing, occurred on August 16, 2023. The total gross proceeds to us at the Closing were \$150.0 million, and after deducting placement agent commissions and offering expenses payable by us, net proceeds were \$140.3 million.

On June 26, 2024, we entered into an underwriting agreement, or the June 2024 Underwriting Agreement, with Jefferies LLC and Goldman Sachs & Co. LLC, as representatives of the several underwriters set forth therein, or, collectively, the Underwriters, to issue and sell 14,361,113 shares of our common stock and pre-funded warrants to purchase 18,972,221 shares of our common stock, or the June 2024 Pre-Funded Warrants, pursuant to an effective shelf registration statement on Form S-3 and a related prospectus and prospectus supplement, or the June 2024 Offering. The offering price to the public was \$2.25 per share of common stock and \$2.249 per June 2024 Pre-Funded Warrant, which is the price to the public of each share of common stock sold in the June 2024 Offering, minus the \$0.001 exercise price per June 2024 Pre-Funded Warrant. The Underwriters purchased the shares and the June 2024 Pre-Funded Warrants from us pursuant to the June 2024 Underwriting Agreement at a price of \$2.115 per share and \$2.114 per pre-funded warrant, respectively. The initial closing of the June 2024 Offering occurred on June 27, 2024 and we received net proceeds of \$70.0 million, after deducting underwriting discounts and commissions and offering expenses. In addition, we granted the Underwriters an option to purchase, for a period of 30 days, up to an additional 5,000,000 shares of our common stock. On July 9, 2024, the Underwriters exercised their option to purchase an additional 3,235,000 shares of common stock and we received additional net proceeds of \$6.7 million, after deducting underwriting discounts and commissions and offering expenses. The total net proceeds received from the June 2024 Offering were \$76.7 million after deducting underwriting discounts, commissions and other offering expenses payable by us.

Funding Requirements

To date, we have not generated any revenues from the commercial sale of approved drug products, and we do not expect to generate substantial revenue for at least the next few years. If we fail to complete the development of our product candidates in a timely manner or fail to obtain their regulatory approval, our ability to generate future revenue will be compromised. We do not know when, or if, we will generate any revenue from our product candidates, and we do not expect to generate significant revenue unless and until we obtain regulatory approval of, and commercialize, our product candidates. We have increased, and expect to continue to increase for the foreseeable future, our research and development expenses, particularly with respect to our Rett clinical trials, as we continue the development of our product candidates and manufacturing processes and conduct discovery and research activities for our preclinical programs. If we obtain approval for any of our product candidates, we expect to incur significant commercialization expenses related to sales, marketing, manufacturing and distribution. We anticipate that we will need substantial additional funding in connection with our continuing operations. If we are unable to raise capital when needed or on attractive terms, we could be forced to delay, reduce or eliminate our research and development programs or future commercialization efforts.

As of December 31, 2024, our material cash requirements consisted of \$28.6 million in total lease payments under our noncancelable leases for equipment, laboratory space and office space. These leases are described in further detail in Note 5 to our

audited consolidated financial statements located in Part IV, Item 15 of this Annual Report on Form 10-K. Our most significant purchase commitments consist of \$12.5 million in cancellable purchase obligations to our CROs and other clinical trial vendors.

We believe that our existing cash and cash equivalents will enable us to fund our operating expenses and capital requirements into the fourth quarter of 2026. We will require additional capital to fund the research and development of our product candidates, to fund our manufacturing activities, to fund precommercial activities of our programs and for working capital and general corporate purposes. The assessment of our ability to meet our future obligations is inherently judgmental, subjective and susceptible to change.

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

- the scope, progress, costs and results of discovery, preclinical development, laboratory testing and clinical trials for TSHA-102 and any current and future product candidates that we advance;
- our ability to access sufficient additional capital on a timely basis and on favorable terms;
- the extent to which we develop, in-license or acquire other product candidates and technologies in our gene therapy product candidate pipeline;
- the costs and timing of process development and manufacturing scale-up activities associated with our product candidates and other programs as we advance them through preclinical and clinical development;
- the number and development requirements of product candidates that we may pursue;
- the costs, timing and outcome of regulatory review of our product candidates;
- our headcount growth and associated costs as we expand our research and development capabilities and establish a commercial infrastructure;
- the costs and timing of future commercialization activities, including product manufacturing, marketing, sales, and distribution, for any of our product candidates for which we receive marketing approval;
- the costs and timing of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending any intellectual property-related claims;
- the costs incurred in defending ourselves in any legal proceedings that we may be subject to;
- the revenue, if any, received from commercial sales of our product candidates for which we receive marketing approval; and
- the costs of operating as a public company.

Identifying potential product candidates and conducting preclinical studies and clinical trials is a time-consuming, expensive and uncertain process that takes many years to complete, and we may never generate the necessary data or results required to obtain marketing approval and achieve product sales. In addition, our product candidates, if approved, may not achieve commercial success. Our commercial revenues, if any, will be derived from sales of product candidates that we do not expect to be commercially available in the near term, if at all. Accordingly, we will need to continue to rely on additional financing to achieve our business objectives. Adequate additional financing may not be available to us on acceptable terms, or at all. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the terms of these equity securities may restrict our ability to operate. The Trinity Term Loan Agreement contains negative covenants, including, among other things, restrictions on indebtedness, liens investments, mergers, dispositions, prepayment of other indebtedness and dividends and other distributions. Any future additional debt financing and equity financing, if available, may involve agreements that include covenants limiting and restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures, entering into profit-sharing or other arrangements or declaring dividends. If we raise additional funds through collaborations, strategic alliances or marketing, distribution or licensing arrangements with third parties, we may be required to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or to grant licenses on terms that may not be favorable to us.

Cash Flows

The following table shows a summary of our cash flows for the years ended December 31, 2024 and 2023 (in thousands):

	For the Year Ended December 31,	
	2024	2023
Net cash used in operating activities	\$ (81,225)	\$ (73,018)
Net cash used in investing activities	(363)	(7,352)
Net cash provided by financing activities	76,684	136,393
Net change in cash, cash equivalents and restricted cash	\$ (4,904)	\$ 56,023

Operating Activities

For the year ended December 31, 2024, our net cash used in operating activities of \$81.2 million primarily consisted of a net loss of \$89.3 million, primarily attributable to our spending on research and development expenses. The net loss of \$89.3 million was partially offset by \$20.5 million in adjustments for non-cash items and other adjustments to reconcile net loss to net cash used in operating activities, primarily due to stock-based compensation expense and impairment of long-lived assets. Additional cash used in operating activities of \$12.4 million, resulting from changes in operating assets and liabilities was primarily due to a decrease in deferred revenue related to the Astellas Transactions.

For the year ended December 31, 2023, our net cash used in operating activities of \$73.0 million primarily consisted of a net loss of \$111.6 million, primarily attributable to our spending on research and development expenses. The net loss of \$111.6 million was partially offset by \$56.6 million in adjustments for non-cash items and other adjustments to reconcile net loss to net cash used in operating activities, primarily due to the change in fair value of warrant liability of \$34.7 million and stock-based compensation expense. Additional cash used in operating activities of \$18.0 million, resulting from changes in operating assets and liabilities was primarily due to a decrease in deferred revenue related to the Astellas Transactions.

Investing Activities

During the year ended December 31, 2024, investing activities used \$0.4 million of cash primarily attributable to the purchase of lab equipment.

During the year ended December 31, 2023, investing activities used \$7.4 million of cash primarily attributable to capital expenditures related to the close out of our in-house manufacturing facility project and payment of a milestone license fee.

Financing Activities

During the year ended December 31, 2024, financing activities provided \$76.7 million of cash, which was primarily attributable to the closing of the June 2024 Offering.

During the year ended December 31, 2023, financing activities provided \$136.4 million of cash, which was primarily attributable to the proceeds from the August 2023 Private Placement.

Critical Accounting Policies and Significant Judgments and Estimates

This management's discussion and analysis of our financial condition and results of operations is based on our financial statements, which have been prepared in accordance with U.S. generally accepted accounting principles, or U.S. GAAP. The preparation of these financial statements requires us to make estimates and judgments that affect the reported amounts of assets, liabilities, and expenses and the disclosure of contingent assets and liabilities in our financial statements. In accordance with U.S. GAAP, we evaluate our estimates and judgments on an ongoing basis, including those related to research and development expenses, stock-based compensation, the Astellas Transactions and accounting for the Trinity Term Loans at fair value. We base our estimates on historical experience, known trends and events, and various other factors that are believed to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions.

We define our critical accounting policies as those accounting principles that require us to make subjective estimates and judgments about matters that are uncertain and are likely to have a material impact on our financial condition and results of operations, as well as the specific manner in which we apply those principles. While our significant accounting policies are more fully described in Note 2 to our audited consolidated financial statements located in Part IV, Item 15 of this Annual Report on Form 10-K, we believe

the following are the critical accounting policies used in the preparation of our financial statements that require significant estimates and judgments.

Research and Development Costs

We have entered into research and development contracts with research institutions and other companies. These agreements are generally cancelable, and related payments are recorded as research and development expenses as incurred. Payments for these activities are based on the terms of the individual agreements, which may differ from the pattern of costs incurred, and are reflected on the balance sheet as prepaid or accrued expenses. We record accruals for estimated ongoing research costs. When evaluating the adequacy of the accrued liabilities, we analyze progress of the studies, including the phase or completion of events, invoices received and contracted costs.

Research and development costs primarily consist of payroll, stock-based compensation, clinical trial expense, certain manufacturing costs, laboratory costs and other supplies, and the cost to acquire third-party licenses.

Costs incurred in obtaining technology licenses through asset acquisitions are charged to research and development expense if the licensed technology has not reached technological feasibility and has no alternative future use.

To date, we have not experienced significant changes in our estimates of accrued research and development liabilities after a reporting period. However, due to the nature of estimates, there is no assurance that we will not make changes to our estimates in the future as we become aware of additional information about the status or conduct of our clinical studies and other research activities.

Stock-Based Compensation

We account for all stock-based payments to employees and non-employees, including grants of stock options, restricted stock awards, or “RSAs” and restricted stock units or, “RSUs” based on their respective grant date fair values. We estimate the fair value of stock option grants using the Black-Scholes option pricing model, which is affected principally by the estimated fair value of shares of our common stock and requires management to make a number of other assumptions, including the expected life of the option, the volatility of the underlying shares, the risk-free interest rate and expected dividends. Expected volatility is based on the historical share volatility of a set of comparable publicly traded companies over a period of time equal to the expected term of the options. Due to the lack of historical exercise history, the expected term of our stock options is determined using the “simplified” method. The risk-free interest rate is determined by reference to the U.S. Treasury yield curve in effect at the time of grant of the award for time periods approximately equal to the expected term of the award. Expected dividend yield is zero based on the fact that we have never paid cash dividends and do not expect to pay any cash dividends in the foreseeable future.

Prior to September 23, 2020, the fair value of common stock underlying our stock options, RSAs and RSUs was estimated by our board of directors considering, among other things, contemporaneous valuations of our common stock prepared by unrelated third-party valuation firms. After the IPO, the fair value of common stock is based on the closing price of our common stock on the Nasdaq Global Select Market as reported on the date of the grant.

The RSAs and RSUs are valued based on the fair value of our common stock on the date of grant. We expense stock-based compensation related to stock options, RSAs and RSUs, which contain service-based vesting conditions, over the requisite service period using the straight-line method. For awards with both performance and service conditions, we recognize expense based on the fair value of the performance awards over the estimated service period using the accelerated attribution method to the extent the achievement of the related performance criteria is estimated to be probable. At each reporting date, we evaluate whether any performance conditions related to a performance-based award have changed. The effect of any change in performance conditions is recognized as a cumulative catch-up adjustment in the period such change occurs. Stock-based compensation costs are generally recorded in research and development expense or general and administrative expense in the consolidated statements of operations based upon the respective employee’s roles within our Company. Forfeitures are recorded as they occur.

Astellas Transactions

In October 2022, we entered into the Securities Purchase Agreement with Astellas, pursuant to which we agreed to issue and sell to Astellas an aggregate of 7,266,342 shares of our common stock, for aggregate proceeds of \$30.0 million. Upon closing of the Private Placement and transferring 7,266,342 shares to Astellas, we recorded the issuance of shares at fair value. Fair value of the shares transferred to Astellas was calculated in accordance with ASC 820, Fair Value Measurement by analyzing our stock price for a period of time prior to and after the transaction date as traded on the NASDAQ. The NASDAQ trading data is considered an active market and a Level 1 measurement under ASC 820. The fair value was determined to be \$13.95 million or \$1.92 per share. The \$16.1

million difference between the \$30.0 million paid by Astellas and the fair market value of shares issued was allocated to the transaction price of the Option Agreement.

We determined that the Option Agreement falls within the scope of ASC 606, *Revenue from Contracts with Customers* as the development of TSHA-102 for the treatment of Rett Syndrome and TSHA-120 for the treatment of GAN are considered ordinary activities for us. In accordance with ASC 606, we evaluated the Option Agreement and identified three separate performance obligations: (1) option to obtain licensing right to GAN, (2) option to obtain licensing right to Rett and (3) performance of research and development activities associated with our Rett program. The transaction price is determined to be \$36.1 million which is comprised of the \$20.0 million Upfront Payment and the \$16.1 million allocated from the Private Placement.

To determine the standalone selling price, or the SSP, of the Rett and GAN options which we concluded represent material rights, we utilized the probability-weighted expected return, or PWERM, method. The PWERM method contemplates the probability and timing of an option exercise. At contract inception, we used significant judgment to estimate the probability of exercise of each option at 50%. The SSP of the Rett research and development activities was estimated using an expected cost-plus margin approach. The standalone selling prices of the material rights and Rett research and development activities were then used to proportionately allocate the \$36.1 million transaction price to the three performance obligations.

Revenue allocated to the material rights will be recognized at a point in time when each option period expires or when a decision is made by Astellas to exercise or not exercise each option. Revenue from the Rett research and development activities will be recognized as activities are performed using an input method, according to the costs incurred as related to the total costs expected to be incurred to satisfy the performance obligation. The transfer of control occurs over this time period and is a reliable measure of progress towards satisfying the performance obligation. During the year ended December 31, 2024, we determined that the total estimated costs to be incurred to satisfy the performance obligation associated with the Rett research and development activities had increased from the cost estimate used for the year ended December 31, 2023.

Fair Value Option

On November 13, 2023 we entered into the Trinity Term Loan Agreement with the Trinity Lenders. The Trinity Term Loan Agreement provides for, on the Trinity Closing Date, \$40.0 million aggregate principal amount of Trinity Term Loans. We drew the Trinity Term Loans in full on the Trinity Closing Date.

We determined that we are eligible to elect the fair value option under ASC 825, *Financial Instruments*. The Trinity Term Loans contains various embedded features and the election of the fair value option allows us to bypass analysis of potential embedded derivatives and further analysis of bifurcation of any recognized financial liabilities. Under the fair value option, the financial liability is initially measured at its fair value on the issue date and subsequently remeasured at estimated fair value on a recurring basis at each reporting date. Changes in the fair value of the Trinity Term Loans, which include accrued interest, if any, are recorded as a component of other expense (income) in the consolidated statements of operations and comprehensive loss. We have not elected to present interest expense separately from changes in fair value and therefore will not present interest expense associated with the Trinity Term Loans. Any changes in fair value caused by instrument-specific credit risk are presented separately in other comprehensive income or loss if material. Under the fair value option, debt issuance costs are expensed as incurred.

In connection with the Trinity Term Loans, we entered into a Success Fee Agreement with Trinity which specifies the terms regarding a fee in the amount of 10% of the principal amount of the funded Trinity Term Loans. The Success Fee is payable upon the achievement of certain corporate development value-inflection milestones. The Success Fee survives the termination of the Trinity Term Loans and expires on the earlier of ten years, or payment in full in cash of the Success Fee. We determined that the Success Fee represents a freestanding financial instrument and should be accounted for as a derivative liability under ASC 815 and recorded a liability within other non-current liabilities on the consolidated balance sheet, at fair value on the Trinity Closing Date and will be marked-to-market at the end of each reporting period with gains and losses recognized as a component of other income (expense) in the consolidated statements of operations. The proceeds from the Trinity Term Loans were allocated to the Success Fee and Trinity Term Loans based on their respective fair values on the Trinity Closing Date. The fair values were determined utilizing a probability-weighted income approach, including variables for the timing of a success event and other probability estimates. The fair value of the Trinity Term Loans is determined to be \$39.2 million and the fair value of the Success Fee liability is determined to be \$0.8 million in the consolidated balance sheet at issuance. We calculated the discounted cash flows of the Success Fee liability, then adjusted for the probability of achievement of certain corporate development value-inflection milestones.

Recent Accounting Pronouncements

See Note 2 to our audited consolidated financial statements located in Part IV, Item 15 of this Annual Report on Form 10-K for a description of recent accounting pronouncements applicable to our financial statements.

Emerging Growth Company and Smaller Reporting Company Status

In April 2012, the JOBS Act was enacted. Section 107 of the JOBS Act provides that an “emerging growth company” can take advantage of the extended transition period provided in Section 7(a)(2)(B) of the Securities Act of 1933, as amended, for complying with new or revised accounting standards. Thus, an emerging growth company can delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We elected the extended transition period for complying with new or revised accounting standards, which delays the adoption of these accounting standards until they would apply to private companies. In addition, as an emerging growth company, we may take advantage of specified reduced disclosure and other requirements that are otherwise applicable generally to public companies. These provisions include:

- an exception from compliance with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002, as amended;
- reduced disclosure about our executive compensation arrangements in our periodic reports, proxy statements and registration statements;
- exemptions from the requirements of holding non-binding advisory votes on executive compensation or golden parachute arrangements; and
- an exemption from compliance with the requirements of the Public Company Accounting Oversight Board regarding the communication of critical audit matters in the auditor’s report on financial statements. We expect that our eligibility to qualify as an “emerging growth company” will end on December 31, 2025, the last day of our fiscal year following the fifth anniversary of the date of our initial public offering. We may choose to take advantage of some but not all of these reduced reporting burdens. We have taken advantage of certain reduced reporting requirements in this Annual Report on Form 10-K and our other filings with the SEC. Accordingly, the information contained herein may be different than you might obtain from other public companies in which you hold equity interests.

We are also a “smaller reporting company,” meaning that the market value of our shares held by non-affiliates is less than \$700 million and our annual revenue was less than \$100 million during the most recently completed fiscal year. We may continue to be a smaller reporting company if either (i) the market value of our shares held by non-affiliates is less than \$250 million or (ii) our annual revenue was less than \$100 million during the most recently completed fiscal year and the market value of our shares held by non-affiliates is less than \$700 million. If we are a smaller reporting company at the time we cease to be an emerging growth company, we may continue to rely on exemptions from certain disclosure requirements that are available to smaller reporting companies. Specifically, as a smaller reporting company, we may choose to present only the two most recent fiscal years of audited financial statements in our Annual Report on Form 10-K and, similar to emerging growth companies, smaller reporting companies have reduced disclosure obligations regarding executive compensation.

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

We are a smaller reporting company as defined by Rule 12b-2 of the Exchange Act and are not required to provide the information required under this item.

Item 8. Financial Statements and Supplementary Data.

Report of Independent Registered Public Accounting Firm

To the Stockholders and the Board of Directors of Taysha Gene Therapies, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Taysha Gene Therapies, Inc. and subsidiaries (the "Company") as of December 31, 2024 and 2023, the related consolidated statements of operations, comprehensive loss, stockholders' equity, and cash flows, for the years then ended, and the related notes (collectively referred to as 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, 2024 and 2023, and the results of its operations and its cash flows for the years then ended, in conformity with accounting principles generally accepted in the United States of America.

Basis for Opinion

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's 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/ Deloitte & Touche LLP

Dallas, Texas
February 26, 2025

We have served as the Company's auditor since 2020.

Taysha Gene Therapies, Inc.
Consolidated Balance Sheets
(in thousands, except share and per share data)

	December 31, 2024	December 31, 2023
ASSETS		
Current assets:		
Cash and cash equivalents	\$ 139,036	\$ 143,940
Restricted cash	449	449
Prepaid expenses and other current assets	2,645	3,479
Assets held for sale	—	2,000
Total current assets	142,130	149,868
Restricted cash	2,151	2,151
Property, plant and equipment, net	7,485	10,826
Operating lease right-of-use assets	8,381	9,582
Other non-current assets	217	304
Total assets	\$ 160,364	\$ 172,731
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	\$ 3,592	\$ 6,366
Accrued expenses and other current liabilities	12,862	12,284
Deferred revenue	9,773	18,106
Total current liabilities	26,227	36,756
Term loan, net	43,942	40,508
Operating lease liability, net of current portion	17,361	18,953
Other non-current liabilities	1,309	1,577
Total liabilities	88,839	97,794
Commitments and contingencies - Note 13		
Stockholders' equity		
Preferred stock, \$0.00001 par value per share; 10,000,000 shares authorized and no shares issued and outstanding as of December 31, 2024 and December 31, 2023	—	—
Common stock, \$0.00001 par value per share; 400,000,000 shares authorized and 204,943,306 and 186,960,193 issued and outstanding as of December 31, 2024 and December 31 2023, respectively	2	2
Additional paid-in capital	677,859	587,942
Accumulated other comprehensive loss	(4,031)	—
Accumulated deficit	(602,305)	(513,007)
Total stockholders' equity	71,525	74,937
Total liabilities and stockholders' equity	\$ 160,364	\$ 172,731

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

Taysha Gene Therapies, Inc.
Consolidated Statements of Operations
(in thousands, except share and per share data)

	For the Year Ended December 31,	
	2024	2023
Revenue	\$ 8,333	\$ 15,451
Operating expenses:		
Research and development	66,001	56,778
General and administrative	28,953	30,047
Impairment of long-lived assets	4,838	1,065
Total operating expenses	99,792	87,890
Loss from operations	(91,459)	(72,439)
Other income (expense):		
Change in fair value of warrant liability	16	(34,718)
Change in fair value of term loan	(4,583)	(1,538)
Loss on debt extinguishment	—	(1,398)
Interest income	6,940	3,572
Interest expense	(102)	(4,998)
Other expense	(110)	(47)
Total other income (expense), net	2,161	(39,127)
Net loss	\$ (89,298)	\$ (111,566)
Net loss per common share, basic and diluted	\$ (0.36)	\$ (0.96)
Weighted average common shares outstanding, basic and diluted	250,134,421	116,121,482

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

Taysha Gene Therapies, Inc.
Consolidated Statements of Comprehensive Loss
(in thousands, except share and per share data)

	<u>For the Year Ended December 31,</u>	
	<u>2024</u>	<u>2023</u>
Net loss	\$ (89,298)	\$ (111,566)
Other comprehensive loss:		
Change in fair value of term loan attributable to instrument specific credit risk	(4,031)	—
Comprehensive loss	<u>\$ (93,329)</u>	<u>\$ (111,566)</u>

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

Taysha Gene Therapies, Inc.
Consolidated Statements of Stockholders' Equity
(in thousands, except share data)

	Common Stock		Additional	Accumulated	Accumulated Other Comprehensive Loss	Total Stockholders' Equity
	Shares	Amount	Paid-in Capital			
Balance as of December 31, 2022	63,207,507	\$ 1	\$ 402,389	\$ (401,441)	\$ —	\$ 949
Stock-based compensation	—	—	7,905	—	—	7,905
Issuance of common stock in private placement, net of placement agent commission and offering costs of \$7,138	123,117,594	1	103,238	—	—	103,239
Issuance of common stock upon vesting and settlement of restricted stock units	566,772	—	—	—	—	—
Issuance of common stock under ESPP	68,320	—	68	—	—	68
Reclassification of pre-funded warrants to equity classification	—	—	74,342	—	—	74,342
Net loss	—	—	—	(111,566)	—	(111,566)
Balance as of December 31, 2023	186,960,193	\$ 2	\$ 587,942	\$ (513,007)	\$ —	\$ 74,937
Stock-based compensation	—	—	13,103	—	—	13,103
Issuance of common stock and pre-funded warrants upon closing of underwritten public offering, net of underwriting discounts and commissions, and other offering costs of \$5,566	17,596,113	—	76,694	—	—	76,694
Issuance of common stock upon vesting and settlement of restricted stock units	234,198	—	(9)	—	—	(9)
Issuance of common stock under ESPP	93,970	—	89	—	—	89
Issuance of common stock upon exercise of stock options	58,832	—	40	—	—	40
Loss on instrument-specific credit risk	—	—	—	—	(4,031)	(4,031)
Net loss	—	—	—	(89,298)	—	(89,298)
Balance as of December 31, 2024	204,943,306	\$ 2	\$ 677,859	\$ (602,305)	\$ (4,031)	\$ 71,525

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

Taysha Gene Therapies, Inc.
Consolidated Statements of Cash Flows
(in thousands)

	For the Year Ended December 31,	
	2024	2023
Cash flows from operating activities		
Net loss	\$ (89,298)	\$ (111,566)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation expense	1,245	1,371
Stock-based compensation	13,103	7,905
Research and development license expense	—	3,500
Change in fair value of warrant liability	(16)	34,718
Issuance costs for pre-funded warrant liability	—	2,567
Non-cash loss on debt extinguishment	—	1,366
Non-cash change in fair value of term loan	(597)	1,278
Impairment of long-lived assets	4,838	1,065
Debt issuance costs expensed under the fair value option	—	867
Non-cash lease expense	1,217	1,182
Other	750	741
Changes in operating assets and liabilities:		
Prepaid expenses and other assets	207	6,011
Accounts payable	(2,920)	(2,295)
Accrued expenses and other liabilities	(1,421)	(6,277)
Deferred revenue	(8,333)	(15,451)
Net cash used in operating activities	(81,225)	(73,018)
Cash flows from investing activities		
Purchase of research and development license	—	(3,500)
Purchase of property, plant and equipment	(374)	(3,869)
Other	11	17
Net cash used in investing activities	(363)	(7,352)
Cash flows from financing activities		
Proceeds from issuance of common stock and pre-funded warrants from underwritten public offering, net of underwriting discounts and sales commissions and other offering costs	76,780	—
Debt issuance costs for term loan	(18)	(399)
Repayment of SVB Term Loan	—	(43,000)
Proceeds from Trinity term loan, net	—	39,550
Proceeds from issuance of common stock and pre-funded warrants from private placement, net of placement agent commissions and other offering costs	—	140,290
Proceeds from issuance of common stock from private placement	—	500
Payment of shelf registration costs	—	(387)
Proceeds from common stock issuances under ESPP	89	68
Other	(167)	(229)
Net cash provided by financing activities	76,684	136,393
Net (decrease) increase in cash, cash equivalents and restricted cash	(4,904)	56,023
Cash, cash equivalents and restricted cash at the beginning of the period	146,540	90,517
Cash, cash equivalents and restricted cash at the end of the period	\$ 141,636	\$ 146,540
Cash and cash equivalents	139,036	143,940
Restricted cash	2,600	2,600
Cash, cash equivalents and restricted cash at the end of the period	\$ 141,636	\$ 146,540
Supplemental disclosure of cash flow information:		
Cash paid for interest	\$ 5,282	\$ 4,952
Supplemental disclosure of noncash investing and financing activities:		
Reclassification of warrants to additional paid-in capital	—	74,342
Allocation of proceeds to Success Fee liability	—	770
Recognition of asset retirement obligation	—	449
Issuance of warrants in connection with private placement	—	252
Property, plant and equipment in accounts payable and accrued expenses	346	—
Offering costs not yet paid	46	18

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

Taysha Gene Therapies, Inc.
Notes to Consolidated Financial Statements

Note 1—Organization and Description of Business Operations

Taysha Gene Therapies, Inc. (the “Company” or “Taysha”) was originally formed under the laws of the State of Texas on September 20, 2019. Taysha converted to a Delaware corporation on February 13, 2020, which had no impact to the Company’s par value or issued and authorized capital structure.

Taysha is a clinical-stage biotechnology company focused on advancing AAV-based gene therapies for severe monogenic diseases of the central nervous system.

Sales Agreement

On October 5, 2021, the Company entered into a Sales Agreement (the “Sales Agreement”) with SVB Securities LLC (f/k/a SVB Leerink LLC) and Wells Fargo Securities, LLC (collectively, the “Sales Agents”), pursuant to which the Company may issue and sell, from time to time in its sole discretion, shares of its common stock having an aggregate offering price of up to \$150.0 million through the Sales Agents. In March 2022, the Company amended the Sales Agreement to, among other things, include Goldman Sachs & Co. LLC as an additional Sales Agent. The Sales Agents may sell common stock by any method permitted by law deemed to be an “at-the-market offering” as defined in Rule 415(a)(4) of the Securities Act, including sales made directly on or through the Nasdaq Global Select Market or any other existing trade market for the common stock, in negotiated transactions at market prices prevailing at the time of sale or at prices related to prevailing market prices, or any other method permitted by law. The Sales Agents are entitled to receive 3.0% of the gross sales price per share of common stock sold under the Sales Agreement. In April 2022, the Company sold 2,000,000 shares of common stock under the Sales Agreement and received \$11.6 million in net proceeds. On December 13, 2024, the Company filed a new shelf registration statement on Form S-3 following the expiration of its prior registration statement, in relation to the registration of common stock, preferred stock, debt securities, warrants and units or any combination thereof up to a total aggregate offering price of \$300.0 million, including up to \$100.0 million shares of common stock that may be offered and sold pursuant to the Sales Agreement. No other shares of common stock have been issued and sold pursuant to the Sales Agreement as of December 31, 2024.

Liquidity and Capital Resources

The Company has incurred operating losses since inception and expects to continue to incur significant operating losses for the foreseeable future and may never become profitable. Losses are expected to continue as the Company continues to invest in its research and development activities. As of December 31, 2024, the Company had an accumulated deficit of \$602.3 million. The Company expects to continue to incur significant expenses and operating losses for the foreseeable future.

On June 26, 2024, the Company entered into an underwriting agreement (the “June 2024 Underwriting Agreement”) with Jefferies LLC and Goldman Sachs & Co. LLC, as representatives of the several underwriters set forth therein (collectively, the “Underwriters”), to issue and sell 14,361,113 shares of the Company’s common stock and, in lieu of common stock to certain investors, pre-funded warrants to purchase 18,972,221 shares of its common stock in an underwritten public offering (the “June 2024 Offering”), pursuant to an effective shelf registration statement on Form S-3 and a related prospectus and prospectus supplement. The offering price to the public was \$2.25 per share of common stock and \$2.249 per pre-funded warrant, which was the price to the public of each share of common stock sold in the June 2024 Offering minus the \$0.001 exercise price per pre-funded warrant. The Underwriters purchased the shares and the pre-funded warrants from the Company pursuant to the June 2024 Underwriting Agreement at a price of \$2.115 per share and \$2.114 per pre-funded warrant, respectively. See Note 10 for additional information. The initial closing of the June 2024 Offering occurred on June 27, 2024. In addition, the Company granted the Underwriters an option to purchase, for a period of 30 days, up to an additional 5,000,000 shares of common stock. On July 9, 2024, the Underwriters exercised their option to purchase an additional 3,235,000 shares of common stock. The total net proceeds from the June 2024 Offering were approximately \$76.7 million, including the proceeds from the Underwriter’s option, after deducting underwriting discounts and commissions and offering expenses.

Future capital requirements will depend on many factors, including the timing and extent of spending on research and development and the market acceptance of the Company’s products. The Company will need to obtain additional financing in order to complete clinical studies and launch and commercialize any product candidates for which it receives regulatory approval. There can be no assurance that such financing will be available or will be on terms acceptable to the Company. As of December 31, 2024, the Company had cash and cash equivalents of \$139.0 million which the Company believes will be sufficient to fund its planned operations for a period of at least twelve months from the date of issuance of these consolidated financial statements. The Company has based this estimate on assumptions that may prove to be wrong, and its operating plan may change as a result of many factors currently unknown to it. As a result, the Company could deplete its capital resources sooner than it currently expects. The Company expects to finance its future cash needs through a combination of equity offerings, debt financings, collaborations, strategic alliances or licensing arrangements. If the Company is unable to obtain funding, the Company would be forced to delay, reduce or eliminate some or all of its research and development programs, preclinical and clinical testing or commercialization efforts, which could adversely affect its business prospects.

Note 2—Significant Accounting Policies

Basis of Presentation

The Company's financial statements have been prepared in conformity with accounting principles generally accepted in the United States of America ("U.S. GAAP") as determined by the Financial Accounting Standards Board ("FASB") Accounting Standards Codification ("ASC") and include all adjustments necessary for the fair presentation of the Company's financial position for the periods presented.

Principles of Consolidation

The accompanying consolidated financial statements include the accounts of Taysha and its wholly owned subsidiaries. All intercompany transactions and balances have been eliminated in consolidation.

Emerging Growth Company

From time to time, new accounting pronouncements are issued by the FASB, or other standard setting bodies and adopted by the Company as of the specified effective date. Unless otherwise discussed, the impact of recently issued standards that are not yet effective will not have a material impact on the Company's financial statements upon adoption. Under the Jumpstart Our Business Startups Act of 2012, as amended, the Company meets the definition of an emerging growth company and has elected the extended transition period for complying with new or revised accounting standards, which delays the adoption of these accounting standards until they would apply to private companies.

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 expenses during the reporting period. The most significant estimates and assumptions in the Company's financial statements relate to the determination of the fair value of the common stock prior to the IPO (as an input into stock-based compensation), estimating manufacturing accruals and accrued or prepaid research and development expenses, the measurement of impairment of long-lived assets, the valuation of the Trinity Term Loans that are carried at fair value, and the allocation of consideration received in connection with the Astellas Transactions. These estimates and assumptions are based on current facts, historical experience and various other factors believed to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities and the recording of expenses that are not readily apparent from other sources. Actual results may differ materially from these estimates. To the extent there are material differences between the estimates and actual results, the Company's future results of operations will be affected.

Risks and Uncertainties

The Company is subject to risks common to companies in the biotechnology industry, including, but not limited to, development by the Company or its competitors of technological innovations, risks of failure of clinical studies, dependence on key personnel, protection of proprietary technology, compliance with government regulations, and ability to transition from preclinical manufacturing to commercial production of products.

The Company's product candidates require approvals from the FDA and comparable foreign regulatory agencies prior to commercial sales in their respective jurisdictions. There can be no assurance that any product candidates will receive the necessary approvals. If the Company was denied approval, approval was delayed or the Company was unable to maintain approval for any product candidate, it could have a materially adverse impact on the Company.

Segments

Operating segments are identified as components of an enterprise about which separate discrete financial information is available for evaluation by the chief operating decision-maker in making decisions regarding resource allocation and assessing performance. The Company views its operations and manages its business as a single operating segment, the gene therapy segment, which is the business of developing AAV-based gene therapies for the treatment of rare monogenic diseases of the central nervous system. See Note 16 for additional information.

As of December 31, 2024 and 2023, the Company did not have any significant long-lived assets located outside of the United States.

Revenue Recognition

The Company recognizes revenue in accordance with ASC 606, *Revenue from Contracts with Customers*, (“ASC 606”). Revenues consist of activities in connection with the Astellas Transactions, including the exclusive option to license intellectual property and the performance of research and development activities. See Note 7 for additional information.

The Company evaluates the agreement to determine if the other party is a customer, and then determines the units of account within the agreement to determine which promised goods or services are distinct. In order for a promised good or service to be considered “distinct” under ASC 606, the customer can benefit from the good or service either on its own or together with other resources that are readily available to the customer (i.e., the good or service is capable of being distinct), and the entity’s promise to transfer the good or service to the customer is separately identifiable from other promises in the contract (i.e., the promise to transfer the good or service is distinct within the context of the contract).

For any units of account that fall within the scope of ASC 606, where the other party is a customer, the Company (i) evaluates the separate performance obligation(s) under each contract, (ii) determines the transaction price, (iii) allocates the transaction price to each performance obligation considering the estimated standalone selling prices of the services and (iv) recognizes revenue when, or as, the Company satisfies the performance obligation(s).

At the inception of an arrangement that includes options for a customer to purchase additional services or products at agreed upon prices in the future, the Company evaluates whether each option provides a material right. An option that provides a material right will be accounted for as a separate performance obligation.

As part of the accounting for arrangements under ASC 606, the Company must use significant judgment to determine the performance obligations, the transaction price, and the standalone selling price (“SSP”) for each performance obligation identified in the contract for the allocation of the transaction price. The SSP is the price at which an entity would sell a promised good or service separately to a customer. Management estimates the SSP of each of the identified performance obligations, maximizing the use of observable inputs. Because the Company has not sold the same goods or services in its contracts separately to any customers on a standalone basis, the Company utilizes similar observable transactions in the marketplace or estimates the SSP of each performance obligation in its customer arrangements at contract inception based on either (1) its estimate of costs to be incurred to fulfill its obligations associated with the performance obligation, plus a reasonable margin, or (2) an estimate that reflects the discount that the customer would obtain when exercising its option adjusted for (i) any discount that the customer could receive without exercising the option and (ii) the likelihood that the option will be exercised. The Company allocates the transaction price to each performance obligation in proportion to its SSP.

A performance obligation is satisfied and revenue is recognized when “control” of the promised good or service is transferred, either over time or at a point in time, to the customer. A customer obtains control of a good or service if it has the ability to (1) direct its use and (2) obtain substantially all of the remaining benefits from it.

Amounts received prior to satisfying the revenue recognition criteria listed above are recorded as deferred revenue in the accompanying consolidated balance sheets. Amounts expected to be recognized as revenue within 12 months of the balance sheet date are classified as current deferred revenue, including the amounts allocated to material rights which are subject to customer exercise at any point. Amounts not expected to be recognized as revenue within the following 12 months of the balance sheet date are classified as deferred revenue, net of current portion. The Company does not incur commission or other costs to fulfill customer contracts and as such, no capitalized contract costs are recorded on the consolidated balance sheets.

Cash and Cash Equivalents

Cash and cash equivalents consist of funds held in a standard checking account, a standard savings account and a money market fund. The Company considers all highly liquid investments with an original maturity of three months or less at the date of purchase to be cash equivalents. As of December 31, 2024, the Company had \$138.3 million in cash equivalents. As of December 31, 2023, the Company had \$142.4 million in cash equivalents.

Restricted Cash

Restricted cash consists of cash that the Company has placed in an escrow account which is pledged as collateral under certain lease agreements and letters of credit.

Concentrations of Credit Risk

Financial instruments that potentially subject the Company to significant concentration of credit risk consist primarily of cash and cash equivalents. Periodically, the Company may maintain deposits in financial institutions in excess of government insured limits. On March 10, 2023, the California Department of Financial Protection and Innovation closed the Silicon Valley Bank, Santa Clara, California (“SVB”), and appointed the FDIC as receiver. On March 12, 2023, the Treasury Department announced that depositors of SVB will have

access to all of their money starting March 13, 2023. On March 14, 2023, the Company regained access to the full amount of its cash that was deposited with SVB. Management believes that the Company is not exposed to significant credit risk as the Company's deposits are held at financial institutions that management continues to believe to be of high credit quality. The Company has not experienced any losses on these deposits.

Fair Value of Financial Instruments

The Company's financial assets and liabilities are accounted for in accordance with ASC 820, *Fair Value Measurements* which defines fair value as the exchange price that would be received for an asset or paid to transfer a liability (an exit price) in the principal or most advantageous market for the asset or liability in an orderly transaction between market participants on the measurement date. The fair value hierarchy requires an entity to maximize the use of observable inputs when measuring fair value and classifies those inputs into three levels:

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

Level 2—Inputs other than Level 1 inputs that are either directly or indirectly observable, such as quoted 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 instrument's anticipated life.

Level 3—Unobservable inputs in which there is little or no market data, which require the reporting entity to develop its own assumptions.

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

The carrying values reported in the Company's consolidated balance sheets for cash and cash equivalents, prepaid expenses and other current assets, accounts payable, accrued expenses and other current liabilities are reasonable estimates of their fair values due to the short-term nature of these items.

Fair Value Option

The fair value option provides an election that allows a company to irrevocably elect to record certain financial assets and liabilities at fair value on an instrument-by-instrument basis at initial recognition. The Company has elected to apply the fair value option to the Trinity Term Loans.

The term loans accounted for under the fair value option election are each a debt host financial instrument containing embedded features that would otherwise be required to be bifurcated from the debt-host and recognized as separate derivative liabilities subject to initial and subsequent periodic estimated fair value measurements in accordance with GAAP. Notwithstanding, when the fair value option election is applied to financial liabilities, bifurcation of an embedded derivative is not required, and the financial liability is initially measured at its issue-date estimated fair value and then subsequently remeasured at estimated fair value on a recurring basis as of each reporting period date.

The portion of the change in fair value attributed to a change in the instrument-specific credit risk is recognized as a component of other comprehensive income or loss if material and the remaining amount of the fair value adjustment is recognized as a component of other income (expense) in the consolidated statements of operations.

Deferred Offering Costs

The Company capitalizes costs directly associated with equity financings until such financings are consummated, at which time such costs are recorded in additional paid-in capital against the gross proceeds of the equity financings. Costs associated with the shelf registration statement on Form S-3, filed with the SEC on October 5, 2021 were capitalized and reclassified to additional paid-in capital on a pro rata basis when the Company completed offerings under the shelf registration. At the end of the three-year term of the shelf registration, the remaining deferred offering costs were charged to operations. Costs associated with the shelf registration statement on Form S-3, filed with the SEC on December 13, 2024 were capitalized and will be reclassified to additional paid-in capital on a pro rata basis when the Company completes offerings under the shelf registration. At the end of the three-year term of the shelf registration, the remaining deferred offering costs, if any, will be charged to operations

Property, Plant and Equipment, net

Property, plant and equipment, net are stated at cost less accumulated depreciation and consist of computer equipment, laboratory equipment and leasehold improvements. Depreciation expense is recognized using the straight-line method over its estimated useful life of three to seven years.

Upon retirement or sale, the cost of assets disposed of and the related accumulated depreciation are removed from the accounts and any resulting gain or loss is included in loss from operations. Expenditures for repairs and maintenance are charged to expense as incurred.

Leases

Effective January 1, 2022, the Company adopted ASC 842, *Leases* using the modified retrospective approach and utilizing the effective dates as its date of initial application.

At the inception of an arrangement, the Company determines whether the arrangement is or contains a lease based on the unique facts and circumstances present in the arrangement. Leases with a term greater than one year are recognized on the balance sheet as right-of-use assets and short-term and long-term lease liabilities, as applicable.

Operating lease liabilities and their corresponding right-of-use assets are initially recorded based on the present value of lease payments over the expected remaining lease term. Certain adjustments to the right-of-use asset may be required for items such as incentives received. The interest rate implicit in lease contracts is typically not readily determinable. As a result, the Company utilizes its incremental borrowing rate to discount lease payments, which reflects the fixed rate at which the Company could borrow on a collateralized basis the amount of the lease payments in the same currency, for a similar term, in a similar economic environment. To estimate its incremental borrowing rate, a credit rating applicable to the Company is estimated using a synthetic credit rating analysis since the Company does not currently have a rating agency-based credit rating.

The Company has elected not to recognize leases with an original term of one year or less on the balance sheet. The Company typically only includes an initial lease term in its assessment of a lease arrangement. Options to renew a lease are not included in the Company's assessment unless there is reasonable certainty that the Company will renew. Assumptions made by the Company at the commencement date are re-evaluated upon occurrence of certain events, including a lease modification. A lease modification results in a separate contract when the modification grants the lessee an additional right of use not included in the original lease and when lease payments increase commensurate with the standalone price for the additional right of use. When a lease modification results in a separate contract, it is accounted for in the same manner as a new lease.

The Company has elected to account for lease and non-lease components together as a single lease component for all underlying assets.

Assets Held for Sale

Assets and liabilities are classified as held for sale when all of the following criteria for a plan of sale have been met: (1) management, having the authority to approve the action, commits to a plan to sell the assets; (2) the assets are available for immediate sale, in their present condition, subject only to terms that are usual and customary for sales of such assets; (3) an active program to locate a buyer and other actions required to complete the plan to sell the assets have been initiated; (4) the sale of the assets is probable and is expected to be completed within one year; (5) the assets are being actively marketed for a price that is reasonable in relation to their current fair value; and (6) actions required to complete the plan indicate that it is unlikely that significant changes to the plan will be made or the plan will be withdrawn. When all of these criteria have been met, the assets and liabilities are classified as held for sale in the balance sheet. Assets classified as held for sale are reported at the lower of their carrying value or fair value less costs to sell. The Company recorded a partial impairment of \$0.6 million during the year ended December 31, 2023 in connection with the classification of certain assets to assets held for sale. Depreciation and amortization of assets ceases upon designation as held for sale.

Impairment of Long-Lived Assets

The Company evaluates its long-lived assets, which consist of property, plant and equipment as well as right-of-use assets, for impairment whenever events or changes in circumstances indicate that the carrying amount of such assets may not be recoverable. Recoverability of assets to be held and used is measured by a comparison of the carrying amount of an asset to the future undiscounted net cash flows expected to be generated by the asset. If such assets are considered to be impaired, the impairment to be recognized is measured by the amount by which the carrying amount of the asset group exceeds the fair value of the asset group. In November 2022, the Company decided not to continue the build-out of the North Carolina manufacturing facility, resulting in a change in use of this asset group. The Company performed an undiscounted cash flow analysis over the long-lived assets associated with the manufacturing facility and determined that the carrying value of the asset group is not recoverable. Significant assumptions used to determine this non-recurring fair value measurement include the time to sublease the facility, the amount of sublease income expected to be generated over the remaining lease term, and the discount rate used to measure the present value of the net cash flows associated with this asset group. During the year

ended December 31, 2022, the Company recorded a non-cash impairment charge of \$36.4 million in connection with the North Carolina manufacturing facility which was allocated on a pro rata basis across the assets within the asset group. The impairment charge was estimated using a discounted cash flow model. During the years ended December 31, 2024 and 2023, the Company recorded additional impairment charges of \$4.8 million and \$0.5 million related to the North Carolina manufacturing facility and equipment. See Note 4 for additional information.

Debt Issuance Costs

Debt issuance costs associated with the Term Loan Agreement (as defined in Note 6) are deferred and presented as a reduction to long-term debt. Debt issuance costs are amortized using the effective interest rate method over the term of the loan. Amortization of deferred debt issuance costs are included in interest expense in the consolidated statements of operations.

Debt issuance costs related to the Trinity Term Loans are expensed as incurred due to the election of the fair value option.

Research and Development

The Company has entered into research and development contracts with research institutions and other companies. These agreements are generally cancelable, and related payments are recorded as research and development expenses as incurred. Payments for these activities are based on the terms of the individual agreements, which may differ from the pattern of costs incurred, and are reflected on the consolidated balance sheets as prepaid or accrued expenses. The Company records accruals for estimated ongoing research costs. When evaluating the adequacy of the accrued liabilities, the Company analyzes progress of the studies, including the phase or completion of events, invoices received and contracted costs.

Research and development costs primarily consist of payroll, stock-based compensation, certain manufacturing costs, laboratory costs and other supplies, and the cost to acquire third-party licenses. Costs incurred in obtaining technology licenses through asset acquisitions are charged to research and development expense if the licensed technology has not reached technological feasibility and has no alternative future use. Payments of such upfront license fees and subsequent development milestones are included as investing cash outflows in the consolidated statements of cash flows.

Stock-Based Compensation

The Company accounts for all stock-based payments to employees and non-employees, including grants of stock options, restricted stock awards (“RSAs”), and restricted stock units (“RSUs”), based on their respective grant date fair values. The Company estimates the fair value of stock option grants using the Black-Scholes option pricing model, which is affected principally by the estimated fair value of shares of the Company’s common stock and requires management to make a number of other assumptions, including the expected life of the option, the volatility of the underlying shares, the risk-free interest rate and expected dividends. Expected volatility is based on the historical share volatility of a set of comparable publicly traded companies over a period of time equal to the expected term of the options. Due to the lack of historical exercise history, the expected term of the Company’s stock options is determined using the “simplified” method. The risk-free interest rate is determined by reference to the U.S. Treasury yield curve in effect at the time of grant of the award for time periods approximately equal to the expected term of the award. Expected dividend yield is zero based on the fact that the Company has never paid cash dividends and does not expect to pay any cash dividends in the foreseeable future.

Prior to September 23, 2020, the fair value of common stock underlying the Company’s stock options, RSAs and RSUs was estimated by the Company’s board of directors considering, among other things, contemporaneous valuations of the Company’s common stock prepared by unrelated third-party valuation firms. After the IPO, the fair value of common stock is based on the closing price of the Company’s common stock as reported on the date of the grant.

The RSAs and RSUs are valued based on the fair value of the Company’s common stock on the date of grant. The Company expenses stock-based compensation related to stock options, RSAs and RSUs which contain only service-based vesting conditions over the requisite service period using the straight-line method. For awards with both performance and service conditions, the Company recognizes expense based on the fair value of the performance awards over the estimated service period using the accelerated attribution method to the extent the achievement of the related performance criteria is estimated to be probable. At each reporting date, the Company evaluates whether any performance conditions related to a performance-based award have changed. The effect of any change in performance conditions is recognized as a cumulative catch-up adjustment in the period such change occurs. Stock-based compensation costs are initially recorded in research and development expense or general and administrative expense in the consolidated statements of operations in a manner consistent with the classification of the respective employee’s payroll costs. Forfeitures are recorded as they occur.

Warrants

The Company accounts for warrants as either equity-classified or liability-classified instruments based on an assessment of the warrant’s specific terms and applicable authoritative guidance in FASB ASC 480, *Distinguishing Liabilities from Equity* (“ASC 480”) and ASC 815, *Derivatives and Hedging* (“ASC 815”). The assessment considers whether the warrants are freestanding financial instruments

pursuant to ASC 480, meet the definition of a liability pursuant to ASC 480, and whether the warrants meet all of the requirements for equity classification under ASC 815, including whether the warrants are indexed to the Company's own common shares and whether the warrant holders could potentially require "net cash settlement" in a circumstance outside of the Company's control, among other conditions for equity classification. This assessment, which requires the use of professional judgment, is conducted at the time of warrant issuance and as of each subsequent reporting period while the warrants are outstanding.

For issued or modified warrants that meet all of the criteria for equity classification, the warrants are required to be recorded as a component of additional paid-in capital at the time of issuance, or when the conditions for equity classification are met, and are not remeasured. For issued or modified warrants that do not meet all the criteria for equity classification, the warrants are required to be recorded at their initial fair value on the date of issuance, and each balance sheet date thereafter. Liability-classified warrants are recorded at their fair value, and the Company adjusts such warrants to fair value at each reporting period. This liability is subject to remeasurement at each balance sheet date until the warrants are exercised or expire, and any change in fair value is recognized in the Company's consolidated statements of operations.

Income Taxes

Income taxes are recorded in accordance with ASC 740, *Income Taxes* ("ASC 740"), which provides for deferred taxes using an asset and liability approach. The Company recognizes deferred tax assets and liabilities for the expected future tax consequences of events that have been included in the financial statements or tax returns. Deferred tax assets and liabilities are determined based on the difference between the financial statement and tax bases of assets and liabilities using enacted tax rates in effect for the year in which the differences are expected to reverse, and net operating loss ("NOL") carryforwards and research and development tax credit ("R&D Credit") carryforwards. Valuation allowances are provided if, based upon the weight of available evidence, it is more likely than not that some or all of the deferred tax assets will not be realized. The Company has recorded a full valuation allowance to reduce its net deferred income tax assets to zero. In the event the Company were to determine that it would be able to realize some or all of its deferred income tax assets in the future, an adjustment to the deferred income tax asset valuation allowance would increase income in the period such determination was made.

The Company accounts for uncertain tax positions in accordance with the provisions of ASC 740. When uncertain tax positions exist, the Company recognizes the tax benefit of tax positions to the extent that the benefit would more likely than not be realized assuming examination by the taxing authority. The determination as to whether the tax benefit will more likely than not be realized is based upon the technical merits of the tax position as well as consideration of the available facts and circumstances. During the year ended December 31, 2024 the Company recorded increases in the amount of gross unrecognized tax benefits of \$1.8 million. During the year ended December 31, 2023, the Company recorded decreases in the amount of unrecognized tax benefits of \$0.4 million. The Company also reduced its uncertain tax positions during 2023 by \$7.8 million related to prior year positions largely as a result of the Section 382 ownership shift analysis performed during 2023 (see Note 12). The unrecognized tax benefits, if recognized, would not affect the effective income tax rate due to the valuation allowance that currently offsets deferred tax assets. The Company does not expect the unrecognized tax benefits to change significantly over the next 12 months. The Company would recognize any corresponding interest and penalties associated with its income tax positions in income tax expense. There was no income tax interest or penalties incurred for the years ended December 31, 2024 and 2023.

Comprehensive Loss

Comprehensive income includes charges and credits to shareholders' equity that are not the result of transactions with shareholders. Our total comprehensive loss consists of net income and changes in fair value attributed to instrument-specific credit risk from the Trinity Term Loans (as defined below). The items of comprehensive loss, with the exception of net loss, are included in accumulated other comprehensive loss in the consolidated balance sheets and statements of shareholders' equity.

Recently Adopted Accounting Pronouncements

In November 2023, the FASB issued Accounting Standards Update ("ASU") No. 2023-07, *Segment Reporting - Improvements to Reportable Segment Disclosures*, to improve segment disclosure requirements under ASC 280, *Segment Reporting*, through enhancing disclosures about significant segment expenses. The guidance requires entities to provide significant segment expenses that are regularly provided to the CODM and other segment expenses included in each reported measure of segment profitability. The ASU also enhances interim segment reporting requirements by aligning interim disclosures with information that must be disclosed annually in accordance with ASC 280. The guidance is effective for annual periods beginning after December 15, 2023, and interim periods beginning after December 15, 2024, applied retrospectively with early adoption permitted. The adoption did not have a material impact on the consolidated financial statements. The Company has included additional disclosures as required by this ASU in Note 16.

Recently Issued Accounting Pronouncements

In November 2024, the FASB issued ASU No. 2024-03, *Income Statement - Reporting Comprehensive Income - Expense Disaggregation Disclosures*, to improve expense disclosure requirements under ASC 220, *Income Statement - Reporting Comprehensive*

Income, through enhancing disclosures about significant segment expenses. The guidance requires entities to provide additional disclosure about specific expenses by requiring entities to disaggregate, in a tabular presentation, each relevant expense caption on the face of the income statement that includes any of the following natural expenses (1) purchases of inventory, (2) employees compensation, (3) depreciation, (4) intangible asset amortization, and (5) depreciation, depletion and amortization recognized as part of oil - and gas - producing activities or other types of depletion expenses. The tabular disclosure would also include certain other expenses, when applicable. The ASU also enhances interim segment reporting requirements by aligning interim disclosures with information that must be disclosed annually in accordance with ASC 220. The guidance is effective for annual periods beginning after December 15, 2026, and interim periods beginning after December 15, 2027, applied either prospectively or retrospectively with early adoption permitted. The Company is still evaluating the impact this ASU will have on its disclosures.

Note 3—Fair Value Measurements

The Company's financial instruments that are measured at fair value on a recurring basis consist of money market funds, the Trinity Term Loans, a success fee derivative liability and certain of the Company's warrant liabilities.

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

	December 31, 2024			
	Total	Level 1	Level 2	Level 3
Assets:				
Cash equivalents – money market funds	\$ 138,308	\$ 138,308	\$ —	\$ —
Total assets	\$ 138,308	\$ 138,308	\$ —	\$ —
Liabilities:				
Trinity Term Loans	\$ 43,942	\$ —	\$ —	\$ 43,942
Success Fee Derivative liability	930	—	—	930
SSI Warrant liability	438	—	—	438
Total liabilities	\$ 45,310	\$ —	\$ —	\$ 45,310
	December 31, 2023			
	Total	Level 1	Level 2	Level 3
Assets:				
Cash equivalents – money market funds	\$ 142,425	\$ 142,425	\$ —	\$ —
Total assets	\$ 142,425	\$ 142,425	\$ —	\$ —
Liabilities:				
Trinity Term Loans	\$ 40,508	\$ —	\$ —	\$ 40,508
Success Fee Derivative liability	800	—	—	800
SSI Warrant liability	454	—	—	454
Total liabilities	\$ 41,762	\$ —	\$ —	\$ 41,762

The Company classifies its money market funds, which are valued based on quoted market prices in an active market with no valuation adjustment, as Level 1 assets within the fair value hierarchy.

The Company's Trinity Term Loans and Success Fee liability are classified as Level 3 measurements under the fair value hierarchy as the fair values were determined based on significant inputs not observable in the market. The fair values were determined utilizing a probability-weighted income approach, including variables for the timing of a success event and other probability estimates. See Note 6 for additional information on the Trinity Term Loans and Success Fee.

The Company's SSI Warrant liability is classified as Level 3 measurements under the fair value hierarchy as the fair values were determined based on significant inputs not observable in the market. The fair values were determined using the Black-Scholes-Merton option pricing model to determine the fair value of the SSI Warrants (as defined below). See Note 10 for additional information on the SSI Warrants.

Note 4—Supplemental Financial Information

Property, plant and equipment, net consisted of the following (in thousands):

	December 31, 2024	December 31, 2023
Leasehold improvements	\$ 2,117	\$ 2,117
Laboratory equipment	3,130	2,868
Computer equipment	707	1,133
Furniture and fixtures	864	864
Construction in progress	4,251	6,823
	<u>11,069</u>	<u>13,805</u>
Accumulated depreciation	(3,584)	(2,979)
Property, plant and equipment, net	<u>\$ 7,485</u>	<u>\$ 10,826</u>

Property, plant and equipment, net includes \$0.7 million and \$1.0 million of assets capitalized as finance leases as of December 31, 2024 and December 31, 2023, respectively.

Depreciation expense was \$1.2 million and \$1.4 million for the years ended December 31, 2024 and 2023, respectively.

During the year ended December 31, 2023, the Company committed to a plan to sell specific pieces of equipment originally intended for use in the Company's manufacturing facility in Durham, North Carolina. The Company determined that this equipment met the requirements to be classified as held for sale as the equipment sales were expected to be completed within one year. During the year ended December 31, 2023, the Company recorded an impairment loss of \$0.6 million which was the difference between the carrying value and fair value less cost to sell. In September 2024, while continuing efforts to sell these specific pieces of equipment, the Company evaluated its long-lived assets for impairment and determined that the carrying value of the North Carolina manufacturing facility asset group and the held for sale equipment may not be recoverable. The Company recorded an impairment loss of \$4.8 million. The impairment charge was estimated using a discounted cash flow model and recorded in the consolidated statements of operations for the year ended December 31, 2024.

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

	December 31, 2024	December 31, 2023
Accrued compensation	\$ 5,242	\$ 3,423
Accrued clinical trial	1,907	1,851
Lease liabilities, current portion	1,877	1,646
Accrued research and development	1,714	3,467
Accrued professional and consulting fees	725	330
Warrant liability	438	454
Accrued property, plant and equipment	207	—
Accrued severance	—	390
Other	752	723
Total accrued expenses and other current liabilities	<u>\$ 12,862</u>	<u>\$ 12,284</u>

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

	December 31, 2024	December 31, 2023
Prepaid clinical trial	\$ 1,112	\$ 802
Prepaid research and development	841	1,412
Prepaid insurance	249	292
Deferred offering costs	135	681
Other	308	292
Total prepaid expenses and other current assets	<u>\$ 2,645</u>	<u>\$ 3,479</u>

Note 5— Leases

The Company leases certain office, laboratory, and manufacturing space.

Dallas Lease

On January 11, 2021, the Company entered into a lease agreement (the “Dallas Lease”) with Pegasus Park, LLC, a Delaware limited liability company (the “Dallas Landlord”), pursuant to which the Company leases approximately 15,000 square feet of office space at 3000 Pegasus Park Drive, Dallas, Texas 75247 (the “Office Space”).

The Dallas Lease commenced on May 27, 2021, and has a term of approximately ten years. The Company has an option to extend the term of the Dallas Lease for one additional period of five years.

The Dallas Landlord has the right to terminate the Dallas Lease, or the Company’s right to possess the Office Space without terminating the Dallas Lease, upon specified events of default, including the Company’s failure to pay rent in a timely manner and upon the occurrence of certain events of insolvency with respect to the Company.

Dallas Lease Expansion

On December 14, 2021, the Company amended the Dallas Lease (the “Dallas Lease Amendment”) with the Dallas Landlord, pursuant to which the Company leases approximately 18,000 square feet of office space adjacent to the Office Space at 3000 Pegasus Park Drive, Dallas, Texas 75247 (the “Expansion Premises”).

The Dallas Lease Amendment commenced on July 1, 2022, and has a term of ten years.

The Company is obligated to pay operating costs and utilities applicable to the Expansion Premises. Total future minimum lease payments under the Dallas Lease Amendment over the initial 10-year term are approximately \$6.0 million. The Company is responsible for costs of constructing interior improvements within the Expansion Premises that exceed a \$40.00 per rentable square foot construction allowance provided by the Dallas Landlord.

The Company has a right of first refusal with respect to certain additional office space on the 15th floor at 3000 Pegasus Park Drive, Dallas, Texas 75247 before the Dallas Landlord accepts any offer for such space.

Durham Lease

On December 17, 2020, the Company entered into a lease agreement (the “Durham Lease”) with Patriot Park Partners II, LLC, a Delaware limited liability company (the “Durham Landlord”), pursuant to which the Company agreed to lease approximately 187,500 square feet of a manufacturing facility located at 5 National Way, Durham, North Carolina (the “Facility”). The Durham Lease commenced on April 1, 2021 and is expected to have a term of approximately fifteen years and six months. The Company has two options to extend the term of the Durham Lease, each for a period of an additional five years.

The Company was not required to provide a security deposit in connection with its entry into the Durham Lease. The Company was responsible for constructing interior improvements within the Facility. The Company was required to place \$2.6 million in an escrow account which was to be released when the improvements were substantially complete. In December 2023, the Company entered into an agreement with the landlord whereby the Company agreed to remove specified leasehold improvements which will be funded by the escrowed funds. The escrow funds are recorded as restricted cash on the consolidated balance sheets as of December 31, 2024 and 2023 with \$0.5 million recorded in current assets and \$2.1 million in noncurrent assets. The Durham Landlord has the right to terminate the Durham Lease upon specified events of default, including the Company’s failure to pay rent in a timely manner and upon the occurrence of certain events of insolvency with respect to the Company.

Summary of all lease costs recognized under ASC 842

The following table summarizes the lease costs recognized under ASC 842 and other information pertaining to the Company’s operating leases for the year ended December 31, 2024 and 2023 (in thousands):

	For the Year Ended December 31,	
	2024	2023
Operating lease cost	\$ 2,664	\$ 2,770
Variable lease cost	811	960
Total lease cost	\$ 3,475	\$ 3,730

Supplemental information related to the remaining lease term and discount rate are as follows:

	December 31, 2024	December 31, 2023
Weighted average remaining lease term (in years) – Finance leases	1.88	2.88
Weighted average remaining lease term (in years) – Operating leases	9.98	10.75
Weighted average discount rate – Finance leases	10.54%	10.52%
Weighted average discount rate – Operating leases	7.84%	7.80%

Supplemental cash flow information related to the Company’s operating leases are as follows (in thousands):

	For the Year Ended December 31,	
	2024	2023
Operating cash flows for operating leases	\$ 2,815	\$ 2,824

As of December 31, 2024, future minimum commitments under ASC 842 under the Company’s operating and finance leases were as follows (in thousands):

Year Ending December 31,	Operating	Finance
2025	2,910	454
2026	2,485	399
2027	2,577	—
2028	2,673	—
2029	2,779	—
Thereafter	14,284	—
Total lease payments	27,708	853
Less: imputed interest	(8,861)	(83)
Total lease liabilities	\$ 18,847	\$ 770
Lease liabilities, current	1,486	391
Lease liabilities, non-current	17,361	379
Total lease liabilities	\$ 18,847	\$ 770

Note 6 – Term Loans

Loan with Trinity Capital

On November 13, 2023 (the “Trinity Closing Date”), the Company entered into a Loan and Security Agreement (the “Trinity Term Loan Agreement”), by and among the Company, the lenders party thereto from time to time (the “Trinity Lenders”) and Trinity Capital Inc., as administrative agent and collateral agent for the Trinity Lenders (“Trinity”). The Trinity Term Loan Agreement provides for, on the Trinity Closing Date, \$40.0 million aggregate principal amount of term loans (collectively, the “Trinity Term Loans”). The Company drew the Trinity Term Loans in full on the Trinity Closing Date.

The interest rate applicable to the Trinity Term Loans is the greater of (a) the WSJ Prime Rate plus 4.50% or (b) 12.75% per annum. The Trinity Term Loans are interest only from the Trinity Closing Date through 36 months from the Trinity Closing Date, which may be extended to 48 months from the Trinity Closing Date upon the satisfaction of certain milestones set forth in the Trinity Term Loan Agreement, after which the Company is required to pay equal monthly installments of principal through November 13, 2028 (the “Maturity Date”). As of December 31, 2024, \$40.0 million was outstanding on the Trinity Term Loan, recorded as Term Loan, net on the consolidated balance sheet.

Future principal debt payments on the Trinity Term Loan Agreement as of December 31, 2024 are as follows (in thousands):

<i>Year Ending December 31,</i>	
2024	\$ —
2025	—
2026	—
2027	18,709
2028	21,291
Total principal payments	<u>\$ 40,000</u>

The Trinity Term Loans may be prepaid in full (i) from the Trinity Closing Date through November 13, 2024, with payment of a 3.00% prepayment premium, (ii) from November 13, 2024 through November 13, 2025, with payment of a 2% prepayment premium, and (iii) from November 13, 2025 through, but excluding, the Maturity Date, with payment of a 1% prepayment premium. On the Trinity Closing Date, the Company paid to Trinity a commitment fee of 1.00% of the original principal amount of the Trinity Term Loans. Upon repayment in full of the Trinity Term Loans, the Company will pay to Trinity an end of term payment equal to 5.00% of the original principal amount of the Trinity Term Loans.

The obligations under the Trinity Term Loan Agreement are secured by a perfected security interest in all of the Company's assets except for certain customarily excluded property pursuant to the terms of the Trinity Term Loan Agreement. There are no financial covenants and no warrants associated with the Trinity Term Loan Agreement. The Trinity Term Loan Agreement contains various covenants that limit the Company's ability to engage in specified types of transactions without the consent of Trinity and the Trinity Lenders which include, among others, incurring or assuming certain debt; merging, consolidating or acquiring all or substantially all of the capital stock or property of another entity; changing the nature of the Company's business; changing the Company's organizational structure or type; licensing, transferring or disposing of certain assets; granting certain types of liens on the Company's assets; making certain investments; and paying cash dividends. As of December 31, 2024, the Company is in compliance with all covenants of the Trinity Term Loans.

The Trinity Term Loan Agreement also contains customary representations and warranties, and also includes customary events of default, including payment default, breach of covenants, change of control, and material adverse effects. Upon the occurrence of an event of default, a default interest rate of an additional 5% per annum may be applied to the outstanding loan balances, and the Trinity Lenders may declare all outstanding obligations immediately due and payable and exercise all of its rights and remedies as set forth in the Trinity Term Loan Agreement and under applicable law.

The proceeds of the Trinity Term Loans were used to repay the Company's obligations under the Term Loan Agreement (as defined below) with Silicon Valley Bank in full. The Term Loan Agreement with Silicon Valley Bank was terminated concurrently with entry into the Trinity Term Loan Agreement.

The Company assessed the terms and features of the Trinity Term Loans and determined that the Company is eligible to elect the fair value option under ASC 825, *Financial Instruments*. The Trinity Term Loans contains various embedded features and the election of the fair value option allows the Company to bypass analysis of potential embedded derivatives and further analysis of bifurcation of any recognized financial liabilities. Under the fair value option, the financial liability is initially measured at its fair value on the issue date and subsequently remeasured at estimated fair value on a recurring basis at each reporting date. Changes in the fair value of the Trinity Term Loans, which include accrued interest, if any, are recorded as a component of other expense (income) in the consolidated statements of operations. The Company has not elected to present interest expense separately from changes in fair value and therefore will not present interest expense associated with the Trinity Term Loans. Any changes in fair value caused by instrument-specific credit risk are presented separately in other comprehensive income or loss if material. Under the fair value option, debt issuance costs are expensed as incurred. The Company incurred \$0.9 million of debt issuance costs, which were recorded within general and administrative expense in the consolidated statements of operations for the year ended December 31, 2023.

In connection with the Trinity Term Loans, the Company entered into a Success Fee Agreement with Trinity which specifies the terms regarding a fee in the amount of 10% of the principal amount of the funded Trinity Term Loans (the "Success Fee"). The Success Fee is payable upon the achievement of certain corporate development value-inflection milestones. The Success Fee survives the termination of the Trinity Term Loans and expires on the earlier of ten years, or payment in full in cash of the Success Fee. The Company determined that the Success Fee represents a freestanding financial instrument and should be accounted for as a derivative liability under ASC 815 and recorded a liability within other non-current liabilities on the consolidated balance sheet, at fair value on the Trinity Closing Date and will be marked-to-market at the end of each reporting period with gains and losses recognized as a component of other income (expense) in the consolidated statements of operations.

The proceeds from the Trinity Term Loans were allocated to the Success Fee and Trinity Term Loans based on their respective fair values on the Trinity Closing Date. The fair values were determined utilizing a probability-weighted income approach, including variables for the timing of a success event and other probability estimates.

The Company determined the fair value of the Trinity Term Loans and the Success Fee using a probability-weighted income approach and recorded the loan at fair value of \$39.2 million and the Success Fee liability at fair value of \$0.8 million in the consolidated balance sheet at issuance.

The Company calculated the discounted cash flows of the Trinity Term Loans using a discount rate of 15.68% and adjusted for the probability of various repayment scenarios. The Company calculated the discounted cash flows of the Success Fee liability, using a discount rate of 15.68% then adjusted for the probability of achievement of certain corporate development value-inflection milestones.

The Company remeasured the fair value of the Trinity Term Loans and Success Fee as of December 31, 2024 using a probability-weighted income approach. The Company calculated discounted cash flows of the Trinity Term Loans using a discount rate of 11.12% and adjusted for the probability of various repayment scenarios. The Company calculated the discounted cash flows of the Success Fee liability, using a discount rate of 11.12% then adjusted for the probability of achievement of certain corporate development value-inflection milestones.

The following table reconciles the change in fair value of the Trinity Term Loans during the years ended December 31, 2024 and 2023 (in thousands):

Trinity Term Loans

Beginning fair value balance at November 13, 2023	\$	39,230
Principal payments		—
Change in fair value reported in statements of operations		1,278
Change in fair value reported in comprehensive loss		—
Ending fair value balance as of December 31, 2023	\$	<u>40,508</u>
Principal payments		—
Change in fair value reported in statements of operations		(597)
Change in fair value reported in comprehensive loss		4,031
Ending fair value balance as of December 31, 2024	\$	<u>43,942</u>

During the year ended December 31, 2024 the Company recorded \$5.2 million of interest expense within change in fair value of term loans, all of which was paid as of December 31, 2024. During the year ended December 31, 2023 the Company recorded \$0.7 million of interest expense within change in fair value of term loans, all of which was paid as of December 31, 2023.

The following table reconciles the change in fair value of the Success Fee liability during the years ended December 31, 2024 and 2023 (in thousands):

Success Fee

Beginning fair value balance at November 13, 2023	\$	770
Change in fair value of Success Fee		30
Ending fair value balance as of December 31, 2023	\$	<u>800</u>
Change in fair value of Success Fee		130
Ending fair value balance as of December 31, 2024	\$	<u>930</u>

Loan with Silicon Valley Bank

On August 12, 2021 (the “Closing Date”), the Company entered into a Loan and Security Agreement (the “Term Loan Agreement”), by and among the Company, the lenders party thereto from time to time (the “Lenders”) and Silicon Valley Bank, as administrative agent and collateral agent for the Lenders (“Agent”). The Term Loan Agreement provided for (i) on the Closing Date, \$40.0 million aggregate principal amount of term loans available through December 31, 2021, (ii) from January 1, 2022 until September 30, 2022, an additional \$20.0 million term loan facility available at the Company’s option upon having three distinct and active clinical stage programs, determined at the discretion of the Agent, at the time of draw, (iii) from October 1, 2022 until March 31, 2023, an additional \$20.0 million term loan facility available at the Company’s option upon having three distinct and active clinical stage programs, determined at the discretion of the Agent, at the time of draw and (iv) from April 1, 2023 until December 31, 2023, an additional \$20.0 million term loan facility available upon approval by the Agent and the Lenders (collectively, the “Term Loans”). The Company drew \$30.0 million in term loans on the Closing Date and \$10.0 million in term loans in December 2021. The Company did not draw on the two additional \$20.0

million tranches prior to expiration on September 30, 2022 and March 31, 2023. The Term Loan Agreement with Silicon Valley Bank was terminated concurrently with entry into the Trinity Term Loan Agreement in November 2023.

The interest rate applicable to the Term Loans was the greater of (a) the WSJ (“Wall Street Journal”) Prime Rate plus 3.75% or (b) 7.00% per annum. The Term Loans were interest only from the Closing Date through August 31, 2024, after which the Company was required to pay equal monthly installments of principal through August 1, 2026, the maturity date.

The Term Loans could have been prepaid in full through August 12, 2023, with payment of a 1.00% prepayment premium, after which they could be prepaid in full with no prepayment premium. An additional final payment of 7.5% of the amount of Terms Loans advanced by the Lenders (“Exit Fee”) was due upon prepayment or repayment of the Term Loans in full. The Exit Fee of \$3.0 million was recorded as debt discount. The debt discount was being accreted using the effective interest method over the term of the Term Loans within interest expense in the consolidated statements of operations.

The obligations under the Term Loan Agreement were secured by a perfected security interest in all of the Company’s assets except for intellectual property and certain other customarily excluded property pursuant to the terms of the Term Loan Agreement.

Upon termination of the Term Loan Agreement with Silicon Valley Bank, the Company made a prepayment of \$43.2 million to satisfy the Company’s principal and interest obligations and related fees under the Term Loan Agreement. The payoff amount paid by the Company in connection with the Term Loans included payment of the Exit Fee of \$3.0 million and accrued interest of \$0.2 million. In connection with the repayment of the Term Loans, the remaining balance of debt discount of \$1.4 million was recognized as a component of other income (expense) in the consolidated statements of operations for the year ended December 31, 2023.

During the year ended December 31, 2023, the Company recognized interest expense related to the Term Loans of \$4.9 million.

Note 7—Astellas Agreements

On October 21, 2022 (the “Effective Date”), the Company entered into the Option Agreement (the “Option Agreement”) with Astellas Gene Therapies, Inc. (f/k/a Audentes Therapeutics, Inc. (d/b/a Astellas Gene Therapy)) (“Astellas”), pursuant to which the Company granted to Astellas an exclusive option to obtain an exclusive, worldwide, royalty and milestone-bearing right and license (A) to research, develop, make, have made, use, sell, offer for sale, have sold, import, export and otherwise exploit, or, collectively, exploit, the product known, as of the Effective Date, as TSHA-120 (the “120 GAN Product”), and any backup products with respect thereto for use in the treatment of Giant Axonal Neuropathy (“GAN”) or any other gene therapy product for use in the treatment of GAN that is controlled by Taysha or any of its affiliates or with respect to which the Company or any of its affiliates controls intellectual property rights covering the exploitation thereof (a “GAN Product”), and (B) under any intellectual property rights controlled by Taysha or any of its affiliates with respect to such exploitation (the “GAN Option”). Subject to certain extensions, the GAN Option was exercisable from the Effective Date through a specified period of time following Astellas’ receipt of (i) the formal minutes from the Type B end-of-Phase 2 meeting between Taysha and the FDA in response to the Company’s meeting request sent to the FDA on September 19, 2022 for the 120 GAN Product (the “Type B end-of-Phase 2 Meeting”), (ii) all written feedback from the FDA with respect to the Type B end-of-Phase 2 Meeting, and (iii) all briefing documents sent by Taysha to the FDA with respect to the Type B end-of-Phase 2 Meeting. In September 2023, Astellas provided written notice of its decision not to exercise the GAN Option.

Under the Option Agreement, the Company also granted to Astellas an exclusive option to obtain an exclusive, worldwide, royalty and milestone-bearing right and license (A) to exploit any Rett Product (as defined below), and (B) under any intellectual property rights controlled by Taysha or any of its affiliates with respect to such exploitation (the “Rett Option,” and together with the GAN Option, each, an “Option”). Subject to certain extensions, the Rett Option is exercisable from the Effective Date through a specified period of time following Astellas’ receipt of (i) certain clinical data from the female pediatric trial and (ii) certain specified data with respect to TSHA-102, such period, the Rett Option Period, related to (i) the product known, as of the Effective Date, as TSHA-102 and any backup products with respect thereto for use in the treatment of Rett syndrome, and (ii) any other gene therapy product for use in the treatment of Rett syndrome that is controlled by Taysha or any of its affiliates or with respect to which the Company or any of its affiliates controls intellectual property rights covering the exploitation thereof (a “Rett Product”).

The parties have agreed that, if Astellas exercises an Option, the parties will, for a specified period, negotiate a license agreement in good faith on the terms and conditions outlined in the Option Agreement, including payments by Astellas of a to be determined upfront payment, certain to be determined milestone payments, and certain to be determined royalties on net sales of GAN Products and/or Rett Products, as applicable.

During the Rett Option Period, the Company has agreed to (A) not solicit or encourage any inquiries, offers or proposals for, or that could reasonably be expected to lead to, a Change of Control (as defined in the Option Agreement), or (B) otherwise initiate a process for a potential Change of Control, in each case, without first notifying Astellas and offering Astellas the opportunity to submit an offer or proposal to the Company for a transaction that would result in a Change of Control. If Astellas fails or declines to submit any such offer within a specified period after the receipt of such notice, the Company will have the ability to solicit third party bids for a Change of Control transaction. If Astellas delivers an offer to the Company for a transaction that would result in a Change of Control, the Company

and Astellas will attempt to negotiate in good faith the potential terms and conditions for such potential transaction that would result in a Change of Control for a specified period, which period may be shortened or extended by mutual agreement.

As partial consideration for the rights granted to Astellas under the Option Agreement, Astellas paid the Company an upfront payment of \$20.0 million (the “Upfront Payment”). Astellas or any of its affiliates shall have the right, in its or their discretion and upon written notice to the Company, to offset the amount of the Upfront Payment (in whole or in part, until the full amount of the Upfront Payment has been offset) against (a) any payment(s) owed to Taysha or any of its affiliates (or to any third party on behalf of the Company) under or in connection with any license agreement entered into with respect to any GAN Product or Rett Product, including, any upfront payment, milestone payment or royalties owed to Taysha or any of its affiliates (or to any third party on behalf of the Company) under or in connection with any such license agreement or (b) any amount owed to Taysha or any of its affiliates in connection with a Change of Control transaction with Astellas or any of its affiliates. As further consideration for the rights granted to Astellas under the Option Agreement, the Company and Astellas also entered into the Astellas Securities Purchase Agreement (as defined below).

Astellas Securities Purchase Agreement

On October 21, 2022, the Company entered into a securities purchase agreement with Astellas (the “Astellas Securities Purchase Agreement”), pursuant to which the Company agreed to issue and sell to Astellas in a private placement (the “Astellas Private Placement”), an aggregate of 7,266,342 shares (the “Astellas Private Placement Shares”), of its common stock, for aggregate gross proceeds of \$30.0 million. The Astellas Private Placement closed on October 24, 2022. Pursuant to the Astellas Securities Purchase Agreement, in connection with the Astellas Private Placement, Astellas has the right to designate one individual to attend all meetings of the Board in a non-voting observer capacity. The Company also granted Astellas certain registration rights with respect to the Astellas Private Placement Shares.

Accounting Treatment

In October 2022, upon closing of the Astellas Private Placement and transferring the 7,266,342 shares to Astellas, the Company recorded the issuance of shares at fair value. Fair value of the shares transferred to Astellas was calculated in accordance with ASC 820, *Fair Value Measurement* by analyzing the Company’s stock price for a short period of time prior to and after the transaction date as traded on the NASDAQ. The NASDAQ trading data is considered an active market and a Level 1 measurement under ASC 820. The fair value was determined to be approximately \$13.95 million or \$1.92 per share. The \$16.1 million difference between the \$30.0 million paid by Astellas and the fair market value of shares issued was allocated to the transaction price of the Option Agreement.

The Company determined that the Option Agreement falls within the scope of ASC 606, *Revenue from Contracts with Customers* as the development of TSHA-102 for the treatment of Rett Syndrome and TSHA-120 for the treatment of GAN are considered ordinary activities for the Company. In accordance with ASC 606, the Company evaluated the Option Agreement and identified three separate performance obligations: (1) option to obtain licensing right to GAN, (2) option to obtain licensing right to Rett and (3) performance of research and development activities in the Rett development plan. The transaction price is determined to be \$36.1 million which is comprised of the \$20.0 million Upfront Payment and the \$16.1 million allocated from the Private Placement.

To determine the standalone selling price (“SSP”) of the Rett and GAN options, which the Company concluded to be material rights, the Company utilized the probability-weighted expected return (“PWERM”) method. The PWERM method contemplates the probability and timing of an option exercise. At contract inception, the Company estimated that the probability of exercise was 50% for each of the GAN and Rett options. The SSP of the Rett research and development activities was estimated using an expected cost plus margin approach. The standalone selling prices of the material rights and Rett research and development activities were then used to proportionately allocate the \$36.1 million transaction price to the three performance obligations. The \$36.1 million transaction price was recorded as deferred revenue on the consolidated balance sheet at the inception of the Astellas Transactions.

The following table summarizes the allocation of the transaction price to the three performance obligations at contract inception (amounts in thousands):

	Transaction Price Allocation	
Option to obtain license for Rett	\$	5,485
Option to obtain license for GAN		2,317
Rett research and development activities		28,257
Total	\$	<u>36,059</u>

Revenue allocated to the material rights will be recognized at a point in time when each option period expires or when a decision is made by Astellas to exercise or not exercise each option. Revenue from the Rett research and development activities will be recognized as activities are performed using an input method, according to the costs incurred as related to the total costs expected to be incurred to satisfy the performance obligation. The transfer of control occurs over this time period and is a reliable measure of progress towards satisfying the performance obligation.

During the year ended December 31, 2024, the Company determined that the total estimated costs to be incurred to satisfy the performance obligation associated with Rett research and development activities had increased from the cost estimate used for the year ended December 31, 2023.

The Company recognized revenue of \$8.3 million and \$13.2 million from Rett research and development activities for the year ended December 31, 2024 and 2023, respectively. In September 2023, Astellas provided written notice of its decision not to exercise the GAN Option. The Company recognized revenue of \$2.3 million from the GAN Option during the year ended December 31, 2023.

As of December 31, 2024, the Company recorded deferred revenue of \$9.8 million within current liabilities in the accompanying consolidated balance sheet. The Company will recognize revenues for these performance obligations as they are satisfied.

Note 8—Research, Collaboration and License Agreements

UT Southwestern Agreement

On November 19, 2019, the Company entered into a research, collaboration and license agreement (“UT Southwestern Agreement”) with the Board of Regents of the University of Texas System on behalf of The University of Texas Southwestern Medical Center (“UT Southwestern”). Under the UT Southwestern Agreement, UT Southwestern is primarily responsible for preclinical development activities with respect to licensed products for use in certain specified indications (up to IND-enabling studies), and the Company is responsible for all subsequent clinical development and commercialization activities with respect to the licensed products. UT Southwestern will conduct such preclinical activities for a two-year period under mutually agreed upon sponsored research agreements that were entered into beginning in April 2020. During the initial research phase, the Company has the right to expand the scope of specified indications under the UT Southwestern Agreement.

In connection with the UT Southwestern Agreement, the Company obtained an exclusive, worldwide, royalty-free license under certain patent rights of UT Southwestern and a non-exclusive, worldwide, royalty-free license under certain know-how of UT Southwestern, in each case to make, have made, use, sell, offer for sale and import licensed products for use in certain specified indications. Additionally, the Company obtained a non-exclusive, worldwide, royalty-free license under certain patents and know-how of UT Southwestern for use in all human uses, with a right of first refusal to obtain an exclusive license under certain of such patent rights and an option to negotiate an exclusive license under other of such patent rights. The Company is required to use commercially reasonable efforts to develop, obtain regulatory approval for, and commercialize at least one licensed product.

On April 2, 2020, the Company amended the UT Southwestern Agreement to include the addition of another licensed product and certain indications, and a right of first refusal to the Company over certain patient dosing patents. No additional consideration was transferred in connection with this amendment. In March 2022, the Company and UT Southwestern mutually agreed to revise the payment schedules and current performance expectations of the current sponsored research agreements under the UT Southwestern Agreement and defer payments by fifteen months. In December 2023, the Company and UT Southwestern mutually agreed to terminate specific sponsored research agreements.

The UT Southwestern Agreement expires on a country-by-country and licensed product-by-licensed product basis upon the expiration of the last valid claim of a licensed patent in such country for such licensed product. After the initial research term, the Company may terminate the agreement, on an indication-by-indication and licensed product-by-licensed product basis, at any time upon specified written notice to UT Southwestern. Either party may terminate the agreement upon an uncured material breach of the agreement or insolvency of the other party. In December 2023, the Company transferred rights to specific indications back to UT Southwestern.

In November 2019, as partial consideration for the license rights granted under the UT Southwestern Agreement, the Company issued 2,179,000 shares of its common stock, or 20% of its then outstanding fully-diluted common stock, to UT Southwestern. The Company does not have any future milestone or royalty obligations to UT Southwestern under the UT Southwestern Agreement other than costs related to maintenance of patents.

Queen’s Agreement

On February 21, 2020, the Company entered into a license agreement (the “Queen’s Agreement”) with Queen’s University at Kingston (“Queen’s”) to obtain the exclusive perpetual, royalty-bearing license, with the right to sublicense through multiple tiers, under certain patent rights and know-how of Queen’s, including certain improvements to such patent rights and know-how, to develop products in any field which use one or more valid claims of the patents licensed under the Queen’s Agreement (the “Licensed Patents”), or the technology, information and intellectual property related to the patents licensed under the Queen’s Agreement (together with the Licensed Patents, the “Licensed Products”), and to make, have made, use, sell, offer for sale, import and export Licensed Products and otherwise exploit such patents and know-how for use in certain specified indications. In exchange for the rights granted to the Company, the Company made a cash payment of \$3.0 million in April 2020 which was recorded within research and development expenses in the consolidated statements of operations since the acquired license does not have an alternative future use. The Company is obligated to make aggregate cash payments of up to \$10.0 million upon the completion of a combination of regulatory milestones and up to \$10.0 million

upon the completion of a combination of commercial milestones. In further consideration of the rights granted, beginning with the Company's first commercial sale of the Licensed Products, the Company will also pay an annual earned royalty in the low single digits on net sales of Licensed Products, subject to certain customary reductions, and a percentage of non-royalty sublicensing revenue ranging in the low double digits. Royalties are payable, on a Licensed Products-by-Licensed Products and a country-by-country basis, until expiration of the last valid claim of a Licensed Patent covering such Licensed Products in such country and the expiration of any regulatory exclusivity for such Licensed Products in such country.

In January 2024, the Company transferred rights back to Queen's for the Licensed Patents. No additional milestone payments were made in connection with the Queen's Agreement during the year ended December 31, 2024.

Abeona CLN1 Agreements

In August 2020, the Company entered into license and inventory purchase agreements with Abeona Therapeutics Inc. ("Abeona") for worldwide exclusive rights to certain intellectual property rights and know-how relating to the research, development and manufacture of ABO-202, an AAV-based gene therapy for CLN1 disease (also known as infantile Batten disease). Under the terms of the agreements, the Company made initial cash payments to Abeona of \$3.0 million for the license fee and \$4.0 million for purchase of clinical materials and reimbursement for previously incurred development costs in October 2020. In exchange for the license rights, the Company recorded an aggregate of \$7.0 million within research and development expenses in the consolidated statements of operations for the year ended December 31, 2020 since the acquired license or acquired inventory do not have an alternative future use. The Company is obligated to make up to \$26.0 million in regulatory-related milestones and up to \$30.0 million in sales-related milestones per licensed CLN1 product. The Company will also pay an annual earned royalty in the high single digits on net sales of any licensed CLN1 products. The license agreement expires on a country-by-country and licensed product-by-licensed product basis upon the expiration of the last royalty term of a licensed product. Either party may terminate the agreement upon an uncured material breach of the agreement or insolvency of the other party. The Company may terminate the license agreement for convenience upon specified prior written notice to Abeona.

In December 2021, a regulatory milestone was triggered in connection with this agreement and therefore the Company recorded \$3.0 million within research and development expenses in the consolidated statements of operations for the year ended December 31, 2021. The milestone fee was paid in January 2022 and classified as an investing cash outflow in the consolidated statements of cash flows. No additional milestone payments were triggered in connection with this agreement during the years ended December 31, 2024 and 2023.

Abeona Rett Agreement

On October 29, 2020, the Company entered into a license agreement (the "Abeona Rett Agreement") with Abeona pursuant to which the Company obtained an exclusive, worldwide, royalty-bearing license, with the right to grant sublicenses under certain patents, know-how and materials originally developed by the University of North Carolina at Chapel Hill, the University of Edinburgh and Abeona to research, develop, manufacture, have manufactured, use, and commercialize licensed products for gene therapy and the use of related transgenes for Rett syndrome.

Subject to certain obligations of Abeona, the Company is required to use commercially reasonable efforts to develop at least one licensed product and commercialize at least one licensed product in the United States.

In connection with the Abeona Rett Agreement, the Company paid Abeona a one-time upfront license fee of \$3.0 million which was recorded in research and development expenses in the consolidated statements of operations for the year ended December 31, 2020 since the acquired license does not have an alternative future use. The Company is obligated to pay Abeona up to \$26.5 million in regulatory-related milestones and up to \$30.0 million in sales-related milestones per licensed Rett product and high single-digit royalties on net sales of licensed Rett products. Royalties are payable on a licensed product-by-licensed product and country-by-country basis until the latest of the expiration or revocation or complete rejection of the last licensed patent covering such licensed product in the country where the licensed product is sold, the loss of market exclusivity in such country where the product is sold, or, if no licensed product exists in such country and no market exclusivity exists in such country, ten years from first commercial sale of such licensed product in such country.

The Abeona Rett Agreement expires on a country-by-country and licensed product-by-licensed product basis upon the expiration of the last royalty term of a licensed product. Either party may terminate the agreement upon an uncured material breach of the agreement or insolvency of the other party. The Company may terminate the agreement for convenience upon specified prior written notice to Abeona.

In March 2022, the Company's CTA filing for TSHA-102 for the treatment of Rett Syndrome was approved by Health Canada and therefore triggered a regulatory milestone payment in connection with this agreement. The Company recorded \$1.0 million within research and development expenses and classified the payment as an investing cash outflow in the consolidated statements of cash flows. In May 2023, the Company dosed the first patient with TSHA-102 in the Phase 1/2 REVEAL trial evaluating the safety and preliminary efficacy of TSHA-102 in adult patients with Rett syndrome and therefore triggered a milestone payment in connection with the Abeona Rett Agreement. The Company recorded \$3.5 million within research and development expenses in the consolidated statements of operations for the year ended December 31, 2023. This milestone fee was paid in August 2023 and classified as an investing cash outflow in the

consolidated statements of cash flows for the year ended December 31, 2023. No additional milestone payments were made or triggered in connection with this agreement during the year ended December 31, 2024.

TSHA-120 for the treatment of GAN

In March 2021, the Company acquired the exclusive worldwide rights to a clinical-stage AAV9 gene therapy program (developed by the Company as TSHA-120) for the treatment of GAN pursuant to a license agreement (the “GAN License Agreement”) with Hannah’s Hope Fund for Giant Axonal Neuropathy, Inc. (“HHF”). In connection with the GAN License Agreement, the Company also obtained rights to collaborate with the National Institute of Neurological Disorders and Stroke (“NINDS”) on a clinical trial for TSHA-120, an intrathecally dosed AAV9 gene therapy for the treatment of GAN.

Under the terms of the GAN License Agreement, in exchange for granting the Company the exclusive worldwide rights to TSHA-120, HHF received an upfront payment of \$5.5 million. No additional milestone payments were made or triggered in connection with the GAN License Agreement during the year ended December 31, 2024. In January 2024, the Company initiated the return of the FDA Investigational New Drug application and transfer of the investigational clinical trial material for TSHA-120 in GAN to NINDS, enabling an opportunity for continued clinical evaluation of TSHA-120 in GAN after the Company discontinued development of TSHA-120 in GAN in September 2023. In January 2024, the Company gave notice of termination of the GAN License Agreement, and such termination became effective in July 2024 when all licensed rights under the GAN License Agreement reverted to HHF.

License Agreement for CLN7

In March 2022, the Company entered into a license agreement with UT Southwestern (the “CLN7 Agreement”) pursuant to which the Company obtained an exclusive worldwide, royalty-bearing license with right to grant sublicenses to develop, manufacture, use, and commercialize licensed products for gene therapy for CLN7, a form of Batten Disease. In connection with the CLN7 Agreement, the Company paid a one-time upfront license fee of \$0.3 million. The Company recorded the upfront license fee in research and development expense in the consolidated statements of operations since the acquired license does not have an alternative future use. The Company is obligated to pay UT Southwestern up to \$7.7 million in regulatory-related milestones and up to \$7.5 million in sales-related milestones, as well as a low, single-digit royalty on net sales upon commercialization of the product. No additional milestone payments were made in connection with this agreement during the years ended December 31, 2024 and 2023.

Note 9—Stock-Based Compensation

On July 1, 2020, the Company’s board of directors approved the 2020 Equity Incentive Plan (“Previous Plan”) which permitted the granting of incentive stock options, non-statutory stock options, stock appreciation rights, RSAs, RSUs and other stock-based awards to employees, directors, officers and consultants. As of September 16, 2020, the approval date of the New Plan (as defined below), no additional awards will be granted under the Previous Plan. The terms of the Previous Plan will continue to govern the terms of outstanding equity awards that were granted prior to approval of the New Plan.

On September 16, 2020, the Company’s stockholders approved the 2020 Stock Incentive Plan (“New Plan”), which became effective upon the execution of the underwriting agreement in connection with the IPO. The number of shares of common stock reserved for issuance under the New Plan automatically increases on January 1 of each year, for a period of ten years, from January 1, 2021, continuing through January 1, 2030, by 5% of the total number of shares of common stock outstanding on December 31 of the preceding calendar year, or a lesser number of shares as may be determined by the Company’s board of directors. Pursuant to this provision, on January 1, 2024, the Company increased the number of shares of common stock reserved for issuance under the New Plan by 9,348,009 shares.

Furthermore, on September 16, 2020, the Company’s stockholders approved the Employee Stock Purchase Plan (“ESPP”), which became effective upon the execution of the underwriting agreement in connection with the IPO. The maximum number of shares of common stock that may be issued under the ESPP will not exceed 362,000 shares of common stock, plus the number of shares of common stock that are automatically added on January 1st of each year for a period of up to ten years, commencing on the first January 1 following the IPO and ending on (and including) January 1, 2030, in an amount equal to the lesser of (i) one percent (1.0%) of the total number of shares of capital stock outstanding on December 31st of the preceding calendar year, and (ii) 724,000 shares of common stock. Pursuant to this provision, on January 1, 2023 and 2024, the Company’s board of directors increased the number of shares of common stock reserved for issuance under the ESPP by 632,075 and 724,000 respectively. The Company has issued an aggregate of 235,363 shares of common stock under the ESPP as of December 31, 2024.

On December 15, 2023, the Company’s board of directors adopted the Taysha Gene Therapies, Inc. 2023 Inducement Plan (the “Inducement Plan”). The Inducement Plan was adopted without stockholder approval pursuant to Nasdaq Listing Rule 5635(c)(4). The Board reserved 4,000,000 shares of the Company’s common stock for issuance under the Inducement Plan. On December 12, 2024, the

Company's board of directors reserved an additional 2,000,000 shares of the Company's common stock for issuance under the Inducement Plan.

The only persons eligible to receive grants of Inducement Awards (as defined below) under the Inducement Plan are individuals who satisfy the standards for inducement grants under Nasdaq Listing Rule 5635(c)(4). The Inducement Plan will be administered by the Board and the Company's Compensation Committee. Inducement Awards may only be granted by: (i) the Compensation Committee, provided such committee is comprised solely of "independent directors" (as defined by Nasdaq Listing Rule 5605(a)(2)) or (ii) a majority of the Company's "independent directors." An "Inducement Award" means any right to receive the Company's common stock, cash or other property granted under the Inducement Plan (including nonstatutory stock options, restricted stock awards, restricted stock unit awards, stock appreciation rights, performance stock awards, performance cash awards or other stock-based awards).

The number of shares available for grant under the Company's incentive plans were as follows:

	Previous Plan	New Plan	Inducement Plan	Total
Available for grant - January 1, 2023	—	1,067,682	—	1,067,682
Plan adjustments and amendments	(667,828)	3,828,203	4,000,000	7,160,375
Grants	—	(5,447,757)	—	(5,447,757)
Forfeitures	667,828	3,714,597	—	4,382,425
Available for grant - December 31, 2023	—	3,162,725	4,000,000	7,162,725
Plan adjustments and amendments	—	9,348,009	2,000,000	11,348,009
Grants	—	(12,442,262)	(3,774,300)	(16,216,562)
Forfeitures	—	632,958	774,000	1,406,958
Available for grant - December 31, 2024	—	701,430	2,999,700	3,701,130

Stock Options

For the year ended December 31, 2024, 11,719,421 shares of common stock under the New Plan and Inducement Plan were awarded with a weighted-average grant date fair value per share of \$1.53. The stock options vest over one to four years and have a ten-year contractual term.

The following weighted-average assumptions were used to estimate the fair value of time-based vesting stock options that were granted during the years ended December 31, 2024 and 2023:

	Year Ended December 31,	
	2024	2023
Risk-free interest rate	4.02 %	3.68 %
Expected dividend yield	—	—
Expected term (in years)	6.1	5.5
Expected volatility	89 %	82 %

The following table summarizes time-based vesting stock option activity, during the years ended December 31, 2024 and 2023:

	Stock Options	Weighted Average Exercise Price	Weighted Average Remaining Contractual Life (in years)	Aggregate Intrinsic Value (in thousands)
Outstanding at January 1, 2023	6,158,078	11.84	8.9	62
Options granted	2,726,871	0.99		
Options cancelled or forfeited	(2,050,562)	10.70		
Options expired	(873,465)	22.21		
Options exercisable at December 31, 2023	5,960,922	\$ 5.75	8.7	\$ 1,960
Options granted	11,719,421	2.02		
Exercised	(58,832)	0.68		
Options cancelled or forfeited	(1,327,123)	2.50		
Options expired	(73,783)	17.01		
Outstanding at December 31, 2024	16,220,605	\$ 3.29	8.7	\$ 1,967
Options exercisable at December 31, 2024	3,595,465	\$ 7.72	7.5	\$ 1,055

The aggregate intrinsic value in the above table is calculated as the difference between the fair value of the Company's common stock at the respective reporting date and the exercise price of the stock options. As of December 31, 2024, the total unrecognized compensation related to unvested time-based vesting stock option awards granted was \$15.5 million, which the Company expects to recognize over a weighted-average period of approximately 2.7 years. During the year ended December 31, 2024 58,832 stock options were exercised. No stock options were exercised during the year ended December 31, 2023.

Performance Stock Options

In February 2023, the Company issued options to purchase 70,235 shares of common stock to employees under the New Plan that contain performance-based vesting conditions, subject to continued employment through each anniversary and achievement of the performance conditions. The grant date fair value of these awards was not material. As of December 31, 2024, 58,346 of the shares subject to the performance-based options were vested and outstanding. No performance-based stock options were exercised during the year ended December 31, 2024.

In May 2023, the Company issued options to purchase 2,166,653 shares of common stock to employees under the New Plan that contain both service and performance-based vesting conditions (the "Original Options"), with a weighted average grant date fair value per share of \$0.50. These Original Options were expected to vest over a 3.6 year term if a combination of clinical, regulatory and financing performance conditions were achieved. No compensation expense was recognized in 2023 related to the Original Options as achievement of the performance conditions was not considered probable. The following weighted-average assumptions were used to estimate the fair value of the options granted in February 2023 and the Original Options that were granted in May 2023:

Risk-free interest rate	4.02 %
Expected dividend yield	—
Expected term (in years)	6.0
Expected volatility	81 %

In December 2023, the Company modified all of the Original Options to amend the clinical and regulatory performance conditions and decreased the number of options granted to 1,516,655 (the "Modified Options"). The Company accounted for the changes in award terms as a modification in accordance with ASC 718, *Compensation - Stock Compensation*. Total compensation cost is equal to the modification date fair value. The Modified Options have a grant date fair value per share of \$1.28. The following assumptions were used to estimate the fair value of the Modified Options:

Risk-free interest rate	3.90 %
Expected dividend yield	—
Expected term (in years)	5.8
Expected volatility	88 %

The Modified Options will vest over 3.0 years. The Company recognized stock-based compensation expense of \$1.2 million and \$0.1 million for the years ended December 31, 2024 and 2023, respectively, related to the Modified Options. As of December 31, 2024, the total unrecognized compensation expense related to the Modified Options was \$0.7 million, which the Company expects to recognize over a weighted average period of approximately 1.6 years using the accelerated attribution method. As of December 31, 2024, 1,516,655 of the Modified Options were outstanding, of which 505,552 vested during the period. No stock options were exercised during the period.

Market-based Stock Options

In February 2023, the Company issued options to purchase 70,233 shares of common stock to employees under the New Plan that contain a market-based vesting condition, subject to continued employment through each anniversary and achievement of the market condition. The grant date fair value of the stock options that contain market-based vesting conditions was not material. As of December 31, 2023, the market condition was not met and all 70,233 shares were forfeited.

Restricted Stock Units

For the year ended December 31, 2024, the Company issued 4,497,141 RSUs to employees under the New Plan. The RSUs are subject to a service-based vesting condition. The service-based RSUs vest in equal annual installments over a one to four-year period. The Company at any time may accelerate the vesting of the RSUs. Such shares are not accounted for as outstanding until they vest.

For the year ended December 31, 2023, the Company issued 81,236 RSUs to employees under the New Plan. The RSUs are subject to a service-based vesting condition. The service-based RSUs vest in equal annual installments over a four-year period. The Company at any time may accelerate the vesting of the RSUs. Such shares are not accounted for as outstanding until they vest.

The Company's default tax withholding method for RSUs granted prior to 2023 is the sell-to-cover method, in which shares with a market value equivalent to the tax withholding obligation are sold on behalf of the holder of the RSUs upon vesting and settlement to cover the tax withholding liability and the cash proceeds from such sales are remitted by the Company to taxing authorities. For RSUs granted in 2023, the Company's tax withholding policy allows the RSU holder to choose to either pay cash to the Company for the tax withholding obligation or elect the net withholding method, in which shares with a market value equivalent to the tax withholding obligation are withheld and the net shares are issued to the RSU holder.

In March 2023, the Company issued 251,296 RSUs to the former President and Chief Executive officer of the Company in connection with his resignation from the Company and Board of Directors. The RSUs vested immediately.

The Company's RSU activity for the years ended December 31, 2024 and 2023 was as follows:

	Number of Shares	Weighted Average Grant Date Fair Value per Share
Nonvested at January 1, 2023	1,257,844	\$ 6.52
Restricted units granted	332,532	1.06
Vested	(556,989)	4.78
Cancelled or forfeited	(658,343)	5.18
Nonvested at December 31, 2023	375,044	\$ 6.63
Restricted units granted	4,497,141	1.83
Vested	(323,031)	7.50
Cancelled or forfeited	—	—
Nonvested at December 31, 2024	4,549,154	\$ 1.82

As of December 31, 2024, the total unrecognized compensation related to unvested RSUs granted was \$6.0 million which is expected to be amortized on a straight-line basis over a weighted-average period of approximately 2.9 years.

Performance and Market-based Restricted Stock Units

In February 2023, the Company issued 81,233 RSUs to employees under the New Plan that contain a combination of performance and market-based vesting conditions, subject to continued employment through each anniversary and achievement of market and performance conditions. The grant date fair value of the RSUs that contain performance and market-based vesting conditions was not material. During the year ended December 31, 2023, 46,562 of the RSUs were forfeited and 34,671 RSUs vested and were settled. No RSUs that contain performance or market-based vesting conditions were granted or outstanding during the year ended December 31, 2024.

Restricted Stock Awards

The Company's former President and Chief Executive Officer, was awarded 769,058 RSAs under the Existing Plan on July 1, 2020, which vested over a three-year term, subject to continuous employment. The fair value of these RSAs at the grant date of July 1, 2020, was \$5.28 per share. On March 2, 2023, the Company's former President and Chief Executive Officer resigned from the Board of Directors, therefore canceling any remaining unvested tranches. No RSAs were granted or outstanding during the year ended December 31, 2024.

The Company's RSA activity for the year ended December 31, 2023 was as follows:

	Number of Shares	Weighted Average Grant Date Fair Value per Share
Nonvested at January 1, 2023	85,494	\$ 5.28
Restricted stock granted	—	—
Vested	(64,120)	5.28
Cancelled or forfeited	(21,374)	5.28
Nonvested at December 31, 2023	—	\$ —

Employee Stock Purchase Plan

In February 2022, the Company's board of directors authorized the first offering under the ESPP. Under the ESPP, eligible employees may purchase shares of Taysha common stock through payroll deductions at a price equal to 85% of the lower of the fair market values of the stock as of the beginning or the end of six-month offering periods. An employee's payroll deductions under the ESPP are

limited to 15% of the employee’s compensation and employees may not purchase more than 1,800 shares of Taysha common stock during any offering period. During the years ended December 31, 2024 and 2023, stock-based compensation expense related to the ESPP was not material.

Stock-based Compensation Expense

The following table summarizes the total stock-based compensation expense for the stock options, ESPP, RSAs and RSUs recorded in the consolidated statements of operations for the years ended December 31, 2024 and 2023 (in thousands):

	For the Year Ended December 31,	
	2024	2023
Research and development expense	\$ 5,631	\$ 2,225
General and administrative expense	7,472	5,680
Total	\$ 13,103	\$ 7,905

Note 10—Warrants

Pre-Funded Warrants

Pre-Funded Warrants Issued in June 2024

On June 26, 2024, the Company entered into the June 2024 Underwriting Agreement with the Underwriters to issue and sell 14,361,113 shares of common stock, and, in lieu of common stock to certain investors, pre-funded warrants to purchase 18,972,221 shares of common stock (the “June 2024 Pre-Funded Warrants”) in the June 2024 Offering. The offering price to the public was \$2.25 per share of common stock and \$2.249 per June 2024 Pre-Funded Warrant, which was the price to the public of each share of common stock sold in the June 2024 Offering, minus the \$0.001 exercise price per June 2024 Pre-Funded Warrant. The Underwriters agreed to purchase the shares and the June 2024 Pre-Funded Warrants from the Company pursuant to the June 2024 Underwriting Agreement at a price of \$2.115 per share and \$2.114 per June 2024 Pre-Funded Warrant, respectively. The initial closing of the June 2024 Offering occurred on June 27, 2024; no additional June 2024 Pre-Funded Warrants were sold upon the exercise of the Underwriters’ option in July 2024.

Each June 2024 Pre-Funded Warrant has an initial exercise price per share of \$0.001, subject to certain adjustments. The June 2024 Pre-Funded Warrants may be exercised at any time until exercised in full, except that a holder will not be entitled to exercise any portion of any pre-funded warrant, which, upon giving effect to such exercise would cause (i) the aggregate number of shares of the Company’s common stock beneficially owned by the holder (together with its affiliates) to exceed 4.99% or 9.99%, as the case may be, of the number of shares of the Company’s common stock outstanding immediately prior to or after giving effect to the exercise, or (ii) the combined voting power of the Company’s securities beneficially owned by the holder (together with its affiliates) to exceed 4.99% or 9.99%, as the case may be, of the combined voting power of all of the Company’s securities then outstanding immediately prior to or after giving effect to the exercise, as such percentage ownership is determined in accordance with the terms of the pre-funded warrants, subject to such holder’s rights under the June 2024 Pre-Funded Warrant to increase or decrease such percentage to another percentage not in excess of 19.99% upon at least 61 days’ prior notice from such holder to the Company.

The Company concluded that the June 2024 Pre-Funded Warrants meet the criteria for equity classification at issuance and were recorded as a component of stockholders’ equity within additional paid-in capital. The June 2024 Pre-funded Warrants are equity classified because they (i) are freestanding financial instruments that are legally detachable and separately exercisable from the equity instruments, (ii) are immediately exercisable, (iii) do not embody an obligation for the Company to repurchase its shares, (iv) permit the holders to receive a fixed number of shares of common stock upon exercise, (v) are indexed to the Company’s common stock and (vi) meet the equity classification criteria. In addition, such pre-funded warrants do not provide any guarantee of value or return.

Pre-Funded Warrants Issued in August 2023

On August 14, 2023, the Company entered into a Securities Purchase Agreement (the “August 2023 Purchase Agreement”) with certain institutional and other accredited investors (the “Purchasers”), pursuant to which the Company agreed to sell and issue to the Purchasers in a private placement transaction (the “August 2023 Private Placement”) (i) 122,412,376 shares (the “PIPE Shares”) of the Company’s common stock, and (ii) with respect to certain Purchasers, pre-funded warrants to purchase 44,250,978 shares of the Company’s common stock (the “2023 Pre-Funded Warrants”) in lieu of shares of the Company’s common stock. The purchase price per share of common stock was \$0.90 per share (the “PIPE Purchase Price”), and the purchase price for the 2023 Pre-Funded Warrants was the Purchase Price minus \$0.001 per PIPE Pre-Funded Warrant.

The 2023 Pre-Funded Warrants have a per share exercise price of \$0.001, subject to proportional adjustments in the event of stock splits or combinations or similar events. The 2023 Pre-Funded Warrants will not expire until exercised in full. The 2023 Pre-Funded Warrants may not be exercised if the aggregate number of shares of common stock beneficially owned by the holder thereof immediately following such exercise would exceed a specified beneficial ownership limitation; provided, however, that a holder may increase or

decrease the beneficial ownership limitation by giving 61 days' notice to the Company, but not to any percentage in excess of 19.99%. The exercise of the 2023 Pre-Funded Warrants was also contingent upon receipt of stockholder approval of an increase in the authorized shares of the Company's common stock (the "Stockholder Approval"), which the Company obtained at a special meeting of stockholders held on November 15, 2023.

The closing of the August 2023 Private Placement occurred on August 16, 2023 (the "PIPE Closing"). The total gross proceeds to the Company at the PIPE Closing were \$150.0 million, and after deducting placement agent commissions and offering expenses payable by the Company, net proceeds were \$140.3 million. The Company used the with-and-without method to allocate the total gross proceeds by first allocating the portion of the proceeds equal to the fair value of the 2023 Pre-Funded Warrants on the PIPE Closing date with the remaining proceeds allocated to the PIPE Shares on a residual basis.

The Company concluded that at the closing of the August 2023 Private Placement in August 2023, the 2023 Pre-Funded Warrants did not meet the criteria for equity classification under the guidance of ASC 815 as the Company did not have sufficient authorized and unissued shares to satisfy the warrants if exercised. The Company recorded the 2023 Pre-Funded Warrants as liabilities at their fair value. This liability is subject to remeasurement at each balance sheet date and any change in fair value is recognized in the Company's consolidated statements of operations. The Company incurred \$9.7 million of placement agent commissions and other issuance costs in connection with the August 2023 Private Placement. The placement agent commissions and other issuance costs were allocated between the PIPE Shares and the 2023 Pre-Funded Warrants on a systematic basis. The Company allocated \$7.1 million to the PIPE Shares which was recorded as a deduction to additional paid-in capital. The remaining \$2.6 million allocated to the 2023 Pre-Funded Warrants were recorded within general and administrative expense in the consolidated statements of operations for the year ended December 31, 2023. The issuance costs allocated to the Pre-Funded Warrants have been added back to net loss when deriving cash flows used in operations, and have been classified as a financing cash outflow in the consolidated statements of cash flows for the year ended December 31, 2023.

The Company measured the fair value of the PIPE Shares and 2023 Pre-Funded Warrants based on the \$0.90 per share Purchase Price. The Company used the relative fair value method to allocate the net proceeds received from the sales of the PIPE Shares and the 2023 Pre-Funded Warrants on the consolidated balance sheet as follows (in thousands):

	Purchase Price Allocation	
PIPE Shares	\$	110,127
Pre-Funded Warrants		39,826
Total	\$	149,953

The Company remeasured the fair value of the 2023 Pre-Funded Warrants using the closing price of the Company's common stock on the Nasdaq Global Market as of November 15, 2023 of \$1.68 per common share upon receipt of Stockholder Approval. The Company recorded a fair value adjustment of \$34.5 million in the consolidated statements of operations for the year ended December 31, 2023 and the warrant liability of \$74.3 million was reclassified into equity as an increase to additional paid-in capital upon receipt of Stockholder Approval.

SSI Warrants

In April 2023, the Company entered into a securities purchase agreement (the "SSI Securities Purchase Agreement"), with two affiliates of SSI Strategy Holdings LLC ("SSI"), named therein (the "SSI Investors") pursuant to which the Company agreed to issue and sell to the SSI Investors in a private placement (the "SSI Private Placement"), 705,218 shares of its common stock (the "SSI Shares") and warrants (the "SSI Warrants") to purchase an aggregate of 525,000 shares of the Company's common stock (the "Warrant Shares"). SSI provides certain consulting services to the Company. Each SSI Warrant has an exercise price of \$0.7090 per Warrant Share, which was the closing price of the Company's common stock on the Nasdaq Global Market on April 4, 2023 and expire ten years after issuance. The SSI Warrants issued in the SSI Private Placement provide that the holder of the SSI Warrants will not have the right to exercise any portion of its SSI Warrants until the achievement of certain clinical and regulatory milestones related to the Company's clinical programs. The SSI Private Placement closed on April 5, 2023. Gross proceeds of the SSI Private Placement were \$0.5 million.

The Company concluded that the SSI Warrants do not meet the criteria for equity classification under the guidance of ASC 815 due to settlement provisions that permit the holder to receive a variable number of shares in the event of a specified fundamental transaction as well as provisions that permit the holder to participate in dividends. As the SSI Warrants do not meet the criteria for equity classification, the Company recorded the warrants as liabilities at their fair value. This liability is subject to remeasurement at each balance sheet date until the warrants are exercised or expire, and any change in fair value is recognized in the Company's consolidated statements of operations.

The Company determined the fair value of the SSI Warrants at issuance was \$0.3 million using the Black-Scholes-Merton option pricing model. The following assumptions were used to estimate the fair value of the warrants at issuance:

Risk-free interest rate	3.46 %
Expected dividend yield	—
Expected term (in years)	5.2
Expected volatility	81 %
Market value of common stock (per share)	\$ 0.71

The fair value adjustment as of December 31, 2023 was \$0.2 million using the Black-Scholes-Merton option pricing model with probability weights applied to each of the SSI Warrants where vesting is contingent upon the achievement of certain clinical and regulatory milestones related to the Company's clinical programs. The fair value adjustment as of December 31, 2024 was less than \$0.1 million using the Black-Scholes-Merton option pricing model. As of December 31, 2024, 316,667 of the SSI Warrants have vested and are exercisable. No warrants were exercised during the period.

The Company estimated the fair value of the SSI Warrant liability using the following assumptions as of December 31, 2024 and 2023:

	December 31, 2024	December 31, 2023
Risk-free interest rate	4.43 %	3.84 %
Expected dividend yield	—	—
Expected term (in years)	4.1	4.5
Expected volatility	87 %	88 %
Market value of common stock (per share)	\$ 1.73	\$ 1.77

The following table summarizes changes in the Company's warrant liability during the years ended December 31, 2024 and 2023 (in thousands):

	Warrant Liability
Balance at January 1, 2023	\$ —
Issuance of SSI Warrants	252
Issuance of 2023 Pre-funded Warrants	39,826
Change in fair value	34,718
Reclass of 2023 Pre-funded Warrants to equity	(74,342)
Balance at December 31, 2023	\$ 454
Change in fair value	(16)
Balance at December 31, 2024	\$ 438

Note 11—Net Loss Per Common Share

Basic net loss per common share is computed by dividing net loss attributable to common stockholders by the weighted-average number of shares of common stock outstanding for the period. Since the Company had a net loss in both periods presented, basic and diluted net loss per common share are the same.

In August 2023, the Company issued liability-classified Pre-Funded Warrants with a nominal exercise price of \$0.001 per share (see Note 10). In accordance with ASC 260, *Earnings Per Share* ("ASC 260"), shares issuable for little to no cash consideration should be included in the number of outstanding shares used to calculate basic loss per share as long as all conditions necessary for exercise are met. The conditions for exercise were met on November 15, 2023, at which time the Pre-Funded Warrants were reclassified into equity. The Pre-Funded Warrants are therefore included as outstanding shares as of November 15, 2023 to calculate the weighted average number of shares outstanding to calculate basic loss per share.

The following table represents the calculation of basic and diluted net loss per common share for the years ended December 31, 2024 and 2023, respectively (in thousands, except share and per share data):

	For the Year Ended December 31,	
	2024	2023
Net loss	\$ (89,298)	\$ (111,566)
Weighted-average shares of common stock outstanding used to compute net loss per common share, basic and diluted	250,134,421	116,121,482
Net loss per common share, basic and diluted	\$ (0.36)	\$ (0.96)

The following common stock equivalents outstanding as of December 31, 2024 and 2023, respectively, were excluded from the computation of diluted net loss per share attributable to common stockholders for the periods presented because including them would have been anti-dilutive:

	December 31, 2024	December 31, 2023
Unvested RSUs	4,549,154	375,044
Stock options	17,795,606	7,535,924
SSI Warrants	316,667	316,667
Total	22,661,427	8,227,635

Note 12—Income Taxes

Provision for income taxes

There is no provision for income taxes because the Company has incurred operating losses and capitalized certain items for income tax purposes since its inception and maintains a full valuation allowance against its net deferred tax assets. The reported amount of income tax expense for the period differs from the amount that would result from applying the federal statutory tax rate to net loss before taxes primarily because of the change in valuation allowance.

Beginning in 2022, the 2017 Tax Cuts and Jobs Act amended Section 174 to eliminate current-year deductibility of research and experimentation (R&E) expenditures and software development costs (collectively, R&E expenditures) and instead require taxpayers to charge their R&E expenditures to a capital account amortized over five years (15 years for expenditures attributable to R&E activity performed outside the United States). The Company generated a deferred tax asset for capitalized R&E expenditures for the years ended December 31, 2024 and 2023 which are fully offset by valuation allowances for each period.

On August 16, 2022, President Biden signed the Inflation Reduction Act of 2022, or the Inflation Act, into law. The Inflation Act contains certain tax measures, including a corporate alternative minimum tax of 15% on some large corporations and an excise tax of 1% on corporate stock buy-backs. The various provisions of the Inflation Act do not have a material impact on the Company's consolidated financial statements.

The effective tax rate of the Company's provision (benefit) for income taxes differs from the federal statutory rate as follows:

	For the Year Ended December 31,	
	2024	2023
Statutory rate	21.00 %	21.00 %
State tax	0.03 %	0.33 %
Research and development tax credits	5.89 %	(18.98) %
Other permanent differences	(0.03) %	(0.67) %
Change in valuation allowance	(23.50) %	8.10 %
Change in fair value of term loan and warrant liability	(1.11) %	(6.83) %
Stock-based compensation	(2.28) %	(2.93) %
Income tax provision (benefit)	0.00 %	0.00 %

Deferred tax assets and valuation allowance

Deferred tax assets reflect the tax effects of NOLs, tax credit carryovers, and temporary differences between the carrying amounts of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes. At December 31, 2024 and 2023, the significant components of the Company's net deferred tax assets and liabilities are as follows (in thousands):

	For the Year Ended December 31,	
	2024	2023
Deferred tax assets:		
Net operating loss carryforwards	\$ 57,034	\$ 47,373
Tax credit carryforwards	7,328	1,961
Accruals and reserves	1,209	1,020
Other	3,429	3,978
Intangibles	4,671	4,888
Non-qualified stock options	4,433	2,585
R&E expenditures	27,709	22,497
Lease liabilities	4,116	4,452
Impairment of long-lived assets	6,115	5,509
Total deferred tax assets	116,044	94,263
Deferred tax liabilities		
Right-of-use assets	(1,912)	(2,224)
Fixed assets	—	(2)
Total deferred tax liabilities	(1,912)	(2,226)
Valuation allowance	(114,132)	(92,037)
Net deferred taxes	\$ —	\$ —

The valuation allowance is equal to the total net deferred tax asset amounts as of December 31, 2024 and 2023. ASC 740 requires that the tax benefit of net operating losses, temporary differences and credit carryforwards be recorded as an asset to the extent that management assesses that realization is "more likely than not." Realization of the future tax benefits is dependent on the Company's ability to generate sufficient taxable income within the carryforward period. Because of the Company's recent history of operating losses, management believes that recognition of the deferred tax assets net of liabilities arising from the above-mentioned future tax benefits is currently not likely to be realized and, accordingly, has provided a valuation allowance.

The valuation allowance increased by \$22.1 million during the year ended December 31, 2024, and decreased by \$9.0 million during the year ended December 31, 2023.

As of December 31, 2024, there were gross federal NOLs of \$268.3 million, gross state NOLs of \$11.7 million, federal tax credit carryforward of \$8.7 million, and state tax credit carryforward of \$1.3 million. The net operating losses and state tax credit carryforward do not expire. As of December 31, 2023, there were gross federal NOLs of \$222.1 million, gross state NOLs of \$11.9 million, federal tax credit carryforward of \$28.6 million, and state tax credit carryforward of \$1.2 million. The federal tax credit carryforward will expire in 2040. The Company files federal, foreign and state income tax returns and, in the normal course of business, the Company is subject to examination by these taxing authorities. All periods since Inception are subject to examination by these taxing authorities, where applicable. There are currently no pending income tax examinations.

Pursuant to Section 382 of the Internal Revenue Code, certain substantial changes in the Company's ownership may result in a limitation on the amount of NOL carryforwards and tax credit carryforwards that may be used in future years. Utilization of the NOL and tax credit carryforwards may be subject to a substantial annual limitation under Section 382 of the Internal Revenue Code of 1986 due to ownership change limitations that have occurred previously or that could occur in the future. These ownership changes may limit the amount of NOL and tax credit carryforwards that can be utilized annually to offset future taxable income and tax, respectively. The Company has completed studies to assess whether an ownership change has occurred through December 31, 2023. Based on these analyses, several ownership changes were identified in 2020 and an additional ownership change occurred in 2023. As a result of the ownership shift that occurred in August 2023, the Company has determined that \$217.9 million of its gross federal NOLs are subject to an annual utilization limitation of \$3.1 million, which can be increased in the five year period post change date for any realized built-in gain. Additionally, there were \$27.1 million of research credits that will expire due to such limitations, resulting in a write-off of the related deferred tax assets and reversal of the corresponding uncertain tax positions and valuation allowance in 2023. The Company will continue to monitor equity movement and its impact on the utilization of the NOLs and credits as the Company could experience additional ownership changes subsequent to December 31, 2023, which may result in additional limitations on the utilization of NOL carryforwards and credits.

Note 13—Commitments and Contingencies

Litigation

From time to time, the Company may be subject to various legal proceedings and claims that arise in the ordinary course of its business activities. The Company records a liability when a particular contingency is probable and estimable.

In January 2024 and April 2024, the Company was named a nominal defendant in two putative stockholder derivative actions filed by stockholders of the Company in the Court of Chancery of the State of Delaware. The lawsuits have since been consolidated and a lead plaintiff has been appointed. In October 2024, the lead plaintiff filed an amended complaint asserting claims relating to the Company’s August 2023 Private Placement against (i) certain of the Company’s current and former directors and officers for breach of fiduciary duty and unjust enrichment; and (ii) certain participants in the Company’s August 2023 Private Placement for aiding and abetting breach of fiduciary duty and unjust enrichment. The complaints seek an unspecified award of damages in the Company’s favor, plus pre-judgment and post-judgment interest, and an award to the plaintiffs for the costs and disbursement of the action, including fees for their attorneys and experts. The board of directors of the Company has formed a special litigation committee to investigate the claims and allegations in the amended complaint. On January 27, 2025, the court entered an order staying the litigation until June 30, 2025, while the special litigation committee conducts its investigation. The Company has not recorded a liability related to these lawsuits because, at this time, the Company is unable to reasonably estimate possible losses or gains or determine whether an unfavorable outcome is either probable or remote.

Commitments

In the normal course of business, the Company enters into contracts that contain a variety of indemnifications with its directors, officers, employees, licensors, suppliers and service providers. The Company’s maximum exposure under these arrangements is unknown at December 31, 2024. The Company does not anticipate recognizing any significant losses relating to these arrangements.

Note 14— Strategic Reprioritization

In March 2022, the Company implemented changes to the Company’s organizational structure as well as a broader operational cost reduction plan to enable the Company to focus on specific clinical-stage programs for GAN and Rett syndrome. Substantially all other research and development activities have been paused to increase operational efficiency.

In connection with prioritization of programs, the Company reduced headcount by approximately 35% across all functions in March 2022. In accordance with ASC 420, *Exit and Disposal Activities*, the Company recorded one-time severance and termination-related costs of \$2.6 million in the consolidated statements of operations for the year ended December 31, 2022, primarily within research and development expenses. In December 2022, the Company further reduced headcount and recorded additional one-time severance and termination related costs of \$1.5 million within research and development and general and administrative expenses. Throughout the first quarter of 2023, the Company further reduced headcount and recorded additional one-time severance and termination related costs of \$2.7 million within research and development and general and administrative expenses.

Payment of these costs are complete as of December 31, 2024. The change in accrued severance during the years ended December 31, 2024 and 2023 is as follows (amounts in thousands):

	Accrued Severance	
Accrued severance as of January 1, 2023	\$	1,463
Severance recorded		2,691
Severance paid		(3,764)
Accrued severance as of December 31, 2023	\$	390
Severance recorded		—
Severance paid		(390)
Accrued severance as of December 31, 2024	\$	—

Note 15— Retirement Plan

In July 2021, the Company adopted a 401(k) retirement savings plan that provides retirement benefits to all full-time employees. Eligible employees may contribute a percentage of their annual compensation, subject to Internal Revenue Service limitations. The Company contributed \$0.5 million and \$0.3 million to the 401(k) retirement savings plan for the years ended December 31, 2024 and 2023, respectively.

Note 16— Segment Information

The Company’s Chief Executive Officer (“CEO”) is the Chief Operating Decision Maker (“CODM”). The CODM allocates resources and makes operating decisions based on financial information presented on a consolidated basis. The CODM does not evaluate profitability below the level of the consolidated company. Accordingly, the Company has determined that it has a single reportable segment and operating segment structure. The Company views its operations and manages its business as a single operating segment, the gene therapy segment, which is the business of developing AAV-based gene therapies for the treatment of rare monogenic diseases of the central nervous system.

The gene therapy segment derives revenue solely from the Astellas Agreements (see Note 7). The accounting policies of the gene therapy segment are the same as those described in the summary of significant accounting policies.

The CODM reviews significant segment expenses including direct program expenses and compensation expenses as part of the assessment of segment profit and loss. The measure of segment assets is reported on the balance sheet as total consolidated assets.

The following table presents significant segment expenses for the years ended December 31, 2024 and 2023 (in thousands):

	<u>For the year ended December 31,</u>	
	2024	2023
Revenue	\$ 8,333	\$ 15,451
Less:		
Research and development program expense		
Program expense	24,646	20,245
Consultants and contractors expense	15,204	20,007
Compensation expense	36,372	26,508
Other segment expense ^(a)	21,409	60,257
Consolidated net loss	\$ (89,298)	\$ (111,566)

(a) Other segment expense included in consolidated net loss includes interest income, depreciation, insurance, travel, software and subscription services, legal, professional and consulting expense, rent and facilities expense, other general and administrative expense, impairment of long-lived assets, change in fair value of term loan, change in fair value of warrant liability and other expense.

Note 17—Subsequent Events

In January 2025, the Company granted options under the New Plan to purchase an aggregate of 6.2 million shares of its common stock at an exercise price of \$1.85 per share, and also granted 3.1 million RSUs. These equity awards vest over a four-year period and are subject to service-based vesting conditions.

In January and February 2025, the Company granted options under the Inducement Plan to purchase an aggregate 0.8 million shares of its common stock at a weighted-average exercise price of \$1.65 per share. These equity awards vest over a four-year period and are subject to service-based vesting conditions.

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

None.

Item 9A. Controls and Procedures.***Evaluation of Disclosure Controls and Procedures***

We maintain “disclosure controls and procedures,” as defined in Rule 13a-15(e) and Rule 15d-15(e) under the Exchange Act that are designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the SEC’s rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is accumulated and communicated to our management, including our principal executive and principal financial officers, as appropriate to allow timely decisions regarding required disclosure.

Our management, with the participation of our Chief Executive Officer and Chief Financial Officer, has evaluated the effectiveness of our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act), as of the end of the period covered by this Form 10-K. Based on such evaluation, our Chief Executive Officer and Chief Financial Officer have concluded that as of December 31, 2024, our disclosure controls and procedures were effective to provide reasonable assurance that the information required to be disclosed by us in this Form 10-K was (a) reported within the time periods specified by SEC rules and regulations, and (b) communicated to our management, including our Chief Executive Officer and Chief Financial Officer, to allow timely decisions regarding any required disclosure.

Management's Report on Internal Control Over Financial Reporting

Our management is responsible for establishing and maintaining an adequate system of internal control over financial reporting, as defined in the Exchange Act Rule 13a-15(f). Management conducted an assessment of our internal control over financial reporting based on the framework established in 2013 by the Committee of Sponsoring Organizations of the Treadway Commission in Internal Control-Integrated Framework. Based on the assessment, management concluded that, as of December 31, 2024, our internal control over financial reporting was effective.

This Annual Report does not include an attestation report of our registered public accounting firm regarding internal control over financial reporting as required by Section 404(c) of the Sarbanes Oxley Act of 2002. Because we qualify as an emerging growth company under the JOBS Act, management’s report was not subject to attestation by our independent registered public accounting firm.

Changes in Internal Control Over Financial Reporting

There were no changes in our internal control over financial reporting identified in management’s evaluation pursuant to Rules 13a-15(d) or 15d-15(d) of the Exchange Act during the quarter ended December 31, 2024 that materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Inherent Limitations on Effectiveness of Internal Controls

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, not absolute, 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. Our management, including our Chief Executive Officer and Chief Financial Officer, believes that our disclosure controls and procedures and internal control over financial reporting are designed to provide reasonable assurance of achieving their objectives and are effective at the reasonable assurance level. However, our management does not expect that our disclosure controls and procedures or our internal control over financial reporting will prevent all errors and all fraud.

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 our 2025 annual meeting of stockholders, or the Proxy Statement, which is expected to be filed not later than 120 days after the end of our fiscal year ended December 31, 2024, under the captions “Information Regarding the Board of Directors and Corporate Governance,” “Election of Directors” and “Executive Officers” and is incorporated herein by reference.

We have adopted the Taysha Code of Business Conduct and Ethics that applies to all officers, directors and employees. The Code of Business Conduct and Ethics is available on our website at www.tayshagtx.com. If we make any substantive amendments to the Code of Business Conduct and Ethics or grants any waiver from a provision of the Code to any executive officer or director, we will promptly disclose the nature of the amendment or waiver on our website.

We have adopted an Insider Trading Policy governing the purchase, sale, and/or other dispositions of the Company’s securities by directors, officers, employees and consultants that is designed to promote compliance with insider trading laws, rules and regulations, as well as procedures designed to further the foregoing purposes. A copy of our insider trading policy is incorporated by reference as Exhibit 19.1 to this Annual Report on Form 10-K. In addition, it is the Company’s intent to comply with applicable laws and regulations relating to insider trading.

Item 11. Executive Compensation.

The information required by this item will be set forth in the Proxy Statement under the captions “Executive Compensation” and “Director Compensation” and is incorporated herein by reference.

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

The information required by this item will be set forth in the Proxy Statement under the captions “Security Ownership of Certain Beneficial Owners and Management” and “Securities Authorized for Issuance under Equity Compensation Plans” and is incorporated herein by reference.

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

The information required by this item will be set forth in the Proxy Statement under the captions “Transactions with Related Persons and Indemnification” and “Independence of the Board of Directors” and is incorporated herein by reference.

Item 14. Principal Accountant Fees and Services.

The information required by this item will be set forth in the Proxy Statement under the caption “Ratification of Selection of Independent Registered Public Accounting Firm” and is incorporated herein by reference.

PART IV

Item 15. Exhibits and Financial Statement Schedules.

Financial Statements

The following report and financial statements of the Company are included in this Annual Report on Form 10-K:

- Report of Independent Registered Public Accounting Firm (PCAOB ID No. 34)
- Consolidated Balance Sheets
- Consolidated Statements of Operations
- Consolidated Statements of Comprehensive Loss
- Consolidated Statements of Stockholders' Equity
- Consolidated Statements of Cash Flows
- Notes to Consolidated Financial Statements

Financial Statements Schedules

All financial statement schedules have been omitted as they are not required, they are not applicable, or the required information is included in the financial statements or notes to the financial statements.

Exhibits

<u>Exhibit Number</u>	<u>Description</u>
3.1	Amended and Restated Certificate of Incorporation (incorporated by reference to Exhibit 3.1 to the Company's Current Report on Form 8-K (File No. 001-39536), filed with the Securities and Exchange Commission on September 29, 2020).
3.2	Amended and Restated Bylaws (incorporated by reference to Exhibit 3.4 to the Company's to the Company's Registration Statement on Form S-1 (File No. 333-248559), filed with the Securities and Exchange Commission on September 17, 2020).
3.3	Certificate of Amendment to the Amended and Restated Certificate of Incorporation of (incorporated by reference to Exhibit 3.1 to the Company's Current Report on Form 8-K (File No. 001-39536), filed with the Securities and Exchange Commission on November 15, 2023).
4.1	Amended and Restated Investors' Rights Agreement, by and among the Company and certain of its stockholders, dated July 2, 2020 (incorporated by reference to Exhibit 4.1 to the Company's Registration Statement on Form S-1 (File No. 333-248559), filed with the Securities and Exchange Commission on September 2, 2020).
4.2	Description of the Company's Common Stock (incorporated by reference to Exhibit 4.1 to the Company's Quarterly Report on Form 10-Q (File No. 001-39536), filed with the Securities Exchange Commission on August 12, 2024).
4.3	Form of Pre-Funded Warrant to Purchase Common Stock (incorporated by reference to Exhibit 4.1 to the Company's Current Report on Form 8-K (File No. 001-39536), filed with the Securities and Exchange Commission on August 14, 2023).
4.4	Form of Warrant to Purchase Common Stock dated April 5, 2023 (incorporated by reference to Exhibit 4.5 to the Company's Registration Statement on Form S-3 (File No. 333-271144), filed with the Securities Exchange Commission on April 5, 2023).
4.5	2024 Pre-Funded Warrant to Purchase Common Stock (incorporated by reference to Exhibit 4.1 to the Company's Current Report on Form 8-K (File No. 001-39536), filed with the Securities and Exchange Commission on June 26, 2024).
10.1†	Research, Collaboration & License Agreement, by and between the Company and The Board of Regents of the University of Texas System on behalf of The University of Texas Southwestern Medical Center, dated as of November 19, 2019 (incorporated by reference to Exhibit 10.1 to the Company's Registration Statement on Form S-1 (File No. 333-248559), filed with the Securities and Exchange Commission on September 2, 2020).
10.2†	Amendment to Research, Collaboration & License Agreement, by and between the Registrant and The Board of Regents of the University of Texas System on behalf of The University of Texas Southwestern Medical Center, dated as of April 2, 2020 (incorporated by reference to Exhibit 10.2 to the Company's Registration Statement on Form S-1 (File No. 333-248559), filed with the Securities and Exchange Commission on September 2, 2020).
10.3†	License Agreement, by and between the Company and Queen's University at Kingston, dated as of February 21, 2020 (incorporated by reference to Exhibit 10.3 to the Company's Registration Statement on Form S-1 (File No. 333-248559), filed with the Securities and Exchange Commission on September 2, 2020).
10.4†#	License Agreement, by and between the Company and Abeona Therapeutics Inc., dated as of August 14, 2020 (incorporated by reference to Exhibit 10.4 to the Company's Registration Statement on Form S-1 (File No. 333-248559), filed with the Securities and Exchange Commission on September 2, 2020).

- 10.5†# [License Agreement, by and between the Company and Abeona Therapeutics Inc., dated as of October 29, 2020 \(incorporated by reference to Exhibit 10.5 to the Company's Annual Report on Form 10-K \(File No. 001-39536\), filed with the Securities and Exchange Commission on March 2, 2021.](#)
- 10.6+ [2020 Equity Incentive Plan and Forms of Stock Option Grant Notice, Stock Option Agreement and Restricted Stock Award Grant Notice \(incorporated by reference to Exhibit 10.5 to the Company's Registration Statement on Form S-1 \(File No. 333-248559\), filed with the Securities and Exchange Commission on September 17, 2020\).](#)
- 10.7+ [2020 Stock Incentive Plan and Forms of Stock Option Grant Notice, Stock Option Agreement, Restricted Stock Unit Grant Notice and Restricted Stock Unit Award Agreement \(incorporated by reference to Exhibit 10.6 to the Company's Registration Statement on Form S-1 \(File No. 333-248559\), filed with the Securities and Exchange Commission on September 17, 2020\).](#)
- 10.8+ [2020 Employee Stock Purchase Plan \(incorporated by reference to Exhibit 10.7 to the Company's Registration Statement on Form S-1 \(File No. 333-248559\), filed with the Securities and Exchange Commission on September 17, 2020\).](#)
- 10.9+ [Form of Indemnification Agreement with Executive Officers and Directors \(\(incorporated by reference to Exhibit 10.8 to the Company's Registration Statement on Form S-1 \(File No. 333-248559\), filed with the Securities and Exchange Commission on September 17, 2020\).](#)
- 10.10+ [Amended and Restated Non-employee director compensation policy \(incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q \(File No. 001-39536\), filed with the Securities and Exchange Committee on August 14, 2023\).](#)
- 10.11+ [Change in Control Severance Plan and Form of Participation Agreement \(incorporated by reference to Exhibit 10.11 to the Company's Registration Statement on Form S-1 \(File No. 333-248559\), filed with the Securities and Exchange Commission on September 17, 2020\).](#)
- 10.12+ [Amended and Restated Offer Letter, effective as of September 24, 2020, by and between the Company and Kamran Alam \(incorporated by reference to Exhibit 10.13 to the Company's Annual Report on Form 10-K \(File No. 001-39536\), filed with the Securities and Exchange Commission on March 3, 2021\).](#)
- 10.13 [Lease, dated December 17, 2020, by and between Patriot Park Partners II, LLC and the Company \(incorporated by reference to Exhibit 10.15 to the Company's Annual Report on Form 10-K \(File No. 001-39536\), filed with the Securities and Exchange Commission on March 3, 2021\).](#)
- 10.14 [Lease Agreement, dated January 8, 2021, by and between Pegasus Park, LLC and the Company \(incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q \(File No. 001-39536\), filed with the Securities and Exchange Commission on August 16, 2021\).](#)
- 10.15 [First Amendment to Lease Agreement, dated December 14, 2021, by and between Pegasus Park, LLC and the Company \(incorporated by reference to Exhibit 10.18 to the Company's Annual Report on Form 10-K \(File No. 001-39536\), filed with the Securities and Exchange Commission on March 31, 2022\).](#)
- 10.16 [Sales Agreement, dated as of October 5, 2021, by and among the Registrant, SVB Leerink LLC and Wells Fargo Securities, LLC \(incorporated by reference to Exhibit 1.2 to the Company's Registration Statement on Form S-3 \(File No. 333-260069\), filed with the Securities and Exchange Commission on October 5, 2021\).](#)
- 10.17 [Amendment No. 1 to Sales Agreement, dated March 30, 2022, by and among the Company, Goldman Sachs & Co. LLC, SVB Securities LLC and Wells Fargo Securities, LLC \(incorporated by reference to Exhibit 10.19 to the Company's Annual Report on Form 10-K \(File No. 001-39536\), filed with the Securities and Exchange Commission on March 31, 2022\).](#)
- 10.18 [Option Agreement, by and between the Company and Astellas, dated October 21, 2022 \(incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K \(File No. 001-39536\), filed with the Securities and Exchange Commission on October 31, 2022\).](#)
- 10.19 [Securities Purchase Agreement, by and between the Company and Astellas, dated October 21, 2022 \(incorporated by reference to Exhibit 10.2 to the Company's Current Report on Form 8-K \(File No. 001-39536\), filed with the Securities and Exchange Commission on October 31, 2022\).](#)
- 10.20 [Registration Rights Agreement, by and between the Company and Astellas, dated October 21, 2022 \(incorporated by reference to Exhibit 10.3 to the Company's Current Report on Form 8-K \(File No. 001-39536\), filed with the Securities and Exchange Commission on October 31, 2022\).](#)
- 10.21+ [Executive Employment Agreement, effective as of December 30, 2022, by and between the Company and Sean Nolan \(incorporated by reference to Exhibit 10.23 to the Company's Annual Report on Form 10-K \(File No. 001-39536\), filed with the Securities and Exchange Commission on March 28, 2023\).](#)
- 10.22+ [Executive Employment Agreement, effective as of December 30, 2022, by and between the Company and Sukumar Nagendran \(incorporated by reference to Exhibit 10.24 to the Company's Annual Report on Form 10-K \(File No. 001-39536\), filed with the Securities and Exchange Commission on March 28, 2023\).](#)
- 10.23 [Loan and Security Agreement, dated November 13, 2023 by and among the Company, and the lenders from time to time party thereto as lenders, and Trinity Capital, Inc. as administrative agent and collateral agent \(incorporated by reference to Exhibit 10.2 to the Company's Quarterly Report on Form 10-Q \(File No. 001-39536\) filed with the Securities and Exchange Commission on November 14, 2023\).](#)
- 10.24+ [Taysha Gene Therapies, Inc. 2023 Inducement Plan \(incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K \(File No. 001-39536\) filed with the Securities and Exchange Commission on December 20, 2023\).](#)

10.25+	Form of RSU Award Grant Notice and RSU Award Agreement under the 2023 Inducement Plan (incorporated by reference to Exhibit 10.2 to the Company's Current Report on Form 8-K (File No. 001-39536) filed with the Securities and Exchange Commission on December 20, 2023).
10.26+	Form of Stock Option Grant Notice and Stock Option Agreement under the 2023 Inducement Plan (incorporated by reference to Exhibit 10.3 to the Company's Current Report on Form 8-K (File No. 001-39536) filed with the Securities and Exchange Commission on December 20, 2023).
10.27	Amendment to 2023 Inducement Plan (incorporated by reference to Exhibit 99.6 to the Company's Registration Statement on Form S-8 (File No. 333-284167) filed with the Securities and Exchange Commission on January 7, 2025).
19.1*	Insider Trading Policy
23.1*	Consent of Deloitte & Touche LLP
24.1*	Power of Attorney (included on signature page)
31.1*	Certification of Principal Executive Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
31.2*	Certification of Principal Financial Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
32.1*##	Certification of Principal Executive Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
32.2*##	Certification of Principal Financial Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
97.1	Taysa Gene Therapies, Inc. Incentive Compensation Recoupment Policy (incorporated by reference to Exhibit 97.1 to the Company's Annual Report on Form 10-K (File No. 001-39536), filed with the Securities and Exchange Commission on March 19, 2024).
101.INS	Inline XBRL Instance Document – the instance document does not appear in the Interactive Data File because XBRL tags are embedded within the Inline XBRL document.
101.SCH	Inline XBRL Taxonomy Extension Schema Document
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document
101.LAB	Inline XBRL Taxonomy Extension Label Linkbase Document
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document
104	Cover Page Interactive Data File (embedded within Inline XBRL document)

* Filed herewith.

† Portions of this agreement (indicated by asterisks) have been omitted because the registrant has determined they are not material and would likely cause competitive harm to the registrant if publicly disclosed.

Certain schedules to this agreement have been omitted in accordance with Item 601(b)(2) of Regulation S-K. A copy of any omitted schedules will be furnished supplementally to the SEC upon request.

+ Indicates management contract or compensatory plan.

These certifications are being furnished solely to accompany this annual report pursuant to 18 U.S.C. Section 1350, and are not being filed for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, and are not to be incorporated by reference into any filing of the registrant, whether made before or after the date hereof, regardless of any general incorporation language in such filing.

Item 16. Form 10-K Summary

Not applicable.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

TAYSHA GENE THERAPIES, INC.

Date: February 26, 2025

By: /s/ Sean Nolan

Sean Nolan
Chief Executive Officer

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Sean Nolan and Kamran Alam, jointly and severally, as his or her true and lawful attorneys-in-fact and agents, with full power of substitution and resubstitution, for him or her and in his or her name, place and stead, in any and all capacities, to sign this Annual Report on Form 10-K of Taysha Gene Therapies, Inc., and any or all amendments thereto, 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 or necessary to be done in and about the premises hereby ratifying and confirming all that said attorneys-in-fact and agents, or his, her 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 report has been signed below by the following persons on behalf of the registrant and in the capacities and on the dates indicated.

<u>Signature</u>	<u>Title</u>	<u>Date</u>
<u>/s/ Sean Nolan</u> Sean Nolan	Chief Executive Officer and Director <i>(Principal Executive Officer)</i>	<u>February 26, 2025</u>
<u>/s/ Kamran Alam</u> Kamran Alam	Chief Financial Officer <i>(Principal Financial Officer and Principal Accounting Officer)</i>	<u>February 26, 2025</u>
<u>/s/ Phillip B. Donenberg</u> Phillip B. Donenberg	Director	<u>February 26, 2025</u>
<u>/s/ Sean Stalfort</u> Sean Stalfort	Director	<u>February 26, 2025</u>
<u>/s/ Sukumar Nagendran, M.D.</u> Sukumar Nagendran, M.D.	Director	<u>February 26, 2025</u>
<u>/s/ Alison Long, M.D., Ph.D.</u> Alison Long, M.D., Ph.D.	Director	<u>February 26, 2025</u>
<u>/s/ Laura Sepp-Lorenzino, Ph.D.</u> Laura Sepp-Lorenzino, Ph.D.	Director	<u>February 26, 2025</u>

TAYSHA GENE THERAPIES, INC.

INSIDER TRADING POLICY

AMENDED AND RESTATED ON MARCH 8, 2024

INTRODUCTION

This policy determines acceptable transactions in the securities of Taysha Gene Therapies, Inc. (the “*Company*”) by our employees, directors and consultants. During the course of your employment, directorship or consultancy with the Company, you may receive important information that is not yet publicly available about the Company or about other publicly-traded companies with which the Company has business dealings (“*inside information*”). Because of your access to this inside information, you may be in a position to profit financially by buying or selling, or in some other way dealing, in the Company’s stock, or stock of another publicly-traded company, or to disclose such information to a third party who does so profit (a “*tippee*”).

INSIDER TRADING POLICY

- A. **Securities Transactions.** Use of inside information by someone for personal gain, or to pass on, or “tip,” the inside information to someone who uses it for personal gain, is illegal, regardless of the quantity of shares, and is therefore prohibited. You can be held liable both for your own transactions and for transactions effected by a tippee, or even a tippee of a tippee. Furthermore, it is important that the appearance of insider trading in securities be avoided. The only exception is that transactions directly with the Company, e.g., option exercises for cash or purchases under the Company’s employee stock purchase plan, are permitted. However, the subsequent sale (including the sale of shares in a cashless exercise program) or other disposition of such stock is fully subject to these restrictions.
- B. **Inside Information.** As a practical matter, it is sometimes difficult to determine whether you possess inside information. The key to determining whether nonpublic information you possess about a public company is inside information is whether dissemination of the information would likely affect the market price of the company’s stock or would likely be considered important, or “material,” by investors who are considering trading in that company’s stock. Certainly, if the information makes **you** want to trade, it would probably have the same effect on others. Remember, both positive and negative information can be material. If you possess inside information, you may not trade in a company’s stock, advise anyone else to do so or communicate the information to anyone else until you know that the information has been publicly disseminated. This means that in some circumstances, you may have to forego a proposed transaction in a company’s securities even if you planned to execute the transaction prior to learning of the inside information and even though you believe you may suffer an economic loss or sacrifice an anticipated profit by waiting. “*Trading*” includes engaging in short
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sales, transactions in put or call options, hedging transactions and other inherently speculative transactions.

There is no bright-line standard for assessing materiality; rather, materiality is based on an assessment of all of the facts and circumstances, and is often evaluated by relevant enforcement authorities with the benefit of hindsight. Although by no means an all-inclusive list, information about the following items may be considered to be inside information until it is publicly disseminated:

1. financial results or forecasts;
2. communications with government agencies, such as the FDA;
3. strategic plans;
4. discovery and development of new product candidates and new technology;
5. details or results of clinical trials of the Company's product candidates;
6. significant changes or developments in suppliers;
7. acquisitions or dispositions of assets, divisions, companies, etc.;
8. pending public or private sales of debt or equity securities;
9. declaration of stock splits, dividends or changes in dividend policy;
10. major contract awards or cancellations;
11. significant regulatory or legislative developments;
12. major new drugs, processes or services, or many developments related to the same;
13. top management or control changes;
14. possible tender offers or proxy fights;
15. significant writeoffs;
16. actual or threatened significant litigation, or the resolution of such litigation;
17. impending bankruptcy of the Company or its key collaborators or partners;
18. gain or loss of significant partners, customers or suppliers;
19. pricing changes or discount policies;

20. establishment of or developments related to corporate partner relationships, strategic partnerships, joint ventures or other collaborations; and
21. notice of issuance of patents.

For information to be considered publicly disseminated, it must be widely disclosed through a press release or SEC filing, and a sufficient amount of time must have passed to allow the information to be fully disclosed. Generally speaking, information will be considered publicly disseminated after two full trading days have elapsed since the date of public disclosure of the information. For example, if an announcement of inside information of which you were aware was made prior to trading on Wednesday, then you may execute a transaction in the Company's securities on Friday.

STOCK TRADING BY DIRECTORS, OFFICERS AND OTHER EMPLOYEES

Because the officers and directors and certain members of management of the Company are the most visible to the public and are most likely, in the view of the public, to possess inside information about the Company, we require them to do more than refrain from insider trading and require that they notify, and receive approval from, a Clearing Officer (as defined below) prior to engaging in transactions in the Company's stock and observe other restrictions designed to minimize the risk of apparent or actual insider trading.

A. Covered Insiders. The provisions outlined in this stock trading policy apply to all directors, officers and employees of the Company. Generally, any entities or family members whose trading activities are controlled or influenced by any of such persons should be considered to be subject to the same restrictions.

B. Trading Blackouts. From time to time, an event may occur that is material to the Company and is known by only a few directors, officers and/or employees. So long as the event remains material and nonpublic, the persons designated by the Chief Executive Officer or Chief Financial Officer may not trade in the Company's securities. In that situation, the Company will notify the designated individuals that neither they nor their Related Persons may trade in the Company's securities. The existence of an event-specific trading blackout should also be considered material nonpublic information and should not be communicated to any other person. Even if you have not been designated as a person who should not trade due to an event-specific trading blackout, you should not trade while aware of material nonpublic information. Exceptions will not be granted during an event-specific trading blackout.

The event-driven trading blackouts do not apply to those transactions to which this policy does not apply, as described under the heading "Exceptions to Trading Blackouts" below.

As of the effective date of this policy, the Company has not instituted an earnings window period. In the event the Company institutes an earnings window period after the effective date of this policy, subject to certain exceptions, officers, directors and employees will be permitted to trade only during a "*window period*" that opens after a specified number of trading days have elapsed after the public dissemination of the Company's annual or quarterly financial results and closes a specified number of days before the end of the quarter.

C. Exceptions to Trading Blackouts.

1. **Option Exercises.** Directors, officers and employees may exercise options for cash granted under the Company's stock option plans without restriction. However, the subsequent **sale** of the stock (including sales of stock in a cashless exercise) acquired upon the exercise of options is subject to all provisions of this policy.

2. **Tax Withholding Transactions.** This Policy does not apply to the surrender of shares directly to the Company to satisfy tax withholding obligations as a result of the issuance of shares upon vesting or exercise of restricted stock units, options or other equity awards granted under the Company's equity compensation plans. Of course, any market sale of the stock received upon exercise or vesting of any such equity awards remains subject to all provisions of this Policy whether or not for the purpose of generating the cash needed to pay the exercise price or pay taxes.

3. **ESPP.** This policy does not apply to the purchase of stock by employees under the Company's Employee Stock Purchase Plan ("**ESPP**") on periodic designated dates in accordance with the ESPP. This policy does, however, apply to any sale of stock acquired pursuant to the ESPP.

4. **10b5-1 Automatic Trading Programs.** In addition, purchases or sales of the Company's securities made pursuant to, and in compliance with, a written plan established by a director or employee (a "**Trading Plan**") that meets the requirements of Rule 10b5-1 under the Securities Exchange Act of 1934, as amended (the "**Exchange Act**") may be made without restriction to any particular period provided that the Trading Plan is properly established. To be properly established, a Trading Plan must be established in compliance with the requirements of Rule 10b5-1 of the Exchange Act and any applicable 10b5-1 trading plan guidelines of the Company. Moreover, all Trading Plans must be reviewed and approved by the Company before being established to confirm that the Trading Plan complies with all pertinent Company policies and applicable securities laws. The Company must be notified of the establishment of any such Trading Plan, any amendments to such Trading Plan and the termination of such Trading Plan.

5. **Gifts.** This Policy does not apply to *bona fide* gifts of Company securities that have been pre-cleared by the Clearing Officer or his designee. Whether a gift is truly *bona fide* will depend on the facts and circumstances surrounding each gift. Pre-clearance must be obtained at least two business days in advance of the proposed gift, and pre-cleared gifts not completed within five business days will require new pre-clearance. The Company may choose to shorten this period.

D. Pre-Clearance and Advance Notice of Transactions. In addition to the requirements of paragraph B above, officers and directors may not engage in any transaction in the Company's securities, including any purchase or sale in the open market, loan, or other transfer of beneficial ownership without first obtaining pre-clearance of the transaction from the Company's Chief Financial Officer or his designee (each, a "**Clearing Officer**") at least two business days in advance of the proposed transaction. The Clearing Officer will then determine whether the transaction may proceed and, if so, will direct the Compliance Officer (as identified in the Company's Section 16 Compliance Program) to assist in complying with the reporting requirements under Section 16(a) of the Exchange Act, if any. Pre-cleared transactions not

completed within ten business days shall require new pre-clearance under the provisions of this paragraph. The Company may, at its discretion, shorten such period of time.

Advance notice of gifts or an intent to exercise an outstanding stock option shall be given to a Clearing Officer. To the extent possible, advance notice of upcoming transactions to be effected pursuant to an established Trading Plan under Section III.C.2 above shall also be given to a Clearing Officer. Upon completion of any transaction, the officer or director or other member of management must immediately notify the Compliance Officer and any other individuals identified in Section 3 of the Company's Section 16 Compliance Program so that the Company may assist in any Section 16 reporting obligations.

E. Prohibition of Speculative or Short-term Trading. No employee or director may engage in short sales, transactions in put or call options, hedging transactions, margin accounts or other inherently speculative transactions with respect to the Company's stock at any time.

F. Short-Swing Trading/Control Stock/Section 16 Reports. Officers and directors subject to the reporting obligations under Section 16 of the Exchange Act should take care not to violate the prohibition on short-swing trading (Section 16(b) of the Exchange Act) and the restrictions on sales by control persons (Rule 144 under the Securities Act of 1933, as amended), and should file all appropriate Section 16(a) reports (Forms 3, 4 and 5), which are enumerated and described in the Company's Section 16 Compliance Program, and any notices of sale required by Rule 144.

G. Prohibition of Trading During Pension Fund Blackouts. In accordance with Regulation BTR under the Exchange Act, no director or executive officer of the Company shall, directly or indirectly, purchase, sell or otherwise acquire or transfer any equity security of the Company (other than an exempt security) during any "blackout period" (as defined in Regulation BTR) with respect to such equity security, if such director or executive officer acquires or previously acquired such equity security in connection with his or her service or employment as a director or executive officer. This prohibition shall not apply to any transactions that are specifically exempted from Section 306(a)(1) of the Sarbanes-Oxley Act of 2002 (as set forth in Regulation BTR), including but not limited to, purchases or sales of the Company's securities made pursuant to, and in compliance with, a Trading Plan; compensatory grants or awards of equity securities pursuant to a plan that, by its terms, permits executive officers and directors to receive automatic grants or awards and specifies the terms of the grants and awards; acquisitions or dispositions of equity securities involving a bona fide gift or by will or the laws of descent or pursuant to a domestic relations order; etc. The Company shall timely notify each director and executive officer of any blackout periods in accordance with the provisions of Regulation BTR.

DURATION OF POLICY'S APPLICABILITY

This policy continues to apply to your transactions in the Company's stock or the stock of other public companies engaged in business transactions with the Company even after your employment or directorship with the Company has terminated. If you are in possession of inside information when your relationship with the Company concludes, you may not trade in the Company's stock or the stock of such other company until the information has been publicly disseminated or is no longer material.

INDIVIDUAL RESPONSIBILITY

Persons subject to this Policy have ethical and legal obligations to maintain the confidentiality of information about the Company and to not engage in transactions in the Company's securities while aware of material nonpublic information. Each individual is responsible for making sure that he or she complies with this Policy, and that any family member, household member or other person or entity whose transactions are subject to this Policy, as discussed under the heading "Persons Subject to this Policy" above, also comply with this Policy. In all cases, the responsibility for determining whether an individual is aware of material nonpublic information rests with that individual, and any action on the part of the Company or any employee or director of the Company pursuant to this Policy (or otherwise) does not in any way constitute legal advice or insulate an individual from liability under applicable securities laws. You could be subject to severe legal penalties and disciplinary action by the Company for any conduct prohibited by this Policy or applicable securities laws. See "Penalties" below.

PENALTIES

Anyone who effects transactions in the Company's stock or the stock of other public companies engaged in business transactions with the Company (or provides information to enable others to do so) on the basis of inside information is subject to both civil liability and criminal penalties, as well as disciplinary action by the Company. An employee, director or consultant who has questions about this policy should contact his or her own attorney or the Clearing Officer of the Company.

AMENDMENTS

The Company is committed to continuously reviewing and updating its policies and procedures. The Company therefore reserves the right to amend, alter or terminate this Policy at any time and for any reason. A current copy of the Company's policies regarding insider trading may be obtained by contacting the Compliance Officer.

TAYSHA GENE THERAPIES, INC.
INSIDER TRADING POLICY
CERTIFICATION

To: Taysha Gene Therapies, Inc.

I, _____, have received and read a copy of the Taysha Gene Therapies, Inc. Insider Trading Policy. I hereby agree to comply with the specific requirements of the policy in all respects during my employment or other service relationship with Taysha Gene Therapies, Inc. I understand that this policy constitutes a material term of my employment or other service relationship with Taysha Gene Therapies, Inc. (or a subsidiary thereof) and that my failure to comply in all respects with the policy is a basis for termination for cause.

(Signature)

(Name)

(Date)

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We consent to the incorporation by reference in Registration Statement Nos. 333-260069, 333-271144 and 333-274264 on Form S-3 and Registration Statement Nos. 333-249130, 333-256013, 333-264025, 333-270915 and 333-276161 on Form S-8 of our report dated February 26, 2025, relating to the financial statements of Taysha Gene Therapies, Inc. appearing in this Annual Report on Form 10-K for the year ended December 31, 2024.

/s/ DELOITTE & TOUCHE LLP

Dallas, Texas
February 26, 2025

**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, Sean Nolan, certify that:

1. I have reviewed this Annual Report on Form 10-K of Taysha Gene Therapies, Inc.;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) 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(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
 - (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
 - (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: February 26, 2025

By: _____ /s/ Sean Nolan
Sean Nolan
Chief Executive Officer
(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, Kamran Alam, certify that:

1. I have reviewed this Annual Report on Form 10-K of Taysha Gene Therapies, Inc.;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) 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(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
 - (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
 - (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: February 26, 2025

By: _____
/s/ Kamran Alam
Kamran Alam
Chief Financial Officer
(Principal Financial Officer and Principal Accounting Officer)

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

Pursuant to the requirement set forth in Rule 13a-14(b) of the Securities Exchange Act of 1934, as amended (the “Exchange Act”) and Section 1350 of Chapter 63 of Title 18 of the United States Code (18 U.S.C. §1350), Sean Nolan, Chief Executive Officer of Taysha Gene Therapies, Inc. (the “Company”) hereby certifies that, to the best of his knowledge:

- (1) The Company’s Annual Report on Form 10-K for the period ended December 31, 2024, to which this Certification is attached as Exhibit 32.1 (the “Annual Report”), fully complies with the requirements of Section 13(a) or Section 15(d) of the Exchange Act; and
- (2) The information contained in the Annual Report fairly presents, in all material respects, the financial condition and result of operations of the Company.

Date: February 26, 2025

By: _____ /s/ Sean Nolan
Sean Nolan
Chief Executive Officer
(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**

Pursuant to the requirement set forth in Rule 13a-14(b) of the Securities Exchange Act of 1934, as amended (the “Exchange Act”) and Section 1350 of Chapter 63 of Title 18 of the United States Code (18 U.S.C. §1350), Kamran Alam, Chief Financial Officer of Taysha Gene Therapies, Inc. (the “Company”) hereby certifies that, to the best of his knowledge:

- (1) The Company’s Annual Report on Form 10-K for the period ended December 31, 2024, to which this Certification is attached as Exhibit 32.2 (the “Annual Report”), fully complies with the requirements of Section 13(a) or Section 15(d) of the Exchange Act; and
- (2) The information contained in the Annual Report fairly presents, in all material respects, the financial condition and result of operations of the Company.

Date: February 26, 2025

By: _____ /s/ Kamran Alam
Kamran Alam
Chief Financial Officer
(Principal Financial Officer and Principal Accounting Officer)
