CPTR Mission, Structure & Goals for Innovation

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Critical Path to TB Drug Regimens
The Challenge

CURRENT REGIMEN DEVELOPMENT PARADIGM:
Existing regimen consists of four drugs

NOVEL COMBINATION TESTING PARADIGM:
Novel regimen development can reduce the time to develop a new TB drug regimen by 75%
Accelerate the development of new, safe, and highly effective regimens for TB by enabling early testing of drug combinations.
CPTR Workgroups and Focus

**Workgroups:**

- Data Standards & Integration
- Biomarkers & Clinical Endpoints
- Preclinical & Clinical Sciences
- Translational Pharmacology (Modeling & Simulation)
- Health Authorities Submission

**Workgroups:**

- Clinical Trials Infrastructure
- Global Regulatory Pathways
- Stakeholder & Community Engagement
- Access & Appropriate Use
CPTR Scientific and Regulatory Innovations

Regulatory Science Consortium

Opportunities for collaboration to complement, enhance and/or accelerate our collective efforts
Role in Enabling & Accelerating the Process:

- Identify tools/methods that can bring the most value
- Reach scientific consensus by sharing expertise, information, data
- Collaborate with regulators on DDT development & use
- Proceed with regulatory authorities when appropriate

*Alignment on tools and data sharing to support their advancement will accelerate our success*
Data Standards and Integration

Key Accomplishments

- Launched CDISC TB Data Standard v1.0
  - Available for use on CDISC website
  - Being implemented in bedaquiline Phase III study design
- TB Data Repository Launched for Data Set Remapping
- Clinical Trial Data Acquisition in Progress:
  - Industry, CDC, & NIAID

Future Milestones

- Enable Modeling with Aggregated Data
  - Potential to add additional terminology as needed (e.g., pediatrics)
  - Data team to support data acquisition, remapping and modeling effort as needed
Biomarkers and Clinical Endpoints

Key Accomplishments

- Liquid Culture Proposed to FDA as a Predictive or Prognostic Biomarker for Clinical Outcome
  - Letter of Intent submitted to FDA
- FDA Division of Anti-Infective Products (DAIP)
  - Review Team in Place
  - In process of first review

Future Milestones

- Respond to FDA DAIP Review Team Comments
- Submit to EMA
- Evaluate Next Generation Endpoints
  - e.g., Imaging biomarkers, molecular markers, etc.
Preclinical and Clinical Sciences

Key Accomplishments

- Gap Analysis of *in vitro* & *in vivo* Preclinical Efficacy Models
- Evaluated & Selected Combination Partners
- Initiated Discussions with Regulatory Agencies Regarding *in vitro* Hollow Fiber Model System
- Agreement to Partner on Data/Method Review

Future Milestones

- Progress Discussion with Regulatory Agencies & Define Next Steps for the Hollow Fiber Model System
- Develop Data & Model Inventory and Analysis
- Report Strengths & Gaps with *in vivo* Models & Develop Research Objectives and Critical Path Studies
- Clinical Sciences Arm to Launch CV/QTc Subteam
Vision: More efficient translation between each stage of drug development

Modeling and Simulation Workgroup

Hollow fiber model
Physiologically-based PK models
Clinical trial simulation tools (drug-disease-trial models)

Network Biology
Pharmacology
Preclinical PKPD
Clinical Pharmacology
Pharmacometrics

Right Pathway
Right Target

Pathway
Target

Right Dose
Drug
Disease

Continuously revise and refine with relevant data (summary and subject-level)
Global Regulatory Pathways

Key Accomplishments

- Developing Pathways for Global Regulatory Efforts
- Provided FDA Bedaquiline Advisory Committee Meeting Materials (Accelerated Approval) to High Burden Countries NRAs

Future Milestones

- Sharing Data From Key TB Clinical Trials with NRAs
  - Address Gaps in Regulatory Review Processes
- Develop a Joint/Parallel Regulatory Review Process for TB Drug Marketing Applications
  - WHO and NRA’s in high burden countries
  - Major opportunity to strengthen the review process for TB drugs
Opportunities for CPTR and PreDiCT-TB

For today

- Panel views on key issues facing the TB field and views on what they have heard
- Understand how both efforts align to meet those needs or identify gaps to consider

For tomorrow

- MOU in place
  - Engage in detailed discussion on our scientific and regulatory goals
  - Develop strategic path forward for partnership
    - Data, cross-talk, gaps etc.

Institute for International Cooperation in Health (IIHI)
Questions for panel

Are there opportunities that you see for synergy / leveraging the outputs of both efforts?

Are there critical gaps that are not being addressed by either effort that would inform such a plan?

Data sharing will be key to many deliverables described today as it prevents duplication, encourages collaboration, and could accelerate the TB drug development process. However, this process remains challenging. Could the panel comment on how they might advise us to leverage this process more effectively?
Questions for panel

The advancement in science described today could inform a more globally harmonized regulatory pathway for the development of novel TB regimens now that we have pathways in place for single TB drug registration. It has been suggested that consortia/PPPs such as IMI and C-Path can help accelerate a pathway for regimen development/regulatory approval via putting forth proposed development plans which would outline the stages of work to be completed from an initial/limited approval through to a full approval.

• Does the panel support this concept?
• Does the Panel have any advice to offer as to how we can make the maximum impact from the work outlined in the presentations and use that work to help inform a development pathway/regulatory pathway that would achieve this goal?
Thank you!

Bill & Melinda Gates Foundation
CRITICAL PATH INSTITUTE
TB ALLIANCE
GLOBAL ALLIANCE FOR TB DRUG DEVELOPMENT
Critical Path to TB Drug Regimens

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