A photograph of two young children, a boy and a girl, sitting on a large log in a field of yellow flowers. The boy is on the left, pointing towards the camera with a smile. The girl is on the right, looking down at something in her hands. They are both shirtless and wearing shorts. The background shows a rural setting with trees and a brick building.

GHIT R&D Forum, December 8th 2017
Tokyo Garden Terrace Kioi Conference

Activating the Power of Japan's Unique
Chemical Compounds for Neglected Diseases

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

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DNDi

Drugs for Neglected Diseases *initiative*

Responding to the Needs of Patients Suffering from Neglected Diseases...



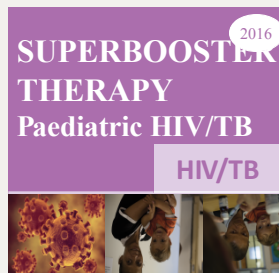
...from Bench to Bedside

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



7 new treatments delivered, recommended, implemented



- ✓ Easy to use
- ✓ Affordable
- ✓ Field-adapted
- ✓ Non-patented

- 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

DNDi's success is only possible through innovative partnerships

Over 160 partnerships worldwide

CRITERIA FOR SUCCESS

- ✓ Share the same vision
- ✓ Mutual understanding
- ✓ Involvement throughout the whole process



Biotechs

Int. Org.
& NGOs

PDPs

Universities
& Research
Institutes

CROs

Pharmaceutical
companies

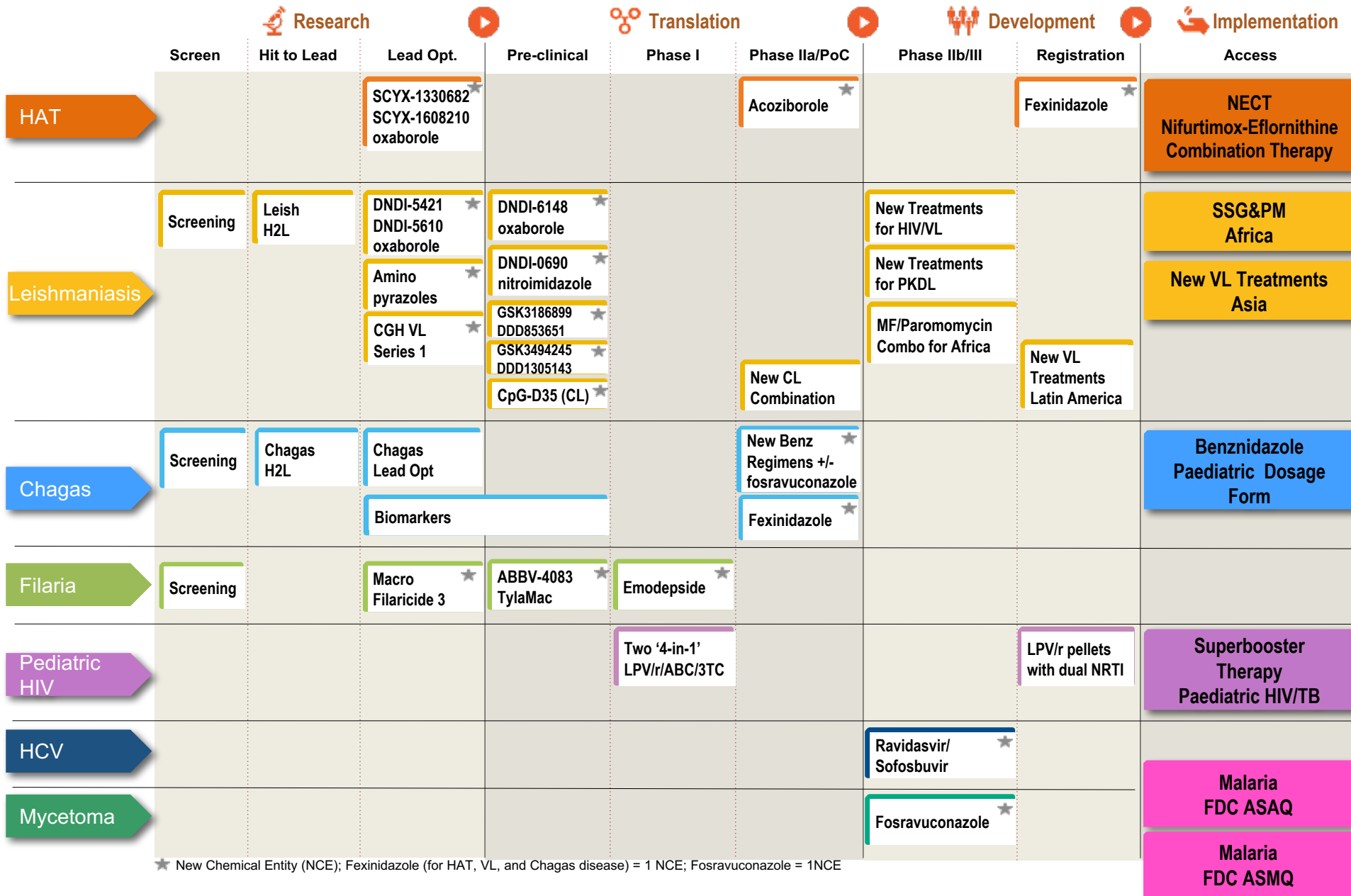
Some current
Japanese partners:

Eisai
Takeda
Shionogi
Daiichi-Sankyo
GeneDesign
Kitasato Institute
Riken Institute
IMC

GHIT Fund

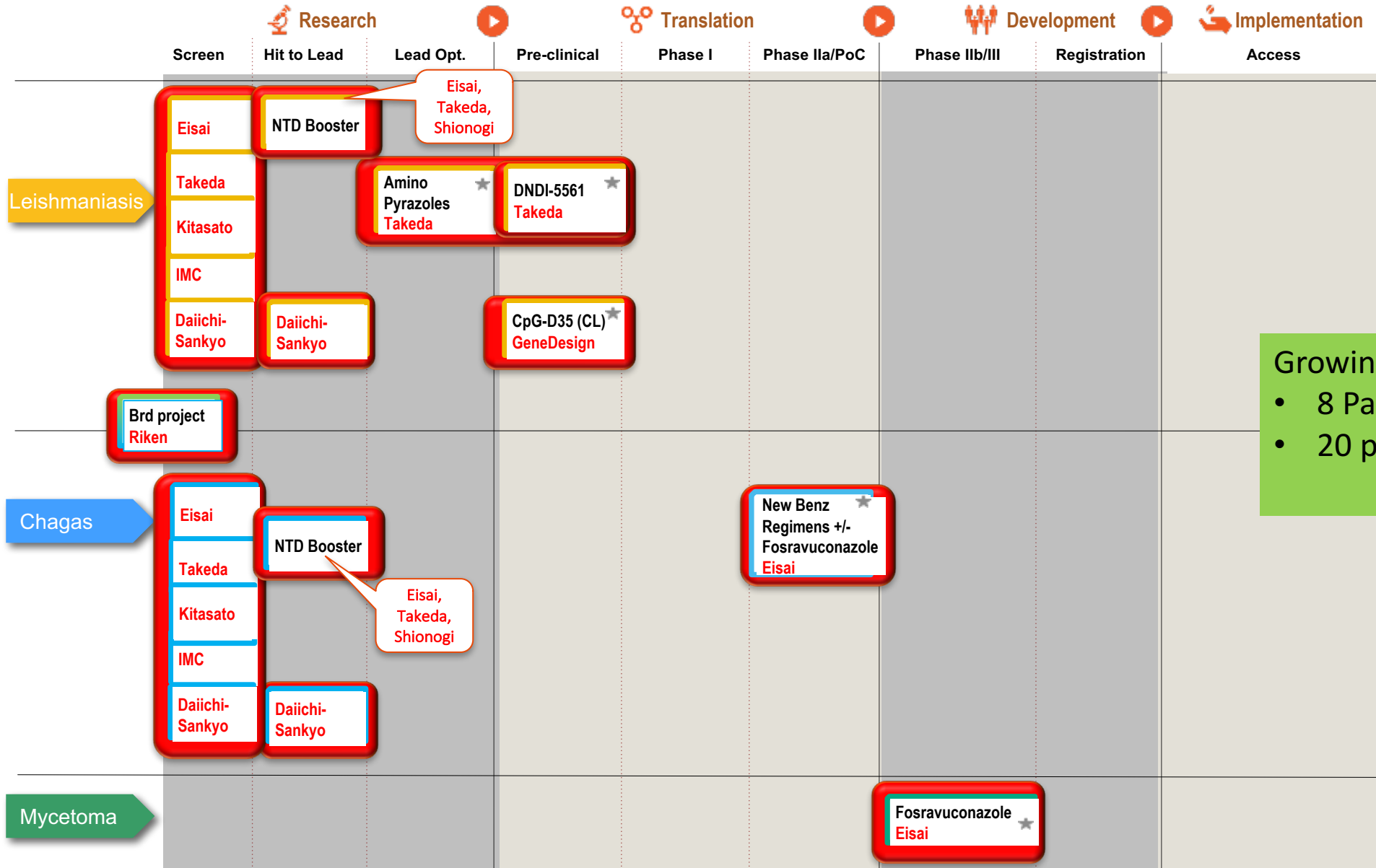
DNDi R&D Portfolio June 2017

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



DNDi R&D Portfolio June 2017

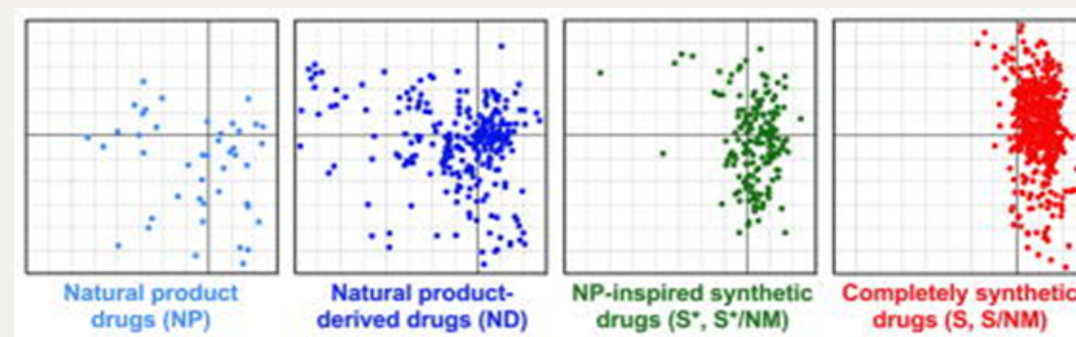
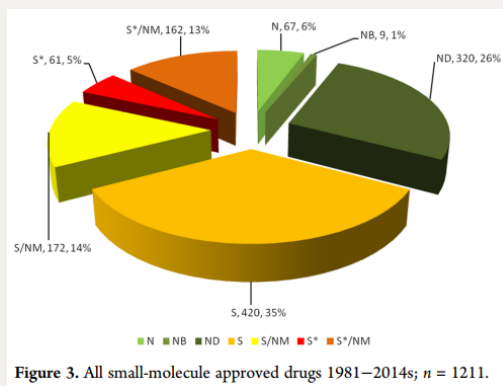
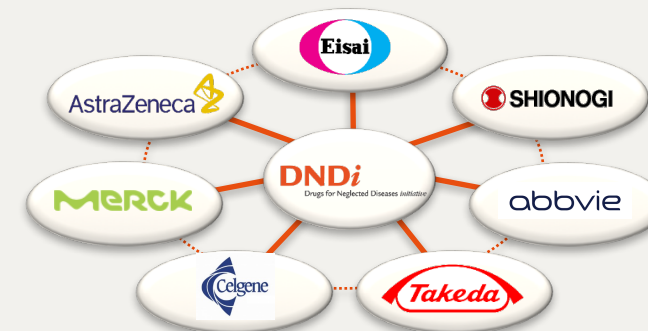
Projects with Japanese partnerships and support from the GHIT Fund providing NCEs



★ New Chemical Entity (NCE)

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



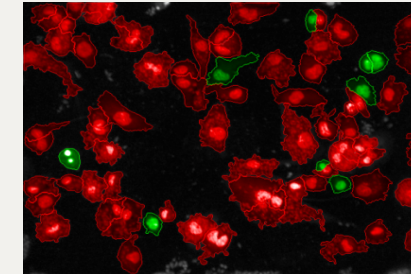
PCA plots of drugs approved by FDA between 1981–2010 parsed by compound origin

Newman DJ, Cragg GM. Natural Products as Sources of New Drugs from 1981 to 2014
J Nat Prod. 2016 25;79(3):629-61

Stratton et al., 2013, Cheminformatic comparison of approved drugs from natural product versus synthetic origins. Bioorg Med Chem Lett. 2015 1; 25(21): 4802–4807

A BIG Experiment in Early Drug Discovery

- Drug discovery for tropical diseases such as Visceral Leishmaniasis and Chagas Disease is neglected
 - Little interest, limited investment, few researchers, *few tools*
- Parasites are very difficult to kill
 - High Throughput Screening hit rates:
 - *L. donovani* (intracellular) <0.05%
 - *T. cruzi* (intracellular) <0.15%



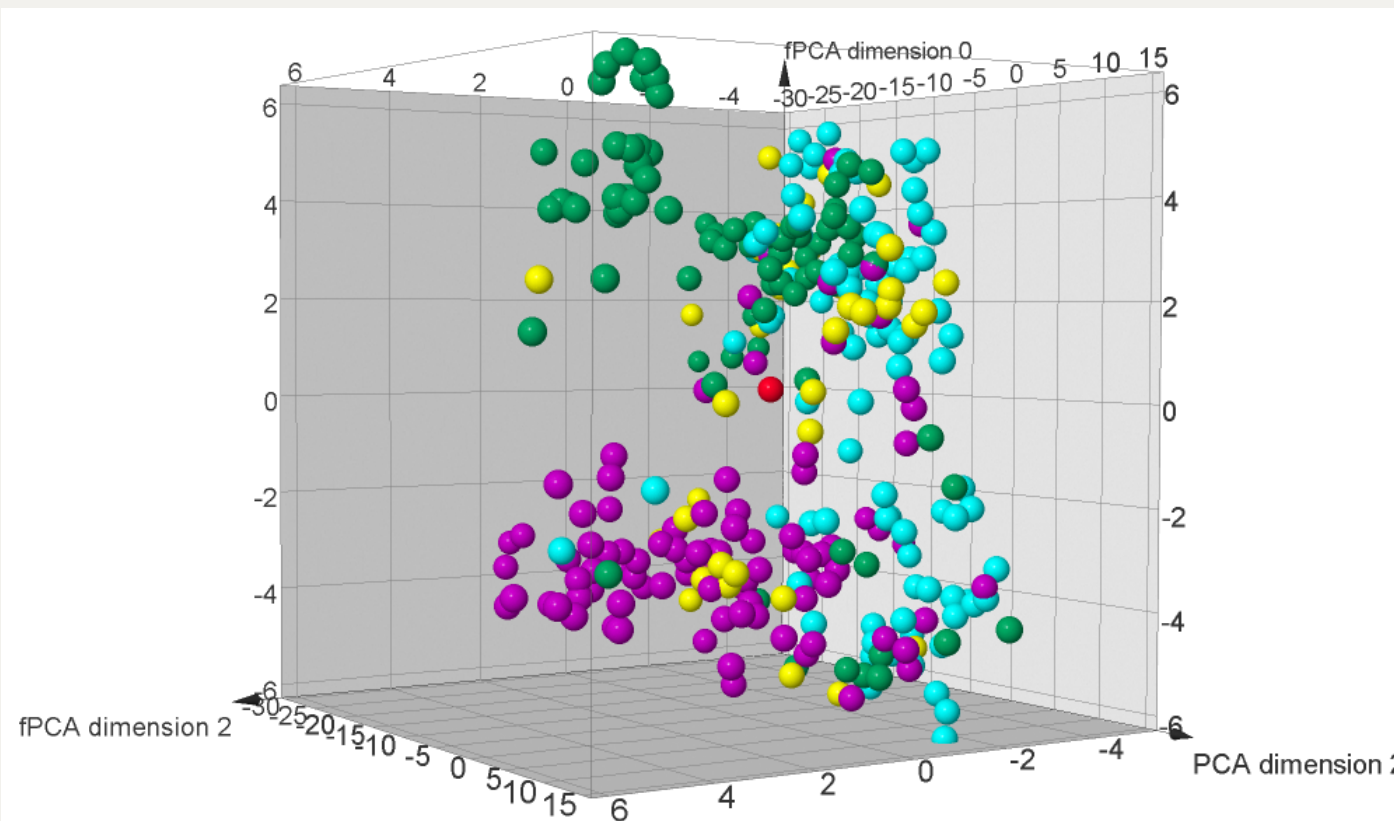
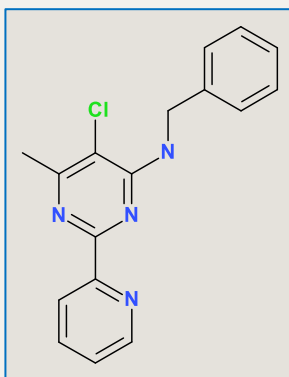
THP1 cells infected with eGFP-*L. donovani* (courtesy of GSK Tres Cantos)

Hits are scarce and precious – need to fully exploit them

- **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

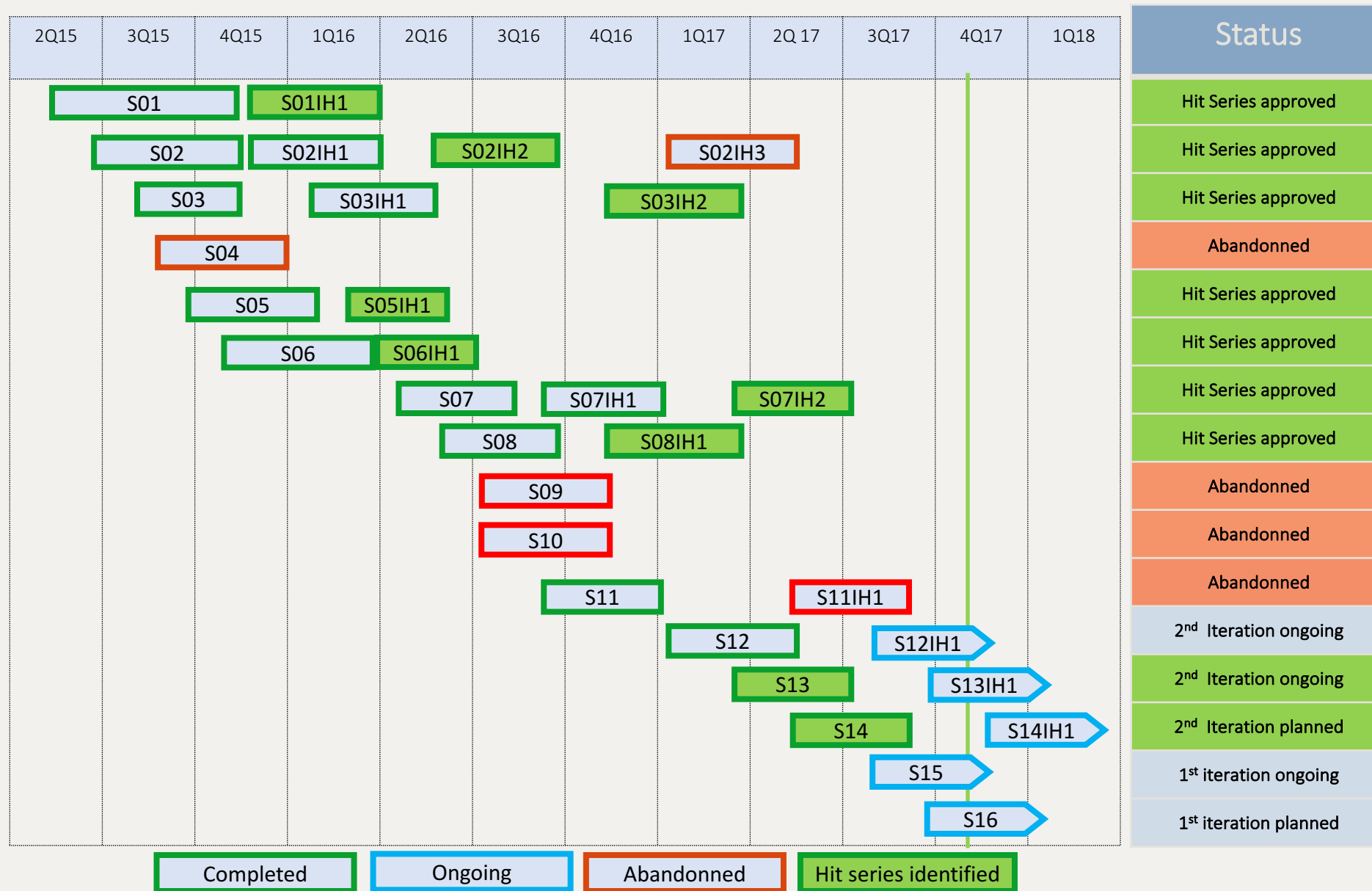
Booster Process - Representative Example

| Source | # hits |
|-----------|--------|
| Seed S01 | 1 |
| Partner A | ~90 |
| Partner B | ~90 |
| Partner C | ~90 |
| Partner D | ~40 |



- Complementary compound collections and different computational approaches efficiently explore chemical space around new hits
- Rapid SAR expansion and scaffold-hopping before expensive optimisation chemistry is needed

Booster: Progress to date

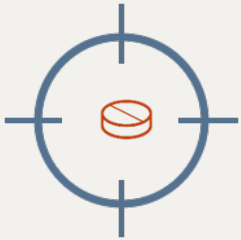


Innovative NTD Booster Project recognised by DNDi

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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Starr International Foundation



Schweizerische Eidgenossenschaft
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