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News Release

Access to Health

Astellas Enters a New Collaborative Research Agreement with AIST to Discover Anti-protozoan Parasite Drugs for the Treatment of Chagas' disease, one of Neglected Tropical Diseases

Tokyo, April 1, 2016 - Astellas Pharma Inc. (TSE: 4503, President and CEO: Yoshihiko Hatanaka, "Astellas") today announced that it has signed a new collaborative research agreement with the National Institute of Advanced Industrial Science and Technology (Headquartered in Tsukuba, President: Ryoji Chubachi, "AIST") to discover anti-protozoan parasite drugs for the treatment of Chagas' disease, one of neglected tropical diseases[1)] ("NTDs").

Astellas is committed to improving "Access to Health[2)]" in the world. As part of the initiative, Astellas has been collaborating with five research institutions in Japan as well as with an international non-profit organization ("NPO") since 2012 to discover new drugs for the treatment of NTDs caused by protozoan parasites belonging to trypanosomatidae (i.e., leishmaniasis[3)], Chagas' disease[4)], and African trypanosomiasis[5)]) that represent significant unmet medical needs ("existing collaborative research").

Under this new agreement, Astellas and AIST will conduct collaborative research to discover new drugs for the treatment of Chagas' disease, using genome editing technology[6)] and a high throughput activity assay[7)] for *Trypanosoma cruzi* (the cause of the disease) that have been obtained through the existing collaborative research. As Chagas' disease is one of the most prevalent NTDs and no specific drugs are available for the disease, the discovery of new effective drugs will help to address a critical unmet need.

Astellas and AIST will work collaboratively to validate whether genes crucial for the survival of *Trypanosoma cruzi* can be pinpointed in a short period of time using gene editing technology. Astellas will mainly be responsible for selecting appropriate genes to be verified, and AIST will lead the gene editing process. After the validation in this collaborative research initiative, the formation of AIST-driven research consortium, in which multiple research institutions will participate to conduct extensive genome editing studies and pursue discovery of new drugs for the treatment of Chagas' disease in a larger framework is planned. Astellas is undergoing a review process to further assess the possibility about joining the consortium.

The existing collaborative research was terminated at the end of the current agreements, as the collaborative research failed in identifying potential compounds with appropriate profiles for the development of anti-protozoan parasite drugs due to the lack of data on target genes critical for the survival of *Trypanosoma cruzi*. Collaborative drug discovery research on anti-dengue virus with two research institutions in Japan has also been terminated, as the research failed to identify promising compounds.

Astellas will continue to be committed to enhancing Access to Health through this new collaborative research for the discovery of new drugs for patients suffering from Chagas' disease in the world.

1) Neglected tropical diseases (NTDs)

NTDs are infections caused by parasites, bacteria and viruses which are rampant mainly among underprivileged people in tropical areas of developing countries. It is estimated that over one billion people worldwide are suffering from the 17 diseases* of NTDs on which the World Health Organization is currently focused. Since these patients do not have enough access to needed medicine and healthcare, NTDs are not only a global health challenge but are said to be associated with poverty and affect economic growth in developing countries.

* List of 17 diseases : Buruli ulcer, Chagas' disease (American trypanosomiasis), cysticercosis, dengue/severe dengue, dracunculiasis (guinea-worm disease), echinococcosis, foodborne trematode infections, human African trypanosomiasis, leishmaniasis, leprosy, lymphatic filariasis, onchocerciasis, rabies, schistosomiasis, soil transmitted helminthiasis, trachoma, endemic treponematoses (including yaws)

2) Access to Health

There are many people with insufficient access to healthcare they need due to the lack of available treatments, poverty, challenges in healthcare systems and limited healthcare information. Astellas recognizes this problem as "Access to Health" issue and works to improve "Access to Health" by engaging in various initiatives.

3) Leishmaniasis

Leishmaniasis occurs in 98 countries, and 310 million people are exposed to risk worldwide. The parasite that leads to this infection is called Leishmania and is transmitted by a sandfly. Leishmaniasis is a poverty-associated disease with several different forms. Visceral leishmaniasis, which is fatal without treatment, and cutaneous leishmaniasis are the most common. Existing treatments are difficult to administer, toxic, and/or costly. Drug resistance also is an increasing problem.

4) Chagas' disease (American trypanosomiasis)

Chagas' disease is endemic in 21 countries across Latin America and kills more people in the region than any other parasite-borne disease, including malaria. More than 25 million people are at risk worldwide most of whom are living in Latin America, and patient numbers are also growing in non-endemic countries such as the United States and Australia, as well as in some European countries. The disease is transmitted by an insect known as the 'kissing bug' and, without treatment, is potentially fatal. Existing treatments are known to have serious safety limitations and their efficacy diminishes the longer the patient has been infected.

5) Sleeping sickness (African trypanosomiasis)

Sleeping sickness is endemic in 36 countries across sub-Saharan Africa and 65 million people are at risk of infection. The disease is transmitted by the tsetse fly's sucking blood. Without treatment in the initial phase, which causes general symptoms, the disease progresses to a second stage where mental debilitation occurs, and

the patient often dies within six months to three years. Although the disease is fatal if left untreated, existing treatments are toxic, difficult to administer, and/or have severe side effects.

6) Genome editing technology for *Trypanosoma cruzi*

This method uses a gene-knockout technology called the "CRISPR/Cas9 system." While gene editing in *Trypanosoma cruzi* had been quite challenging, recent research revealed that the CRISPR/Cas9 system is useful for this purpose. This has improved the feasibility of extensive analyses of gene functions using the gene knockout technology. AIST is building various platforms which enable gene editing using a high-throughput activity assay.

7) High throughput activity assay for *Trypanosoma cruzi*

When the growth of *Trypanosoma cruzi* is inhibited through genome editing or by administering compounds, *Trypanosoma cruzi* undergoes certain changes in growth rate, shape, and mobility that are visible under a microscope. AIST has an image analysis technology that quantifies the changes in appearance of microorganisms and further aims to combine this technology with automatic microscopes to assess the vitality of *Trypanosoma cruzi* using the high-throughput activity assay.

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. We focus on Urology, Oncology, Immunology, Nephrology and Neuroscience as prioritized therapeutic areas while advancing new therapeutic areas and discovery research leveraging new technologies/modalities. We are also creating new value by combining internal capabilities and external expertise in the medical/healthcare business. Astellas is on the forefront of healthcare change to turn innovative science into value for patients. For more information, please visit our website at www.astellas.com/en.

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