

BUSINESS PLAN

2015-2023



A dynamic portfolio approach
to address neglected patients' needs

DNDi

Drugs for Neglected Diseases *initiative*

The R&D landscape for neglected but large gaps remain

➔ Review of the Business Plan to ensure impact for patients

Every four to five years, DNDi reviews and updates its Business Plan in order to ensure the organization stays attuned to current and emerging patient needs.

Since its inception, DNDi has advocated for public leadership and a sustainable, publicly-driven framework for essential health R&D. In 2010, a Business Plan review for the period of 2011 to 2018 was conducted, at which time two new disease areas were added to DNDi's portfolio (filarial diseases and paediatric HIV), with a renewed commitment to its core disease activities (human African trypanosomiasis, leishmaniasis, and Chagas disease).

A plan was put in place to complete and transfer malaria activities to partners. The plan also aimed to substantially increase the role of Regional Offices and better define DNDi's engagement in facilitating patient access to treatments.

In 2014, DNDi initiated the process for its next Business Plan to cover the period from 2015 to 2023. Through an extensive consultation exercise involving founding partners and key stakeholders worldwide, DNDi analysed the R&D landscape, assessed new and emerging R&D gaps, explored the involvement of other players in addressing these needs, and identified future trends. As a result, an adapted decision-making process has been implemented to ensure that the organization remains responsive to neglected patients' needs and the appropriate models were designed.

WHO WE ARE

The Drugs for Neglected Diseases *initiative* (DNDi) was established in 2003 to address specific research and development (R&D) needs of neglected patients by filling a virtually empty drug pipeline, where market and policy failures had left millions with either ill-adapted treatments or no treatments at all. DNDi was set up by key research and health institutions, notably from the public sector in neglected-disease-endemic countries, with seed funding from Médecins Sans Frontières/Doctors Without Borders (MSF)'s 1999 Nobel Peace Prize. DNDi is an independent, international not-for-profit R&D organization working to bring new treatments to neglected patients. To date, DNDi has delivered six new treatments and built the largest-ever drug pipeline for some of the most neglected diseases, with a mix of improvements on existing drugs and entirely new chemical entities (NCEs).

DNDI'S FOUNDING PARTNERS

Médecins Sans Frontières/Doctors Without Borders (MSF) • Indian Council of Medical Research • Kenya Medical Research Institute • Oswaldo Cruz Foundation, Brazil • Ministry of Health, Malaysia • Institut Pasteur, France • World Health Organization (WHO) Special Programme for Research and Training in Tropical Diseases (TDR), permanent observer

The following is a summary of this new Business Plan 2015-2023, adopted by the Board of Directors in 2015. It reinforces the principles on which the organization is built:

- 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 (IP) management and licensing;
- the fostering of innovative, collaborative partnerships; and
- the diversification of funding sources to ensure scientific independence.

DNDi will build on its collaborative R&D model, retaining the core focus on some of the most neglected diseases while providing flexibility to extend its disease scope to better address urgent unmet patient needs within the rapidly changing global health R&D landscape.

patients has improved

➔ An unsustainable biomedical innovation system

As illustrated during the R&D landscaping phase of the Business Plan process, there is growing recognition and consensus that the current system for biomedical innovation has failed to deliver adequate and affordable health technologies, particularly for the world's poor. Epidemiological trends are now shifting, with low- and middle-income countries (LMICs) increasingly experiencing a double-burden of non-communicable and communicable diseases. Compounding this situation, estimates show that by 2020 the majority of the world population living on less than USD 2 per day will be in emerging economies, and will be unable to access medical innovations if the current challenges in innovation and access are not addressed.

This shifting epidemiological trend brings risks of emerging infectious diseases, such as anti-microbial resistance, which threatens the health of the entire world. Following the peak of the Ebola crisis, initiatives

have been and will be proposed to address the need for a global fund and mechanism, which should align rather than further fragment prioritization, coordination, and funding of R&D efforts to accelerate innovation and ensure equitable treatment access for a wide range of diseases.

However, the current system of biomedical innovation is becoming unsustainable for all countries, irrespective of disease area or income classification, because of three main drivers of unmet need:

- R&D priorities do not sufficiently originate from low- and middle-income countries and do not prioritize patients' needs;
- medical innovation is not linked to equitable access;
- market-based incentives aligned with the current intellectual property system do not adequately address global public health needs of poor people.

Within this context, the need is greater than ever for organizations such as DNDi to stimulate innovation in a way that guarantees equitable access and to continuously explore new pathways for drug development, while advocating for systemic change. In order to better respond to the changing landscape, DNDi has modified its mission statement to enable the organization to:

- address the needs of people suffering from neglected diseases, the scope of which goes beyond the most neglected communicable diseases;
- adopt a more dynamic portfolio approach to R&D, allowing for more flexible, proactive, and diversified operational models;
- continue efforts to strengthen research capacity in endemic countries;
- more forcefully advocate for public responsibility and a more enabling and sustainable R&D framework that guarantees both innovation and equitable patient access to health technologies.

KEY ACHIEVEMENTS TO DATE (2003-2015)

• Six treatments delivered

Malaria: two fixed-dose combination (FDC) treatments: artesunate-amodiaquine (ASAQ FDC) and artesunate-mefloquine (ASMQ FDC)

Human African trypanosomiasis: nifurtimox-eflornithine combination therapy (NECT)

Visceral leishmaniasis in Africa: sodium stibogluconate and paromomycin combination therapy (SSG&PM)

Visceral leishmaniasis in Asia: a set of therapies, including drug combinations with paromomycin and miltefosine, and liposomal amphotericin B

Chagas disease: a paediatric dosage form of benznidazole

- Pipeline of over **30 projects** spanning **six disease areas**
- **Fifteen entirely new chemical entities (NCEs)** in the R&D pipeline
- **Over 130 institutional partnerships**, the majority of which are in disease-endemic countries
- **Team of 150 staff**, more than half of whom are in disease endemic countries, and some 600 people working on DNDi projects within partner organizations
- **Over EUR 350 million raised to date**, equally from public and private sources
- **Three regional disease-specific clinical trial platforms** and two technology transfers

DNDi’s core focus is maintained while the organization adapts to evolving needs

➔ Vision

To improve the quality of life and the health of people suffering from neglected diseases by using an alternative model to develop drugs for these diseases and by ensuring equitable access to new and field-relevant health tools.

In this not-for-profit model, driven by the public sector, a variety of players collaborate to raise awareness of the need to research and develop drugs for those neglected diseases that fall outside the scope of market driven R&D. They also build public responsibility and leadership in addressing the needs of these patients.

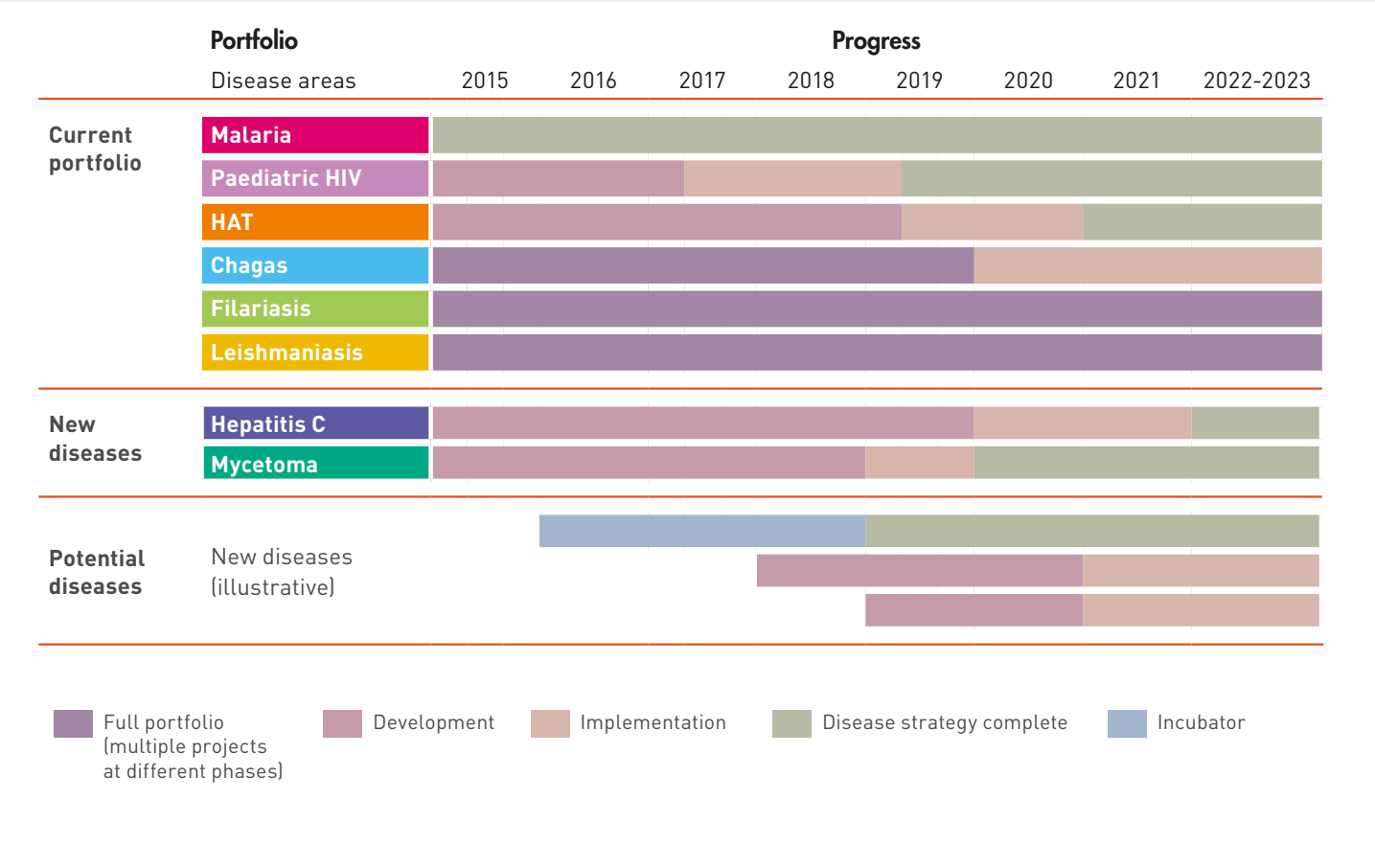
➔ Mission

- To develop new drugs or new formulations of existing drugs for **people suffering from neglected diseases**. Acting in the public interest, DNDi bridges existing research and development (R&D) gaps in essential drugs for these diseases by initiating and coordinating drug R&D projects in collaboration with the international research community, the public sector, the pharmaceutical industry, and other relevant partners.
- DNDi’s **primary focus** has been the development of drugs for the **most neglected diseases**, such as human African trypanosomiasis (HAT, or sleeping sickness), visceral leishmaniasis (kala-azar), and Chagas disease, while considering engagement in **R&D projects for other neglected patients** (e.g. malaria, paediatric HIV, filarial infections) and development of diagnostics and/or vaccines

to address unmet needs that others are unable or unwilling to address.

- In pursuing these goals, DNDi enables R&D networks built on global collaborations. While harnessing existing support capacities in countries where the diseases are endemic, DNDi contributes to **strengthen capacities in a sustainable manner**, including through know-how and technology transfers in the field of drug R&D for neglected diseases.
- In order to address the evolving needs of public health importance and maintain DNDi’s commitment to delivering on the objectives of the current portfolio of diseases, **a dynamic portfolio approach** is adopted. This enables DNDi to take on new disease areas with various operating models, while completing objectives in current diseases.

Illustrative portfolio progression through a dynamic R&D approach



A more dynamic approach to addressing neglected patients' needs

A dynamic portfolio approach has been developed in order to enable DNDi to maintain its primary focus on the most neglected diseases, while providing flexibility to extend the scope of diseases to address current and future unmet and/or urgent patient needs. It involves a detailed decision-making and evaluation framework for the selection of new opportunities, as well as for phasing out projects when they reach completion, as was recently the case for malaria.

The process entails a phase of idea sourcing, in which patient needs and opportunities are explored with partners, followed by idea translation, where feasibility studies are conducted and options validated in order to prepare for a Board decision, following Scientific Advisory Committee review. The

final phase comprises the selection of a model, in which the project is further defined and prepared for launch if approved. Ultimately, decisions to enter into new projects will always be based on patient needs, existing R&D opportunities, an absence of other actors in the field, and ability to engage operational partners.

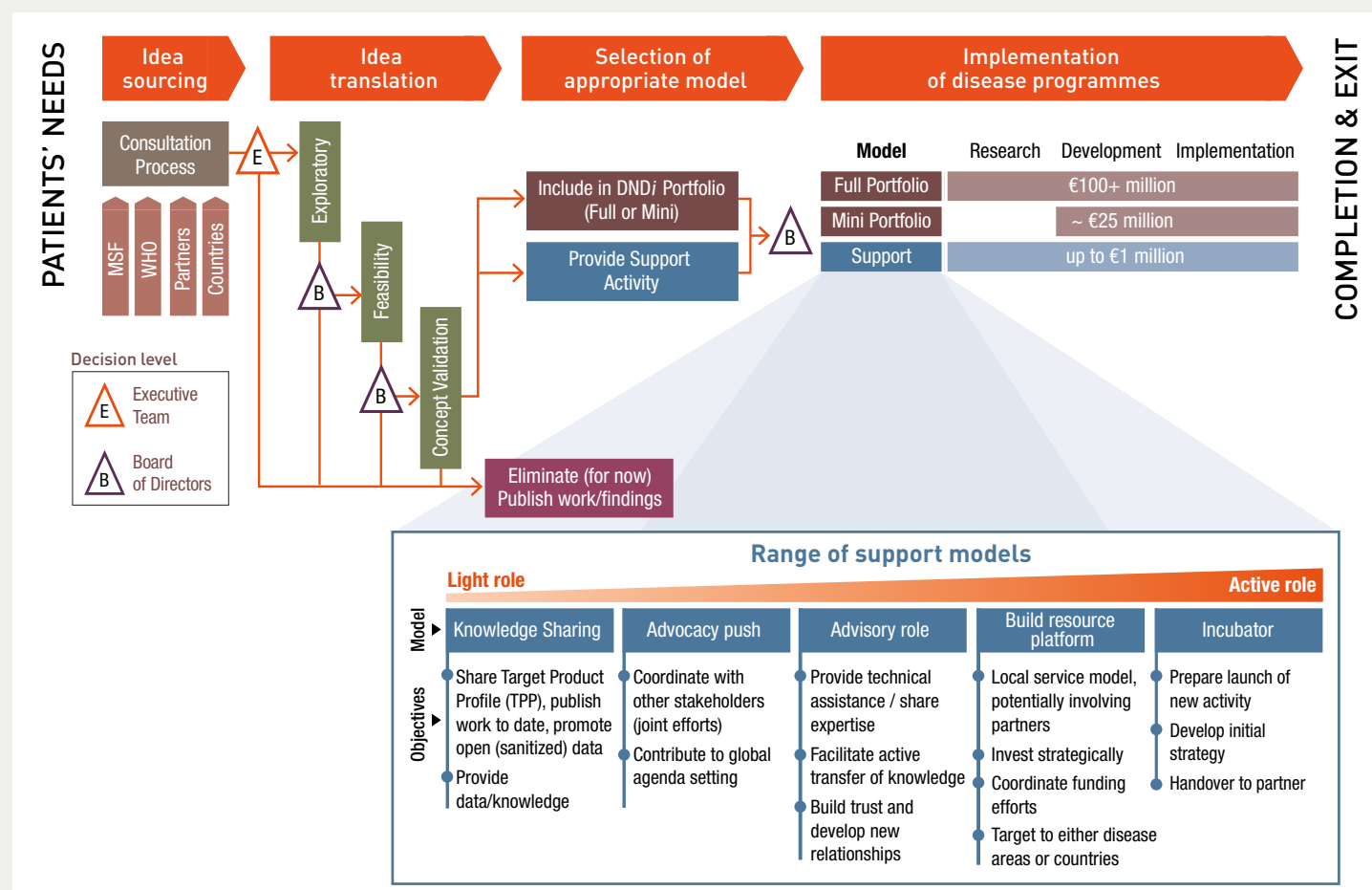
Because not every disease area will require the same amount of effort and investment from DNDi, a range of operating models has been designed to tailor DNDi's involvement and allow for responding to global health R&D needs as they arise.

New projects may require a multiplicity of models to address unmet needs, ranging from light approaches (such as knowledge-sharing or helping with an advocacy push) to

more active approaches (including building new resource platforms or serving as an incubator for an idea that may ultimately be externalized. This could be achieved by integration into the existing portfolio, with definition of clear exit criteria, a defined ideal outcome for knowledge sharing, or an advisory role. Anti-microbial resistance (AMR), for example, could benefit from an incubator model, as this would enable a separate team to develop the idea further in order to prepare for the launch of a new not-for-profit entity.

By piloting five different support models, DNDi can achieve greater impact and build on its experience in addressing unmet medical needs without jeopardizing areas of focus and/or draining resources (both human and financial).

A new decision-making framework allows for a dynamic portfolio comprised of different (regional) models for selection of new opportunities



DNDi's long term objective: 16 to 18 new of EUR 650 million by 2023

DNDi will remain invested in the most neglected diseases. Over time, additional disease areas and support models will be integrated, with the possibility of being initiated and led by Regional Offices.

Current

LEISHMANIASIS

A safe, effective, low-cost, and short-course oral combination treatment for visceral leishmaniasis (VL); a new treatment for post-kala azar dermal leishmaniasis; treatment options for HIV/VL co-infected patients; a new first-line treatment regimen for VL in Latin America; and a new treatment for cutaneous leishmaniasis (CL).

CHAGAS DISEASE

An effective and safe oral treatment for the chronic and acute forms of Chagas disease, including new benznidazole regimens and combinations, in addition to new chemical entities expected to emerge from the discovery pipeline.

HUMAN AFRICAN TRYPANOSOMIASIS (HAT)

An oral, safe, effective treatment for both stages of the disease, in support of disease elimination targets, and project completion.

FILARIAL DISEASES

A new treatment for adults and children with lymphatic filariasis or onchocerciasis that is a macrofilaricide (a drug to kill adult worms), oral, short-course, well tolerated, affordable, and adapted to tropical climates.

PAEDIATRIC HIV

Two new four-in-one paediatric formulations containing the protease inhibitor lopinavir/ritonavir (LPV/r) and two nucleoside reverse transcriptase inhibitors (NRTIs: abacavir or zidovudine and lamivudine); one stand-alone paediatric booster (ritonavir) for HIV-TB co-infected children; complete this project or transition into other paediatric drug formulation projects.

New

MYCETOMA

A pragmatic short-term approach based on an existing therapeutic opportunity: DNDi and partners will conduct a clinical trial in mycetoma patients to test fosravuconazole, the best-in-class azole candidate drug from laboratory tests, to safely treat patients suffering from mycetoma.

HEPATITIS C VIRUS (HCV)

To meet the specific needs of HCV patients in low- and middle-income countries: DNDi's objective is to develop an affordable public health tool using direct-acting antivirals (DAAs). DNDi will partner with the governments of Thailand and Malaysia and suppliers to conduct clinical trials of new DAAs to support scientific evidence for public health decision making. Due to the rapidly changing HCV environment, DNDi will also support access-related activities in this field.

Exploratory

ANTI-MICROBIAL RESISTANCE (AMR)

In close collaboration with WHO and other key stakeholders, DNDi may incubate a task force to assess the potential of a new global initiative to respond to the unmet needs in the field of AMR R&D, with the expectation that the initiative become independent after 18 months.

Complete

MALARIA

After producing two treatments for malaria, DNDi handed over the projects to the Medicines for Malaria Venture and has ceased activities in this disease area.

2015

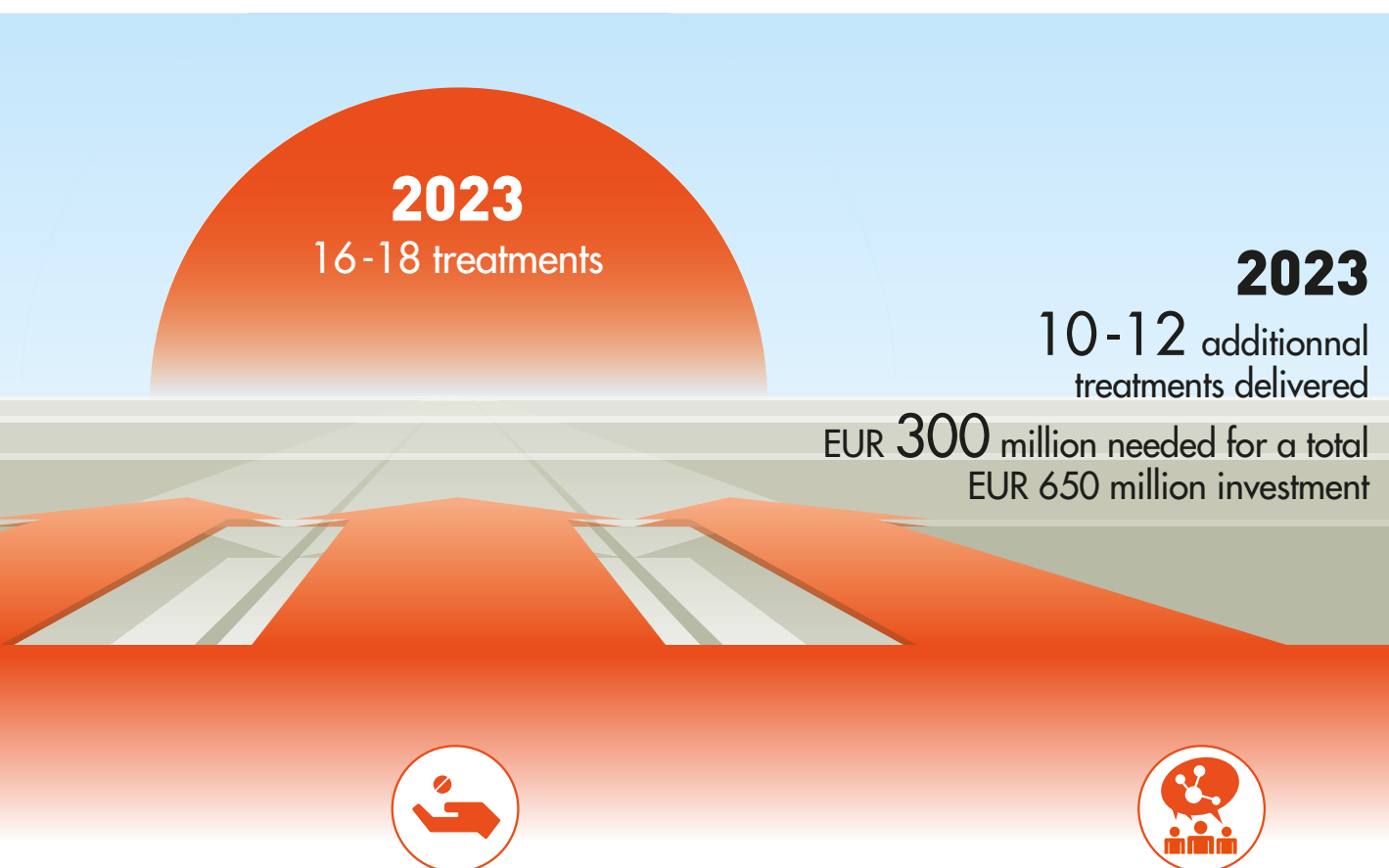
6 treatments delivered
EUR 350 million raised



Influence the R&D landscape for neglected diseases

- DNDi advocates for enhanced political leadership, sustainable financing, and sound public policies that will encourage greater needs-driven R&D.
- DNDi will take concrete steps in analysing, piloting, and bringing evidence from its alternative and open models of innovation; pro-access management of intellectual property and licensing; practice of de-linking product pricing from R&D costs; and promotion of innovative regulatory pathways.
- Global policy advocacy efforts will be focused on the creation of a global fund and mechanism for innovations of public health importance through the engagement of public health leaders in low- and middle-income countries.

treatments developed with a total investment



Develop treatments for people suffering from neglected diseases

- As defined within this new Business Plan, the primary objective of DNDi is to deliver a total of 16 to 18 treatments by 2023 (including the six delivered as of September 2015).
- Expanding on R&D networks built across regions, DNDi will reach this objective while testing several models of implementation.
- Three new chemical entities (NCEs), including combinations with one NCE, will be developed and the portfolio will span approximately ten disease areas during a 20-year period (2003-2023).

Strengthen research capacity

DNDi enables R&D networks while harnessing existing support capacities in low- and middle-income countries by:

- Maintaining and building R&D platforms (e.g. transforming one platform in Africa into a sustainable resource platform for clinical studies);
- Promoting regionally driven initiatives (e.g. lead optimization programmes in Latin America and India);
- Facilitation of patient access to treatments;
- Training to support R&D efforts in disease-endemic countries; and
- Transfer of technology to local manufactures.

Regional Offices will lead these efforts.

An organizational roadmap for growth

Proximity to patients is key to support the ongoing work to address neglected patients' needs

DNDi has taken concrete steps to invest in the expansion and **development of its Regional Offices**, particularly those in neglected-disease-endemic regions. To ensure its activities are carried out in close proximity to the patients who DNDi was created to serve, regional R&D projects, networks of excellence, capacity strengthening programmes, access activities, and advocacy will be taken up increasingly by Regional Offices.

Growth is controlled and stable, increasing to EUR 50 million per year

While over the past eight years, DNDi's budget nearly tripled and to reach the targeted objectives of the organization, the projected growth for the next Business Plan period will stabilize, reaching approximately 30% over a period of nine years. Furthermore, the dynamic portfolio approach will lead to a balance of investment between the initial disease areas and new programmes.

In view of a lean structure, overhead costs will remain low, at approximately 12.5%. Other social mission, including advocacy and capacity strengthening, will remain stable at 15%, with the remaining 72.5% for R&D activities.

Based on an analysis of its model, DNDi estimates the cost of development to range from EUR 6-20 million for an improved treatment, and EUR 30-40 million for a new chemical entity (NCE). However, the attrition rate for drug discovery and development in the field of infectious diseases and the inherent risk of failure should be taken into account, bringing the cost range of an improved treatment to EUR 10-40 million, and EUR 100-150 million for an NCE. These estimations do not include the in-kind contributions from DNDi's many partners.

The 2023 vision relies on an estimated budget of EUR 440 million for the 2015-2023 period, including EUR 340 million associated to the current portfolio of diseases and activities (with 'other social mission') and EUR 100 million for new opportunities.

Thirty per cent of financial needs already secured

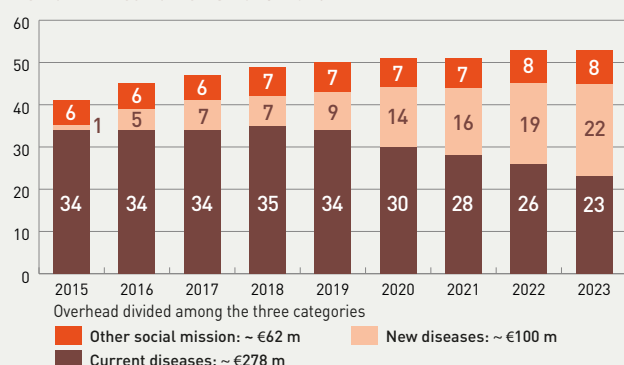
At the launch of this Business Plan in September 2015, EUR 140 million of the EUR 440 million needed to develop 10-12 additional treatments by 2023 has already been secured. DNDi aims to continue to raise a majority of unrestricted or portfolio-wide funding and to maintain a balance between public and private sources, with no single donor contributing more than a quarter of the overall budget. It is expected that emerging economies and innovative funding mechanisms will play an increasingly important role in the donor landscape.

The people behind our work

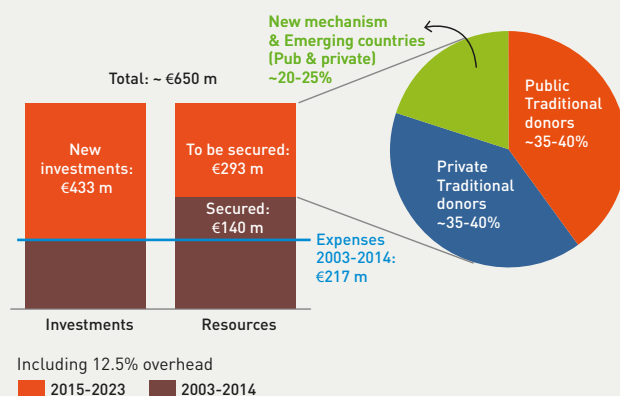
The majority of human resources growth will occur in the Regional Offices (80% of new staff), to reach over 210 staff (up from currently 150) by 2023. The ratio of DNDi staff and individuals at other institutions working on DNDi projects will remain stable at approximately 1:4. Building on its 'virtual model', DNDi remains committed to coordination and facilitation roles with partners and stakeholders.

Projections including the dynamic portfolio will require an average annual budget of EUR 48-50 million

BUDGET PROJECTIONS 2015-2023



New Business Plan 2015-2023: EUR 440 million EUR 140 million already secured (30%)



➔ DNDi's work is only possible through its partnerships

None of the work of the organization is possible without the passionate and motivated people from diverse backgrounds, spanning public, private, and non-governmental sectors. The people and partners behind the success of DNDi worldwide embody the values of the organization in its patient-driven approach, best science and quality for the most neglected, commitment to building partnerships, pragmatism and responsibility, and spirit of entrepreneurship and innovation.