DNDi
Drugs for Neglected Diseases *initiative*

Product – Development - Partnership

- Non-profit drug research & development (R&D) organization founded in 2003
- Addressing the needs of the most neglected patients
- Harnessing resources from public institutions, private industry and philanthropic entities

8 regional offices working close to patients in:
Brazil, Democratic Republic of Congo, Kenya, South Africa, Malaysia, India, Japan, USA

Founding Partners
Indian Council for Medical Research (ICMR), Kenya Medical Research Institute (KEMRI), Malaysian MoH, Oswaldo Cruz Foundation Brazil, Médecins Sans Frontières (MSF), Institut Pasteur France, WHO/TDR (permanent observer)

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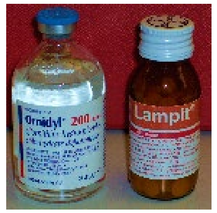
8 new treatments delivered since 2007

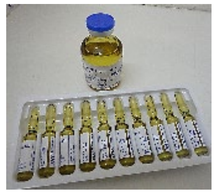
- ✓Easy to use
- ✓Affordable
- ✓Field-adapted
- ✓Non-patented

2007 **ASAQ**
Malaria
>500 million patients reached

2008 **ASMQ**
Malaria
Used in Africa and Asia



2009 **NECT**
Sleeping sickness
100% of stage-2 patients



2010 **SSG&PM**
Visceral leishmaniasis in E Africa
Now 1st line in all countries

2011 **PAEDIATRIC BENZNIDAZOLE**
Chagas disease
Two sources developed

2011 **NEW VL TREATMENT ASIA**
Visceral leishmaniasis in Asia
Support to disease elimination

2018 **FEXINIDAZOLE**
Sleeping sickness
Approved by European Medicines Agency, first all-oral treatment

2019 **4-in-1 Pediatric Formulation**
Paediatric HIV
Quadrimune under Review by FDA, under 1 USD

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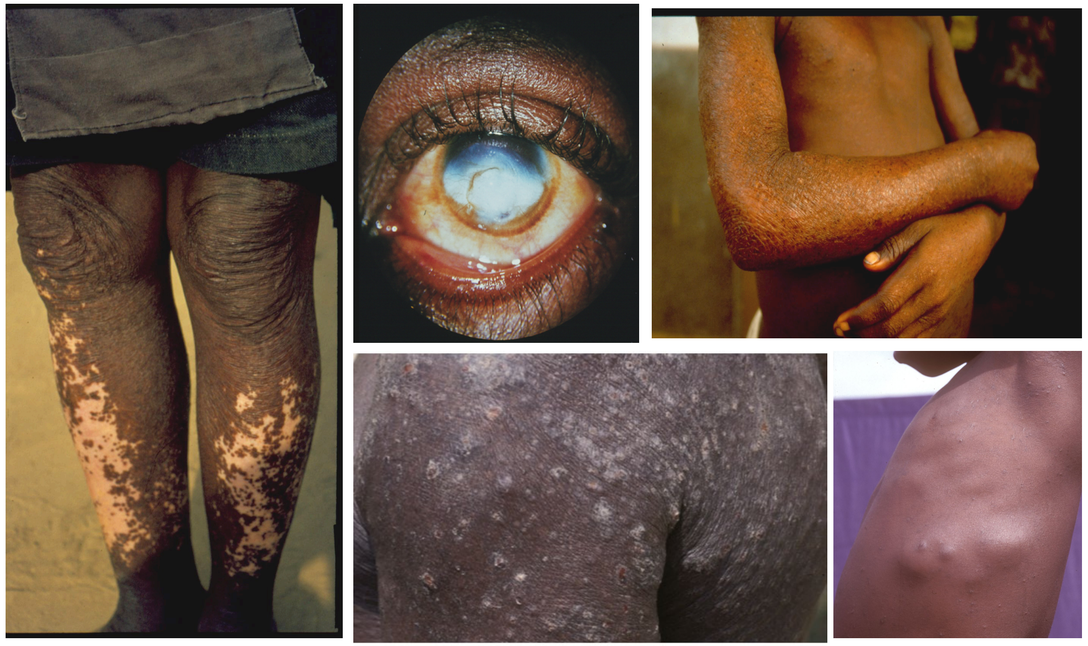
New tools to eliminate onchocerciasis

Where are we?
Mass Drug Administration (MDA, ivermectin)
Ivermectin does not kill the adult worms
Sustainable Development Goals cannot be met with current tools

Common strategic goals:
Expanding coverage of MDA programs
Adopting Test-and-Treat approaches in affected areas
Developing new drugs with superior efficacy to ivermectin



Over **20 million** people infected
About **200 million** people at risk
4 million people suffer from severe itching or dermatitis
1.34 DALY`s lost in 2017

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Use Case for a Macrofilaricide

Case 1: TNT - Programmatic approach

- Test-and-Treat strategies (TNT), for treatment of patients in endemic areas outside MDA campaigns when diagnostic tools are available, especially in “mop up” campaigns after the disease burden has been reduced by MDA programs and is no longer cost effective, or in areas that are difficult to treat
- Test-and-not-Treat (TaNT) campaigns in areas where *Loa loa* is co-endemic , when the macrofilaricidal drug also has rapid microfilaricidal activity

Case 2: TNT - Case Management

- Symptomatic patients
- Patients diagnosed positive for onchocerciasis

Case 3: MDA

- MDA, if safety and tolerability profile is suitable, in order to drastically reduce the number of MDA cycles from 10-15 years as currently required.

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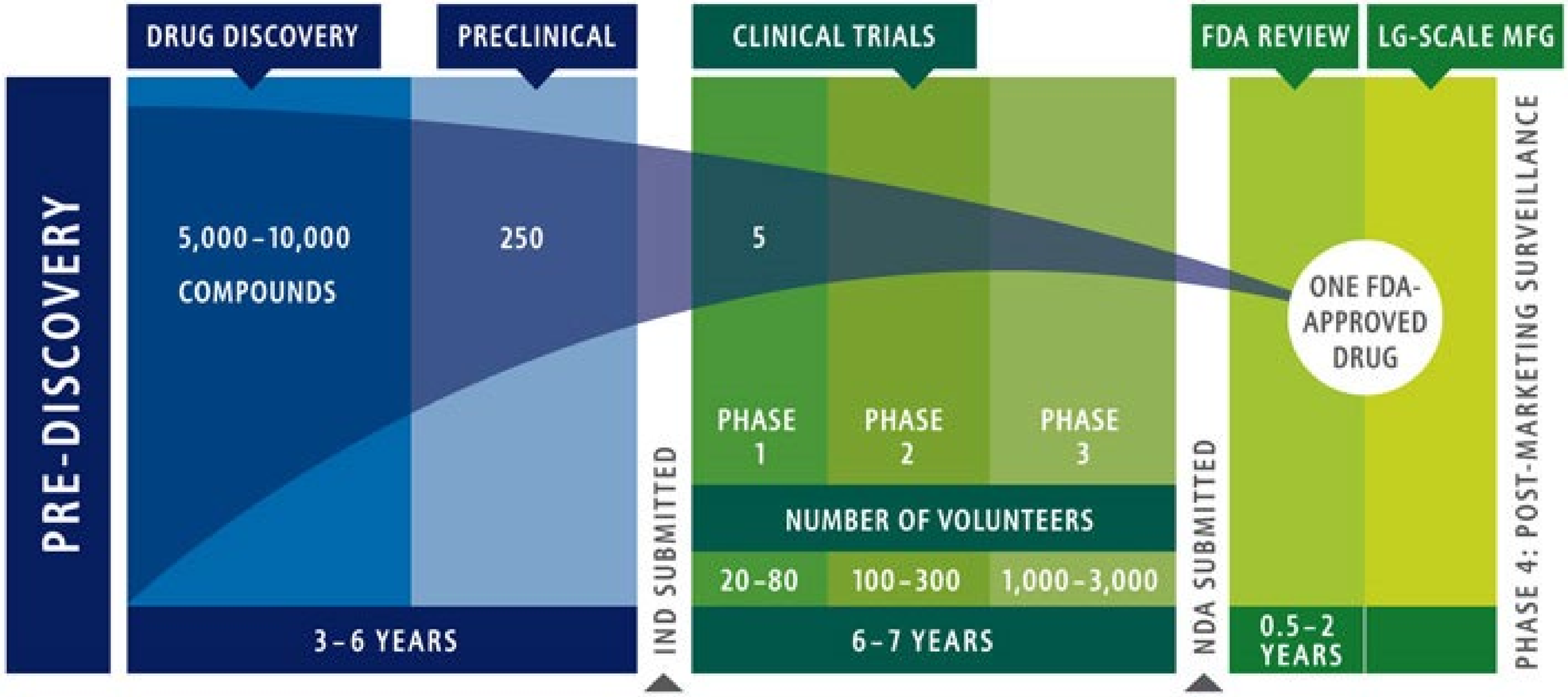
R&D: A long and risky road



Source: Pharmaceutical Research and Manufacturers of America

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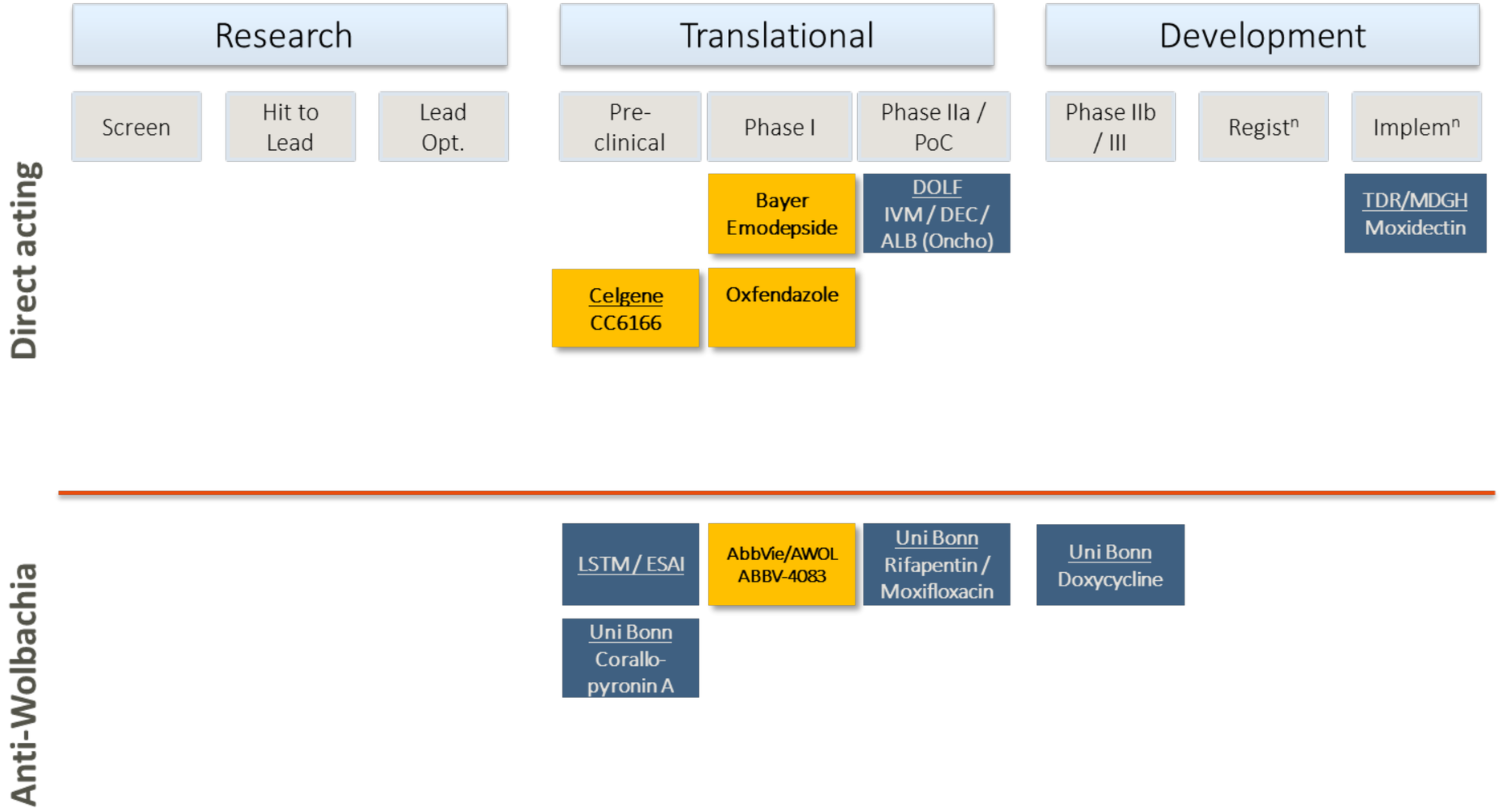
Filarial Landscape



DNDi projects

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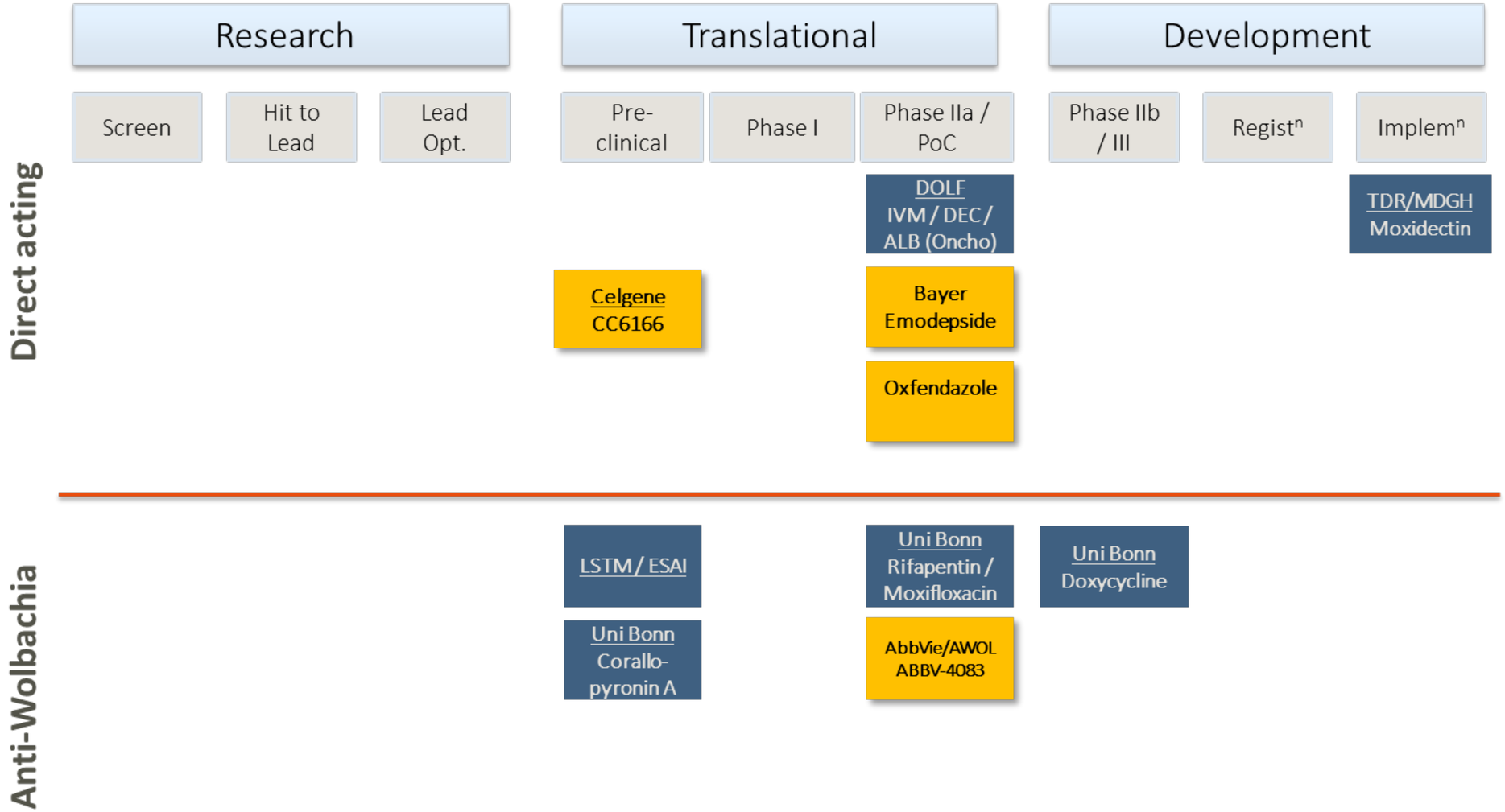
Filarial Landscape



DNDi projects

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DND*i* Macrofilaricide program

Project activities:
- Development of macrofilaricidal drugs against Onchocerciasis.

Project stage:
- Currently, emodepside, ABBV-4083 (TylAMac®) and have passed the First-In-Human study (Phase 1) and will be tested for efficacy and safety in infected humans.
- Oxfendazole has passed the First-In-Human study (Phase 1)

Countries:
- Ghana, DRC to start with proof of concept for emodepside and ABBV-4083

Duration (emo/ABBV-4083):
- Complete development: until 2032
- For proof of concept 2022/2023

Reducing Development Time Lines & Costs
Repurposing of drugs
Liase with veterinary drug developers
Bayer Pharma, Bayer Animal Health
AbbVie

ABBV-4083 - TylAMac

- Synthetic derivative of tylosin A (common veterinary macrolide antibiotic)
- Highly potent against *Wolbachia* (>200-fold more potent than doxycycline)

✓ Tox-package completed

✓ IND (Investigational New Drug) application 11/2017

✓ Phase 1 Single Ascending Dose study completed

✓ Scientific advice meeting held with FDA

Dale Kempf

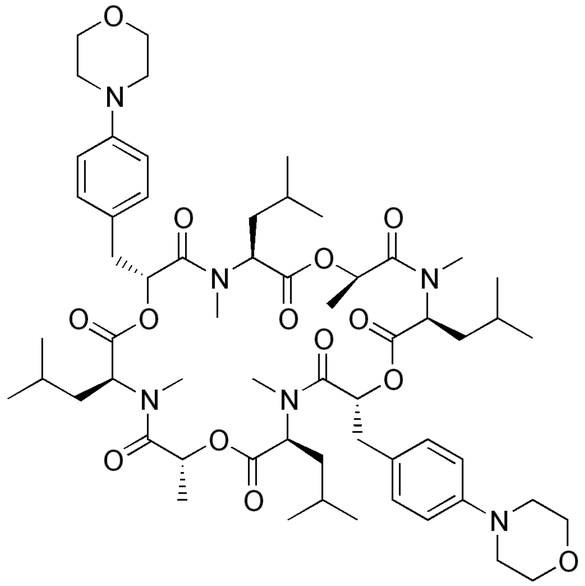
Emodepside - Profender

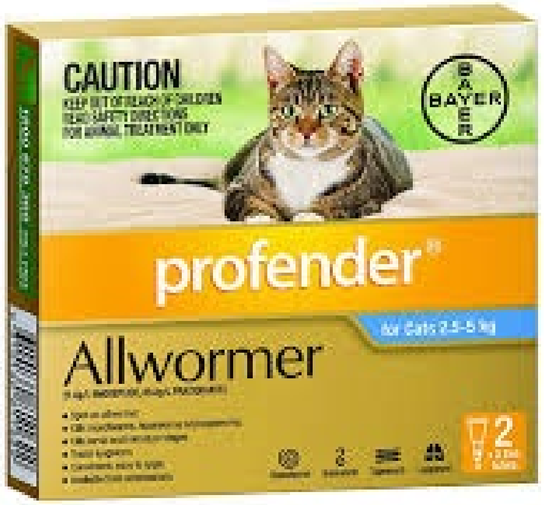
Emodepside

- Cyclooctadepsipeptide
- Veterinary anthelminthic with broad activity

Active against

- different nematode species
- different larval stages
- gastrointestinal and tissue parasites
- micro- and macrofilaricidal activity on filarial parasites





✓ preclinical studies completed

✓ Veterinary toxicology package available

✓ First-In-Human clinical studies completed

✓ Scientific advice meeting held with FDA

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Study Endpoints

Proof-of-Concept Endpoints:

- Absence of microfilaridermia
- Embryogenesis inhibition
- Adulticidal effect
- *Wolbachia* depletion (surrogate)

Proof-of-Concept Design:

- Dose range

Regulatory Endpoint:

- Absence of microfilaridermia after 24 months
    - Long term sterilizing, clinical benefit

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Oxfendazole

Oxfendazole

- broad spectrum benzimidazole anthelmintic
- Veterinary anthelminthic with broad activity

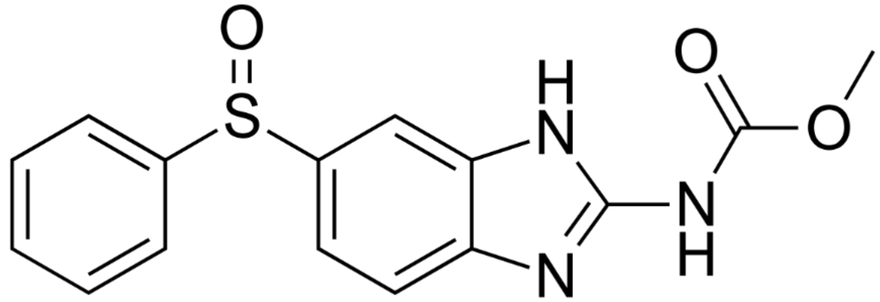
Active against

- roundworm, strongyloides and pinworms
- macrofilaricidal activity on filarial parasites

✓ preclinical studies completed

✓ First-In-Human clinical studies completed (ODG)

✓ Scientific advice meeting held with FDA



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Summary

Develop a new safe and field-adapted drug with long-term sterilizing / macrofilaricide activity

- To implement in TNT/TaNT, case management
- DNDi candidates passed Phase 1
- Emodepside and ABBV-4083 will be tested for safety and efficacy
- No healthy drug discovery pipeline exists
- Similar challenges in other helminth areas

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Partners

Institut de Recherche pour le Développement
FRANCE

Celgene

abbvie

BAYER

Research Foundation in Tropical Diseases and Environment
Buea Cameroon

universitäts klinikum bonn

Imperial College London

WASHINGTON UNIVERSITY IN ST. LOUIS · 1853 ·

MUSÉUM NATIONAL D'HISTOIRE NATURELLE

NPIMR
Northwick Park Institute for Medical Research

Erasmus
ERASMUS UNIVERSITEIT ROTTERDAM

LSTM
LIVERPOOL SCHOOL OF TROPICAL MEDICINE

leti
ceatech

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SWOT Analysis for helminth control	
Strength • Elimination programs have reduced morbidity due to helminth infections • Abrogation of transmission in some areas and countries • Awareness for neglected patient groups increases	**Weakness** • Relies on extremely limited number of (sub-) optimal tools • Current drugs do not kill/eliminate adult worms (Oncho, Trichuriasis) • Transmission unbroken in many areas • No sensitive diagnostics available
Opportunities MDA • Transfer of successful programs • Collaborations national level R&D • Common targets in various helminth species • Large body of knowledge on the animal health market • Advanced compounds available that have a complete tox package or have already been used in humans, but have no registration	**Threats** • Potential spread of drug resistance • Compliance issues with drug treatment • Migration of infected individuals into post-control regions • Vulnerable populations often not targeted

Horizon 2020
European Union Funding
for Research & Innovatic

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HELP

Helminth Elimination Platform

Swiss TPH

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