Taysha Announces Exclusive Option from UTSW to License Worldwide Rights to Clinical-Stage AAV9 Gene Therapy Program for CLN7 Disease, a Research Collaboration with UTSW to Develop Next-Generation Construct for CLN7 and a Grant Award to Batten Hope

CLN7 program currently in Phase 1 clinical proof-of-concept trial with preliminary data anticipated by year-end 2021

Intrathecal dosing of the high dose first-generation construct resulted in nearly complete normalization of impaired open field and motor function and more than doubled median life expectancy in MSFSD8 knockout mice; data to be presented at upcoming 17th Annual International Congress on Neuronal Ceroid Lipofuscinosis

Taysha also enters into a research collaboration with UT Southwestern to develop next-generation construct for CLN7 disease, which is expected to improve potency, safety profile, packaging efficiency and manufacturability over first-generation construct

Initiation of a planned pivotal CLN7 clinical trial with next-generation construct anticipated in 2022, with reference to human proof-of-concept data generated from first-generation construct

Provides a grant to Batten Hope, the leading CLN7 patient advocacy group, to support patient awareness, disease education and newborn screening initiatives

Estimated prevalence of CLN7 disease is 4,000 patients worldwide

Taysha expected to have five clinical stage programs by year-end 2021

Webcast today at 8:00 AM Eastern Time

DALLAS--(BUSINESS WIRE)--Oct. 5, 2021-- Taysha Gene Therapies, Inc. (Nasdaq: TSHA), a patient-centric, pivotal-stage gene therapy company focused on developing and commercializing AAV-based gene therapies for the treatment of monogenic diseases of the central nervous system (CNS) in both rare and large patient populations, today announced that it has obtained an exclusive option from UT Southwestern (UTSW) to license worldwide rights to a clinical-stage AAV9 gene therapy replacement program for the treatment of CLN7 disease. The company has also entered into a research collaboration with UTSW to develop a next-generation construct for the treatment of CLN7 disease, which is expected to improve potency, safety profile, packaging efficiency and manufacturability over the first-generation construct. Completion of the next-generation construct design is anticipated by year-end 2021, with commercial-grade GMP material expected in 2022.

The first-generation construct for the CLN7 program was developed in the laboratory of Steven Gray, Ph.D., Associate Professor at UT Southwestern Medical Center and Chief Scientific Advisor for Taysha, with financial support from Mila's Miracle and Batten Hope, the leading CLN7 patient advocacy groups. The CLN7 program is currently in a Phase 1 clinical proof-of-concept trial run by UTSW, and Taysha expects the availability of preliminary human proof-of-concept clinical safety and efficacy data from the first-generation construct by year-end 2021. Taysha intends to initiate a planned pivotal trial using a next-generation construct in 2022, with reference to the human proof-of-concept clinical data being generated from the first-generation construct.

In addition, Taysha has provided a grant to Batten Hope to support patient awareness, disease education and newborn screening initiatives.

CLN7 disease is a rare, fatal and rapidly progressive neurodegenerative disease that is a form of Batten disease. CLN7 is caused by autosomal recessive mutations in the *MFSD8* gene that results in lysosomal dysfunction. Disease onset occurs around two to five years of age, with death often ensuing in young adolescence. Patients experience gradual nerve cell loss in certain parts of the brain and typically present with seizures, vision loss, speech impairment and mental and motor regression. Currently, there are no approved therapies to treat CLN7 disease, which impacts an estimated 4,000 patients globally.

Preclinical data in rodents supported advancement of the first-generation construct into a Phase 1 clinical proof-of-concept study in patients with CLN7 disease. In an *in vivo* efficacy study, intrathecal (IT) administration of the first-generation construct to MFSD8 knockout mice with high or low doses resulted in clear age and dose effects with early intervention and high dose achieving the best therapeutic benefits. IT high dose of the first-generation construct in younger knockout mice resulted in: 1) widespread MFSD8 mRNA expression in all tissues assessed; 2) nearly complete normalization of impaired open field and rotarod performance at 6 and 9 months post injection; 3) more than doubled median life expectancy (16.82 months versus 7.77 months in untreated knockout mice); and 4) maintained healthy body weight for a prolonged period of time. Toxicology studies in wild type rodents demonstrated safety and tolerability of IT administration of the first-generation construct. These preclinical data will be presented by Xin Chen, Ph.D., Assistant Professor, Department of Pediatrics at UT Southwestern, in an oral presentation at the 17th Annual International Congress on Neuronal Ceroid Lipofuscinosis on October 8, 2021.

"The CLN7 program is a strategic addition to our gene therapy pipeline focused on monogenic CNS diseases. Encouraging preclinical data generated in relevant rodent models suggest that the first-generation construct has the potential to reduce overall disease pathology, preserve motor function and ultimately prolong survival," said RA Session II, President, Founder and Chief Executive Officer of Taysha. "The first-generation construct is currently in a Phase 1 clinical proof-of-concept trial with two patients dosed to date, and we look forward to the availability of preliminary data by year-end. With human proof-of-concept clinical data to reference, we expect to advance a next-generation construct into a planned pivotal trial in 2022, which we anticipate should improve potency, safety, packaging efficiency and manufacturability over the first-generation construct. Importantly, we are also pleased to announce our grant to Batten Hope, the leading CLN7 disease nonprofit patient advocacy organization, to support patient awareness, disease education and newborn screening initiatives. We believe a gene therapy approach has the potential to address a significant unmet need in an estimated 4,000 patients globally."

Gina Hann, Batten Hope Founder, President and Treasurer, added, “Our mission is to support families with children suffering from terminal and rapidly progressive neurodegenerative diseases like CLN7. We are honored to receive Taysha’s support to raise awareness, increase newborn screening and help patients gain access to potentially transformative treatments that offer hope and therapeutic advancement for conditions with significant unmet needs.”

UTSW is currently enrolling patients in an investigator-sponsored Phase 1 open-label, dose escalation clinical proof-of-concept trial at Dallas Children’s Hospital for an intrathecally dosed AAV9-based gene replacement therapy for the treatment of infantile CLN7 disease. The primary endpoint of the trial is safety and tolerability by incidence and severity of treatment related serious adverse events. Secondary efficacy endpoints include the Clinical Global Impression, neuropsychological, ataxia and motor function assessments and quality of life. The design rationale and a discussion of outcome measures for this clinical trial will be presented as a poster at the upcoming 17th Annual International Congress on Neuronal Ceroid Lipofuscinosis. To date, one patient has been dosed at 5x10^{14} total vg and a second patient was dosed at 1x10^{15} total vg as measured by the qPCR method. UTSW continues to enroll patients in this Phase 1 study at 1x10^{15} total vg and expects to dose additional patients in the near term. Preliminary safety and efficacy data are expected by the end of 2021.

With the addition of the CLN7 program, Taysha expects to have five clinical stage programs by year-end. As such, the TSHA-104 program for the treatment of SURF1-associated Leigh syndrome will transition to the company’s collaborators at UTSW to complete IND-enabling studies, followed by a planned investigator-initiated clinical trial by the end of 2022. Taysha will continue to support the SURF1 natural history study in partnership with UTSW.

Financial terms of the agreements were not disclosed.

Webcast Information

Taysha management will host a webcast today at 8:00 am ET / 7:00 am CT to discuss today’s news. To participate, please access the following link: http://lifesci.rampard.com/WebcastingAppv5/Events/eventsDispatcher.jsp?Y2lk=MTQ1MQ==. The live webcast and replay may also be accessed by visiting Taysha’s website at https://ir.tayshagtx.com/news-events/events-presentations. An archived version of the webcast will be available on the website for 60 days.

About Taysha Gene Therapies

Taysha Gene Therapies (Nasdaq: TSHA) is on a mission to eradicate monogenic CNS disease. With a singular focus on developing curative medicines, we aim to rapidly translate our treatments from bench to bedside. We have combined our team’s proven experience in gene therapy drug development and commercialization with the world-class UT Southwestern Gene Therapy Program to build an extensive, AAV gene therapy pipeline focused on both rare and large-market indications. Together, we leverage our fully integrated platform—an engine for potential new cures—with a goal of dramatically improving patients’ lives. More information is available at www.tayshagtx.com.

Forward-Looking Statements

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. Words such as “anticipates,” “believes,” “expects,” “intends,” “projects,” and “future” or similar expressions are intended to identify forward-looking statements. Forward-looking statements include statements concerning the potential of our product candidates, as well as the CLN7 program, to positively impact quality of life and alter the course of disease in the patients we seek to treat, our expectations regarding the benefits of a next-generation construct for CLN7, our research, development and regulatory plans for our product candidates, the potential for these product candidates to receive regulatory approval from the FDA or equivalent foreign regulatory agencies, and whether, if approved, these product candidates will be successfully distributed and marketed, and the potential market opportunity for these product candidates. Forward-looking statements are based on management’s current expectations and are subject to various risks and uncertainties that could cause actual results to differ materially and adversely from those expressed or implied by such forward-looking statements. Accordingly, these forward-looking statements do not constitute guarantees of future performance, and you are cautioned not to place undue reliance on these forward-looking statements. Risks regarding our business are described in detail in our Securities and Exchange Commission (“SEC”) filings, including in our Annual Report on Form 10-K for the full-year ended December 31, 2020, and our Quarterly Report on Form 10-Q for the quarter ended June 30, 2021, both of which are available on the SEC’s website at www.sec.gov. Additional information will be made available in other filings that we make from time to time with the SEC. Such risks may be amplified by the impacts of the COVID-19 pandemic. These forward-looking statements speak only as of the date hereof, and we disclaim any obligation to update these statements except as may be required by law.

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