Since its inception in 2003, DNDi has defined itself as an experiment in ‘innovation for access,’ a laboratory for alternative mechanisms that deliver affordable products answering to an unaddressed medical need. Our scale is by definition small: our purpose is not, and never has been, to act as the solution to systemic failures of biomedical R&D.

Our six achievements to date, attained in collaboration with our partners, bear witness to the pertinence of that initial ideal and the success of the model – with two new antimalarial fixed-dose combinations, the world’s first child-friendly medication for Chagas disease, and changes to national or international guidelines, thanks to successful clinical trials for sleeping sickness and for visceral leishmaniasis treatments in Africa and Asia.

More than a decade later, it is our pleasure to take stock once again.
An unchanged vision, an expanded mission

In 2014 and 2015, we embarked on an extensive consultation exercise with our founding partners and key stakeholders, as well as with leading global health actors, to ensure the organization remains attuned to current and emerging patients’ needs and the evolving R&D landscape.

The outcome of the consultation, enshrined in the new Business Plan for 2015 to 2023, maintains our focus on the most neglected diseases by adopting a dual strategy: on the one hand, pursuing incremental innovation to bring therapeutic benefits to patients by repurposing, reformulating, or combining existing drugs; and on the other, seeking to discover and develop entirely new chemical entities, with the aim of bringing radically improved oral treatments without which sustainable control or elimination of these diseases can never become a reality.

Discovering and developing treatments to respond to neglected tropical diseases like sleeping sickness, visceral and cutaneous leishmaniasis, Chagas disease, and filaria remain at the core of our work. Adding to this focus on the most neglected of the neglected, a new research and development project will focus on new treatments for mycetoma, a devastating infection – recently introduced on the official WHO list of neglected tropical diseases – which, left untreated, eventually results in amputation.

While our core focus remains unchanged, we acknowledge that the shortcomings of the existing system of research and development extend far beyond the neglected diseases at the core of DNDi’s portfolio.

From our consultations, three main findings emerged to help us draw lessons for the future of DNDi’s model and operations: first, R&D priorities do not sufficiently originate from low- and middle-income countries (LMICs); secondly, patients’ needs are not prioritized, and many treatment needs, for example for Ebola or mycetoma, are left unaddressed; and finally, market incentives that solely rely on intellectual property and exclusivity rights do not adequately address health needs in LMICs, with certain public health needs like antimicrobial resistance left unanswered as a result.

We also noted changes in global health epidemiology, with for example the
emergence of new infectious disease risks and LMICs facing a double burden of both communicable and non-communicable diseases. The political context of global health is also evolving, with the lack of equitable access to new health tools increasingly seen as a problem, including in high-income countries as, for example, in hepatitis C.

The challenge is therefore better understood as one of “neglected diseases, neglected patients and populations in neglected health and social systems” – that is, of ensuring that the global R&D system meets the needs of all, especially of the poorest and most vulnerable populations in the most neglected settings.

**A dynamic and pragmatic approach to ensure DNDi can respond to changing needs**

Given the complexities of drug discovery and development, the timelines of a research and development organization are lengthy. By essence, our commitments and objectives are long term. The challenge lies in continuing to meet these, while also ensuring DNDi remains relevant and responsive to the evolving needs of patients.

Within this rapidly changing landscape, DNDi’s new Business Plan for 2015 to 2023 aims to give the organization the flexibility to address urgent unmet patients’ needs, by introducing the concept of a dynamic portfolio as a tool to guide the evolution of DNDi’s activities. This will involve identifying and selecting new opportunities through a detailed decision-making and evaluation framework, as well as for phasing out projects when they reach completion and/or are not part of our core activities, as was recently the case for our malaria portfolio that was transferred to the Medicines for Malaria Venture.

Ultimately, decisions to enter into new projects will always be based on patients’ needs, existing R&D opportunities, an absence of other actors in the field, and ability to engage operational partners.
This is what led DNDi to include paediatric HIV into its portfolio in 2011. Even though there is a strong R&D effort to develop better HIV/AIDS treatments for adults, very little research is done for HIV-positive children. Current treatment options are insufficient, as little investment has been made to ensure the safety and efficacy of antiretrovirals in treating children. They are neglected patients.

We now tackle hepatitis C: Despite an abundant pipeline of potential new drugs, developing country research needs are largely unaddressed, and existing products are unaffordable. The therapeutic advances brought about by direct-acting antivirals are not reaching patients. In an exciting new project launched in April 2016, DNDi aims to foster a public health approach to the disease, by facilitating the development of an affordable pan-genotypic treatment. DNDi will also change how it does things. Not every disease area will require the same amount of effort and investment. A range of different operating models can be used, from integration into DNDi’s R&D portfolio, to various levels of more time-limited support such as knowledge sharing, advocacy, building new resource platforms, or serving as an incubator for an idea that may ultimately be externalized.

By allowing for more flexible and diversified operational models, DNDi can tailor the breadth and depth of its engagement to a specific global health R&D need as it arises without jeopardizing our focus or draining resources. Resistance to antibiotic treatments, for example, emerged as a key unmet medical need in our landscape analysis, and was considered best addressed through an incubator model, with a dedicated team (see p. 9).

### The roadmap towards 2023

In our 13 years of existence, DNDi has developed, implemented, or delivered six new treatments, for malaria, sleeping sickness, Chagas, and leishmaniasis, and developed a pipeline of over 30 projects. By our 20th anniversary in 2023, our ambition is to have delivered 16 to 18 new treatments, including two to three new chemical entities.

Reaching this ambitious objective relies on an estimated budget of EUR 650 million covering the 20 year period since the creation of DNDi until 2023,
of which close to EUR 400 million has already been secured to date.

We will stay focused on the key elements that have been essential to our success: our partnerships with private sector actors, key for us to access the necessary expertise and data to bring a treatment through to the hands of patients; the support of public actors, which has been the lifeline of our endeavours; and the participation of research communities and civil society in endemic countries to ensure patients’ needs remain at the forefront of our efforts. For this particular reason, this business plan will be translated into a regional strategic plan, with the expansion and development of DNDi’s regional offices, particularly those in neglected disease-endemic regions. These close associations, for some now more than a decade long, will remain a fundamental part of the set-up of DNDi and assure the process of mutual learning for change for the benefit of the most neglected populations in the most neglected health and social systems.

In the new Business Plan, the founding principles upon which DNDi is built are also reinforced:

• a patients’ needs-driven approach;
• a steadfast commitment to promote open sharing of research knowledge and data while ensuring an access-oriented approach to intellectual property;
• the fostering of innovative, collaborative partnerships with public and private sectors;
• the diversification of funding sources to ensure independence.
GARD: A new partnership to fill critical gaps in antibiotic R&D

“Antimicrobial resistance threatens the very core of modern medicine and the sustainability of an effective, global public health response to the enduring threat from infectious diseases. Without harmonized and immediate action on a global scale, the world is heading towards a post-antibiotic era in which common infections could once again kill.”


A joint initiative by WHO and DNDi, the vision of the Global Antibiotic Research and Development (GARD) Partnership is to develop new antibiotic treatments addressing antimicrobial resistance and to promote their responsible use for optimal conservation, while ensuring equitable access for all, with a focus on global health needs.

The initiative ties in with the Global Action Plan on Antimicrobial Resistance adopted in 2015, which required the WHO Secretariat to propose options for the establishment of new partnerships to identify priorities for new treatments, diagnostics, and vaccines to fight resistant pathogens.

In November 2015, WHO and DNDi jointly organized a technical consultation that reaffirmed the initiative, with participants from pharmaceutical and biotechnology companies, other product development partnerships, academia, civil society, and health authorities from countries of all income levels, including Brazil, Canada, Chile, China, Egypt, India, Japan, Malaysia, Qatar, South Africa, Thailand, the US, Zambia, and seven European countries and the European Commission.

In December 2015, the DNDi Board of Directors approved the hosting of the incubation of the GARD Partnership, which was formally launched in May 2016.

New incentive mechanisms

A critical issue is the failure of current incentive mechanisms to replenish the empty antibiotic R&D pipeline. GARD will provide an important alternative to the traditional market-driven approach, by focusing on products that the pharmaceutical industry has not and will not develop for lack of profitability.

To overcome this hurdle, alternative business models and incentives need to be tested, including ‘delinkage’ of the cost of R&D from volume-based sales and price of treatments. Learning from DNDi’s experience of the partnership model for product development in the field of neglected diseases, GARD will test new incentive mechanisms that stimulate R&D but also contribute to responsible use, while facilitating equitable access to new antibiotic treatments.

Political and financial support from governments

At the time of its launch, GARD secured seed funding commitments from the Federal Ministry of Health of Germany, the Netherlands’ Ministry of Health Welfare and Sports, the South African Medical Research Council, and the United Kingdom Department for International Development as well as from Médecins Sans Frontières, totalling over EUR 2 million of the projected EUR 3 million required for the incubation phase.

Hosted by DNDi, the GARD team is responsible for building the scientific strategy and a product pipeline, developing the GARD business plan, setting up a scientific working group and steering committee, and establishing the operational structure. GARD’s governance is de facto embedded into DNDi’s during this start-up phase.

WHO will provide support in priority setting, stewardship, and access; report back to its Member States; secure close collaboration with the AMR Secretariat, relevant WHO departments, the Essential Medicines List team, and the Global Health R&D Observatory; and provide other technical input where needed.

Staphylococcus Aureus bacteria culture.
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More details on each person available on DNDi’s websites
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Regional Offices

AFRICA
DRC

KENYA

* Member of the Strategic Committee

More details on each person available on DNDi’s websites
EUR 43 MILLION BUDGET FOR 155 DNDi CORE STAFF AND CLOSE TO 700 ESTIMATED FTEs WORLDWIDE

Major growth for HAT disease and in the recent portfolios, as well as in feasibility studies

Since its inception in 2003, DNDi expenditure totals EUR 260 million. In 2015, expenditure amounted to EUR 43 million, +18% (+EUR 6.6 M) compared to 2014. This increase is principally due to HAT projects expenditure (+EUR 1.6 M) and the projects recently entered in the portfolio (+EUR 1.2 M for filarial diseases; +EUR 1.1 M for the HIV portfolio (+EUR 1.6 M) and the projects recently entered in the portfolio (+EUR 1.2 M for filarial diseases; +EUR 1.1 M for the HIV paediatric project, and +EUR 0.5 M for feasibility studies).

In addition, the variation of exchange rates in 2015, and particularly the higher price of the US dollar (+17%) and the Swiss franc (+9%) against the Euro, led to a significant increase in our accounts, as these are held in Euros (+ +EUR 3 M, accounting for -8% out of the total 18% 2015 growth).

The operating gain of EUR 0.28 million is partly canceled because of exchange rate loss (EUR 0.16 million).

HUMAN RESOURCES EVOLUTION 2014-2015

Growth of activities (+18%) sustained by staff increase (+13%)

In 2015, DNDi recruited an additional 18 people (24 people in 2014), which represents an increase of 13%. Recruitment occurred mainly at headquarters in Geneva, with 15 new people (+24%), and with 3 new positions in regional offices (ROs) - Kinshasa, Tokyo, and Rio de Janeiro (+4%). The increase in the Geneva R&D team is mainly due to the strengthening of the R&D coordination (4 FTE in Geneva and 2 in Japan) and HAT disease (+2 FTE in Geneva and 1 FTE in Kinshasa). Other new positions are mostly dedicated to External Affairs (Communication and Fundraising activities +4 FTE). Staff in ROs is now of an equivalent number (50%) to staff based in headquarters (50%). Also noteworthy: of the 16 recruitments completed in 2016 by the end of April, 5 are in the headquarters (4 replacements and 1 new position), and 11 implemented in ROs (3 replacements and 8 new positions).

For 2015, the exact amount of FTE working at DNDi was calculated taking into account start date, end date, and percentage of time for each person working at DNDi; giving a total of 139 FTE with 155 people working at DNDi.

FOUNDSING PARTNERS

In 2003, seven public and private institutions came together to form DNDi: Médecins Sans Frontières (MSF) • Doctors Without Borders • Oswaldo Cruz Foundation, Brazil • Indian Council for Medical Research, India • Kenya Medical Research Institute, Kenya • Ministry of Health, Malaysia • Institut Pasteur, France • The Special Programme for Research and Training in Tropical Diseases (WHO-TDR)
Stabilization of the Social Mission ratio

In 2015, DNDi’s non-social mission ratio remains highly stable compared to 2014. The growth in non-social mission (+EUR 0.8 M) and social mission expenditures (+EUR 5.8 M) were balanced, at 18% each. However, these steady figures mask some specific points worth highlighting:

- The External Affairs department covering Communications, Advocacy, Policy affairs, and Fundraising activities experienced one of the highest growths in 2015 of all departments, with a 33% increase (+EUR 1.1 M).
- Activities related to Strengthening Capacities, with 7% growth (+EUR 0.2 M), and General Administration, with 10% growth (+EUR 0.3 M) maintained the same level of activity compared to 2014, with the rise in expenditure mostly due to the increase in the CHF & USD exchange rates against the EUR.

Comparison of percentage of partnerships with the public institutional sector (research institutes, public hospitals, academic groups, universities, PDPs, and other not-for-profit organizations) with numbers of partnerships with the private sector (pharmaceutical and biotechnology companies and contract research organizations).

Steady growth in number of partnerships

The number of contracts finalized each year follows a trend similar to that of R&D partners & service providers with a financial compensation of over EUR 5,000. There is a regular annual increase of between 5% and 15%, with 5% in 2013 and 12% in 2015.

*Except confidentiality agreements; some new contracts may be extensions.