


FIGHTBACK

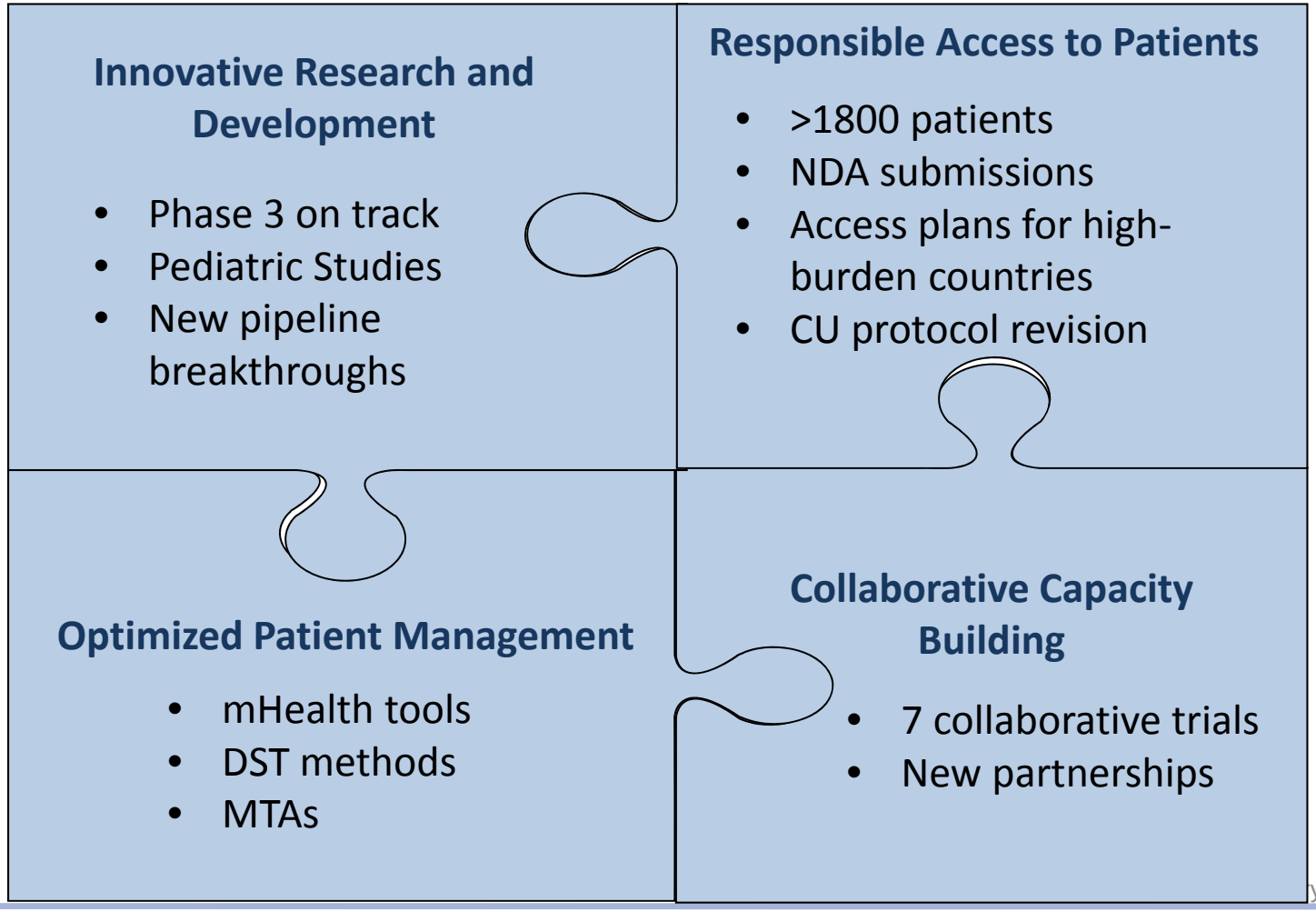
Liverpool, October 2016

Progress in Otsuka's FighTBack Initiative


Otsuka

TB innovation for tomorrow.

FighTBack Update 2016



FighTBack: Innovative R&D

Delamanid's Phase 3 trial

- Last patient, last visit completed. Currently working on data cleaning and data-base lock. Publication of results expected in early 2018.
- Though blinded, no newly identified safety concerns noted to date.

Pediatric Studies

- Study of safety and efficacy of delamanid in ages 6-17 completed and preliminary results submitted to WHO and also in discussion with EMA.
- First-ever MDR-TB pediatric formulation under assessment.
- Enrolment of 3-5 year old age group is ongoing, followed by 0-3 year olds starting early 2017.

FighTBack: Innovative R&D

Second New Anti-TB Compound

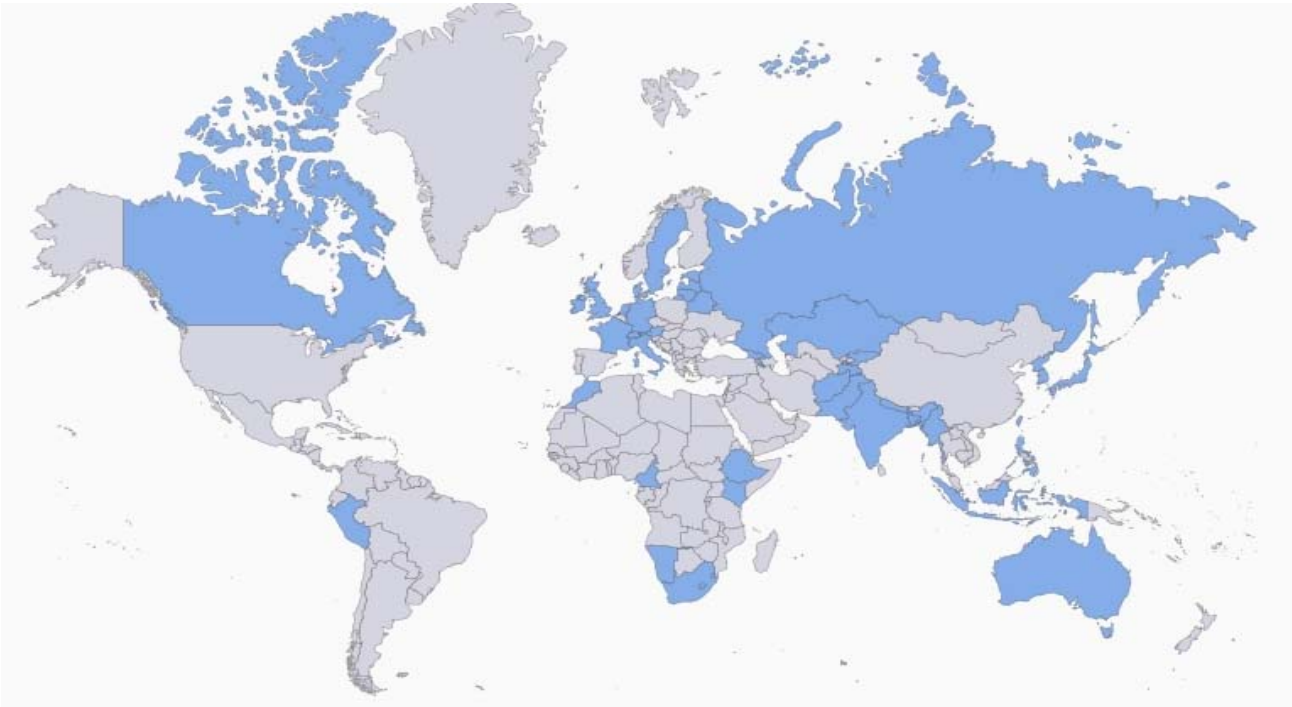
- IND package completed for second new anti-TB compound: OPC-167832.
- Different mechanism of action than delamanid and other anti-TB compounds.
- First subjects are already being enrolled in a Phase 1 single ascending dose study.
- Collaboration with the Gates Foundation to develop a pan-TB approach, in line with WHO's TPP.

Innovative Tool for Drug Development and Treatment Monitoring

- Continuing research on LAM-based assay for use as a drug development and treatment monitoring tool.
  - Collaborating with CPTR to seek Qualification as Drug Development Tool/Method

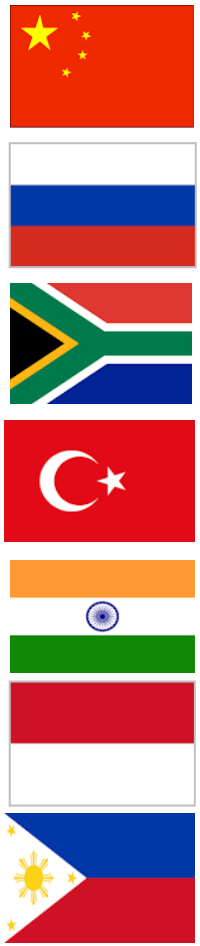
FighTBack: Responsible Access to Patients

Countries where delamanid has been supplied for the treatment of M/XDR-TB as part of expanded access, compassionate use, or under normal programmatic conditions as of October 2016



Number of countries = 45
High MDR-TB burden countries = 16

FighTBack: Responsible Access to Patients



- Over **1,800 patient courses** of **delamanid** supplied for treatment **in 45 countries** for compassionate use, expanded access programs, or under normal programmatic conditions.
- Over 120 compassionate use requests approved thus far from 12 countries
  - Protocol revision: allows concomitant use with BDQ, children above 6 years old, and pregnant women—if no alternatives exist.
  - All requests are reviewed by an internal committee of experts and by experts of the WHO/ERS Consilium.
- **Regulatory Status:**
  - New approval in 2016: **Hong Kong**
  - NDAs submitted: **China, Indonesia, Turkey, Philippines**
  - NDAs in preparation: **Peru, Vietnam, Russia, India, South Africa**

FighTBack: Early Outcomes with Delamanid Treatment

Setting	2 Month Culture Status	6 Month Culture Status	QTcF>500ms or Change>60ms
Japan	25/28 (89.3%)	20/20 (100%)	0/28 (0%)
Korea	20/21 (95.2%)	5/5 (100%)	N/A
Latvia	N/A	26/29 (89.7%)	N/A
Estonia	N/A	6/10 (60.0%)	N/A
PIH – endTB	N/A	N/A	0/14 (0%)
MSF – endTB, CU, other	18/27 (66.7%)	24/27 (88.9%)	8/213 (3.8%)
Compassionate Use (CU)	N/A	41/53 (77%)	2/68 (2.9%)

Notes
- Patients are MDR-TB, preXDR-TB, and XDR-TB for each setting
- Culture Status defined as at least last culture result after 2 and 6 months of delamanid treatment, respectively
- Culture Status includes culture positive and culture negative patients at baseline
- Culture Status includes patients completing 2 and 6 months of delamanid treatment, respectively
- QTcF data provided for any patient receiving delamanid
- Data reported for MSF also included in Compassionate Use data
- Data provided in aggregate for each Setting

Data Acknowledgements:
Japan = Fukujuji Hospital, Osaka Prefectural Medical Center for Respiratory and Allergic Diseases, National Hospital Organization (NHO) Higashinagoya National Hospital, NHO Kinki-Chuo Chest Medical Center and NHO Ibarakihigashi National Hospital; **Korea** = Pusan National University Hospital, Masan National TB Hospital, Pusan National University Yangsan Hospital, Chonbuk National University Hospital, Ulsan University Hospital, Severance Hospital; **Latvia** = L. Kuska; **Estonia** = M. Danilovits; **PIH** = C. Mitnick; **MSF** = F. Varaine

FighTBack: Responsible Access to Patients

Expanded Access Programs

- endTB
  - 400 patient donation in Dec 2015 to MSF
  - Early outcomes presented at Liverpool

- Working closely with South Africa's Department of Health and Right to Care to provide delamanid through a pre-approval pilot project for about 200 MDR-TB patients, including:
    - Children ages 12-18
    - HIV co-infected patients
    - Diabetes patients with poor treatment outcomes

  - Current status: Waiting for MCC approval. The developed protocol has been endorsed by the Department of Health and Right to Care.

- Discussions ongoing with India's RNTCP and ICMR

FighTBack: Responsible Access to Patients - GDF

- Delamanid available through Stop TB Partnership's GDF since Feb 2016
  - Procurement open to countries eligible for TB financing from the Global Fund and following WHO guidelines for the proper management of MDR-TB in quality-assured programs.
- Orders should be placed directly through GDF's website
- 850 treatment courses shipped thus far (550 to ship in December)
  - Orders primarily for MSF, but also from Kazakhstan, Belarus, Swaziland, Cameroun, Afghanistan, Dominican Republic, Senegal

FighTBack: Optimized Patient Management

Total Disease Management System

- Bridging treatment and diagnostic innovations with mHealth tools
- Working with partners on development of mobile technology to improve patient management and treatment adherence

- Otsuka has provided delamanid powder and transferred 7H11-based DST method to 23 labs in 15 countries
  - ➢ 43 MTAs executed for delamanid powder requests from external research institutions (100% approval rate)

- Actively working with partners to develop DST methods that are faster, more convenient and accessible

FighTBack: Collaborative Capacity Building

Sponsor	Study title	Started (✓)
Korea CDC	MDR-END: Treatment Shortening of MDR-TB Using Existing and New Drugs	✓
US NIH	A5300B/PHOENIx: Protecting households on exposure to newly diagnosed index Multidrug-Resistant Tuberculosis patients	
US NIH	ACTG 5343: Evaluating the safety, tolerability, and pharmacokinetics of bedaquiline and delamanid, alone and in combination, for Drug-Resistant Pulmonary Tuberculosis	✓
US NIH	IMPAACT 2005: DLM for MDR/HIV paediatric patients w/o injectable	
US NIH	ACTG 5356: Linezolid dose ranging in combination with DLM	
US NIH	DMID/VTEU: Standard regimen vs. DLM plus injectable-free regimen for MDR-TB	
UNITAID/MSF/ PIH	endTB: OBR vs. 5 different 6-month treatment shortening, injectable-free regimens	
USAID	Evaluate six-month regimen (DLM + BDQ + 1 or 2 other TB medicines) for patients with drug resistance to isoniazid, rifampicin and a quinolone.	

Conclusion

- Partnerships and collaborations are essential to ensure antimicrobial stewardship of new TB medications and ensure rational use of delamanid
- Availability through GDF opens procurement to countries eligible for TB financing from the Global Fund and following WHO guidelines; regular communications and forecasting essential to ensure timely and seamless procurement
- Otsuka is continuing to work with a broad array of global health partners to responsibly scale up access to delamanid and improve the current standard of care
- Otsuka's commitment to fighting TB remains unwavering. The development of a new anti-TB compound in partnership with key stakeholders opens the possibility for a pan-TB regimen