Innovation & Access for Neglected Populations

Key Challenges & Perspectives for Latin America

Dr Joel Keravec, Latin America Executive Director

DNDi
Drugs for Neglected Diseases initiative
Latin America Landscape

Social inequalities ➔ Health Access inequalities

- 34% residents live in poverty, with more than 12% living in extreme poverty
- 125 M out of 580 M no access to health services

Considerable disparities in health & social devpt indicators

- Persistence of high maternal and infant mortality rates, diarrheal and respiratory diseases in low resources settings
- Drug resistant infectious agents emergence (MDR-TB)
- Inadequate food, drug safety system & sanitation
- Violence undermines well-being and security
Latin America & the double burden of diseases

*Infectious and Non Communicable Diseases represent new challenges*

- **Expansion of people moving from urban to metropolitan areas:**
  Deforestation & exposure to vectors previously sylvatic

- **Urbanization > 78% => changes in disease epidemiology patterns:**
  Chagas, Leishmaniosis transmission and Malaria in urban/peri-urban areas

- **Emerging and re-emerging conditions such as arbovirus;**
  Zika, Dengue, Chikungunha, Yellow Fever ...

- **Emerging Non Communicable & Chronic diseases** (Hypertension, cancer, chronic respiratory diseases, diabetes ...)

- **NCDs = 55% of the disability-adjusted life-years (DALYs),**
  communicable, maternal, perinatal and nutritional conditions (27%) and injuries (18%)

Fragile health systems need to adjust to new complexities & increasing healthcare costs
R&D Landscape: Overview of challenges & opportunities

- **Brazil, Argentina and Mexico leaders** in # of clinical trials
  - Predominance of Phase 3 vs Phase 1 trials
    - Nearly 2/3 are phase 3 trials
    - 2.4% are phase 1 trials
  - Significant differences in regulatory requirements & slow pace of harmonization ("convergency")
  - Fiocruz announced accelerated clinical trials process for Zika..

- **Pharmaceutical industries** responsible for 7 out of 10 studies conducted across the region.

- But in Brazil, ~40% of studies conducted by universities, public institutions or other independent researchers

- **Increasing number of well-qualified investigators:**
  - 110% increase of # of journal articles by in the last 10 years as compared to 15-50% in the US and Europe
  - On going capacity-building

Sources: [https://clinicaltrials.gov/ct2/results/map?recr=Open&no_unk=Y](https://clinicaltrials.gov/ct2/results/map?recr=Open&no_unk=Y) (assessed 30 May 2016)
The Science Citation Index and Social Science Citation Index
Since 2003 DNDi LA is supported by a diverse & complementary network:

- Liaison office established with FIOCRUZ
- Technical collaboration w/ Malaysia and reversed TT w/ CIPLA – India
- ASMQ partnership with FARMANGUINHOS and MoH of Brazil

2003

- ASMQ registered in Brazil
- Expansion of registration worldwide

2008

- Regional Chagas Campaign: «Time to Treat»

2009

- Clinical trials expansion to Bolivia and Argentina

2010

- Registration of Ped. Benznidazol for Chagas
- Collaboration with LAFEPE

2011

- Creation of DNDi Argentina
- MOU with key public and private partners in Argentina
- Funding from MSF-Brazil and Institut Pasteur in Uruguay

2012

- Conducted regional consultations
- Public Funding from BNDES
- Private donation, family Moreau
- Funding of Ruta-N in Colombia

2013

- Expansion into Leishmaniosis: VL in Brazil and CL projects
- Carlos Slim Prize
- Mapping presence in Mexico
- Strategic Partnership and funding SCTIE (MoH) and FIOCRUZ
- Strengthened relationship with MSF sections in Latin America

2014

- New scope: Implement DNDi Business Plan 2015-2023
- Access projects in Latin America
- Pilots in Colombia, Mexico and USA
- Approval for creation of DNDi Colombia
- WHO PreQ for ASMQ filed

2015

- Looking at 2016 & Beyond...

2014, 2015
Beyond 2016, perspectives for expansion of DNDi activities

Legal entities in Brazil, Argentina & Colombia

- Focus on new treatments for Chagas & Leishmaniosis
- Screening & Lead Optimization
- New Business Plan
  - Hep C, Mycetoma,
  - Antimicrobial Resistance
- Expand Activities in Chile, Venezuela, Guatemala, Honduras, El Salvador...
- Chagas & Leish Access Plans
- Strategic surveillance on other emerging challenges
Chagas Disease: clinical trials in the region (1)

**The Gap**

Treatment for Chronic and Acute phases, to be used in all regions, with a good safety profile, short treatment duration (< 30 days)

**E1224 trial (phase 2, Proof of Concept)**
- DNDi-CH-E1224-001 / NCT01489228
- Bolivia, 2011 – 2013 (Awarded DNDi Project of the Year)

**Drug-drug Interaction (phase 1 trial)**
- Combination between E1224 and Benznidazole
- Argentina, 2014
Chagas Disease: clinical trials in the region (2)

The Gap

Treatment for Chronic and Acute phases, to be used in all regions, with a good safety profile, short treatment duration (< 30 days)

FEXI Trial (phase 2, Proof of Concept)
- Clinical study report by end June 2016
- Bolivia 2014-2016

BENDITA Trial (phase 2, Proof of Concept)
- Benznidazol New improved treatments and associations
- Bolivia, Argentina and Spain
- Expected enrolment starting September 2016
Cutaneous leishmaniasis: clinical trials in the region

**Anfoleish - Phase Ib/II** (Colombia)
- Enrolment completed Nov 2015
- Final report expected September 2016.

**Combination thermoterapy + miltefosine - Phase II** (Peru, Colombia)
- Approvals from regulatory authorities by Q3-2016.
- Trial start expected September 2016.

Topical & oral drugs, safe, effective against all forms of CL, with superior cosmetic results, at low-cost and easy to use.
A Key Role for Regional Disease Platforms

- Defining patient needs and Target Product Profile (TPP)
- Strengthening local capacities
- Conducting clinical trials (Phase II/III studies)
- Facilitating Registration of new therapies
- Accelerating implementation of new therapies, ensure therapies reach patients

LEISHMANIASIS

HAT

CHAGAS

DNDi

Network of Investigators and Collaborators in Leishmaniasis

LEAP

LEISHMANIASIS
Chagas Clinical Research Platform (CCRP)

- Since 2009, a network of health agencies and scientists in the Americas and around the world.
- Annual meetings, trainings, standardization of protocols, regulatory aspects, newsletter publications and integration of ethical principles.

**Main activities:**

- Identify and/ map gaps in Chagas R&D
- Conduct capacity building & training to support clinical trials
- Strengthen CCRP in endemic and non-endemic countries
- Support activities for to scale up of diagnosis & treatment working closely with policy makers and other stakeholders
RedeLEISH: Network of investigators and collaborators in Leishmaniasis

The CCRP aims to:

- Strengthen capacity for implementation of clinical trials
- Promote technical and scientific information sharing
- Promote consensus on research priorities
- Discuss R&D challenges and strategies to ensure public health impact of new treatment options

Launched in Brazil 2014
Expansion in LATAM in 2015
More than 70 members from 8 countries and 38 institutions
Technical Committee: 6 representatives of key partner institutions
Collaborative projects: Species identification project in Brazil
WEBFORUM launched in 2015: more than 100 contributions
Second Annual Meeting held in Medellín, Colombia in 2014

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DNDi
Drugs for Neglected Diseases initiative
Out of 150-180 million people suffer from Hepatitis C
10 million live in Latin America

85% of HCV infected people live in low- and middle-income countries
Generic licensing has created gaps for access in high-HCV burden middle-income countries, but there is an opportunity to change the current paradigm in Latin America

**Strengths of region**

- Strong civil society with advocacy capacity
- Prevalent genotypes (1 and 3) less challenging to treat
- Local and robust manufacturing capacity
- Overall research capacity to conduct trials
- IP aspects:
  - Ravidasvir non exclusive license for DNDi in LA
  - but sofosbuvir already strategically patented in some countries

[Map of DNDi license with alternate treatments for HCV]
Chagas: An old public health problem requiring innovative solutions...

- 6 million cases in Latin America
- Around 10,000 deaths/year
- Globally the economic burden is around U$ 1 billion
- Less than 1% of Chagas infected individuals has access to treatment
Despite some advances in the Chagas landscape, no significant changes in access occurred.

Major gaps still remain between the estimates of the number of people living with Chagas disease and those actually diagnosed and receiving treatment.

DNDi is focusing on developing NCE + New Access Strategies:

- On-going pilot projects
- Advocacy campaigns with the Global Chagas Coalition and other partners
- Partnership models

Chagas Access Challenges: How to address this major access gap?

- USA
- Mexico
- Colombia
- Brazil
- Gran Chaco
Towards a Comprehensive Chagas Access Plan: A Joint Initiative of DNDi, Chemo Group/FMS

DNDi, Mundo Sano and Chemo team up to register benznidazole in US and Latin America

Plans will boost access to Chagas treatment throughout Americas

• to register adult (100mg) and paediatric (12.5mg) benznidazole (BZN) with the US FDA, as well as in Mexico, Colombia and other LA endemic countries

• to ensure sustainable access to benznidazole

• to develop a far reaching access plan in the region, in consultation with partners
Developing a pragmatic approach for interventions: from production challenges to a fully functional pharmaceutical system for Access
Working towards a renewed Access Vision & Innovative Strategies for Chagas with partners: enabling a paradigm shift

Creating strategies with partners to define interventions, development & and use of new tools to reduce overall Chagas burden

Source / southern cone initiative: A. Moncayo: Chagas Disease: Current Epidemiological Trends after the Interruption of Vectorial and Transfusional Transmission in the Southern Cone Countries “incidence of new infections by T. cruzi in the whole continent has decreased by 70%”
Capacities, willingness, commitments are there:

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<th>Category</th>
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<td>Elimination of some NTDs</td>
<td>in Colombia or Mexico</td>
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<td>Alliance</td>
<td>for a joint effort to the crisis of Zika &amp; regional research collaboration</td>
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<td>New initiatives</td>
<td>Lead Optimization Initiative (LOLA), GARD, ...</td>
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<td>Platforms, Networks</td>
<td>Partners, Academia</td>
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<td>Multi-lateral organizations &amp; Regional</td>
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**DNDi is a living laboratory: a rich think tank & catalyst in action for change: not just in what we do but how we do it:**

- Strengthening regional capacity for R&D
- Promote evidence based policy changes
- Advocate for new models & bring neglected populations to high level agenda
- What we can learn & share with our partners to develop creative solutions

=> Link global ideas & translate models with interventions at local levels & channels for access

=> How local levels can nurture global health debates and new ideas to demonstrate & promote sustainable changes

Concluding Remarks: How to build together a strong regional agenda for Innovation & Access
Perspectives and Plans

CL:
- Explore other opportunities for development of topical formulations
- Phase III trial thermotherapy + miltefosine
- Continue with screening and preclinical development of new oral compounds

VL:
- Evidence-based treatment recommendation change
- Plan for further studies to improve efficacy with good safety profile for treatment of VL in Brazil

REDELEISH:
- Consolidate the development of RedeLeish in LA
- Promote implementation of collaborative projects

ACESS:
- Develop regional strategy in alignment with the global concerted strategy for access

Gracias
Obrigado