

Press Release

Gene Therapy Research Institution and Astellas Executes Option Agreement for Sporadic ALS Gene Therapy Program

TOKYO, September 14, 2018 –Gene Therapy Research Institution Co., Ltd. (head office: Kawasaki, Kanagawa; President: Katsuhito Asai, “GTRI”) and Astellas Pharma Inc. (TSE: 4503, head office: Tokyo, President and CEO: Kenji Yasukawa, Ph.D., “Astellas”) today announced that they have entered into an option agreement for the exclusive negotiation of rights to global development and commercialization of the gene therapy program GT0001X for the treatment of sporadic amyotrophic lateral sclerosis (ALS)¹.

ALS is a neurodegenerative disorder that selectively impairs motor neurons, gradually leading to a decrease and loss in strength of muscles in the limbs, throat, tongue, and those required for respiration. There are an estimated 55,000 patients with ALS in Japan, the United States, and the EU5 countries (United Kingdom, Germany, France, Spain, and Italy). The prevalence rate in patients ≥ 60 years of age is as many as 20 to 30 per 100,000 people. The cause of ALS is unknown and no effective therapy to stop the progression of this disease has been established. In patients with sporadic ALS, which accounts for $\geq 90\%$ of the whole ALS population, decreased activity of adenosine deaminase acting on RNA 2 (ADAR2)², an RNA-editing enzyme, has been reported to be a possible cause of the disease.

GT0001X is a modified adeno-associated virus (mAAV) vector expressing human ADAR2. In conditional ADAR2 knockout mice, degeneration of anterior horn cells and the resulting motor dysfunction were prevented by mAAV-mediated delivery of ADAR2³. Currently, GTRI has been developing GT0001X in the pre-clinical stage for the treatment of sporadic ALS. In the future, the clinical efficacy and safety will be investigated.

“Gene therapy using AAV vectors is about to enter the era of full-scale development in all over the world,” said Shin-ichi Muramatsu, MD, Ph.D., Chief Scientific Officer of GTRI. “This gene therapy is highly safe, and widely applicable especially in the field of neurodegenerative diseases and congenital metabolic diseases. GTRI is developing it for many indications. We will conduct clinical trials for sporadic ALS, which is a serious neurodegenerative disease currently without definitive treatment, as our first step. Taking this opportunity, I would like to accelerate development of other programs as well for patients suffering from intractable diseases.”

“This agreement demonstrates Astellas’ commitment to actively looking to turn state-of-the-art scientific and technological advances into VALUE for patients,” said Naoki Okamura, Chief Strategy Officer, Astellas. “Astellas is continuously making efforts to develop medical solutions and new drugs in focused therapeutic areas with high unmet medical needs, an approach that includes collaborating with external partners

performing cutting-edge science. With this agreement, we endeavor to potentially deliver a novel treatment for patients suffering from ALS.”

Astellas reflected the impact from this agreement in its financial forecasts of the current fiscal year ending March 31, 2019.

(1) **Sporadic amyotrophic lateral sclerosis:** There are familial ALS in which ALS patients exist in the blood relatives. It is said that the familial ALS is about 10% of the ALS patient, and the remaining 90% is sporadic ALS

(2) **ADAR2 (Adenosine deaminases acting on RNA2):** ADAR2 is an RNA-editing enzyme that binds double-stranded RNA and converts adenosine to inosine

(3) **EMBO Mol Med. 2013 Nov, vol. 5, no.11, p. 1710-1719.**

About GTRI

Gene Therapy Research Institution Co., Ltd., based in Kawasaki, Japan, is a biotech company dedicated to development of AAV vector-mediated gene therapy for intractable diseases. For more information, please visit our website at <http://www.en.genetherapy-ri.com/>

About Astellas

Astellas Pharma Inc., based in Tokyo, Japan, is a company dedicated to improving the health of people around the world through the provision of innovative and reliable pharmaceutical products. For more information, please visit our website at <https://www.astellas.com/en>

Cautionary Notes

In this press release, statements made with respect to current plans, estimates, strategies and beliefs and other statements that are not historical facts are forward-looking statements about the future performance of Astellas. These statements are based on management’s current assumptions and beliefs in light of the information currently available to it and involve known and unknown risks and uncertainties. A number of factors could cause actual results to differ materially from those discussed in the forward-looking statements. Such factors include, but are not limited to: (i) changes in general economic conditions and in laws and regulations, relating to pharmaceutical markets, (ii) currency exchange rate fluctuations, (iii) delays in new product launches, (iv) the inability of Astellas to market existing and new products effectively, (v) the inability of Astellas to continue to effectively research and develop products accepted by customers in highly competitive markets, and (vi) infringements of Astellas’ intellectual property rights by third parties.

Information about pharmaceutical products (including products currently in development) which is included in this press release is not intended to constitute an advertisement or medical advice.

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Contacts for inquiries or additional information:

Gene Therapy Research Institution Co., Ltd
HR & General Affairs Department
TEL: +81-44-589-5900 FAX: +81-44-589-5901

Astellas Pharma Inc.
Corporate Communications
TEL: +81-3-3244-3201 FAX: +81-3-5201-7473