New Drugs for Neglected Diseases

Research Partnership for Technological Innovation (PITE-FAPESP) to discover novel drug candidates for the treatment of parasitic tropical diseases

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PUBLIC HEALTH-DRIVEN R&D

DND*i* was created to address the needs of neglected patients

Sleeping sickness

Chagas disease

Mycetoma

Filarial diseases

Leishamaniasis

HIV

Hepatitis C

Anti – Microbial Resistance

… and next?

LEISHMANIASIS

Towards a new generation of treatments

1 BILLION
people at risk across the globe

20,000-30,000
deaths annually

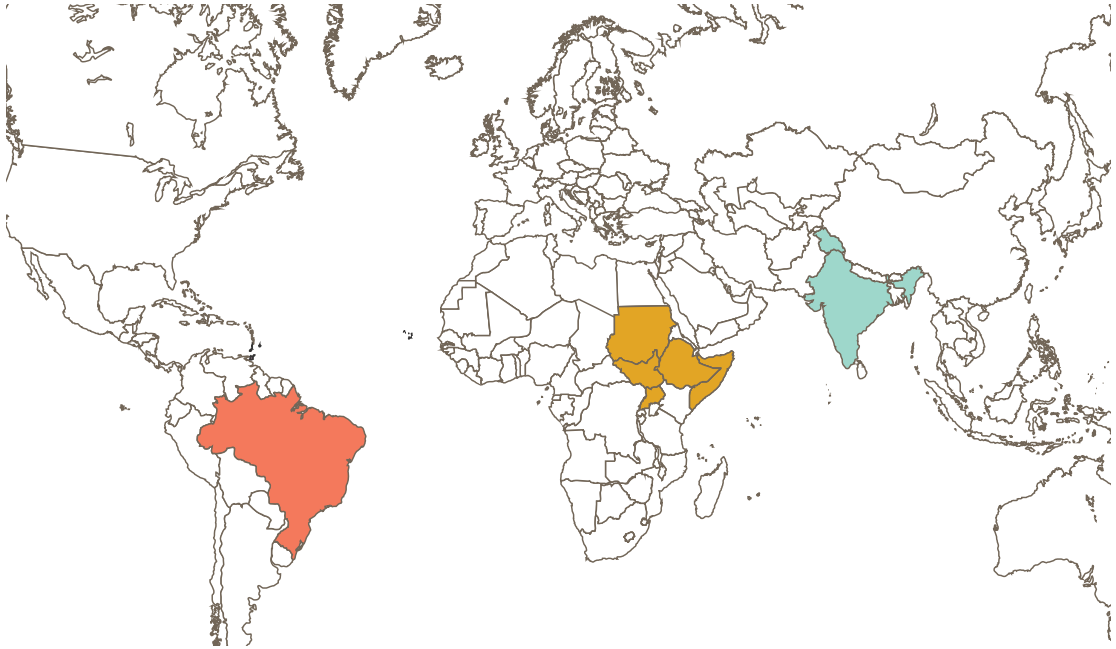
TREATMENT CHALLENGE

Treating leishmaniasis depends on:

- The form of the disease (**Visceral leishmaniasis, Post-kala-azar dermal leishmaniasis, Cutaneous leishmaniasis)**
- The species of infecting parasite
- The country: treatment responses differ from region to region
- Co-existing infections such as HIV make treatment more difficult.

VISCERAL LEISHMANIASIS

Treatment challenges

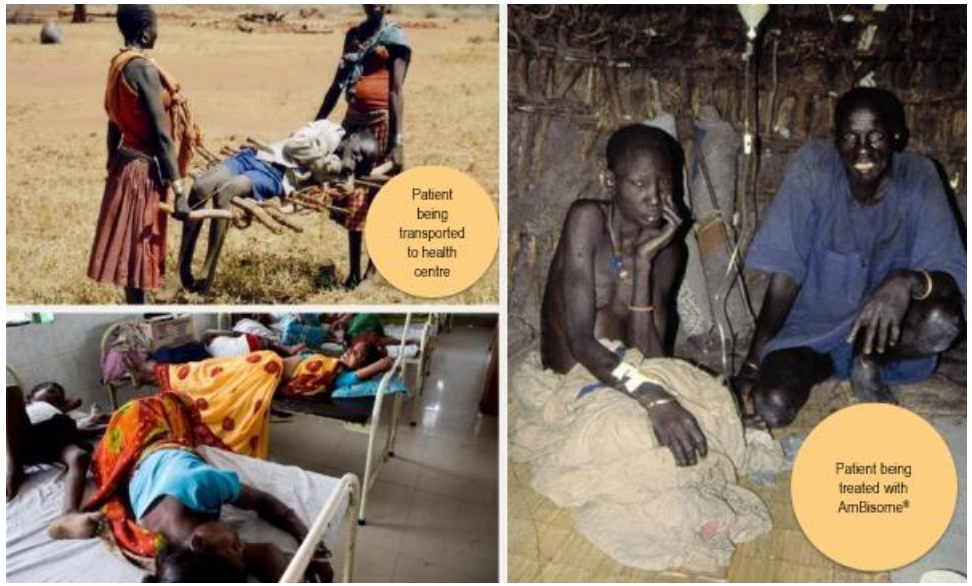


BRAZIL
- ***1st line treatment:*** **Glucantime**
- ***2nd line treatment:*** **AmBisome®**

EASTERN AFRICA
- ***1st line treatment*:** **SSG&PM**
- ***2nd line treatment*:** **AmBisome® or SSG**

SOUTH ASIA
- ***1st line treatment:*** **Single dose AmBisome®**
- ***2nd line treatment:*** **PM+MF**

Treating leishmaniasis depends on many variables:
- The form of the disease
- The species of infecting parasite
- The country, as treatment responses differ from region to region
- Co-existing infections such as HIV make treatment more difficult.
- Drugs not adapted to local context



CHAGAS DISEASE

In search of shorter, better treatments to stop a silent killer

6-7 MILLION
people infected by the *T. cruzi* parasite that causes Chagas

FEWER THAN
10%
diagnosed - and only a small number receive the treatment they need

70 MILLION
people are at risk

TREATMENT CHALLENGES:

- Only two drugs available, both old.
- Benznidazole, is effective, but treatment is 8 weeks, and 2 out of 10 people can't complete it due to the side effects.

A shared mission to meet patients' needs

TARGET PRODUCT PROFILE – VISCERAL LEISHMANIASIS

Target Product Profile for Visceral Leishmaniasis

As a prerequisite to building the strategy, the target product (treatment) profile (TPP) has been established. It is based on discussions with various visceral leishmaniasis experts, consultation with visceral leishmaniasis national control programmes in endemic countries, and specifically with leading physicians and health workers who deal with this disease on a daily basis. Our TPP is reviewed and revised annually, and shared with other investigators openly.

The priority is to develop a safe, effective, oral, short-course (11 days maximum) visceral leishmaniasis drug to replace current treatments. This will improve and simplify current case management. The aim is to develop combinations of drugs that are effective against visceral leishmaniasis in all foci of the disease.

Target Product Profile for Visceral Leishmaniasis New Chemical Entities

	Optimal Target Profile	Minimal Target Profile
Target Label	VL and PKDL	VL
Spp	All species	*L. donovani*
Distribution	All areas	Either India or Africa
Target Population	Immunocompetent and immunosuppressed	Immunocompetent
Clinical Efficacy	> 95%	> 90%
Resistance		Active against resistant strains
Safety and Tolerability	No AEs requiring monitoring	1 monitoring visit in mid/end – point
Contraindications	None	Pregnancy/lactation
Interactions	None – Compatible for combination therapy	None for malaria, TB, and HIV therapies
Formulation	Oral / im depot	Oral / im depot
Treatment Regimen	1/day for 10 days po/ 3 shots over 10 days	bid for <10 days po; or <3 shots over 10 days
Stability	3 yrs in zone 4	Stable under conditions that can be reasonably achieved in the target region (> 2 yr)
Cost	< $10 / course	< $80 / course

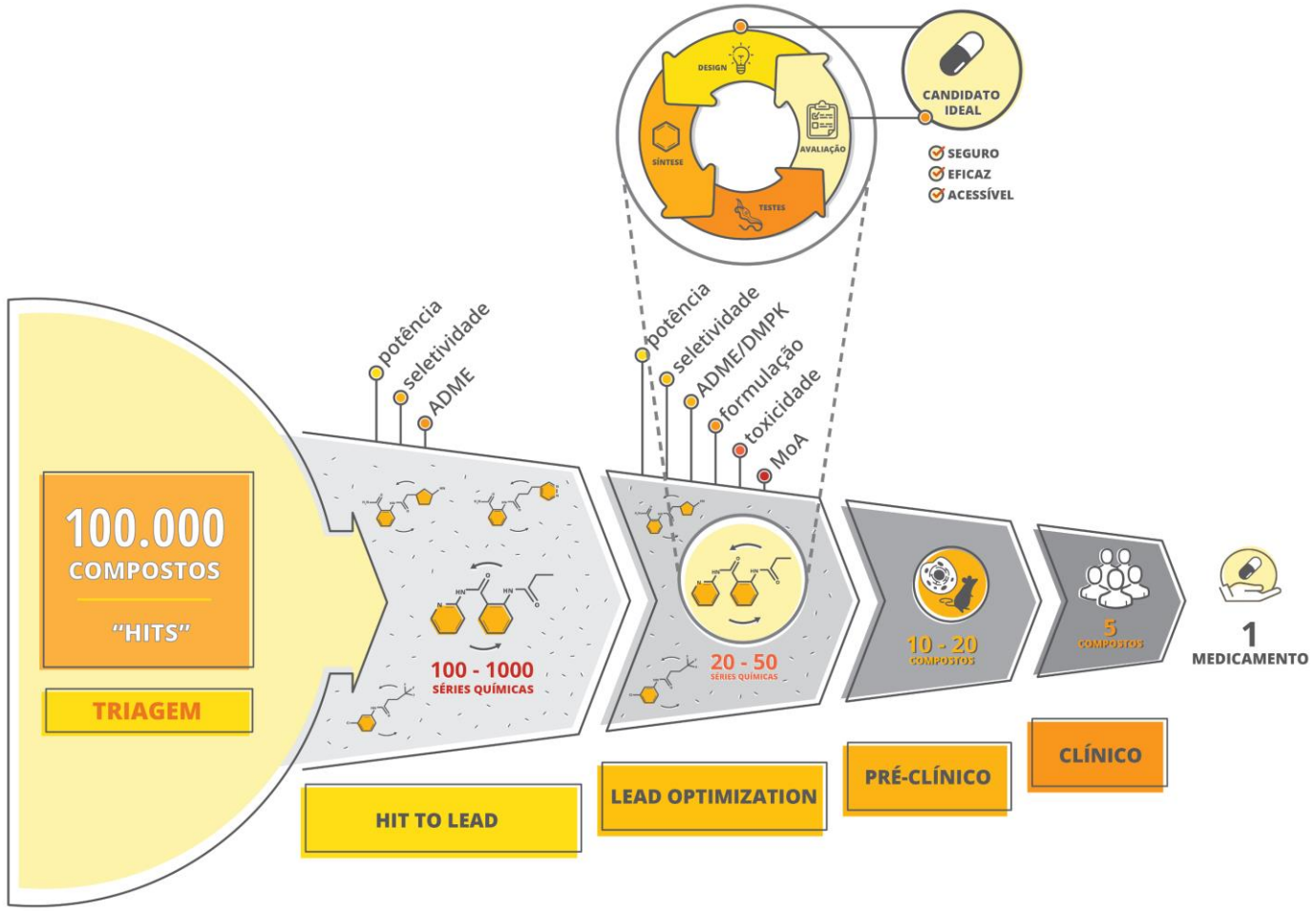
- Agreed objectives (TPPs) set in collaboration with disease platforms to meet patients' needs
- Projects have a clear focus on delivery of new treatments
- The consortium is gaining and sharing drug discovery experience by addressing parasitic diseases of Brazil, Latin America and globally

CHAGAS DISEASE TARGET PRODUCT PROFILE

	Acceptable	Ideal
Target population	Chronic	Chronic and Acute
Geographic Distribution	All regions	All regions
Efficacy	Non inferior to benznidazole standard dose* in all regions (parasitological)	Superiority to benznidazole standard dose to different phases of disease (acute and chronic) (parasitological)
Safety	Superiority to benznidazole* in the frequency of definitive treatment discontinuations for medical indication (clinical and laboratory)**	Superiority to benznidazole* in the frequency of definitive treatment discontinuations for medical indication (clinical and laboratory)**
Contraindications	Pregnancy	No contraindications
Precautions	No genotoxicity**; No pro-arrythmic potential	No genotoxicity; No teratogenicity; No pro-arrythmic potential
Interactions	No clinically significant interaction with anti-arrythmic and anticoagulants drugs	No clinically significant interaction
Presentation	Oral/Parenteral (short POC)*** Age-adapted	Oral Age-adapted
Stability	3 years, climatic zone IV	5 years, climatic zone IV
Dosing regimen	Oral – any duration Parenteral – <7 days	<30days
Cost	Current treatments	Lowest possible

* As per WHO recommendation
** No genotoxicity is a condition only for NCEs
*** Need for parenteral treatment for severe disease

PITE: Science and partnerships in Brazil with international partners



FAPESP

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Drugs for Neglected Diseases *initiative*

MMV
Medicines for Malaria Venture

USP

UNICAMP

BEST SCIENCE
FOR THE MOST NEGLECTED







Thank you!

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