

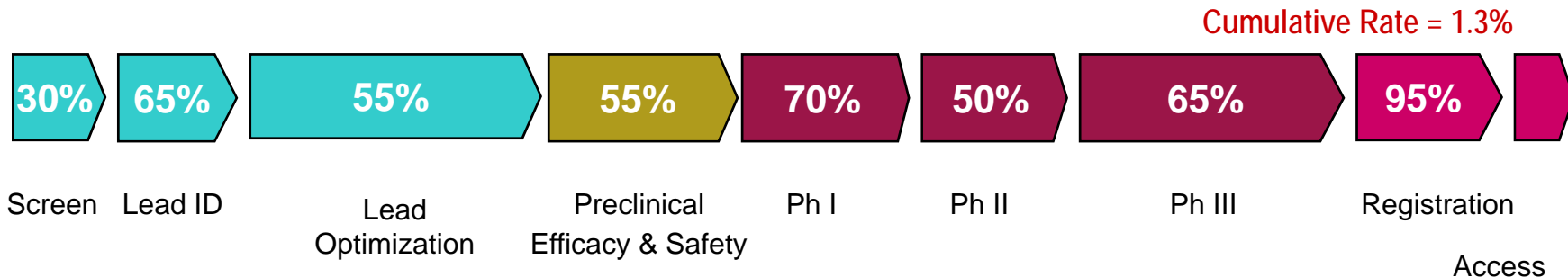
# Advancing R&D Projects Through Partnering

Shing Chang, PhD  
R&D Director, DNDi



# Research, Development, Access

- Research
  - Building a pipeline for the future
- Development
  - 6 to 8 new treatments
- Access
  - Patients access to improved treatments



# Characteristics of Our Discovery Strategy

- Understanding of the field conditions and patient needs
- TPP (Targeted Product Profile) to guide our programs
- “Low hanging fruits” approach to address urgent needs
- Consortia for centralized LO
- Targeting selected classes of compounds
- Working with partners with shared mission and commitment

# Diverse Compounds and Libraries through Partnerships

Hits & leads	
Scynexis IPK Epichem LicA Anacor Chemroutes IRD NITD GATB GSK	WEHI Eskitis Kitasato Institute Genzyme Nycomed Altana Basilea Intervet CDRI Otsuka U.Washington
Screening center	
London School of Hygiene & Tropical Medicine Swiss Tropical Institute Antwerp University	

# Accessing Compound Classes with Known Activity Against Parasites

- Partnership with GSK
  - To identify promising compounds via screening of existing GSK libraries and tapping into MMV-GSK research on malaria
  - Initial work focused on two classes known to be active against parasites
    - 4 (1H) pyridones and cysteine protease inhibitors
- Partnership with Anacor
  - Interesting exaborolo compounds active against *T. brucei* and *T. cruzi* in vitro

# Accessing the Wealth of Natural Products Screening

- Partnership with Eskitis Institute, Australia
  - Screening a unique library of natural product extracts that are enriched for drug-like molecules using proprietary “Lead-like Enhancement Technology
- Partnership with Kitasato Institute, Japan
  - Screening a unique library of microbial secondary metabolites and plant extracts

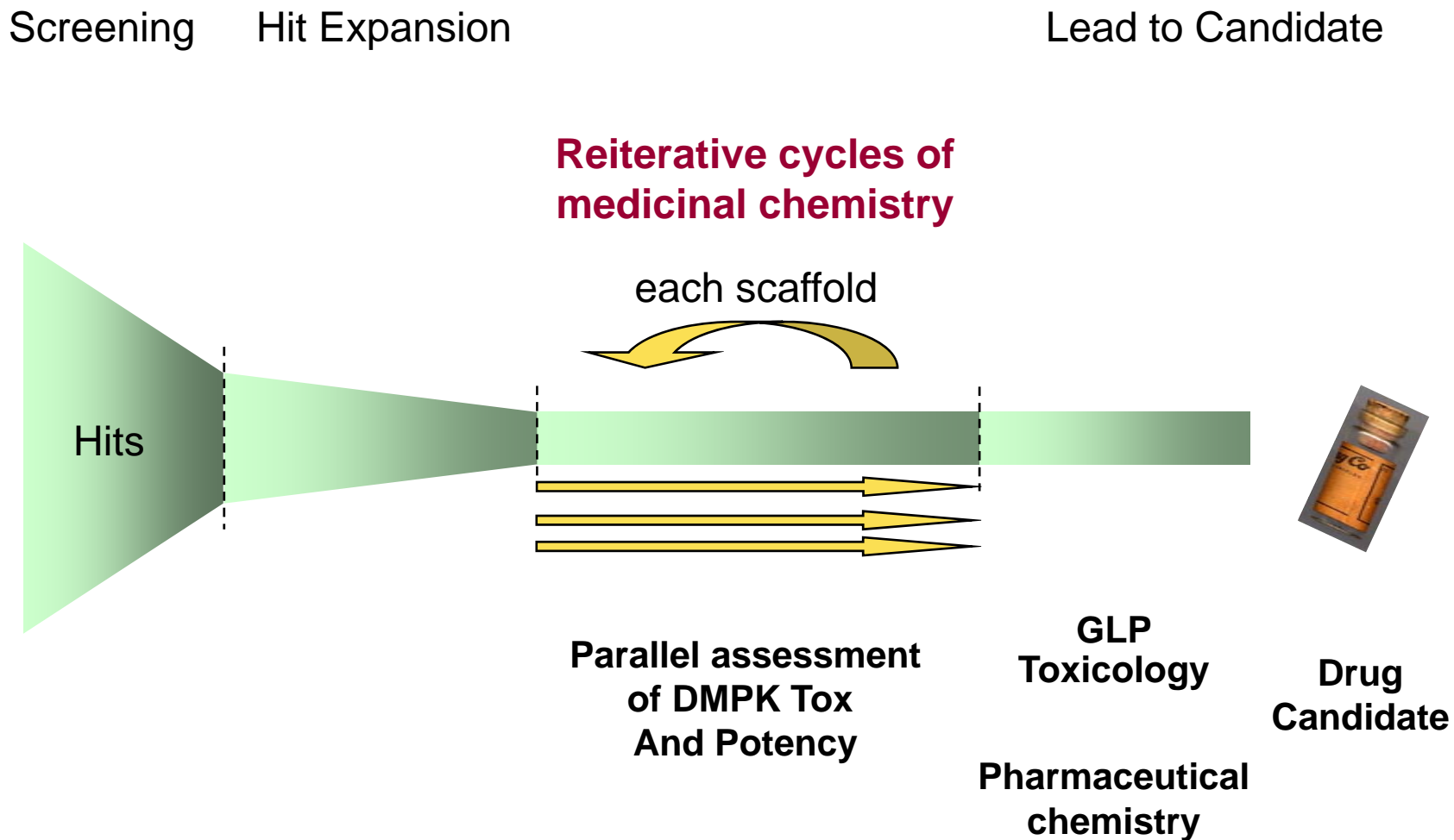


# Accessing New Drug Discovery Technologies

- Partnership with Institute Pasteur of Korea
  - High throughput Image Screen for *leishmania*
  - Use macrophage infected with intracellular amastigotes under BSL-3 conditions



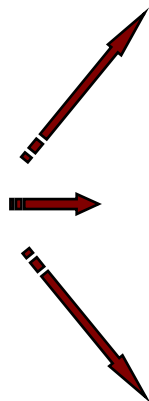
# Lead Optimization





# Optimizing Leads Through Disease-focused Consortia

Hits & Leads from Screening Partners



**HAT Lead Optimization**

Scynexis, Pace

**VL Lead Optimization**

Advinus  
Central Drug Research Institute

**Chagas Lead Optimization**

CDCO, Murdoch,  
Epichem, Ouro Preto

# A Robust and Dynamic Portfolio 2004-2008



- Nitroimidazoles (All)
- Microtubule Inhibitors (HAT)
- GSK (All)
- Kitasato Natural Substances (HAT)
- CDRI (HAT)
- Eskitis Natural Products (HAT)
- IPK (VL)

**HAT Consortium:**  
Scynexis, Pace Univ

**VL Consortium:**  
Advinus, CDRI

**Chagas Consortium:**  
CDCO, Epichem, Murdoch Univ

*Exploratory Screening:*  
Anacor, Chemroutes, Univ of Ouro Preto, Fiocruz, IICB, IRD, LicA  
LSHTM, MerLion, Otsuka, STI, TDR, Univ of Antwerp, University of Dundee, WEHI, ...

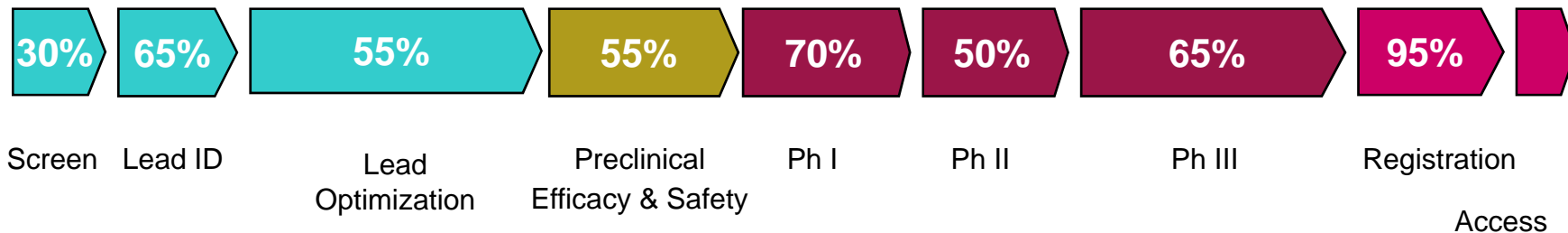
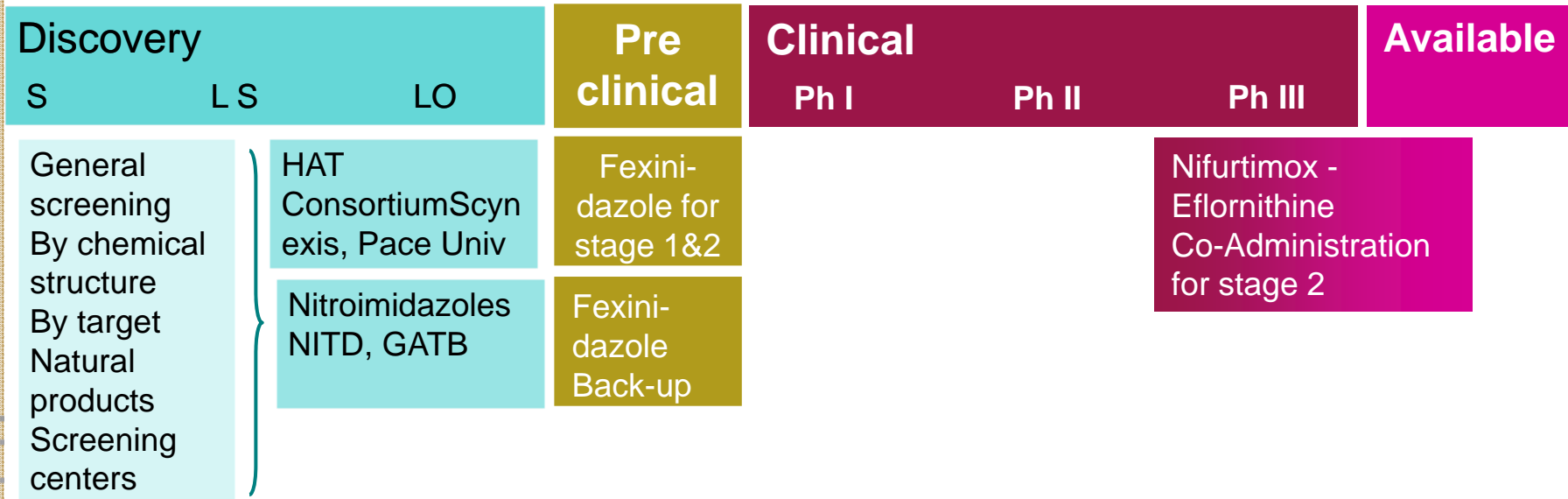
- Azoles (Chagas)
- Amphotericin B Polymer (VL)
- Buparvaquone (VL)
- Fexinidazole (HAT)
- Exploratory*

- Paromomycin (VL in Africa)
- AmBisome (VL in Africa)
- Paediatric Benznidazole (Chagas)
- Combination Therapy (VL in India)
- Nifurtimox - Eflornithine Co-Administration (HAT)
- Exploratory*

**ASMQ (Malaria)**  
Fixed-Dose Artesunate/Mefloquine

**ASAQ (Malaria)**  
Fixed-Dose Artesunate/Amodiaquine

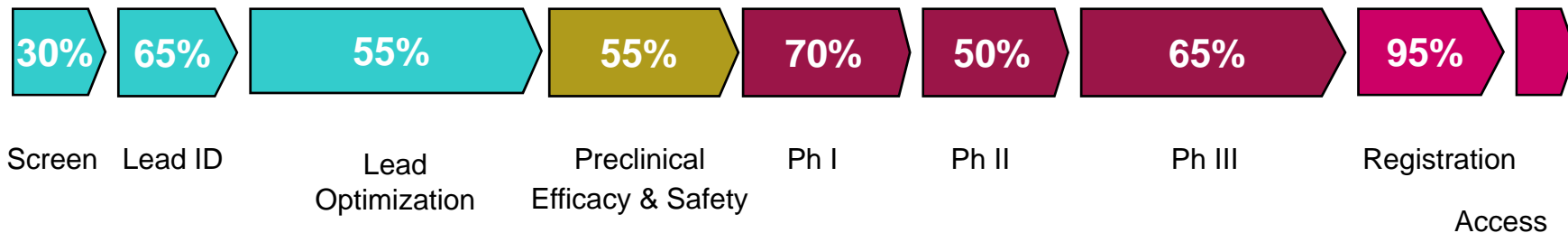
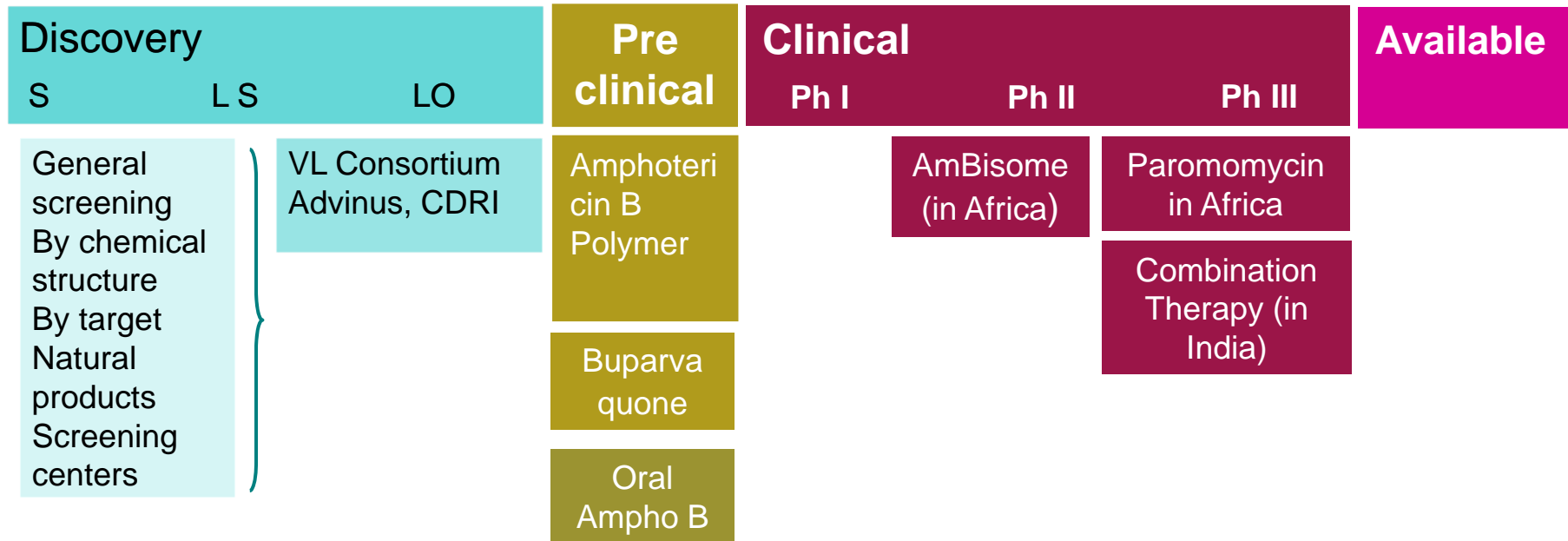
# DNDi Preclinical & Clinical Portfolio - Human African Trypanosomiasis



# HAT Strategy Challenges

- Make combination of nifurtimox and eflornithine available for patients
- Develop an accelerated clinical plan for fexinidazole
- Select best regulatory strategy
- Identify new preclinical candidates
- Success with lead optimization projects

# DNDi Preclinical & Clinical Portfolio - Visceral Leishmaniasis

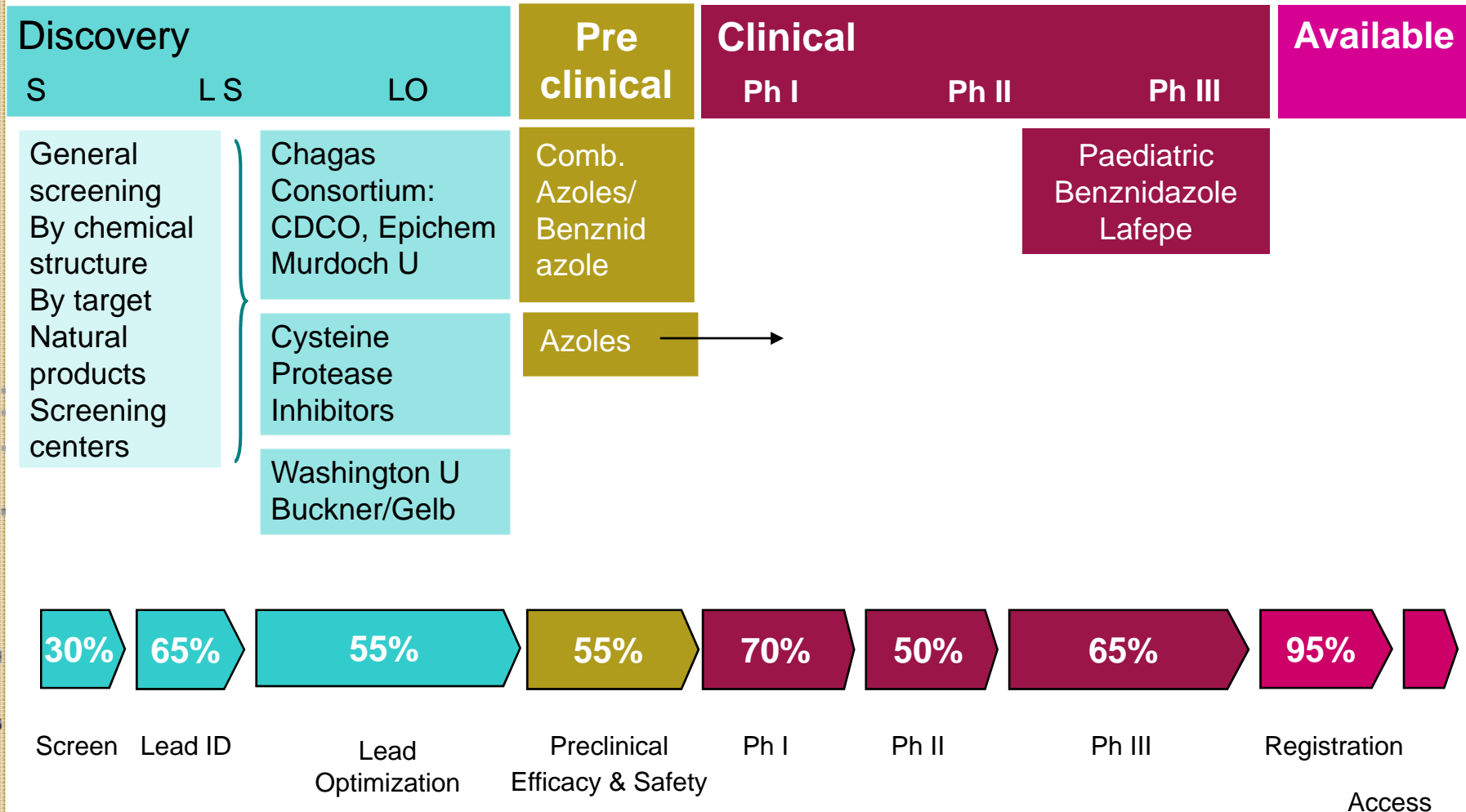




# VL Strategy Challenges

- Select the most appropriate drug combination tailored for different regions:
  - Asia
  - East Africa
  - Latin America
- Develop better preclinical candidates to be used in combination therapy
  - efficacy/safety
  - easy use
  - affordability
- Select new compounds from lead optimization program

# DNDi Preclinical & Clinical Portfolio - Chagas



# Chagas Challenges: Need for new drugs at all stages

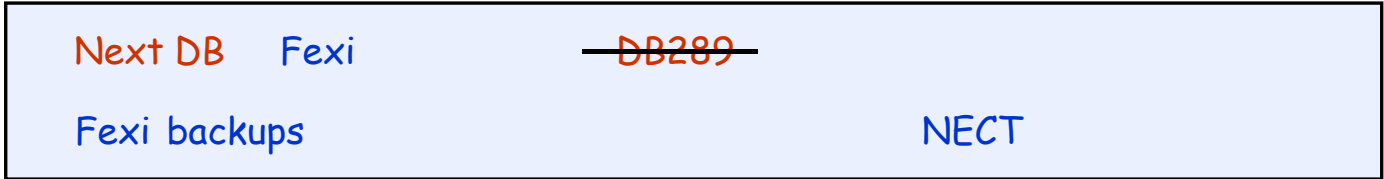
- Therapeutic switching
  - Azole class such as ravuconazole (Eisai) and posaconazole (Schering-Plough)
  - Active in animal efficacy models
- Paediatric strength of benznidazole
  - Currently not available; known to be effective in children in acute phase
- Develop a new treatment for indeterminate/early chronic disease through the advancement of lead optimization
  - One project per year

# Preclinical and Clinical Projects – Portfolio in the Field by Disease

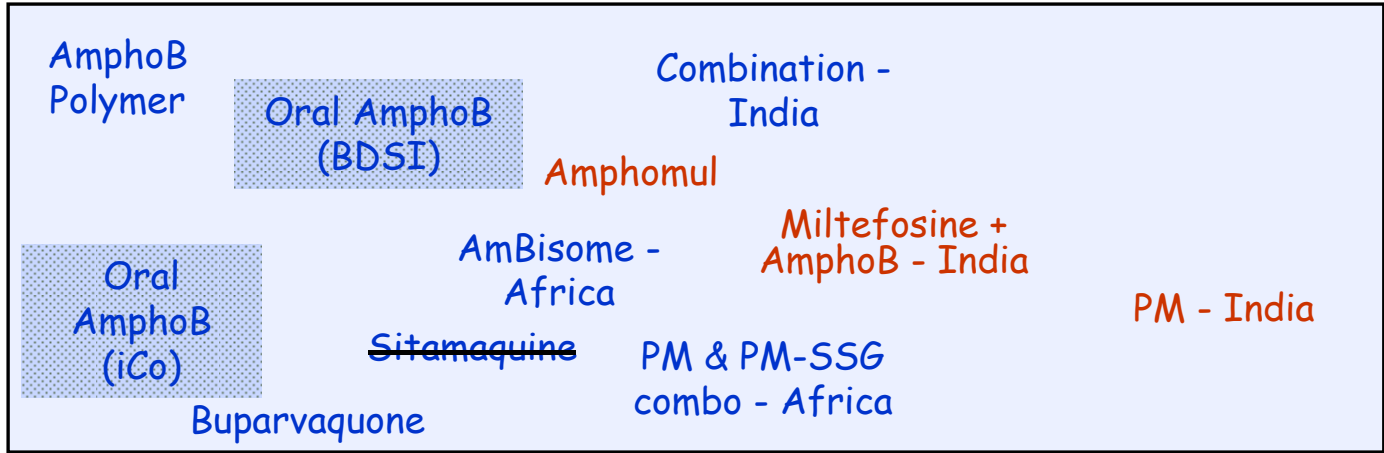
Chagas



HAT



VL



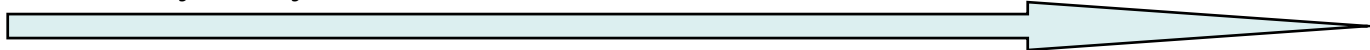
- DNDi projects
- Non-DNDi
- In discussion

Preclinical  
Efficacy & Safety

Clinical

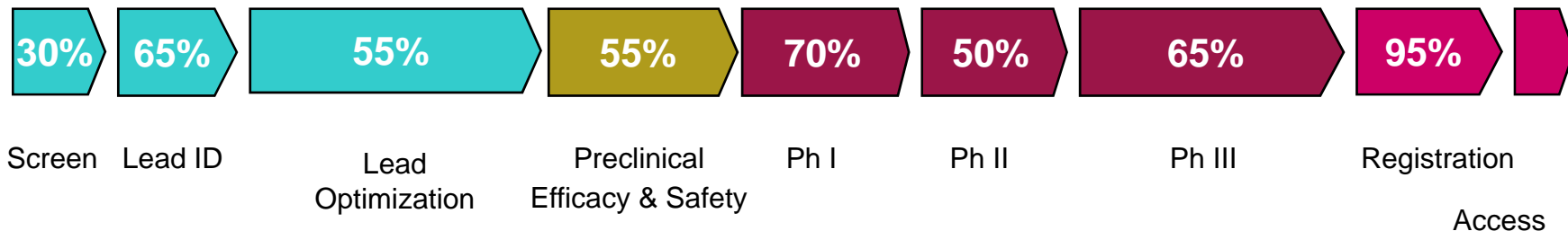
Registration

Ph IV



# Access

- DNDi has delivered 2 projects
  - Challenges remain
- Solid partnerships being built
- Post-registration: an ongoing challenge & process
  - How to deliver?





# Strategic Partnering to Address Access for Neglected Patients

As facilitator, DNDi ensures:

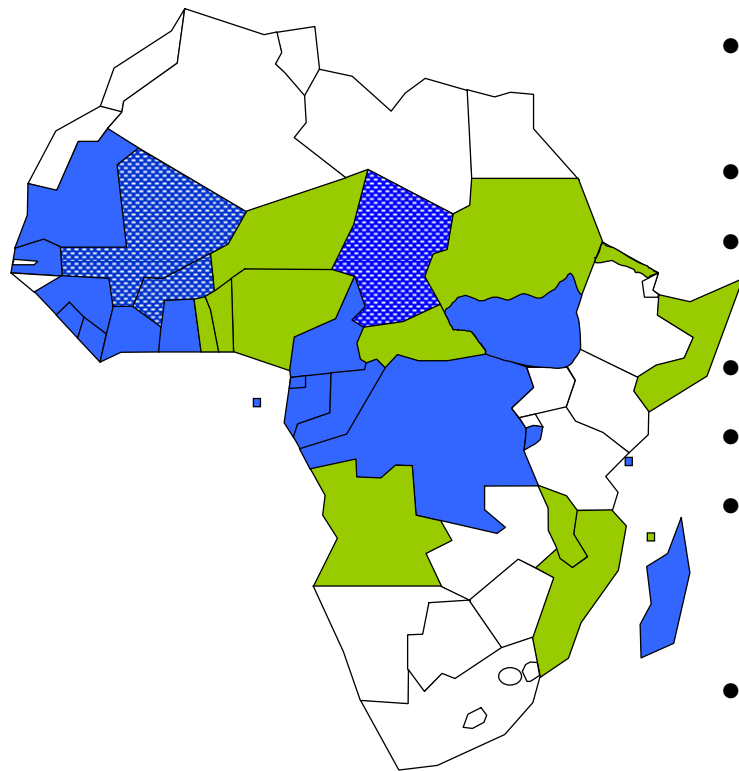
- Timely registration in endemic countries (WHO prequalification)
- Implementation through successful procurement and distribution strategy
- Changing international and national treatment guidelines
- Rational use of new treatment
- Pharmacovigilance
- Monitoring of drug resistance
- Advocacy to support implementation






Shoklo Malaria Research Unit

# Overcoming Access Challenges Reaching Neglected Patients

## Strategic Partnering to Implement Tools: **ASAQ**



-  countries ASAQ 1st line treatments
-  Countries ASAQ is one of 1st-line treatments
-  countries ASAQ can be of benefit

- Registered by sanofi-aventis in 21 countries
- Prequalification pending
- sanofi-aventis distributes ASAQ and Coarsucam
- 1.5 M treatments distributed
- Global fund, Unitaid, AFMm
- Recommended in 16 countries as first line treatment, and by WHO (geographic extension: India)
- Rational use (Effectiveness study in Liberia/Specific groups, DNDi, MSF, Epicentre)
- Pharmacovigilance study in Ghana (DNDi, MMV, sanofi-aventis, In-depth)
- Information materials

# As DNDi and our partners blaze the trail together...

...we continue to  
advance our  
projects, and to  
address the  
needs of the  
neglected  
patients

