

Agilis GTRI Japan Inc.

Agilis Biotherapeutics, LLC, a US biotechnology company developing gene therapy, has established the joint venture Agilis GTRI Japan Inc., together with the Gene Therapy Research Institution Co., Ltd., a Japanese bio-venture company. In February 2017, Agilis GTRI Japan Inc. established a R&D center for gene therapy drug in Kawasaki, Japan. Its aim is to obtain Japan's first approval of gene therapy drugs for intractable central nervous system diseases such as AADC deficiency and Parkinson's disease.

Agilis GTRI Japan Inc. (hereinafter called "AGJ"), which develops gene therapy drugs, established an R&D center in the King Skyfront area in Tonomachi, Kawasaki in February 2017. This center is located in the "Life Innovation Center," a hub for the commercialization and industrialization of regenerative medicine and cell therapy established by Kanagawa Prefecture as part of a public-private joint project.

Within the Life Innovation Center, home to a concentration of cutting-edge life science industries and research organizations, AGJ develops and manufactures adeno-associated virus (AAV) vectors¹ for gene therapy treating intractable central nervous system diseases such as AADC deficiency and Parkinson's disease. Once the AAV vector is administered to a patient, it infects the target cells, and the gene inserted in the vector works within the cells to produce a medicinal protein.



Life Innovation Center, where AGJ's office is located

Gene therapy of intractable central nervous system diseases

AADC deficiency is an autosomal recessive inherited disease where aromatic L-amino acid decarboxylase (AADC), an enzyme responsible for synthesizing the neurotransmitters, does not work due to congenital gene mutation. It causes symptoms such as insufficient autonomic function and difficulty in moving the body. It is an intractable disease and there are only around 100 reported cases in the world. Katsuhito Asai, President of AGJ, says, "There are only six known patients in Japan so far." In April 2016, the disease was included in Japan's list of intractable diseases. In contrast, there are 150,000 Parkinson's disease patients in Japan. If AGJ's gene therapy drugs are approved, it will open the way to treatment for intractable diseases for which no cure exists such as ADDC deficiency and Parkinson's disease.

Partnership with Japanese bio-venture company which has an advanced technology

The parent company, Agilis Biotherapeutics, LLC (hereinafter called "Agilis"), is a bio-venture company established in Cambridge, Massachusetts, the US in 2013. It is a world leader in the clinical development of gene therapy for AADC deficiency and has provided treatment to the largest number of patients in the world. Agilis is recognized as having the

¹ Non-pathogenic virus used for delivering the gene of interest into a target cell.

most extensive experience and advanced technologies in AADC gene therapy. In December 2015, the Gene Therapy Research Institution Co., Ltd., a Japanese bio-venture company conducting research in the same field (hereinafter called “GTRI”), offered a partnership to Agilis.

Possessing top gene therapy technology using AAV vectors, GTRI is one of only a few companies in the world developing gene therapies in the central nervous system and neurology fields. The decisive factor for Agilis in accepting the partnership with GTRI was “the pipelines² that GTRI has in Japan and the progress of their research and development of the manufacturing technology of such pipelines,” said Mr. Asai. AGJ aims to strengthen the foundation of gene therapy drug development in Asia utilizing the advanced manufacturing technologies of Japanese companies and the experience of Agilis in gene therapy. In July 2016, about a half year after the offer of partnership, a business cooperation agreement was concluded through consultation provided by JETRO, and a joint venture, AGJ, was established in August of the same year.

Incentive for setting up a R&D site in Japan

Mr. Asai said, “We had determined to form a business tie-up as GTRI offered a partnership, but I didn't expect that we could establish a joint venture so soon.” According to him, the Subsidy Program for Global Innovation Centers³ provided by JETRO played a significant role in enabling them to establish the joint venture in just a half year as the program subsidized the expenses for the establishment of the R&D center. Mr. Asai said, “In the course of discussion on the business tie-up, I was

informed by GTRI of the subsidy program supporting the regenerative medicine field. Without this subsidy, the joint venture might not have been established yet.” AGJ also utilized the National Strategic Special Zones system and municipal incentives including the “Select Kanagawa 100” program, a subsidy system to attract companies to Kanagawa Prefecture. He said, “The cost reduction at the time of establishment was very attractive.”



An air-conditioning control room in the R&D facility built with the subsidy. The facility must maintain conditions complying with the standards of manufacturing and quality management of regenerative medicine products of the subsidy.

Toward the first manufacturing of gene therapy drugs in Japan

Currently, 10 staff members, including Mr. Asai and eight researchers, are preparing for the manufacture of gene therapy drugs in the Life Innovation Center. Their first goal is to obtain approval of compliance with GCTP, a standard for manufacturing and quality management of regenerative medicine products. Mr. Asai said, “We are making every effort to prepare for obtaining approval of GCTP compliance. Without this approval, we cannot start clinical trials. As this process takes some time, we are also concurrently studying how to expand the laboratory's current manufacturing

² Drug candidates that are in the phase of either research, development, approval or marketing. Drug candidate compounds.

³ Implemented from January 2016 to March

2017 with an extra budget for fiscal 2015. It supports projects in the IoT and regenerative medicine fields where foreign companies work in collaboration with Japanese companies in Japan.

scale to a commercial production level.” Upon obtaining approval, the company will then prepare for international multicenter clinical trials in the center. Mr. Asai talked about his passion for manufacturing gene therapy drugs, saying, “Using the international multicenter clinical trial framework, we can utilize the results of trials in Japan in our application for approval in the US and Europe. The standards of most other countries are no more stringent than those of Japan. We want to make this center a regional base for Asia and Europe as well as a base of manufacturing and marketing in the future.” The company has received inquiries about the clinical trial in Japan from overseas patients eager to be considered as candidates.”

Not only is this cutting-edge treatment being developed by AGJ expected to be the sole highly-safe treatment for AADC deficiency and Parkinson’s disease, but the application of its technology is also expected to establish treatment strategies for other genetic diseases.

Detailed support by JETRO

JETRO provided the company with various services including the provision of information on subsidies, consultation on the establishment of joint ventures, introduction of an administrative procedures specialist, and arrangement for a meeting with local governments, utilizing its local network. Mr. Asai talked about JETRO's services, saying, “The staff of both the head office and the Yokohama office carefully supported us. They gave us very detailed and kind advice on the overall administrative procedures.”



Katsuhito Asai, President of Agilis GTRI Japan Inc.

(Interviewed in June 2017)

History of Agilis GTRI Japan Inc.

- 2013 Foundation of Agilis Biotherapeutics, LLC (US)
- 2014 Foundation of Gene Therapy Research Institution Co., Ltd.
- 2016 Conclusion of business cooperation agreement between Agilis Biotherapeutics, LLC and Gene Therapy Research Institution Co., Ltd
Joint foundation of Agilis GTRI Japan Inc. by the companies above.
- 2017 Establishment of R&D center in Tonomachi district of Kawasaki, Kanagawa

Agilis GTRI Japan Inc.

- Foundation: 2016
- Business overview: Research and development of gene therapy drugs for AADC deficiency and Parkinson's disease.
- Parent company Agilis Biotherapeutics, LLC
(group):
- Address: (Head office) 3-25-22, Tonomachi, Kawasaki-ku, Kawasaki, Kanagawa 210-0821, Japan

Support from JETRO

- Consultation related to the establishment of the joint venture
- Introduction of administrative procedures specialists
- Provision of information on subsidies
- Arrangement for a meeting with the Kanagawa Prefectural Government.