

General symposium at 137th. Annual meeting of Pharmaceutical Society of Japan (Sendai)

Receipt number: 1039

Title of the symposium: "Partnership for NTDs drug discovery originated in Japan"

Time & Date: 13:15-15:15 25th. March 2017

Venue: Meeting room2, 1st floor, Exhibition wing at Sendai International Center

Organizer(s):

- Haruki Yamada, Ph.D., Tokyo University of Pharmacy and Life Science, DNDi Japan
- Kiyoshi Kita, Ph.D., School of Global Health, Nagasaki University



Nearly 200 audiences attended

Order and contents of the speech

- 13:15-13:20: Welcome speech and intent of the symposium
(Haruki Yamada, Tokyo University of Pharmacy and Life Science)
- 13:20-13:40: Current status and issues on NTDs treatments”
(Kiyoshi Kita, School of Global Health, Nagasaki University)
- 13:40-13:50: Role of DNDi as PDP
(Haruki Yamada, Tokyo University of Pharmacy and Life Science)
- 13:50-14:05: Our challenge through Drug Discovery Booster for drug discovery treating Leishmaniasis
(Charles Mowbray, DNDi)
- 14:05-14:25: Pros and cons of NTD Booster and our R&D efforts against NTDs
(Yoshinori Yamano, Shionogi)
- 14:25-14:45: NTDs projects with DNDi (other than Booster) and other PDPs funded by GHIT Fund
(Yoshinori Ikeura, Takeda)
- 14:45-15:05: Development of E1224 and clinical study on Mycetoma and our R&D efforts on Filariasis.
(Nao-aki Watanabe, Eisai)
- 15:05-15:15 Wrap up, Q&A
(Kiyoshi Kita, School of Global Health, Nagasaki University)

Summary of contents

- ✚ Welcome speech and intent of the symposium
(Haruki Yamada, Tokyo University of Pharmacy and Life Science)

A new mechanism of developing drugs for NTDs, from which approximately one sixth of global population are suffering, is awaited because such drugs have limited marketability due to patients' distribution mostly in low-income countries. Recently new platforms created by global Product Development Partnerships for drug development consisting of pharmaceutical companies, universities, research institutions and funding agencies are achieving significant results step by step. It is the aim of the symposium in which we discuss roles of and issues on academia in order to facilitate drug discovery based on the latest success of Public Private Partnerships for NTDs drug discovery originated in Japan.

We ask speakers to introduce current prevalence of NTDs, research and development of drugs for those diseases, latest developments made through "Drug Discovery Booster", capabilities of PDPs that can cover drug discovery, clinical studies in endemic countries and access to medicine. In addition, we hope speakers from pharmaceutical companies would disclose expectations on future collaboration with academia and touch episodes of some impacts brought to employees by their involvement in NTDs drug development.

🚩 Current status and issues on NTDs treatments"

(Kiyoshi Kita, School of Global Health, Nagasaki University)

Infectious diseases have been classified as several groups such as "Emerging and re-emerging diseases". Emerging diseases are the infectious diseases that are recognized newly and were never known in public health globally (AIDS, EBOLA hemorrhagic fever and cryptosporidiosis etc). On the other hand, with regard to re-emerging diseases, the number of patients increased by a revival although that of patients decreased once to a extent with little problem in public health (tuberculosis, malaria, Salmonella and cholera etc).

In addition, "Neglected Tropical Diseases; NTDs" have been paid attention currently. WHO listed 18 infectious diseases including Mycetoma, which has been added recently. NTDs have been neglected by societies, nations, the global communities and pharmaceutical companies because NTDs are the diseases coming from poverty. Control programs for NTDs should be

performed as well as three major infectious diseases. NTDs include virus infections such as Dengue fever and rabies, bacterial infection such as cholera, leprosy and Buruli-ulcer, and 10 parasitic infections (trypanosomiasis, a soil-mediated helminthiasis and echinococcus etc). Among the problems that should be solved about NTDs, drug discovery and development are the most behind because they are the infectious disease of the poor people who are not able to buy "medicine". I would like to introduce the current conditions of the anti-NTDs medicines and future direction in this lecture.

✚ Role of DNDi as PDP

(Haruki Yamada, Tokyo University of Pharmacy and Life Science)

A new system for drug development is awaited because the drugs for NTDs have limited marketability. DNDi is a non-profit organization and one of PDPs founded in 2003 based in Geneva in order to drive development of new treatments for NTDs with global partners such as private companies, governmental organizations and academia. DNDi is developing drugs for Filariasis and Mycetoma which is the 18th. NTD to be listed by WHO, as well as for Human African Trypanosomiasis, Leishmaniasis and Chagas diseases as its core targets. Based on patients' needs in endemic regions, DNDi is also developing affordable treatments for Hepatitis C and new formulations for Paediatric HIV. Drug development in DNDi is shared with global partners by processes such as early discovery, lead optimization, non-clinical studies, translational research, clinical studies in endemic countries and implementation of new treatments according to each disease area. DNDi has created a consortium called "NTDs Drug Discovery Booster" in order to accelerate drug discovery and save time for the research. The consortium is expected to succeed through its revolutionary new system for drug discovery which could overcome existing barriers between pharma companies. DNDi also started incubation of GARD partnership together with WHO to address multiple-drug resistant bacteria and its diffusion that becomes a great threat to developing countries.

✚ Our challenge through Drug Discovery Booster for drug discovery treating Leishmaniasis

(Charles Mowbray, DNDi)

The NTD Drug Discovery Booster is an innovative collaboration designed to swiftly and efficiently maximise the Structure-Activity Relationship (SAR) space around new chemical hits and leads targeting *Leishmania donovani* and *Trypanosoma cruzi*, the Kinetoplastid parasites responsible for visceral leishmaniasis and Chagas disease respectively. In partnership with our consortium partners, we have implemented a novel in silico screening process that allows us to advance various chemical series through the hit-to-lead process via the mining of each pharmaceutical company's vast chemical library in an iterative and collaborative manner. The innovation of the NTD Booster lies in the companies simultaneously accepting to share with DNDi upfront structural and biological information about a promising chemical series that is essential for its rapid development.

We demonstrate that this original, cooperative approach allows us to rapidly expand the SAR around hits, as well as detect scaffold hops and series deviations that would otherwise go unexplored in a more classical hit-to-lead strategy. We also identify the clear advantages of accessing and mining several proprietary chemical libraries in parallel iterations, as well as reveal some interesting observations and learnings around overlaps between corporate library collections and the advantages of different in silico screening approaches.

✚ Pros and cons of NTD Booster and our R&D efforts against NTDs
(Yoshinori Yamano, Shionogi)

Neglected tropical diseases are causing threats to human health worldwide, but many pharmaceutical companies have not fully conducted the discovery activities against such infectious diseases due to the limiting opportunities for profits. In order to resolve these issues, the collaboration between government, academia and industry, and the utilization of public funds are actively promoted. The examples of our research collaboration to promote these activities will be shown as follows. First is the participation of the booster project, which is led by DNDi with five pharmaceutical companies by using GHIT fund. The discovery process for the anti-infective drugs against Leishmaniasis and Chagas' disease has been accelerated by being provided with a structural variety of compounds from different companies. Second is

the collaboration with TB alliance and the research institute of tuberculosis to discover the anti-tuberculosis drugs. Third is the collaboration with Hokkaido university research center for zoonosis control to discover anti-infective drugs against various viruses such as Dengue virus, Chikungunya virus, and Zika virus. These activities are expected to be successful by combining strength from each organization such as the compound library from companies and the unique evaluation systems from academia.

- 🚩 NTDs projects with DNDi (other than Booster) and other PDPs funded by GHIT Fund
(Yoshinori Ikeura, Takeda)

The discovery of innovative medicines for the patients of the Neglected Tropical Diseases is challenging

Based on our corporate philosophy, "Takeda-ism" (Integrity: Fairness, Honesty and Perseverance) and according to the corporate mission to "strive towards better health for people worldwide through leading innovation in medicine", we are challenging to participate into the pharmaceutical research that contribute to the discovery of outstanding products for the patients of the Neglected Tropical Diseases by utilizing our advanced technologies for drug discovery research and our proprietary compound libraries with collaboration of PDPs.

In this symposium, the projects for the drug discovery research with PDPs through GHIT Fund to identify innovative medicines for tuberculosis or Neglected Tropical Diseases, for example, the project, "Lead optimization of the aminopyrazole series for visceral leishmaniasis" with DNDi by utilizing our sophisticated knowledge for medicinal chemistry; and the project, "Neglected Tropical Diseases Drug Discovery Booster" to accelerate and expand discovery of new drugs for Leishmaniasis and Chagas disease together with the other pharmaceutical companies providing diverse compounds libraries and lead identification technologies. Our research strategy to improve access to global healthcare for patients of the Neglected Tropical Diseases will be also presented to discuss for open innovation by the collaboration with PDPs and other organizations which have diverse experts and differentiated technologies.

- ✚ Development of E1224 and clinical study on Mycetoma and our R&D efforts on Filariasis.
(Nao-aki Watanabe, Eisai)

Not only the three major infectious diseases, tuberculosis, malaria, and HIV/AIDS, but also neglected tropical diseases (NTDs) such as lymphatic filariasis (LF) and Chagas disease (CD) that we in Japan don't so hear about impair billions of peoples' health in developing countries. Mycetoma was designated the 18th NTD by WHO this year, and many NTDs should be still eliminated in the world. LF was eliminated in Japan, but more than 100 million of people in the world suffer from LF. CD is a protozoal infection from which 8 million of people suffer mainly in Latin America. Through various public-private partnerships, we are going to improve access to medicines worldwide and at various stages of medicine creation, from the discovery of medicine seeds, clinical studies in patients, to the supply of medicines.

In this symposium, I will introduce Eisai's approach to NTDs, 1) free provision of DEC (diethylcarbamazine) tablets to WHO for LF patients, 2) Phase 2 clinical studies of antifungal E1224 for CD in Bolivia and for mycetoma in Sudan in collaboration with Drugs for Neglected Diseases initiative, 3) some projects at compound screening stage to clinical study stage to create new medicines for CD, malaria, or tuberculosis, mainly supported by Global Health Innovative Technology Fund, and 4) WIPO Re-Search project in which we provide compounds and know-hows to contribute to NTDs research.