

Astellas Enters Collaborative New Drug Discovery Research with AIST for Neglected Tropical Diseases Caused by Protozoan Parasites

- Through Drug Design Using Fragment Evolution -

Tokyo, Japan, October 22, 2012 – Astellas Pharma Inc. (Tokyo:4503, “Astellas”) announced today that it has signed a collaborative drug discovery research agreement with the National Institute of Advanced Industrial Science and Technology (“AIST”) to efficiently discover new drugs for the treatment of neglected tropical diseases (“NTDs”)⁽¹⁾ caused by protozoan parasites.

NTDs, prevalent mainly among the poor in tropical areas of developing countries, are infectious diseases spread by parasites or bacteria. As it is estimated that approximately one billion people are affected with NTDs worldwide, NTDs are a serious healthcare issue that is being addressed on a global scale. Among them, diseases caused by protozoan parasites, such as leishmaniasis⁽²⁾, Chagas disease⁽³⁾ and sleeping sickness⁽⁴⁾ are with high unmet medical needs for treatment and development of new therapeutic drugs.

This collaborative research aims to contribute to the new drug discovery for the treatment of such diseases caused by protozoan parasites.

Astellas will use a unique drug designing method which it has developed using small molecular weight fragments (Fragment Evolution, “FE”) as a key technology in this collaborative research with AIST. FE consists of three main steps:

[Step 1: Exploration of fragment hits]

Small compounds (molecular weight of 150-300 Da) used in the FE are called “fragments”. Among these, ones efficiently interacting with target protein are fragment hits. They are selected from the Astellas’ compound library (fragment libraries) through bioassays and physicochemical analyses such as NMR (nuclear magnetic resonance). In this step, a large amount of highly purified target proteins are used.

[Step 2: Clarification of binding patterns of fragment hits]

The binding of all fragment hits to the target proteins are structurally examined by high throughput x-ray crystallographic analysis.

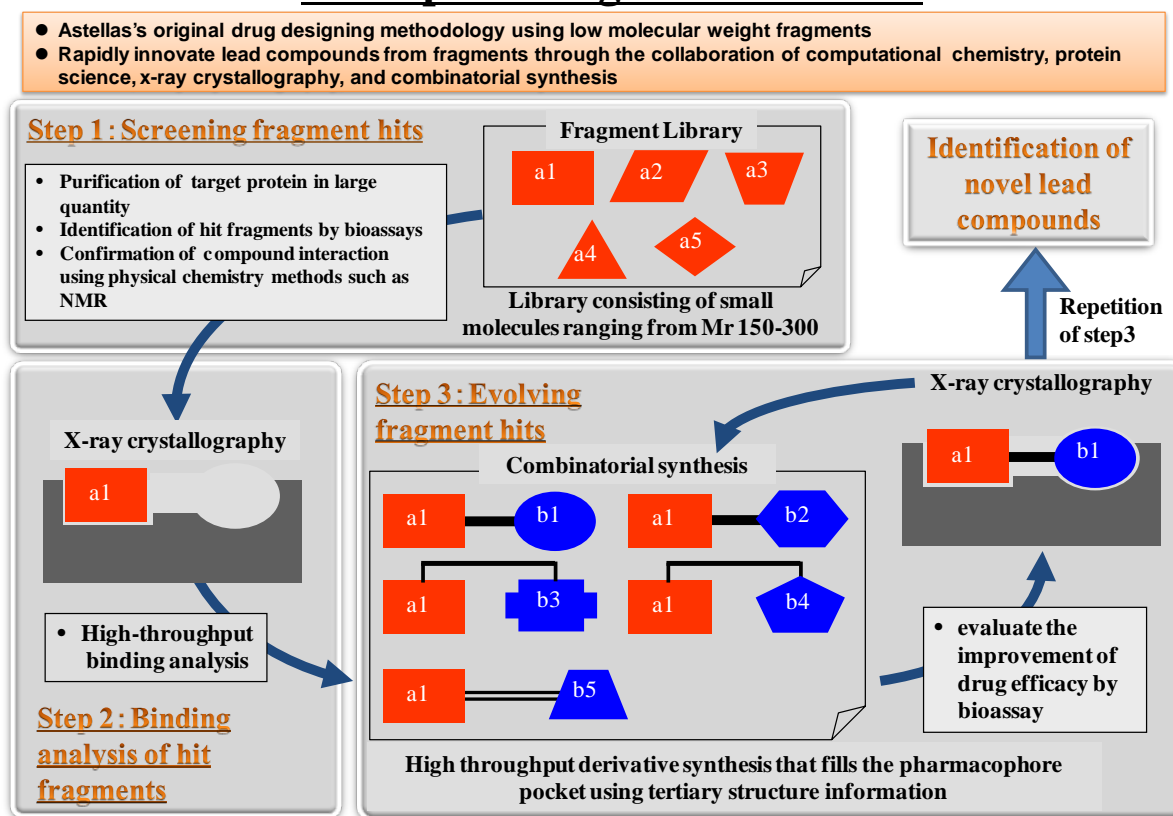
[Step 3: Evolution of fragment hits]

Taking a full advantage of an enormous amount of three-dimensional structural information obtained, combinatorial syntheses (high throughput synthesis of fragment derivatives using an

automatic synthesizer) are efficiently performed in order to fill the active pockets. The inhibitory activity and binding patterns of the fragment derivatives are further evaluated, resulting in the improvement in inhibition.

Ultimately, lead compounds are obtained through the repetition of this evolution process (improvement of fragment activity) explained in Step 3.

Concept of Fragment Evolution



AIST has accumulated technologies for the construction of bioassay systems, NMR technologies for assessing binding of candidate compounds to proteins in solution, and technologies for supporting and analyzing protein production and crystallization. These technologies are expected to be used in Step 1 and Step 2, which are extremely important steps in the FE. In this collaborative research, Astellas and AIST plan to combine their technologies with the aim of improving the efficiency of the FE.

Astellas is committed to improving “Access to Health*” in developing countries through its partnership initiatives, including this collaborative research with AIST. As part of the contribution to Access to Health, Astellas is committed to undertake an initiative of drug discovery for patients infected with and suffering from NTDs in the world by utilizing its know-how and assets of drug discovery research.

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National Institute of Advanced Industrial Science and Technology (AIST)

AIST is one of the biggest public research institutes in Japan which supports Japan's industry in six diverse fields: Environment and Energy; Life Science and Biotechnology; Information Technology and Electronics; Nanotechnology, Materials and Manufacturing; Metrology and Measurement Science; and Geological Survey and Applied Geoscience.

AIST has headquarters in Tokyo and Tsukuba and has AIST network throughout Japan which consists of eight research bases other than AIST Tsukuba that focus on unique research fields. Over 2,000 researchers of around 3,000 total employees conduct organic cooperation with industry, universities and governments based upon the "Open Innovation Hub" concept in which organization, human resources and institutions of AIST are utilized. This concept leads research and development to innovation.

Astellas Pharma Inc. (Astellas)

Astellas' raison d'être is to contribute toward improving the health of people around the world through the provision of innovative and reliable pharmaceutical products. Astellas has approximately 17,000 employees worldwide. The organization is committed to becoming a global category leader in Urology, Immunology (including Transplantation) and Infectious Diseases, Oncology, Neuroscience and DM Complications and Kidney Diseases. For more information on Astellas Pharma Inc., please visit the company website at www.astellas.com/en.

* Access to Health : Unmet medical needs remain in many therapeutic areas. Furthermore, there are many people who are unable to access adequate medical care due to poverty or weak health systems. Astellas recognized these remaining issues as "Access to Health" and proactively addresses them as responsible corporate citizen.

(1) Neglected tropical diseases (NTDs)

NTDs are infections caused by parasitic worms and bacteria which are mainly endemic in tropical areas of developing countries. It is estimated that over 1 billion people are affected worldwide with the 17 diseases** of NTDs on which currently WHO is focusing on. 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.

** Group 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) Leishmaniasis

Leishmaniasis occurs in 98 countries, and 350 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.

(3) 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. In total, 100 million people are at risk worldwide and patient numbers are growing in non-endemic countries such as the United States and Australia, as well as 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.

(4) Sleeping sickness (human African trypanosomiasis, or HAT)

Sleeping sickness threatens millions of people in sub-Saharan Africa. The disease is transmitted by the bite of the tsetse fly. 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. Existing treatments are toxic, difficult to administer, and/or have severe side effects. The disease is fatal if left untreated.

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