

**BEST SCIENCE**  
FOR THE MOST NEGLECTED

**DNDi**

Drugs for Neglected Diseases *initiative*

## GHIT PDP Webinar

Byron Arana  
DNDi Geneva, Switzerland

Head of the Cutaneous  
Leishmaniasis Clinical Program

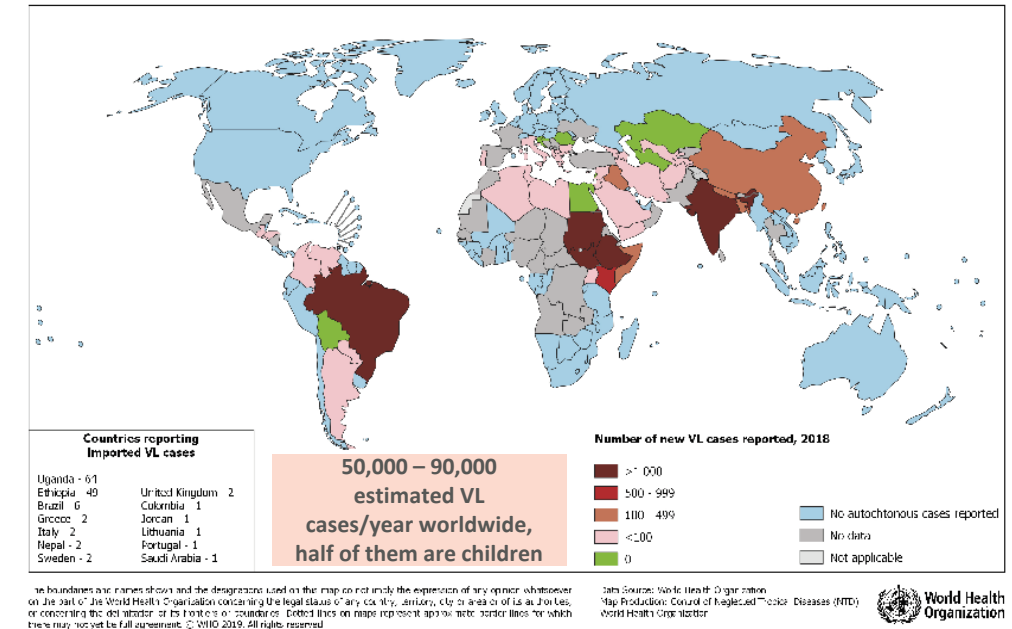
20 October 2021

# Leishmaniasis: 98 countries, 1 billion people at risk

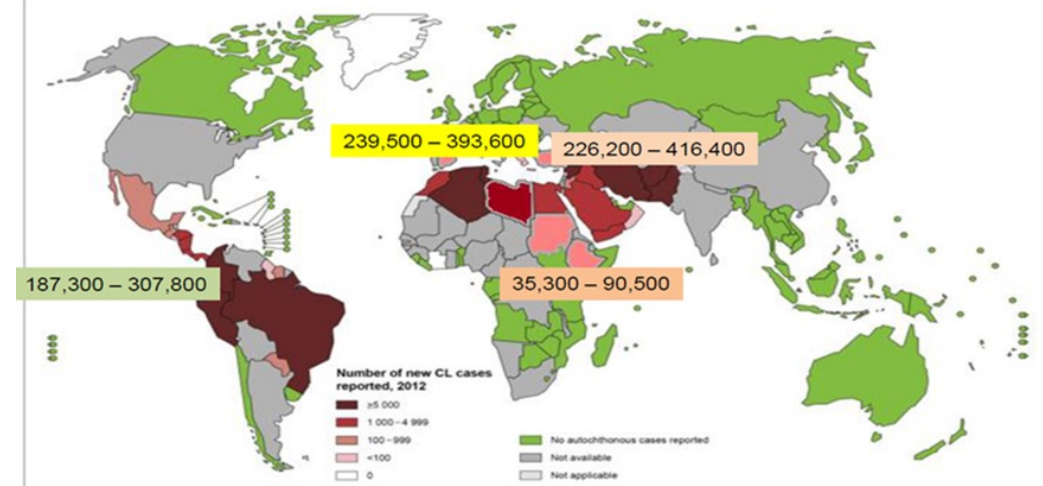
- Leishmaniasis is a **complex vector-borne disease** with different clinical manifestations:
  - Primary targets for the programme: VL and CL.
  - Secondary targets: PKDL, HIV-VL, complicated CL.
- Linked to **environmental changes** such as deforestation, building of dams, irrigation schemes and urbanization\*.
- Affects some of the **poorest people on earth**\*.
- Prone to **outbreaks**, mainly related to displacement of vulnerable population due to conflict.
- 700,000 to 1.4 million new cases occur annually**\*; 14,454 deaths associated with leishmaniasis

\* WHO, 2020

Status of endemicity of visceral leishmaniasis worldwide, 2018



Endemicity of Cutaneous Leishmaniasis



# Cutaneous Leishmaniasis

- Endemic in **88 countries**
- **0.7 to 1.2 million new CL** cases annually worldwide.
- Every **30 seconds** there is a new case of CL
- Eastern Mediterranean region contribute to ~60% of global CL burden
- >12 species and dozens of proven vectors and reservoirs
- No vaccine
- No chemoprophylaxis
- Limited number of drugs with variable efficacy

## Diseases Severity



**No Tx**

**Local topical**

**Systemic oral**

**Syst. Parenteral**

**Combinations**

Small lesion, *L. major* or *L. mexicana*

IL antimonials  
Liquid Nitrogen  
Thermotherapy

Miltefosine

MA / SSG  
Pentamidine  
Amphotericin B

TT + MF  
SbV + Allopurinol  
SSG + Pentoxifylline

Variable efficacy, high rate of AEs, lengthily schemes, low compliance

**Topical & oral drug, safe, effective against all forms of CL, at a low-cost and be adapted for use in rural areas**

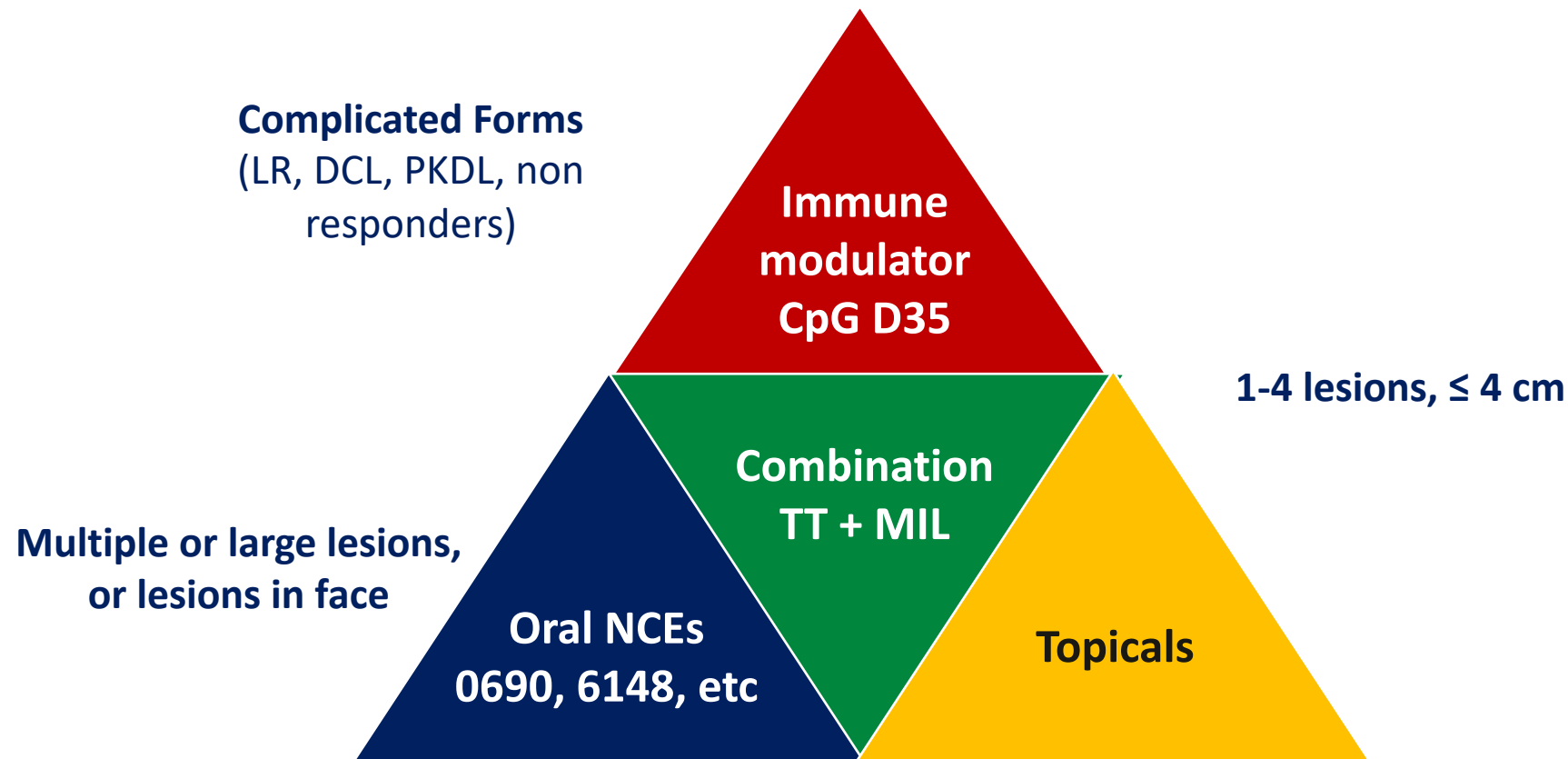


# CL Scarring, stigma and mental health problem



# DNDi Cutaneous leishmaniasis strategy

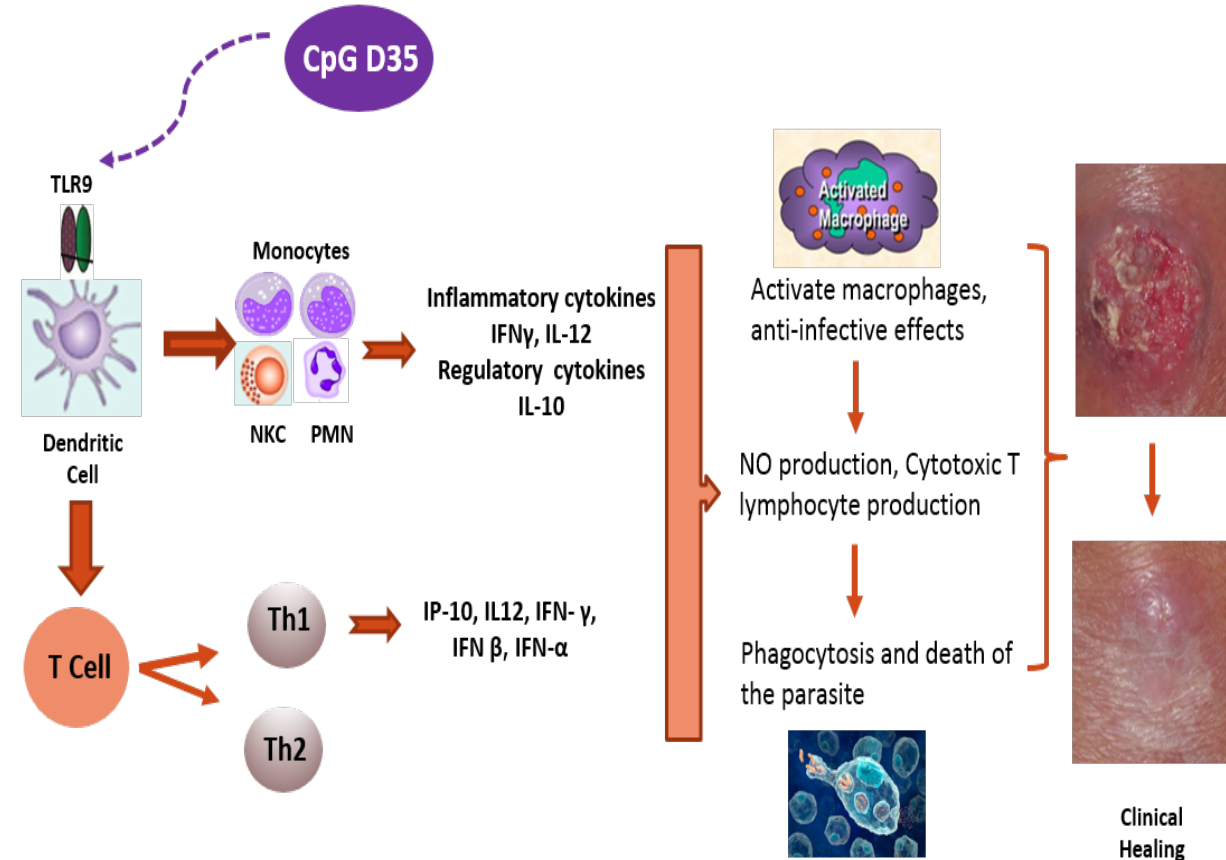
To achieve short, safe, non-invasive, efficacious, affordable, and field-friendly treatments for CL or at least for lesions caused by *L. tropica* and *L. braziliensis*.



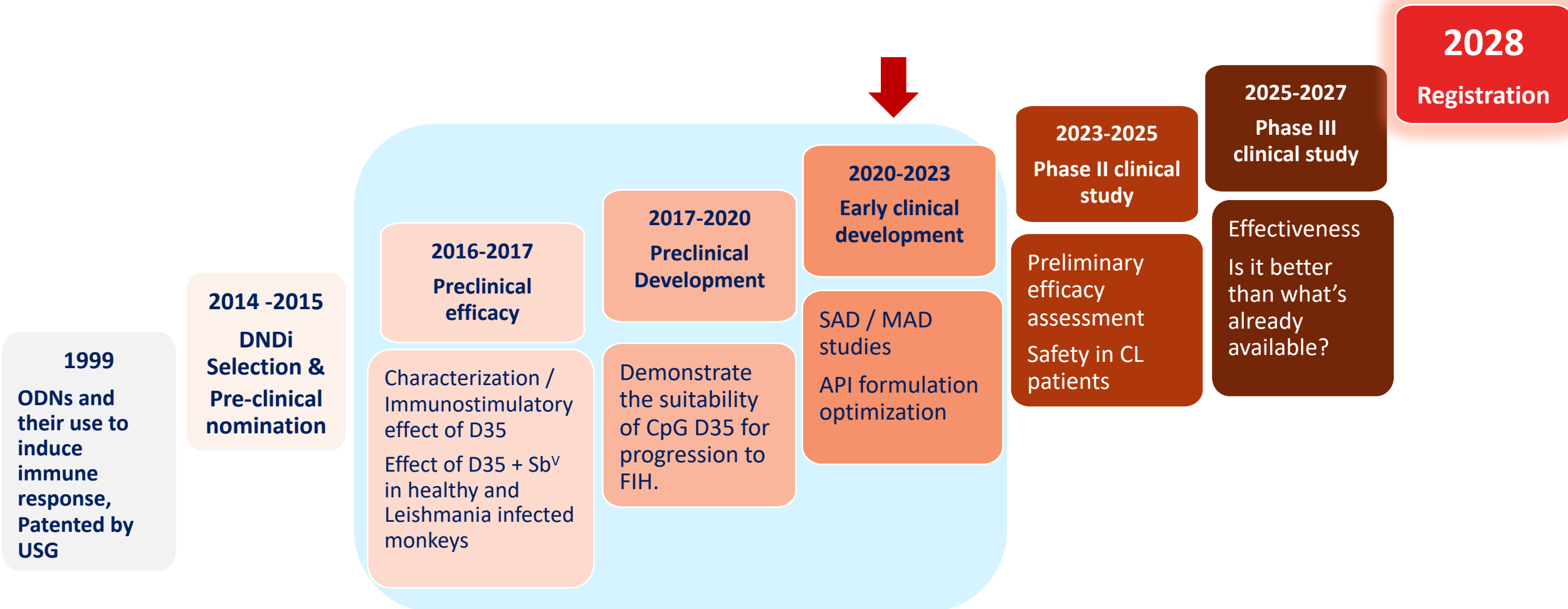
# CpG ODN D35

- ❖ Patent owned by the US government and licensed to DNDi. D. Verthelyi, D. Klinman and K. Ishii are named as inventors on the patent covering D35 filed on April 1999.
- ❖ CpG D35 is a Class A (also known as class D) synthetic oligonucleotide, TLR9 agonist, designed to activate the innate immune system and enhance the effector mechanism to control *Leishmania* infection.
- ❖ It has been tested in a monkey CL model (with *L. major* and *L. amazonensis*) with encouraging results (reduction of pathogenicity, enhanced healing - even without an antiparasitic drug)
- ❖ Preclinical and CMC studies have been completed by DNDi with the support from GHIT and in collaboration with GeneDesign and Tokyo University
- ❖ First in human study (SAD in HV) is being conducted in UK and MAD in CL patients will start in mid 2022
- ❖ CpG D35 is planned to be administered for CL treatment in combination with an oral antiparasitic drug.

## Mode of Action



# CpG D35: A long Journey



# CpG D35: A global collaboration of drug development expertise

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GHIT

Fund

Global Health Innovative Technology Fund

Intertek

 **GeneDesign, Inc.**

**FDA**

 **World Health Organization**

  
**OHIO**  
UNIVERSITY

  
**大阪大学**  
OSAKA UNIVERSITY

 **NACC**  
NAGASAKI UNIVERSITY

  
**ISC**  
Instituto  
de Salud  
Carlos III

  
**Patheon**  
A HEALTHIER WORLD. DELIVERED.

  
**東京大学**  
THE UNIVERSITY OF TOKYO



# CpG D35 in the time of COVID-19

COVID-19 has impacted in different ways the development of the project

- The lockdown and stay-at-home orders by the end of 2020 and beginning of 2021 caused a drop in the number of study participants, forcing the CROs to postpone the initiation of new studies.
- Many CROs were fully involved in conducting large studies on COVID-19 vaccines and not accepting new projects.
- Because the effects of CpG D35 in the immune system, an exclusion period of one month before and after receiving a COVID-19 vaccine has been imposed for all participants.
- The fear that CpG D35 interact with the host immune system is making potential participants being more hesitant to participate in a FIH study of an injectable product.

# Lessons learned

- GHIT funds has created an especial environment with Japanese pharmaceutical companies and international organizations fostering global partnership committed to patients' needs, creating medicines and vaccines against diseases for which there is a lack of R&D funding.
- Japanese pharma companies, research organizations and universities bring unique resources and capabilities including alternative drug discovery approaches, chemical classes not found abundantly in other libraries, technologies, insights and experiences gained through the whole process of product development.
- Oligonucleotides are not simple small molecules, so both the discovery and manufacturing require work with experts at the forefront of oligonucleotide. Having the opportunity to work with one of the creators of CpG D35 and with a pharma company with the expertise on GMP manufacturing oligos is exceptional and prized experience.
- Working in international environment always brings some challenges, often related to communication and culture, time zones differences and others but the politeness, diplomacy and Japan's gastronomy compensates in abundance any of the challenges.



**Thank You**