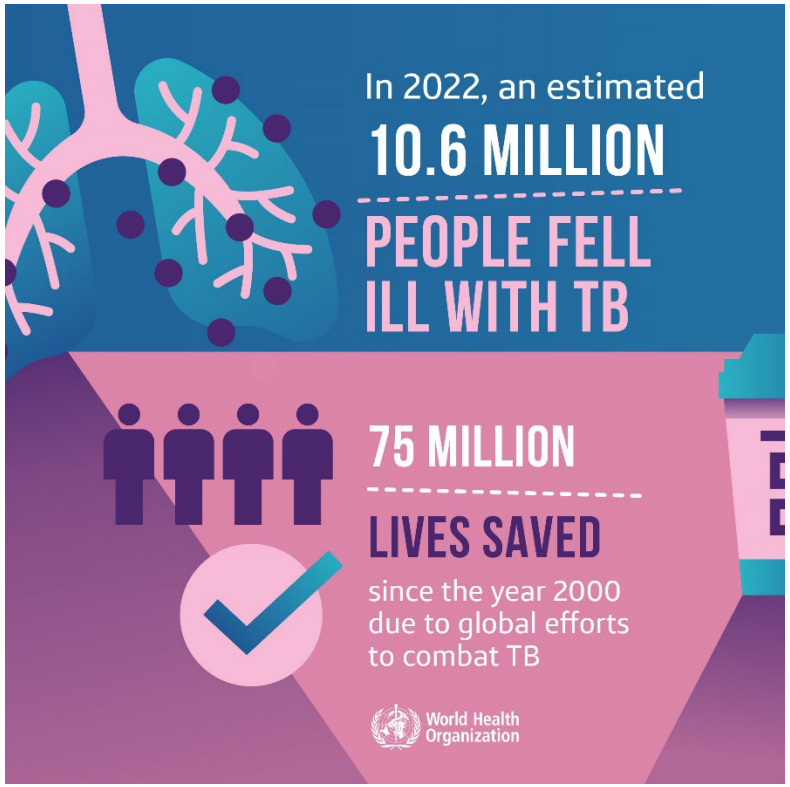
BILL & MELINDA GATES *foundation*

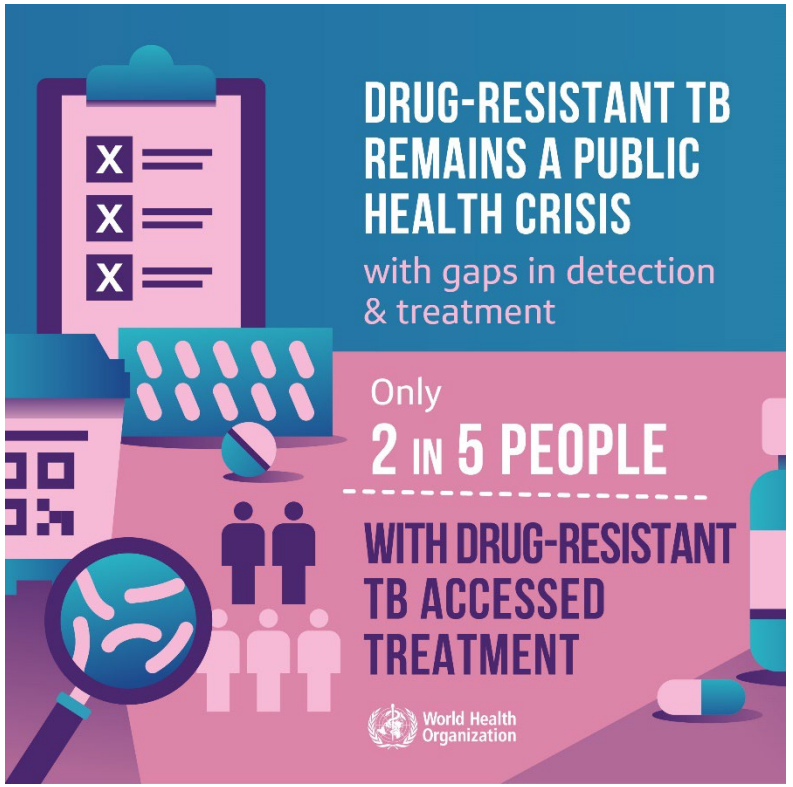
The TB Drug Accelerator: A Public-Private Model for Antibiotic Development

Ken Duncan

Tuberculosis

Source: WHO Global tuberculosis report 2023





The Pan-TB Target Regimen Profile (TRP)

TRP Criteria	Hypotheses
Pan-TB **(No relevant resistance, No Susceptibility Testing required)**	***ENABLE a Simple Test & Treat Paradigm***: Fewer patients lost to the system after diagnosis (Dx) Decreases time from Dx to Treatment → Less time to transmit (no waiting for drug susceptibility testing or failure on HRZE)
Shorter (≤2mos)	Clear differentiation from Standard of Care (SoC) ***Shorter*** → Improves Adherence → Improves Outcome → Less transmission
Safe and Well Tolerated	***No baseline or ongoing safety monitoring.*** Enables Test & Treat Paradigm. Well tolerated → Improves Adherence → Improves Outcome → Less Transmission
Simpler	**All Oral**, **Once daily** dosing, No clinically relevant Drug-Drug Interactions w/ other TB drugs, ARVs, or hormonal contraceptives (supporting a simple Test & Treat approach). FDC.
Efficacy **(Non-Inferior to SoC)**	Favorable outcome non-inferior to SoC (e.g., >90% favorable outcome 1 year after treatment start) Minimizes the **Efficacy – Effectiveness GAP** Short, Forgiving regimen will minimize impact of non-adherence → Improve Outcome → Less Transmission
Affordable	Low barrier to uptake → Impact [e.g., DS Standard of Care ~ $30/course]

TB Drug Accelerator

A consortium created to drive cutting edge drug discovery alongside investments in innovative technology platforms that inform the selection of targets, optimization of drugs and building of combinations, with partners including:

Pharma/Biotech

abbvie · janssen · Eisai · LEGENIA · GSK · MERCK · evotec

Non-Profit Research Institutes

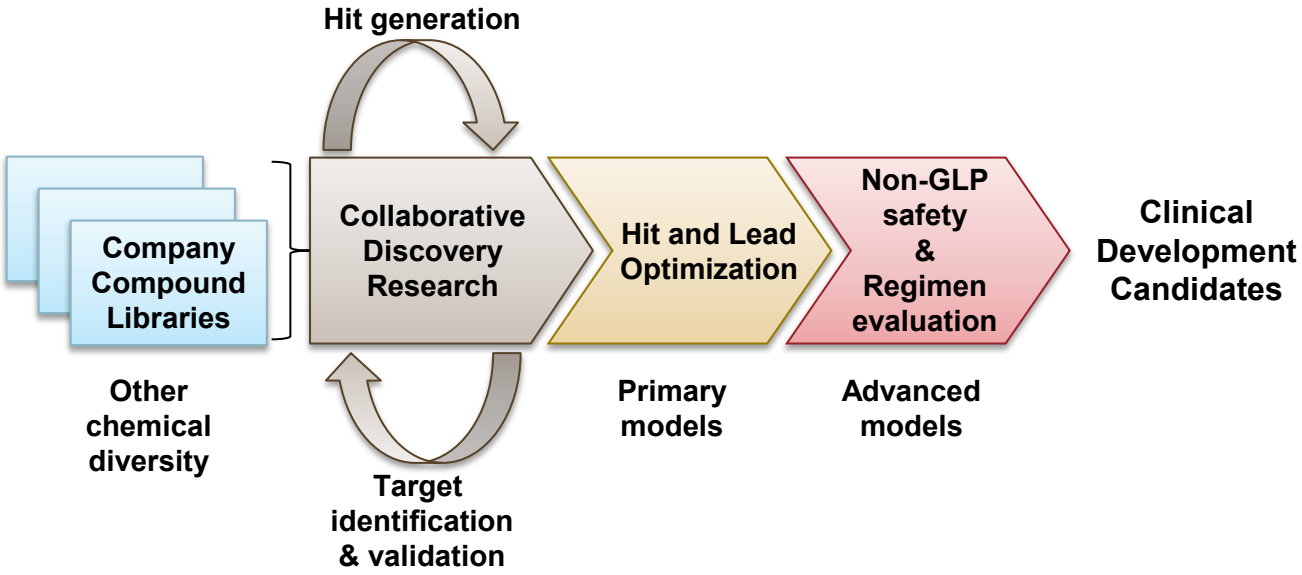
Calibr at Scripps Research · NIH National Institute of Allergy and Infectious Diseases · Seattle Children's Hospital · Research · Foundation · Bill & Melinda Gates Medical Research Institute · TB Alliance · GHDDI · Drug Discovery Unit · H3D · HZI Helmholtz Centre for Infection Research

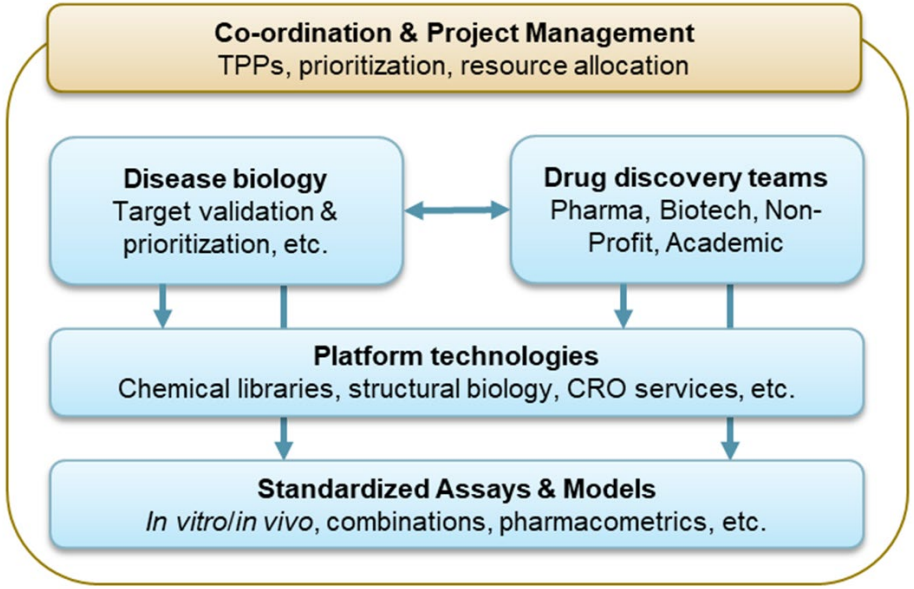
Academia

Harvard School of Public Health · IDM Institute of Infectious Disease and Molecular Medicine · Tufts · The Rockefeller University · Colorado State University · Texas A&M · CDI Center for Discovery & Innovation · Cornell University College of Veterinary Medicine · Weill Cornell Medicine · UCSF

TBDA members **disclose results** and chemical structures within the consortium

Commitment to data sharing, and **global access** to drug candidates





Status: 21 active projects at H2L and LO

Output: 12 clinical drug candidates (7 active through Phase 2)

Science linked to Product Development

Integration of new science with immediate impact on novelty, productivity, and quality

The Tuberculosis Drug Accelerator at year 10: what have we learned?

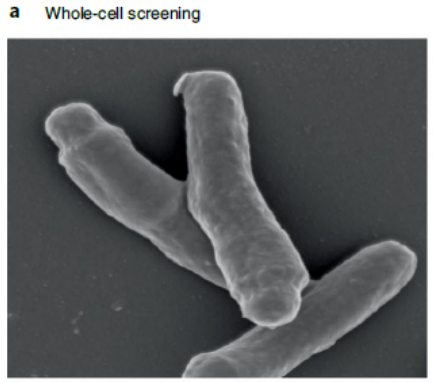
The Tuberculosis Drug Accelerator, an experiment designed to facilitate collaboration in tuberculosis drug discovery by breaking down barriers among competing labs and institutions, has reached a 10-year landmark. We review the consortium's achievements, advantages and limitations and advocate for the application of similar models to other diseases.

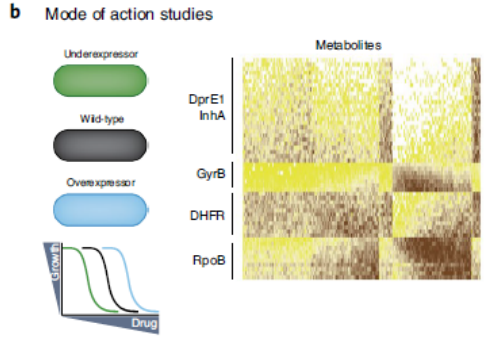
Bree B. Aldridge, David Barros-Aguirre, Clifton E. Barry III, Robert H. Bates, Steven J. Berthel, Helena I. Boshoff, Kelly Chibale, Xin-Jie Chu, Christopher B. Cooper, Véronique Dartois, Ken Duncan, Nader Fotouhi, Fabian Gusovsky, Philip A. Hipskind, Dale J. Kempf, Joël Lelièvre, Anne J. Lenaerts, Case W. McNamara, Valerie Mizrahi, Carl Nathan, David B. Olsen, Tanya Parish, H. Michael Petrassi, Alexander Pym, Kyu Y. Rhee, Gregory T. Robertson, Jeremy Michael Rock, Eric J. Rubin, Betsy Russell, David G. Russell, James C. Sacchettini, Dirk Schnappinger, Michael Schrimpf, Anna M. Upton, Peter Warner, Paul Graham Wyatt and Ying Yuan

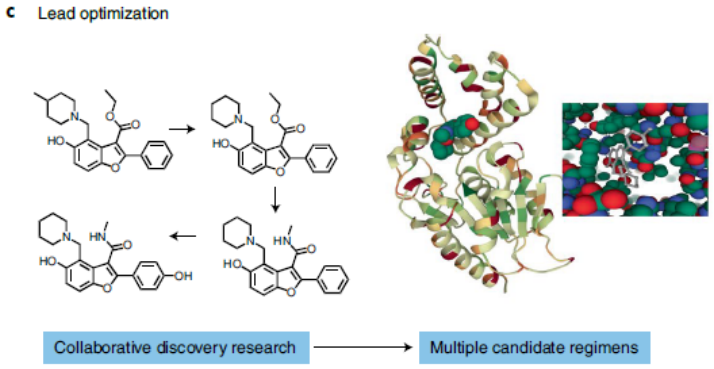
Nature Medicine **27**, 1333-1337 (2021)

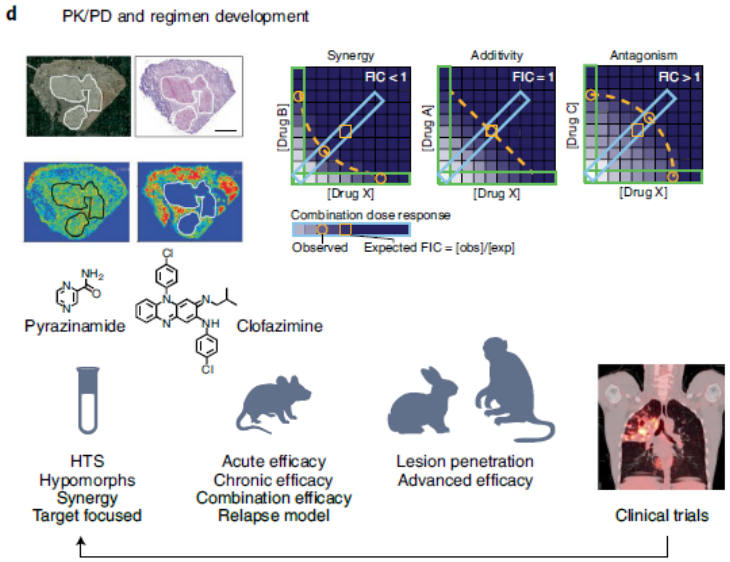
tbdrugaccelerator.org

Overview of TBDA activities

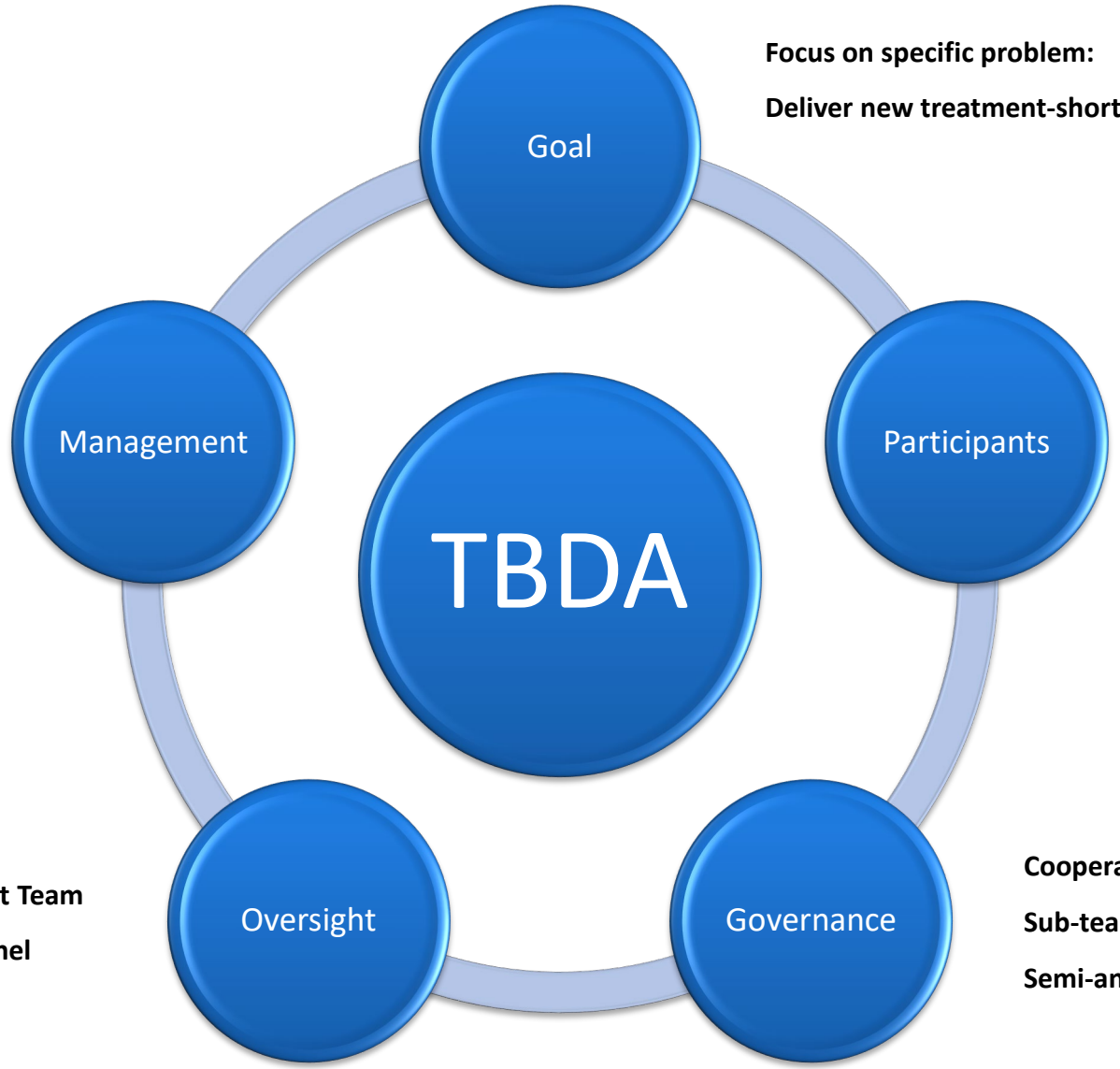








Features of the TBDA model



Focus on specific problem:

Deliver new treatment-shortening drug combinations for TB

Pharma, Biotech, research institutes, academia

Cooperation and Data Sharing Agreement

Sub-teams, topic-specific working groups

Semi-annual meetings

Portfolio Management Team

Scientific Advisory Panel

Leadership, goal setting

Portfolio and project management

Would a TBDA-like discovery program boost innovation and productivity in AMR product development?

AMR encompasses many pathogens, Use Cases, Target Product Profiles

- Focus on a narrow indication

Relatively cost effective and different way to build an innovative portfolio of products

- Managed portfolio eliminates redundancies
- Efficient transfer of new insights to product development

Consider drug combinations to guard against emergence of resistance

- Acknowledge development challenges and risks