The NTD Drug Discovery Booster: an innovative collaboration for hit expansion

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Activating the Power of Japan’s Unique Chemical Compounds for Neglected Diseases
Responding to the Needs of Patients Suffering from Neglected Diseases

DNDi’s PRIORITY: Neglected Patients

- Mycetoma
- Hep C
- Sleeping sickness
- Chagas disease
- Malaria
- Pediatric HIV
- Leishmaniasis
- Filarial diseases

DNDi’s Mission

- To develop new drugs or new formulations of existing drugs
- To strengthen capacities in a sustainable manner
- To adopt a dynamic approach to portfolio diseases

...from Bench to Bedside
7 new treatments delivered, recommended, implemented

- 30 projects, 8 diseases areas
- 13 entirely new chemical entities (NCEs)
- Over 160 partnerships, most in endemic countries
- 160 staff, half in endemic countries & 700 people working on DNDi projects
- EUR 400 million raised equally from public and private sources
- 4 regional disease-specific clinical trial platforms/ networks and several technology transfers

- Easy to use
- Affordable
- Field-adapted
- Non-patented
DNDi’s success is only possible through innovative partnerships

CRITERIA FOR SUCCESS
- Share the same vision
- Mutual understanding
- Involvement throughout the whole process

Over 160 partnerships worldwide

Some current Japanese partners:
- Eisai
- Takeda
- Shionogi
- Daiichi-Sankyo
- GeneDesign
- Kitasato Institute
- Riken Institute
- IMC
- GHIT Fund
### DNDi R&D Portfolio June 2017

#### 7 new treatments available and up to 16 new chemical entities in the pipeline

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<th>Screen</th>
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<th>Lead Opt.</th>
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New Chemical Entity (NCE); Fexinidazole (for HAT, VL, and Chagas disease) = 1 NCE; Fosravuconazole = 1 NCE
Projects with Japanese partnerships and support from the GHIT Fund providing NCEs

DNDi R&D Portfolio June 2017

Growing portfolio
- 8 Partners
- 20 projects
Unique compounds from Japan

- Screening of drug-like small molecules from Japanese pharmaceutical companies and research institutes
- Some interesting hits identified
- NTD Drug Discovery Booster used to accelerate these new discoveries
- Japanese natural products


PCA plots of drugs approved by FDA between 1981–2010 parsed by compound origin
Drug discovery for tropical diseases such as Visceral Leishmaniasis and Chagas Disease is neglected – Little interest, limited investment, few researchers, \textit{few tools}

Parasites are very difficult to kill – High Throughput Screening hit rates:
- \textit{L. donovani} (intracellular) $<0.05\%$
- \textit{T. cruzi} (intracellular) $<0.15\%$

\textit{Hits are scarce and precious – need to fully exploit them}

\textbf{The NTD Drug Discovery Booster Goals:}
- Expand precious HTS hits and enable scaffold-hopping to find new hits
- Benefit from the pooling of structures and information
- Accelerate discovery and reduce costs
- Experiment with a new open innovation approach to drug discovery
• Complementary compound collections and different computational approaches efficiently explore chemical space around new hits
• Rapid SAR expansion and scaffold-hopping before expensive optimization chemistry is needed
Booster: Progress to date

- **Status**
  - Hit Series approved
  - Abandoned
  - 2nd Iteration ongoing
  - 2nd Iteration planned
  - 1st iteration ongoing
  - 1st iteration planned

- **Booster: Progress to date**

  - S01IH1
  - S02IH1
  - S03IH1
  - S04IH1
  - S05IH1
  - S06IH1
  - S07IH1
  - S08IH1
  - S09IH1
  - S10IH1
  - S11IH1
  - S12IH1
  - S13IH1
  - S14IH1
  - S15IH1
  - S16IH1

- **Status**
  - Hit series identified

- **1st iteration**
  - S01
  - S02
  - S03
  - S04
  - S05
  - S06
  - S07
  - S08
  - S09
  - S10
  - S11

- **2nd iteration**
  - S01IH1
  - S02IH1
  - S03IH1
  - S04IH1
  - S05IH1
  - S06IH1
  - S07IH1
  - S08IH1
  - S09IH1
  - S10IH1
  - S11IH1
  - S12IH1
  - S13IH1
  - S14IH1
  - S15IH1

- **1Q18**
  - Hit Series approved
  - Abandoned
  - 2nd Iteration ongoing
  - 2nd Iteration planned
  - 1st iteration ongoing
  - 1st iteration planned

- **2Q15**
  - Hit Series approved

- **3Q15**
  - Hit Series approved

- **4Q15**
  - Hit Series approved

- **1Q16**
  - Hit Series approved

- **2Q16**
  - Hit Series approved

- **3Q16**
  - Hit Series approved

- **4Q16**
  - Hit Series approved

- **1Q17**
  - Hit Series approved

- **2Q17**
  - Hit Series approved

- **3Q17**
  - Hit Series approved

- **4Q17**
  - Hit Series approved

- **1Q18**
  - Hit Series approved

- **2Q18**
  - Hit Series approved

- **3Q18**
  - Hit Series approved

- **4Q18**
  - Hit Series approved

- **1Q19**
  - Hit Series approved

- **2Q19**
  - Hit Series approved

- **3Q19**
  - Hit Series approved

- **4Q19**
  - Hit Series approved

- **1Q20**
  - Hit Series approved

- **2Q20**
  - Hit Series approved

- **3Q20**
  - Hit Series approved

- **4Q20**
  - Hit Series approved

- **1Q21**
  - Hit Series approved

- **2Q21**
  - Hit Series approved

- **3Q21**
  - Hit Series approved

- **4Q21**
  - Hit Series approved

- **1Q22**
  - Hit Series approved

- **2Q22**
  - Hit Series approved

- **3Q22**
  - Hit Series approved

- **4Q22**
  - Hit Series approved

- **1Q23**
  - Hit Series approved
Innovative NTD Booster Project recognised by DNDi

Project of the year 2016
NTD Booster Summary

• A novel approach accelerating discovery of new drugs for NTDs

• A unique partnership of Japanese companies, the GHIT Fund and other international partners

• Diversity of chemistry and scientific approaches already yielding several promising projects

• Useful learning for growing partnership with applicability to other global health projects

• Special environment created in Japan by the GHIT Fund and Japanese pharmaceutical companies

• Global partnership committed to patients’ needs

• Precious Japanese contributions to synthetic and natural compound screening, the NTD Booster, and drug discovery and development projects
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NTD Drug Discovery Booster

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