03. STRENGTHENING EXISTING CAPACITIES

Through a global network of collaborations, DNDi’s disease-specific platforms aim to answer patients’ needs in supporting local research and implementation programmes and in ensuring technology transfers to guarantee sustainable access to the treatments delivered.
Regional networks working to ensure sustainable solutions

True to its vision and mission, DNDi works closely with partners in disease-endemic countries to strengthen existing clinical research capacity as well as to build new capacity where necessary. These efforts to support research and implementation programmes are also vital to ensuring sustainable access to the treatments delivered. Furthermore, with this vision of sustainability, DNDi also aims at transferring technology, in particular manufacturing processes, to industrial partners in endemic regions.

PILLARS OF DNDi’S BUSINESS MODEL

Since its inception in 2003, DNDi has worked to integrate capacity strengthening in all of its projects as well as to promote technology transfer where possible in order to increase the chances of registration, uptake, and sustainable access of new treatments. The regional platforms, set up at the outset of DNDi as part and parcel of its business model, are essential pillars of DNDi’s work. At the cornerstone of their mission, the platforms define patient needs and provide a solid basis for appropriate and sustainable research, by creating clinical trial methodologies in compliance with Good Clinical Practices (GCP) standards, while taking into consideration the local conditions in which such trials are conducted.

Three regional disease-specific platforms in Latin America and Africa collaborate to support R&D programmes on Chagas disease (Chagas Clinical Research Platform), visceral leishmaniasis (Leishmaniasis East Africa Platform – LEAP), and sleeping sickness, or Human African Trypanosomiasis (HAT Platform). They have the specificity of bringing together regional actors, notably Ministries of Health and National Control Programmes, regulatory agencies, academia, clinicians, civil society groups, and pharmaceutical companies with a common goal of addressing patient needs in the local and national contexts where the diseases are endemic. The platforms utilize, capitalize upon, and reinforce clinical capacities in endemic regions, and address infrastructural requirements where necessary. They provide on-site training in clinical research in sometimes very remote settings, which are the most challenging research environments.

In 2010, the LEAP platform was critical to making available DNDi’s first new treatment for visceral leishmaniasis – the combination of SSG&PM, see page 28 – and in obtaining recommendation of SSG&PM by the WHO Expert Committee on the Control of Leishmaniases as first-line treatment for VL in East Africa. The HAT Platform was instrumental in facilitating the implementation and access of NECT for stage 2 sleeping sickness in 10 endemic countries by working closely with national authorities.

A YEAR OF COLLABORATION AND ACHIEVEMENTS

In addition, training was a vital part of DNDi’s regional efforts to strengthen existing capacities in 2010. In the field of sleeping sickness, a Good Clinical Practices (GCP) training course was organized in Kenya, while Ethics Committee training courses were delivered in Rwanda and Central African Republic by the HAT Platform. The Leishmaniasis East African Platform (LEAP) organized GCP training in Kenya and the newly launched Chagas Clinical Research Platform (CCRP) held a GCP course at its first platform meeting in Argentina.
TWO TECHNOLOGY TRANSFER PROJECTS PAVE THE WAY TO INCREASING ACCESS

For DNDi, the transfer of technology consists of transferring the industrial development know-how to partners in endemic regions to ensure a wide-spread distribution of new treatments. It implies providing the required regulatory files and information in order to maintain competitive prices and to reinforce the technological and scientific capacities of endemic countries. In 2010, DNDi actively participated in the process of technology transfer between Farmanguinhos and Cipla (for ASMQ) and is preparing the transfer of technology to an additional partner for ASAQ.

ASMQ: FROM BRAZIL TO INDIA AND BEYOND

In order to facilitate access of ASMQ in Southeast Asia, a South-South technology transfer between Farmanguinhos/Fiocruz in Brazil and Cipla Ltd in India, the agreement for which was signed in 2008, came to completion in 2010 with support and facilitation by DNDi. This technology transfer for the artesunate-mefloquine fixed-dose combination (ASMQ FDC, see page 36) was the first of its kind between a company in Brazil and one in India, and was even more unique in that it involved a transfer from a public entity, Farmanguinhos, to a private company, Cipla Ltd.

Successful transfer of technology necessitates true partnership, as it is more than just a question of offering acquired information. The Farmanguinhos-Cipla technology transfer required the alignment of procedures to Good Manufacturing Practices (GMP) to achieve similar and comparable products that meet international requirements in order to benefit patients in all endemic countries.

ASAQ: ON THE STARTING BLOCKS FOR TECHNOLOGY TRANSFER IN AFRICA

ASAQ, the artesunate-amodiaquine fixed-dose combination (see page 37), was the first treatment developed by DNDi in partnership with sanofi-aventis (launched in 2007), and is produced in Morocco. Developed as a non-patented product, the technology transfer for ASAQ to a second partner in Africa is a vital part of DNDi’s strategy to increase patient access to this treatment, according to the market demand forecast of 100 million treatments.

In 2010, DNDi, with support from a group of experts, assessed various potential partners in Africa in order to ensure that all criteria for a successful technology transfer were met. By the close of 2010, a partner in Tanzania – Zenufa – was selected and negotiations are well underway.

Disease platforms in 2010

CHAGAS CLINICAL RESEARCH PLATFORM

Founded: 2009 in Uberaba, Brazil

Representatives from the following organizations participated in the first CCRP meeting: Pan American Health Organization (PAHO); Department for the Control of Neglected Tropical Diseases, WHO; Ministries of Health and National Control Programmes of high burden endemic countries (Argentina, Bolivia, Brazil, Mexico); Hospital de Niños Ricardo Gutiérrez, Argentina; Instituto Nacional de Parasitología Dr. M Fátala Chabén, Argentina; Hospital de Niños de Jujuy, Argentina; Hospital Público Materno Infantil – Salta, Argentina; Centro de Chagas y Patología Regional, Santiago del Estero, Argentina; Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET), Argentina; Instituto Oswaldo Cruz, Brazil; Instituto de Pesquisa Evandro Chagas–Fiocruz, Brazil; Centro de Pesquisas René Rachou–Fiocruz, Brazil; Universidad Mayor de San Simon–Platform of Integral Care for Patients with Chagas Disease, Bolivia; CRESIB-Hospital Clinic Barcelona, Spain; Médecins Sans Frontières; Institut de Recherche pour le Développement, France; Eisa, Japan.

Objectives: To support its R&D activities on Chagas disease, DNDi launched the Chagas Clinical Research Platform (CCRP). The platform brings together partners, experts, and stakeholders to provide support for evaluation and development of new treatments for Chagas disease. The CCRP aims to facilitate clinical research, provide a forum for technical discussions, develop a critical mass of expertise, and strengthen institutional research capacities. In addition, it will identify and review priority needs, work towards standardization of methodology to assess drug efficacy to treat T. cruzi infection, review alternatives for using current drugs approved (new schemes, doses, combination) and special scenarios (resistance).

Achievements and Activities in 2010

- Meetings: The CCRP held its first meeting in Buenos Aires, Argentina, in March 2010 to update the target product profile (TPP) for Chagas disease.
- Clinical trials: Three studies are planned for 2011 for which the CCRP will provide support in terms of preparation and implementation. A population pharmacokinetics study of the paediatric formulation of benznidazole will be conducted in Buenos Aires, Argentina, and in endemic areas of the north of the country. With its partners in Bolivia, the CCRP will also implement a study to evaluate and optimize the polymerase chain reaction (PCR) for diagnosis and assessment of therapeutic response in patients with chronic indeterminate Chagas disease, and a study to evaluate the safety and efficacy of E-1224, a pro-drug of ravuconazole.
- Capacity Strengthening: A training course on Good Clinical Practices (GCP) was offered to investigators involved in the planned studies. 38 people trained in 2010.
- Access: The CCRP will increasingly work as a channel to raise awareness on issues related to access to existing drugs and will be involved in the implementation of paediatric benznidazole, developed through a partnership between DNDi and the Brazilian public laboratory LAFEPE, planned for 2011.
networks for global impact

HUMAN AFRICAN TRYPANOSOMIASIS HAT PLATFORM
Founded: 2005 in Kinshasa, Democratic Republic of the Congo

Members: National Control Programmes of most affected endemic countries; Swiss Tropical and Public Health Institute (Swiss TPH), Switzerland; Institute of Tropical Medicine in Antwerp (ITMA), Belgium; Institut National de Recherche Biomédicale (INRB), DRC; Centers for Disease Control and Prevention (CDC), USA; Kenya Agricultural Research Institute – Trypanosomiasis Research Centre (KARI-TRC), Kenya; MSF/Epicentre; Foundation for Innovative New Diagnostics (FINDI); WHO-TDR; Regional networks such as Eastern Africa Network for Trypanosomiasis (EANETT), Pan African Bioethics Initiative (PABIN), the African Malaria Network Trust (AMANET).

Objectives: To build and strengthen treatment methodologies and clinical trial capacity in HAT-endemic countries, so that new treatments for this fatal disease can be rapidly and effectively evaluated, registered, and made available to patients. After the success of the Nifurtimox-Ellorchin Combination Therapy (NECT), included in the WHO’s List of Essential Medicines for the treatment of stage 2 HAT, the primary goals of the HAT Platform are to develop appropriate clinical trial methodologies for HAT, overcome system challenges related to administrative and regulatory requirements, strengthen clinical trial capacity (human resources, infrastructure, equipment), and share information and strengthen ties among endemic countries.

Achievements and Activities in 2010

- **Treatments:** As of December 2010, NECT was available in 10 African countries and 2.1% of patients were treated. More than half (62%) of the patients were now treated with NECT in African endemic countries.
- **Clinical trials:** Participation in the ongoing NECT-Field studies. Preparation of the clinical trials for a new oral drug (Fexinidazole) in the Democratic Republic of the Congo for 2011.
- **Capacity Strengthening:** Good Clinical Practices (GCP) training for researchers; Ethics Committee training; HAT patient examination training for clinical monitors and general practitioners. 208 people trained in 2010.
- **Communication:** Two newsletters were published in 2010. TV and radio presentations were given on NECT.
- **Meetings:** Joint HAT Platform–EANETT Annual Scientific Meeting, Nairobi, 2010: contributions to this meeting provided suggestions for a profile to target research for new molecules for HAT; other scientific congresses.
- **Supply:** Advocacy in member countries towards quick adoption of NECT as first-line treatment for second stage HAT.

LEISHMANIASIS EAST AFRICA PLATFORM (LEAP)
Founded: 2003 in Khartoum, Sudan

Members: Center for Clinical Research, Kenya; Medical Research Institute, Kenya; Ministry of Health, Kenya; Institute of Endemic Diseases, University of Khartoum, Sudan; Federal Ministry of Health, Sudan; Addis Ababa University, Ethiopia; Gondar University, Ethiopia; Federal Bureau of Health, Ethiopia; Makerere University, Uganda; Ministry of Health, Uganda; Médecins Sans Frontières; i+ Solutions; Institute for OneWorld Health (iOWH); AMC/KIT/University of Sotervaart, Amsterdam, The Netherlands; London School of Hygiene and Tropical Medicine (LSHTM), UK.

- 50 individual members, representing over 20 institutions
- Over 1,100 patients enrolled in clinical trials by the end of 2010
- Approximately 1,000 patients treated outside clinical trials per year

Objectives: The overall aim of the platform is to strengthen clinical research capacity, which is lacking in part due to the remoteness and geographic spread of the patients, most of whom live in the most impoverished regions of Africa. This platform also serves as a base for ongoing educational cooperation between the countries in the East African region and standardization of procedures and practices within the region, as far as is possible within the confines of local regulations. LEAP evaluates, validates, and registers new treatments that address regional needs for VL.

Achievements and Activities in 2010

- **Treatments:** Following up on the results of the study comparing the paromomycin (PM) and sodium stibogluconate (SSG) in monotherapies, and the shorter course combination of PM and SSG, the WHO Expert Committee on the Control of Leishmaniasis recommended, in March 2010, the use of the SSG&PM as first-line treatment for VL in East Africa. Sudan applied this recommendation at the close of 2010, implementing SSG&PM as a first-line treatment.
- **Clinical trials:** DND and LEAP have completed the study LEAP 0104, a multi-centre clinical trial comparing the paromomycin (PM) and sodium stibogluconate (SSG) as monotherapies, and the shorter course combination of SSG and PM. The AMBI 0106 study aims at determining the minimum effective single dose of AmBisome® in Ethiopia and Sudan. The objective of the LEAP 0208 study is to assess the safety and efficacy of miltefosine in monotherapy and in combination with AmBisome® in Kenya and Sudan as a second shorter-course combination treatment. Evaluation of rapid diagnostic kits for VL is also ongoing in Kenya.
- **Capacity Strengthening:** Clinical monitors, Data and Safety Monitoring Board (DSMB) members, and investigators received training in Good Clinical Practices (GCP); key members were trained on a case-by-case basis in career development, and researchers were trained in parasite classification research through technology transfer and training courses. 63 people trained in 2010.
- **Infrastructure:** A treatment and laboratory training centre was opened in Doka, Sudan, in 2010. Ongoing improvements were made to a data centre in Nairobi to set up a GCP-compliant data-management system using open source software.

Strengthening Existing Capacities