

DNDi advocates for increased public responsibility and a more enabling environment for neglected disease R&D.



LESSONS LEARNED FROM 10 YEARS OF INNOVATIVE R&D

Marking its 10-year anniversary in 2013, DNDi explored the lessons learned from a decade of experience in research and development (R&D) of new treatments for neglected diseases. This analysis aimed at taking stock of key aspects of DNDi's business model in order to stimulate discussions on ways forward for sustainable financing and coordinating mechanisms.

Innovative R&D models that have emerged over the past decade have played an important role in what can be seen as a positive evolution of the neglected disease R&D landscape. A retrospective analysis of ten years of DNDi's activities highlighted the four pillars driving its innovative, 'virtual', not-for-profit drug development model: patient-centricity; open access to knowledge and patient access to treatments; financial and scientific independence; and building and sustaining solid alliances with public and private partners, notably in endemic countries. The analysis of its business model also offers insight into DNDi's R&D costs. Through case studies, the report shows that it is possible to develop and deliver quality, adapted, and affordable treatments to address the needs of the poorest populations. The cost of development for DNDi is relatively low: it ranges from EUR 6-20⁽¹⁾ million for an improved treatment, to EUR 30-40⁽¹⁾ million for a new chemical entity. With the usual attrition rate in the field of infectious diseases, the cost of development of an improved treatment would typically be EUR 10-40⁽¹⁾ million and EUR 100-150 million for a new chemical entity.⁽¹⁾

Key components for success

After ten years of experience and lessons learned, DNDi has identified key components for success, which could serve as perspectives for the next decade, to address global health needs in developing countries:

- put the specific needs of patients in developing countries upfront, at the start of the innovation process
- break the link between the cost of R&D and the price of products

Towards a Global Framework: Financing and coordination of R&D for the health needs of developing countries: 'VL Global R&D and Access Initiative' demonstration project

In May 2013, a resolution on NTDs was adopted⁽²⁾ during the 66th World Health Assembly, and following the recommendations of the WHO Consultative Expert Working Group on Financing and Coordination (CEWG), an R&D observatory⁽³⁾ was established and experts entered into the process of selecting 'demonstration projects'.⁽⁴⁾ The latter were expected to 'utilize collaborative approaches, including open knowledge approaches for R&D coordination; promote de-linkage of the cost of R&D from product price; and propose and foster financing mechanisms including innovative, sustainable, and pooled funding'.

In March 2014, the WHO, with experts and Member States, shortlisted DNDi's project on visceral leishmaniasis, 'VL Global R&D and Access initiative', with three other projects (out of 22 proposals), allowing the start of its implementation under the aegis of the WHO.

The objective of this policy process is to provide evidence on innovative mechanisms to fund and coordinate public health R&D, to address unmet medical needs of developing countries and to contribute to further discussions on a sustainable global framework, as recommended by the CEWG. The outcome of these projects will be assessed at the WHA in 2016.

(1) These estimations do not include the in-kind contributions from DNDi's many partners. (2) http://www.who.int/neglected_diseases/mediacentre/WHA_66.12_Eng.pdf (3) http://www.who.int/phi/documents/dwp1_global_health_rd_observatory_16May13.pdf (4) http://www.who.int/phi/documents/dwp4_demo_projects_16may13.pdf

- ensure that the fruits of innovation are accessible and affordable
- integrate global health R&D monitoring, coordination, and financing
- strengthen and harmonize regulatory capacities in endemic regions to facilitate implementation of new health technologies.

Public leadership still needed

Despite the promise of initial successes in DNDi's portfolio, product development partnerships cannot constitute the unique solution to the systemic lack of R&D to address the needs of patients who have no purchasing power, and where there is no incentive to drive innovation. Current efforts will not be transformed into sustainable change if the foundations for a new global framework that stimulates essential health R&D are not laid (see box page 51).

To generate public health breakthroughs, it is mandatory to consolidate sustainable public and private partnerships, with partners from endemic countries, based on priorities.

In addition, to ensure further development and advance promising technologies through the global R&D pipeline for neglected diseases, increased and innovative funding as well as new incentives are needed.

Push for policy change to scale-up testing and treatment: The Global Chagas Disease Coalition

Launched in December 2012 as a collaborative alliance to prioritize the disease on the international and regional health agendas, the Global Chagas Disease Coalition⁽¹⁾ has advocated through several public events in 2013, among them the 'Chagas Week' held in April in Bolivia (the country with the highest Chagas disease burden worldwide) and a side-event at the American Society of Tropical Medicine and Hygiene (ASTMH) meeting in November, hosted by PAHO in the USA. The ultimate aim of the coalition is to advocate for the policy changes necessary to ensure that health systems can and do diagnose and treat all patients with Chagas disease, and to reverse the ratio of only 1% of all patients currently receiving treatment.



DNDi's 10-YEAR ANNIVERSARY

ENGAGING WITH STAKEHOLDERS AND ASSESSING PROGRESS AND CHALLENGES

Following events held in Malaysia and in New York in 2012 to kick-off the 10th anniversary of DNDi, two key public events took place in 2013 where DNDi stakeholders gathered to discuss the success of the past decade and, more importantly, the challenges ahead.

A gathering of over 450 participants, co-organized with KEMRI in Nairobi, reviewed all aspects of R&D in Africa. A scientific meeting in Paris of over 440 participants, hosted at the Institut Pasteur in December, focused on innovation in research for neglected patients.

Other disease-specific events were organized throughout the year, namely the 'Chagas Week' in Bolivia in April, which comprised a week-long series of meetings with key partners and Chagas experts worldwide.



(From left to right)

- 1 Prof. Hannah Akuffo, EDCTP; Dr Tom Ellman, MSF; Dr Wilfred Mbacham, Biotechnology Centre, Cameroon; Dr Margareth Ndomondo-Sigonda, AMRH-NEPAD
- 2 Dr Philippe Douste-Blazy, UNITAID
- 3 Hon. James Macharia, Cabinet Secretary, Ministry of Health of Kenya; Mark Bor, Permanent Secretary (2013), Ministry of Public Health and Sanitation, Kenya; Dr Solomon Mpoke, Director, KEMRI
- 4 Dr Elias Zerhouni, Sanofi
- 5 Dr Charles Clift, Chatham House; Dr Christophe Paquet, AFD; Dr Line Matthiessen, European Commission; Dr Philippe Douste-Blazy, UNITAID; Dr Joanne Liu, MSF; Dr Bernard Pécoul, DNDi



(1) Partners include the Sabin Vaccine Institute and Texas Children's Hospital Center for Vaccine Development and National School of Tropical Medicine at Baylor College of Medicine, the Mundo Sano Foundation, CEADES Salud y Medio ambiente, the Barcelona Institute for Global Health - ISGlobal, and DNDi, with the support of the International Federation of People Affected by Chagas Disease (FINDECHAGAS), and the Instituto Carlos Slim de la Salud, and Médecins Sans Frontières (MSF).

Selected Scientific Publications and Press Articles

Two Analogues of Fenarimol Show Curative Activity in an Experimental Model of Chagas Disease by Martine Keenan, Jason H. Chaplin, Paul W. Alexander, Michael J. Abbott, Wayne M. Best, Andrea Khong, Adriana Botero, Catherine Perez, Scott Cornwall, R. Andrew Thompson, Karen L. White, David M. Shackelford, Maria Koltun, Francis C. K. Chiu, Julia Morizzi, Eileen Ryan, Michael Campbell, Thomas W. von Geldern, Ivan Scandale, Eric Chatelain, and Susan A. Charman. *J Med Chem*, December 2013

An Unfolding Tragedy of Chagas Disease in North America by Peter J. Hotez, Eric Dumonteil, Miguel Betancourt Cravioto, Maria Elena Bottazzi, Roberto Tapia-Conyer, Sheba Meymandi, Unni Karunakara, Isabela Ribeiro, Rachel M. Cohen, Bernard Pécoul. *PLoS Negl Trop Dis.*, October 2013

The drug and vaccine landscape for neglected diseases (2000—11): a systematic assessment by Belen Pedrique, Nathalie Strub-Wourgaft, Claudette Some, Piero Olliaro, Patrice Trouiller, Nathan Ford, Bernard Pécoul, Jean-Hervé Bradol. *The Lancet Global Health*, October 2013

Validation of Two Rapid Diagnostic Tests for Visceral Leishmaniasis in Kenya by Jane Mbui, Monique Wasunna, Manica Balasegaram, Adrian Laussermayer, Rashid Juma, Simon Njoroge Njenga, George Kirigi, Mark Riongoita, Roberto de la Tour, Joke van Peteghem, Raymond Omollo, François Chappuis. *PLoS Negl Trop Dis.*, September 2013

Les Echos

Développer des médicaments pour dix fois moins cher : le pari réussi de DNDi

EL MUNDO

El primer ensayo en Bolivia, una tibia esperanza contra el Chagas

The New York Times

Neglected Diseases Still Are, Well, Neglected

Le Monde

UN NOUVEAU MODÈLE CONTRE LES MALADIES NÉGLIGÉES



PLOS and DNDi: A Decade of Open Access and NTD R&D

EL PAIS

Médicos contra el abandono

FINANCIAL TIMES

Collaborative approach pays off in area of neglected diseases



Drug Development Lags for Neglected Diseases

Pharmacokinetics and pharmacodynamics utilizing unbound target tissue exposure as part of a disposition-based rationale for lead optimization of benzoxaboroles in the treatment of Stage 2 Human African Trypanosomiasis by Stephen Wring, Eric Gaukel, Bakela Nare, Robert Jacobs, Beth Beaudet, Tana Bowling, Luke Mercer, Cyrus Bacchi, Nigel Yarlett, Ryan Randolph, Robin Parham, Cindy Rewerts, Jacob Platner and Robert Don. *Parasitology*, September 2013.

Screening strategies to identify new chemical diversity for drug development to treat kinetoplastid infections by Rob Don and Jean-Robert Loset. *Parasitology*, August 2013.

Efficacy of artesunate-amodiaquine and artemether-lumefantrine fixed-dose combinations for the treatment of uncomplicated *Plasmodium falciparum* malaria among children aged six to 59 months in Nimba County, Liberia: an open-label randomized non-inferiority trial by Schramm B, Valeh P, Baudin E, Mazinda CS, Smith R, Pinoges L, Sundaygar T, Zolia YM, Jones JJ, Comte E, Bruneel A, Branger M, Jullien V, Carn G, Kiechel J, Ashley EA, and Guérin PJ. *Malaria Journal*, July 2013.

Effects of the benzimidazole anthelmintic drug flubendazole on rat embryos *in vitro* by Monica Longo, Sara Zanoncelli, Paolo Angelo Colombo, Michael Oscar Harhay, Ivan Scandale, Charles Mackenzie, Timothy Geary, Nicole Madrill, Guy Mazué. *Reprod Toxicol.*, April 2013

The story of artesunate-mefloquine (ASMQ), innovative partnerships in drug development: case study by Wells S, Diap G and Kiechel J-R. *Malaria Journal*, February 2013

EUR 63 Million Secured in 2013

The year 2013 was an exceptional one for DNDi, as the organization raised over EUR 63 million in multiyear grants for the next five years. In compliance with its funding strategy, DNDi continued to diversify funding sources with engagement of new donors such as the Norwegian Agency for Development Cooperation and the Global Health Innovative Technology Fund (GHIT), a new funding mechanism set up by public and private Japanese partners. Such partnerships contribute to the coherence of DNDi's fundraising policy, which aims to maintain a balance of public and private support, minimize – as much as possible – earmarked donations for more flexibility in managing projects, and ensure that no one donor contributes more than 25% of the overall budget.

Three major donors reiterated their commitments: The UK Department for International Development (DFID), Médecins Sans Frontières (MSF), and the Swiss Agency for Development and Cooperation.

Other long-term DNDi donors such as the Bill and Melinda Gates Foundation, the European Union (EU FP7), and the Republic and Canton of Geneva awarded new grants.

By the close of the year, all donors combined had committed a total of over EUR 282 million to DNDi since its launch in 2003. The overall funding goal for DNDi is to secure EUR 400 million by 2018.

NEW GRANTS IN 2013

UK Government / DFID

GPB 30 million (2013-2018)

The UK Department for International Development (DFID) renewed its support to DNDi for the third time since 2006, allocating £ 30 million (EUR 35 million) over the coming five years to fight neglected diseases (excluding paediatric HIV). This grant is part of DFID's larger investment of £ 138 million in nine product development partnerships.

European Union (EU FP7)

EUR 3 million (2013-2015)

The European Union Seventh Framework Programme granted EUR 3 million to DNDi to support the AfriCoLeish project, which aims to test new treatments for kala-azar and co-infection of the disease with HIV in Ethiopia and Sudan.

Norwegian Agency for Development Cooperation (NORAD)

NOK 15 million (2013-2015)

DNDi received support from NORAD for the first time. This grant of NOK 15 million (EUR 1.85 million), to be disbursed over three years (2013-2015), will be dedicated to the development of an oral treatment for sleeping sickness, as well as to strengthen local capacities through the HAT Platform.

Global Health Innovative Technology Fund (GHIT/Japan)

USD 158,000 (2013)

In 2013, DNDi and DNDi Japan, based in Tokyo, welcomed the launch of the Global Health Innovative Technology Fund (GHIT), an initiative supported by the Japanese government, several Japanese pharmaceutical companies, and the Bill and Melinda

Médecins Sans Frontières (MSF)

EUR 20 million (2014-2018)

MSF renewed its support to DNDi as a founding partner: EUR 4 million per year for the next five years to support the development of new treatments for neglected diseases. MSF will also continue to be a major strategic and operational partner of DNDi as it participates at the highest level of DNDi governance, facilitates implementation of clinical studies, and shares DNDi's vision in advocacy activities.

Gates Foundation, to support and stimulate R&D projects for neglected diseases. GHIT awarded DNDi with a first grant of USD 158,000 directed towards screening activities.

Bill and Melinda Gates Foundation

USD 2 million (2013-2014)

In 2011, the Bill and Melinda Gates Foundation supported DNDi with a two-year grant of USD 2 million for screening activities. In 2013, the foundation provided a supplemental grant for the identification of a new drug candidate for filarial diseases.

Republic and Canton of Geneva

CHF 500,000 (2013-2015)

For the third time since 2004, the Republic and Canton of Geneva, Switzerland, renewed its support to DNDi with a three-year grant of CHF 500,000. This is the second grant directed towards R&D for sleeping sickness.

Carlos Slim Foundation, Mexico

USD 100,000 (2013)

DNDi Latin America received the 2013 'Carlos Slim Health Award' of USD 100,000 for 10 years of exceptional work and achievements in R&D to deliver new treatments

Swiss Agency for Development and Cooperation (SDC)

CHF 8 million (2013-2016)

Following its initial support of CHF 4 million granted in 2010, the SDC has reiterated its commitment to the fight against neglected tropical diseases with support to DNDi's R&D projects. This new grant is part of the SDC's global strategy to contribute to the Millennium Development Goals.

for neglected patients in the region of Latin America.

Rockefeller Foundation, USA

USD 100,000 (2013)

DNDi was awarded the Rockefeller Foundation's 'Next Century Innovators Award'. This prize of USD 100,000 will be directed towards R&D activities across all DNDi's portfolio.

BBVA Foundation, Spain

USD 400'000 (2013)

DNDi was honoured with the BBVA Foundation's 'Frontiers of Knowledge and Culture Award for Development Cooperation'. This award of EUR 400,000 will be directed towards R&D activities across all DNDi's portfolio.

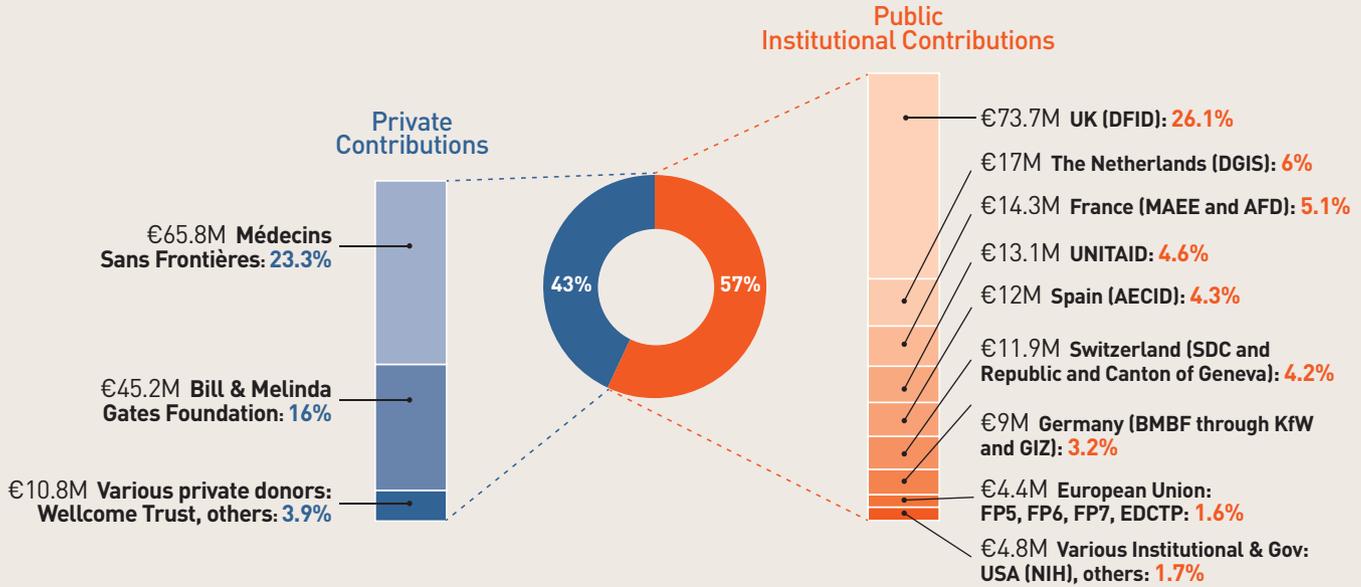
UBS Optimus Foundation, Switzerland

CHF 750,000 (2013-2016)

UBS Optimus Foundation, following previous grants since 2005, awarded DNDi this additional grant towards the Paediatric HIV portfolio to support development of a new therapeutic formulation for children co-infected with HIV and TB.

Maintaining balanced and diversified funding is essential to DNDi's vision and independence

EUR 282 MILLION COMMITTED TO DNDi FOR 2003-2018 (AS PER DECEMBER 2013)



To develop its activities and meet its objectives, DNDi seeks diversified sources of funding from public and private sources, which include financial contributions from governments, public institutions, private individuals, foundations, founding partners, and innovative funding mechanisms.

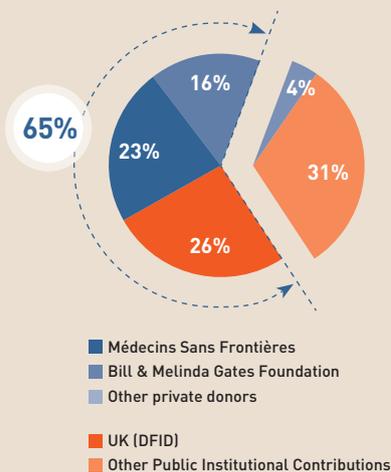
The diversification of donors significantly increased in 2013 with 7 new donors. DNDi welcomed: Norway-NORAD, BBVA Foundation, Brazil-MoH/BNDS, a private donor in Brazil (Moreau Family), Japan-GHIT, Carlos Slim Foundation, and the Rockefeller Foundation.

Concerted efforts are made to ensure that, at maturity (by 2018), no one donor contributes more than 25% toward DNDi's Business Plan and that half of DNDi's budget is covered by public funds and half by private funds.

In 2012, public funding (projected to 2018) was at 53%, with 47% private support. This tendency was reinforced in 2013 with public funding at 57% and 43% from private support. This is mainly due to the fact that two major public donors (UK-DFID and Switzerland-SDC) renewed their long-term commitments, which amount to EUR 41.8 M (15% of total income committed).

THREE MAIN FUNDERS TO DNDi 2003-2013

DNDi, in striving to guarantee its scientific and financial independence from any one specific donor, has maintained a healthy range of funding sources. A ten year analysis shows that the three main donors (Médecins Sans Frontières, DFID, and the Bill & Melinda Gates Foundation) represent two-thirds of total grants to DNDi overall.



Successful shift toward unrestricted funding

Over the past few years, DNDi has managed to maintain a balance between restricted and unrestricted grants. While the ratio is relatively balanced, this requires substantial effort. Unrestricted funding has been part of DNDi's success to date as it has allowed the organization to respond quickly to research opportunities and also to terminate projects that do not meet targeted goals set forth in the Business Plan. In 2013, DNDi received significant unrestricted contributions from UK-DFID, MSF, and Switzerland-SDC which shifted the scale toward unrestricted funding.

CUMULATED 2003-2018: EUR 282 MILLION

