

Society

Astellas is cooperating with a range of stakeholders in an effort to address social issues which affect people throughout the world. We are also working to enhance the sustainability of society through our activities, including addressing Access to Health issues, fostering advancement in medical science and providing support to local communities.

Access to Health

There are many people with insufficient access to the healthcare they need due to the lack of available treatments, poverty, challenges in healthcare systems and limited healthcare information. Astellas recognizes this problem as the Access to Health issue, and works to improve Access to Health by engaging in various initiatives. Astellas believes that the relationships with governments and the local partners it develops through these initiatives will generate synergies with its business activities over the long term.

Initiatives to Combat Tropical Diseases by Harnessing Astellas' Unique Strengths

Collaborative Research to Discover Anti-Protozoan Parasite Drugs

In April 2016, Astellas signed a new collaborative research agreement with the National Institute of Advanced Industrial Science and Technology (AIST).

The collaborative research is targeting Chagas disease, one of the neglected tropical diseases (NTDs)^{*1} caused by protozoan parasites belonging to trypanosomatidae^{*2}, for which a new drug is urgently needed to address unmet medical needs. Since 2012, Astellas has been collaborating with five research institutions in Japan as well as with an international non-profit organization^{*3} to discover new drugs for the treatment of NTDs caused by protozoan parasites belonging to trypanosomatidae. By utilizing the knowledge obtained through this collaborative research, Astellas and AIST will now pursue collaborative research to discover new drugs for the treatment of Chagas disease.

Astellas and AIST will work collaboratively to validate whether genes crucial for the survival of *Trypanosoma cruzi* (the cause of the disease) can be pinpointed in a short period of time using genome editing technology. Through this new collaborative research, Astellas will endeavor to amass the scientific knowledge that will lead to the discovery of new drugs for patients suffering from Chagas disease around the world.

In case this approach is validated, the formation of an AIST-driven research consortium, in which multiple research institutions will participate to conduct extensive genome editing studies on the genes of *Trypanosoma cruzi* and pursue discovery of new drugs for the treatment of

Chagas disease in a larger framework, is planned. Astellas also plans to consider joining the consortium.

^{*1} Neglected tropical diseases (NTDs): NTDs are infections caused by parasites and bacteria 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 these infections.

^{*2} In addition to Chagas disease, leishmaniasis and African trypanosomiasis are also caused by protozoan parasites belonging to trypanosomatidae.

^{*3} Collaborative research has also been undertaken with the University of Tokyo, the Tokyo Institute of Technology, Nagasaki University, the High Energy Accelerator Research Organization, AIST and the international non-profit organization Drugs for Neglected Diseases initiative (DNDi).

Collaborative Research on a Rice-Based Oral Vaccine

In June 2016, Astellas signed a new collaborative development agreement with the Institute of Medical Science, the University of Tokyo (IMSUT) on the rice-based oral vaccine "MucoRice-CTB" against diarrheal diseases caused by cholera and enterotoxigenic *Escherichia coli* (*E.coli*).

In developing countries, diarrhea caused by pathogenic bacteria such as *Vibrio cholerae* and enterotoxigenic *E.coli*, is a major cause of death among infants and young children. However, existing cholera vaccines present several issues, including the need to store and transport the vaccines at a constant low temperature, and their ineffectiveness against enterotoxigenic *E.coli*. MucoRice-CTB is stable at room temperature and easily produced. Therefore, it is expected to meet the unmet medical needs of existing cholera vaccines.

MucoRice-CTB is a rice-based oral vaccine expressing a cholera toxin B (CTB) subunit in the intrinsic storage protein of rice using genetic engineering. It was developed by Prof. Hiroshi Kiyono, Project Researcher Yoshikazu Yuki and their colleagues at the International Research and Development Center for Mucosal Vaccines, IMSUT.

Under the agreement, IMSUT provides investigational medicines and study data, etc., which are necessary for phase 1 and 2 of clinical trials of MucoRice-CTB for cholera and enterotoxigenic *E.coli*, and Astellas is responsible for conducting and managing the clinical trials.

Through this collaborative development, Astellas will work to develop vaccines against infectious diseases affecting developing countries.

Development of Pediatric Formulation for Schistosomiasis

Schistosomiasis is one of the most prevalent parasitic diseases in developing countries centered on Africa and South America. The disease has a particularly high incidence rate among children. The existing 'gold standard' treatment for schistosomiasis is praziquantel. However, one challenge is that praziquantel tablets are difficult to administer to preschool age children, including infants and toddlers, mainly due to the risk of choking stemming from their large size and the drug's bitter taste.

Having set up a consortium with other pharmaceutical

companies, research institutions and international non-profit organizations, Astellas is developing a pediatric formulation of praziquantel.

The pediatric formulation newly developed by Astellas uses its original drug formulation technology. The pediatric formulation was designed to be smaller than the existing tablet and to be orally dispersible so that it can be taken even without water, with reduction of bitterness. In addition, the pediatric formulation can be manufactured using simple production technology, while holding down production costs, and the tablets are stable even in the hot and humid environment of tropical areas. Astellas has transferred the technology and expertise needed to develop the pediatric formulation to a consortium partner in Brazil, thereby helping to build local pharmaceutical manufacturing capabilities.

The consortium is conducting Phase II clinical trials. Astellas continues to provide its expertise and technology to the consortium.



Newly developed pediatric formulation (top) and existing tablet (bottom)



Members of the Pediatric Praziquantel Consortium Team ©Lygature 2015

Action on Fistula

Action on Fistula*¹, a program focused on urology, is led by the charity Fistula Foundation and funded by €1.5 million provided by Astellas. In the three years through 2017, the initiative launched its activities with the aim of transforming the lives of more than 1,200 women in Kenya living with this condition and building capacity in the country by training doctors who can perform surgeries.

The program is making progress ahead of its targets. As of the end of April 2016, the program had successfully treated 1,210 women with life-changing reconstructive surgery. It has established a fistula treatment network comprising 7 hospitals and has increased the number of fistula surgeons in the country. The initiative is also undertaking a major outreach program with community workers identifying patients and encouraging them to access available treatment.

*1 For details, please visit the following website:

<http://www.astellas.eu/action-on-fistula/>

*2 An obstetric fistula is a hole that develops between the vagina and rectum or bladder, causing incontinence. It is caused by prolonged hard labor lasting several days when emergency care is unavailable. Untreated, fistulas can lead to chronic medical problems including ulcerations, kidney diseases and nerve damage in the legs, and can cause economic hardship in some cases if patients are excluded from society. The United Nations Population Fund estimates 3,000 new cases of obstetric fistulas occur annually in Kenya.



Fistula surgeons in Kenya

Progress in the Action on Fistula Program (May 2014-May 2016)

Patients successfully treated with reconstructive surgery	1,210 patients
Trained and certified doctors to the standard level of competency	5 Kenyan doctors
Centers in the Fistula Treatment Network	7 centers
FIGO* ¹ -accredited fistula training center	Established the Gynocare Fistula Center
Reached counties* ² of Kenya	40 counties
Trained community health volunteers	211 volunteers
Conducted outreach activities	4,339 activities
Reached community members with fistula messages	206,000 members

*1 FIGO: International Federation of Gynecology and Obstetrics

*2 Kenya is divided into 47 counties. There are several units of governance below the county level. These units include subcounties, wards, and villages.

Special Programme for Research and Training in Tropical Diseases

Through the Special Programme for Research and Training in Tropical Diseases (TDR) of the World Health Organization, Astellas accepted research fellows from developing countries and provided them with job training on management skills related to clinical development. In October 2015, one trainee from the Republic of Mali, the third trainee of the programme, began training at Astellas' clinical development division in the U.S., and is scheduled to complete the training by September 2016.

Support for Patients

Astellas conducts a variety of activities to provide assistance to patients fighting illnesses, and their family members, on a global basis.

Astellas promotes Starlight Partners Activities in Japan as part of efforts to support the self-reliance and development of patient associations. Astellas Peer Support Training Sessions are held for a wide range of participants, including patients and their families, along with those who have recently formed patient associations. In these training sessions, activities include programs for participants to learn attentive listening skills, which enable colleagues who have faced the same issues or have experienced the same problems to serve as consulting partners to one another. In fiscal 2015, Astellas Peer Support Training Sessions were held in three locations across Japan, attended by 29 organizations and 42 people.

Group-Wide Volunteer Activities Changing Tomorrow Day

Astellas Group employees around the world are contributing to their local communities by conducting a diverse range of volunteer activities as part of Changing Tomorrow Day based on the themes of promoting healthcare and maintaining the environment. In fiscal 2015, more than 7,400 employees participated.

Changing Tomorrow Day Held in Fiscal 2015

Region	Participants	Volunteering hours	Number of locations	Number of countries
Japan	3,665	3,447	132	1
Americas	2,179	10,220	121	3
EMEA	472	3,812	33	29
Asia & Oceania	1,133	6,278	14	9
Total	7,449	23,757	300	42

Astellas Foundations

Astellas has established foundations in Japan, the Americas, EMEA, Asia and Oceania in order to provide financial assistance for research and other support to foster advancement in medical science, conduct philanthropic activities in local communities, and contribute relief funds to assist with disaster recovery efforts. The foundations are operated in accordance with the laws of the regions where they are active.

Of these foundations, Astellas USA Foundation carries out activities focused on health and education, including support for activities to ensure healthy lives and promote well-being for all at all ages, one of the United Nations' Sustainable Development Goals.

In fiscal 2015, with a focus on health, Astellas USA Foundation helped to immunize more than 200,000 children against measles in Latin America, in addition to providing funding for enhancements to the pediatric wings of local hospitals. To strengthen the focus on education, Astellas USA Foundation supported fostering the next generation through STEM* education. Astellas USA Foundation provided grants for eight specialized programs, thereby providing thousands of students with mentoring and hands-on learning to cultivate critical thinking and problem-solving skills, and raising their awareness about careers in STEM.

* STEM: Science, Technology, Engineering, and Math.

For further information on Astellas' society activities, please visit the following website:

 <http://www.astellas.com/en/csr/social/>

Message from Collaborative Researcher in the Project to Discover Anti-protozoan Parasite Drugs

I was deeply impressed with Astellas' front-line focus, dedication and integrity as a pharmaceutical company.

At the final reporting conference of the NTDs Drug-discovery Research Consortium, my supervisor asked me to share my thoughts on working for the project over the past three years. Without hesitation, I answered, "It was very enjoyable."

Through this drug-discovery research consortium initiated in 2012, we learned about Astellas' front-line focus, something that came as a big surprise to all of us. This front-line focus encompasses Astellas' research methods devoted to drug discovery and its speed of research, which is far faster than that of academia, as well as its scale and calm, level-headed decision-making. Astellas' researchers showed an incredible dedication to their work. They delivered progress reports with such an intensity that the audience would often be left in stunned silence after the presentations. That is what the process of developing a new drug is like. However, as a for-profit enterprise engaged in a social contribution effort, Astellas always conducted itself with the utmost integrity. I am deeply impressed with and grateful for Astellas' generosity in making this approach to the project possible.

In fiscal 2016, our collaborative research is about to enter the next stage of focusing on the treatment of Chagas disease as the target. To make the drug-discovery research more meaningful, the new project will commence research by seeking to identify the genes crucial for the survival of *Trypanosoma cruzi*,

the pathogenic protozoa that causes Chagas disease, and making those genes the target candidate for drug discovery. In this stage, the project will use the genetically engineered pathogenic protozoa produced by the research consortium since 2012 to efficiently create gene-deficient strains and use genetic editing technology to identify the genes.

Another feature of the new project is that it will be set up as a consortium at AIST that will be open to participation by multiple companies. The 2015 G7 Elmau Summit Leaders' Declaration underscored the need for developed countries to take steps to fight NTDs. Against this backdrop, Professor Satoshi Omura received the Nobel Prize in Physiology or Medicine. Under these social conditions, and in the sense of carrying on the legacy of the research consortium's work to date, AIST has been given an immense role to play in leading this project. We can easily anticipate that a wide range of difficulties lie ahead. That is precisely why we must advance to the next stage with extraordinary determination.

Another benefit of participating in this collaborative research has been the friendships I have developed with numerous colleagues. They are the reason why the past three years have been so enjoyable. For their sake too, I would like to continue working hard on this project.



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