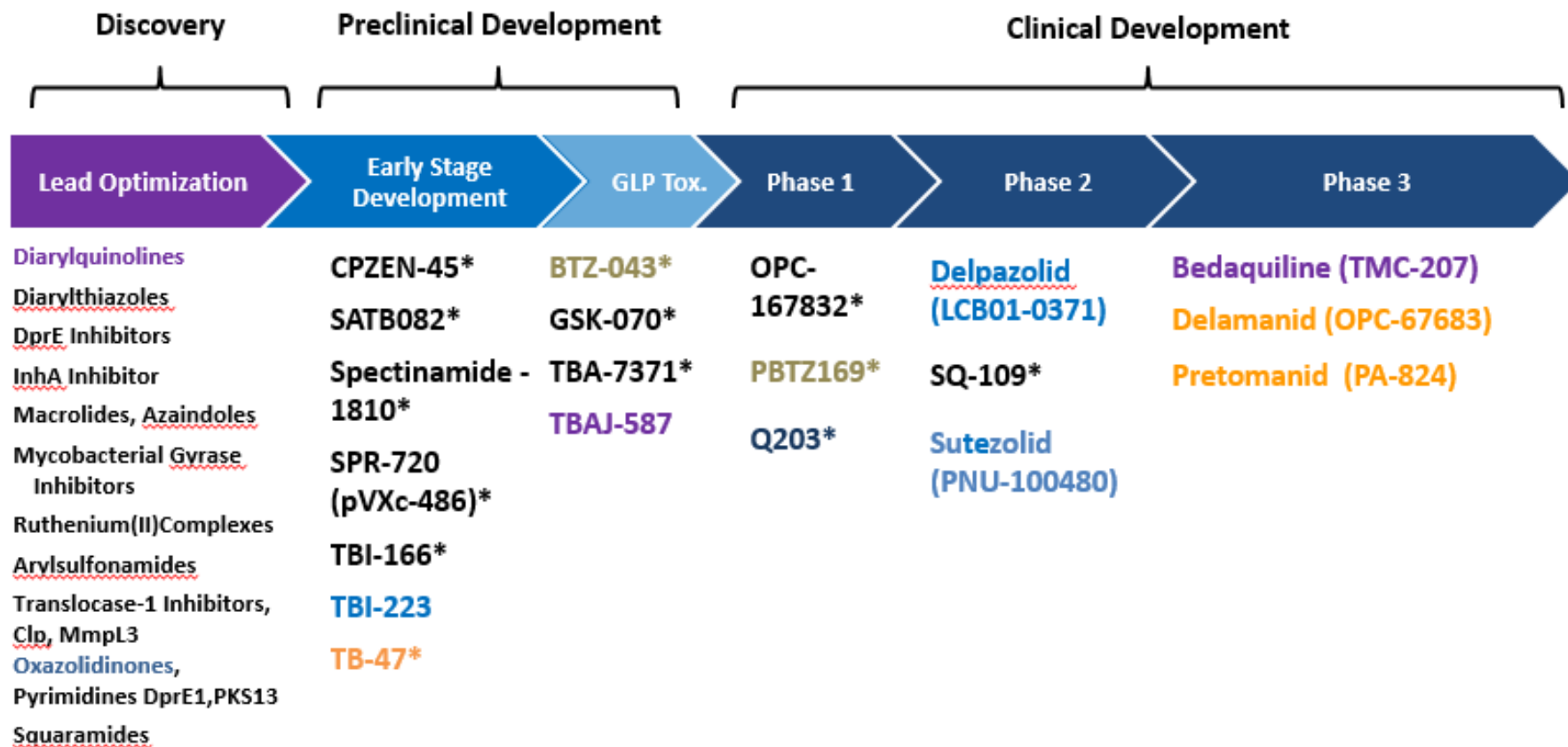# Critical Path to TB Drug Regimens
Global Collaboration for Accelerating Novel TB Regimen Development

Debra Hanna, Executive Director, Critical Path to TB Drug Regimens

NOV 2017

Global New TB Drug Pipeline [1]

Discovery   **Preclinical Development**   **Clinical Development**

Lead Optimization	Early Stage Development	GLP Tox.	Phase 1	Phase 2	Phase 3
Diarylquinolines	CPZEN-45*	BTZ-043*	OPC-167832*	Delpazolid (LCB01-0371)	Bedaquiline (TMC-207)
Diarylthiazoles	SATB082*	GSK-070*			Delamanid (OPC-67683)
DprE Inhibitors	Spectinamide - 1810*	TBA-7371*	PBTZ169*	SQ-109*	Pretomanid (PA-824)
InhA Inhibitor		TBAJ-587	Q203*		
Macrolides, Azaindoles	SPR-720 (pVXc-486)*			Sutezolid (PNU-100480)	
Mycobacterial Gyrase Inhibitors	TBI-166*				
Ruthenium(II)Complexes	TBI-223				
Arylsulfonamides	TB-47*				
Translocase-1 Inhibitors, Clp, MmpL3					
Oxazolidinones,					
Pyrimidines DprE1,PKS13					
Squaramides					

*New chemical class. Known chemical classes are color coded: fluoroquinolone, rifamycin, oxazolidinone, nitroimidazole, diarylquinoline, benzothiazinone, imidazopyridine amide.

[1] New Molecular Entities not yet approved, being developed for TB or only conditionally approved for TB. Showing most advanced stage reported for each. Details for projects listed can be found at
http://www.newtbdrugs.org/pipeline/clinical

Ongoing projects without a lead compound series identified can be viewed at
http://www.newtbdrugs.org/pipeline/discovery

WORKING GROUP ON NEW TB DRUGS

www.newtbdrugs.org

Updated: June 2017
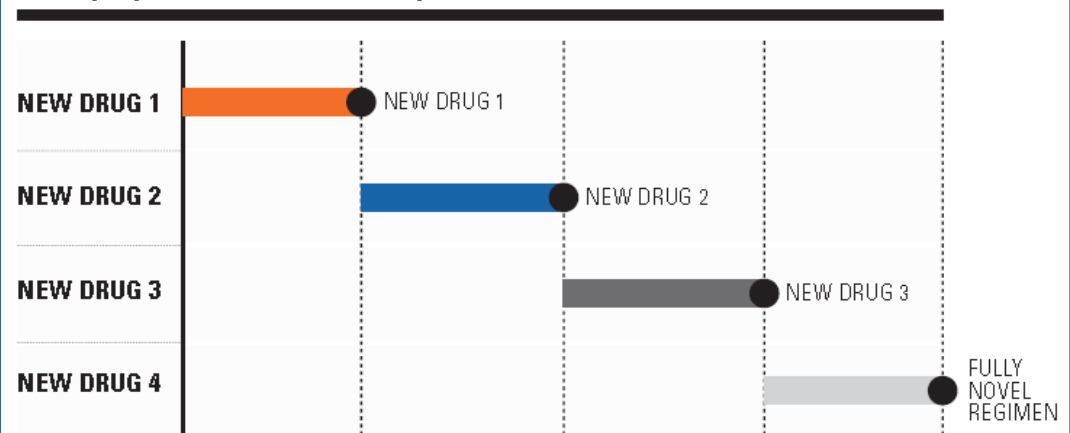
CRITICAL PATH INSTITUTE

Advance TB drug pipeline emphasizing combination study approaches informed by *translational science*

Define, based on evidence, best drug development tools to de-risk compounds and improve understanding of efficacy

Define, based on evidence, novel biomarkers to inform improved trial design and adaptivity
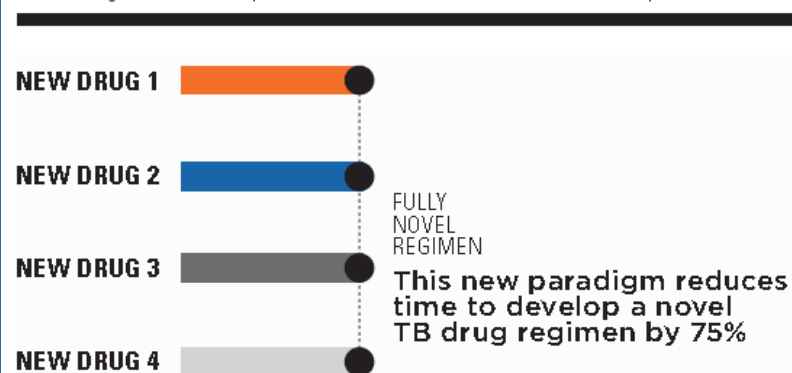
CURRENT REGIMEN DEVELOPMENT PARADIGM:

Existing regimen consists of four drugs

- NEW DRUG 1 — NEW DRUG 1
- NEW DRUG 2 — NEW DRUG 2
- NEW DRUG 3 — NEW DRUG 3
- NEW DRUG 4 — FULLY NOVEL REGIMEN

NOVEL COMBINATION TESTING PARADIGM:

Novel regimen development can reduce the time to develop a new TB drug regimen by 75%:

- NEW DRUG 1
- NEW DRUG 2
- NEW DRUG 3   FULLY NOVEL REGIMEN
- NEW DRUG 4

This new paradigm reduces time to develop a novel TB drug regimen by 75%

MISSON, FOCUS AREAS AND FUNDER

The Critical Path to TB Drug Regimens (CPTR) is a global, cross-sector initiative that aims to speed the development of a safer and shorter duration TB drug regimen

Four Critical Areas of Focus:

- Advance drug development tools and methodologies to support go/no-go decisions during each stage of research and development

- Acquire and curate supportive data through establishment of collaboration network to support new methods and tool validation

- Develop pathways for new TB treatment regimens that include drugs that are not yet individually approved

- Provide regulatory excellence in the development, validation, and advancement of these drug development tools and methodologies

BILL & MELINDA GATES foundation

CRITICAL PATH INSTITUTE

CPTR INITIATIVE MEMBERS AND PARTNERS

Government/Regulatory participants

CDC · FDA · European Medicines Agency · World Health Organization · imi Innovative Medicines Initiative · National Institutes of Health · National Institute of Allergy and Infectious Diseases · DAIDS RSC Regulatory Support Center

Industry members

AstraZeneca · Pfizer · SANOFI · Celgene GLOBAL HEALTH · Cepheid A better way. · VERTEX THE SCIENCE of POSSIBILITY · epistem · gsk GlaxoSmithKline · BIOMÉRIEUX · Alere · QIAGEN · Otsuka · Janssen PHARMACEUTICAL COMPANIES of Johnson-Johnson · tibotec · Abbott Molecular · SEQUELLA Incorporated · ThermoFisher SCIENTIFIC · BD

Nonprofit research members

TB ALLIANCE GLOBAL ALLIANCE FOR TB DRUG DEVELOPMENT · BILL & MELINDA GATES foundation · EDCTP · TAG Treatment Action Group · REAGAN - UDALL FOUNDATION FOR THE Food and Drug Administration · PATH A catalyst for global health · FIND foundation for innovative new diagnostics · Stop TB Partnership

Academic Partners

Baylor Institute for Immunology Research	O'Neill Institute at Georgetown Law Center	University College of London
Case Western Reserve University TB Research Unit	Radboud University	University of Arkansas for Medical Sciences
Colorado State University	RESIST-TB [Boston University]	University of Cape Town
Duke University	Rutgers [University Of Medicine & Dentistry]	University of Liverpool
Forschungszentrum Borstel	St. George's, University of London	University of St. Andrews
Harvard University	Stanford University	University of Virginia
Johns Hopkins University	Stellenbosch University	University of Texas Health Science Center at San Antonio
London School of Hygiene and Tropical Medicine	University of Florida	University of Toronto
Munich University	University of California, San Francisco	Uppsala University, Dept. of Pharmaceutical Biosciences
NYU		Vanderbilt University School of Medicine

GLOBAL, CROSS-SECTOR PARTNERSHIP

CRITICAL PATH
INSTITUTE

ACADEMIA

INDUSTRY

PATIENT ADVOCACY GROUPS

HEALTH ORGANIZATIONS

CRITICAL PATH INSTITUTE

Critical Path to TB Drug Regimens

REGULATORY AGENCY INPUT

Eight Pharmaceutical Partners

Non-Profit Product Development Partners

Eighteen Diagnostic Companies

Twenty-six Academic Institutions

Twenty Non-Governmental Agencies

Five Governmental Agencies

Shared Data
Shared Resources
Shared Costs
Shared Risks

Research And Discovery	Preclinical Studies	Phase I Trial	Phase II Trial	Phase III Trial

REGULATORY AGENCY REVIEW

SHARED LEARNING CAN SHORTEN THE TIMELINE

CRITICAL PATH INSTITUTE

- ✓ Data Sharing and Data Standardization
- ✓ Biomarker Development and Qualification
- ✓ Drug Development Tool Advancement and Qualification
- ✓ Development and Implementation of Modeling and Simulation Tools

Adapted from *"A virtual space odyssey"*, Cath O'Driscoll (2004)
http://www.nature.com/horizon/chemicalspace/background/odyssey.html

DATA COLLABORATION IS CRITICAL
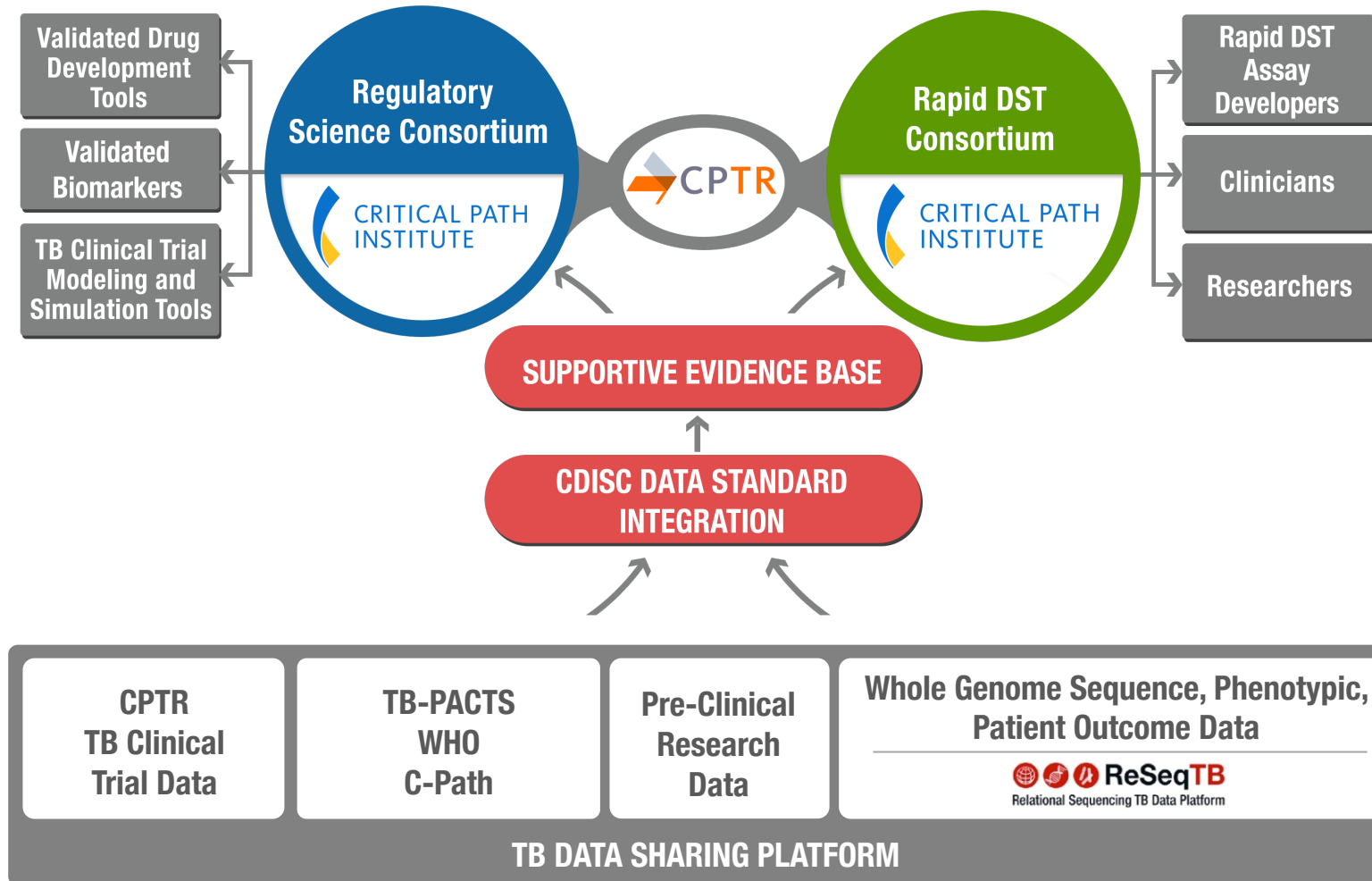
GLOBAL CPTR DATA CONTRIBUTIONS
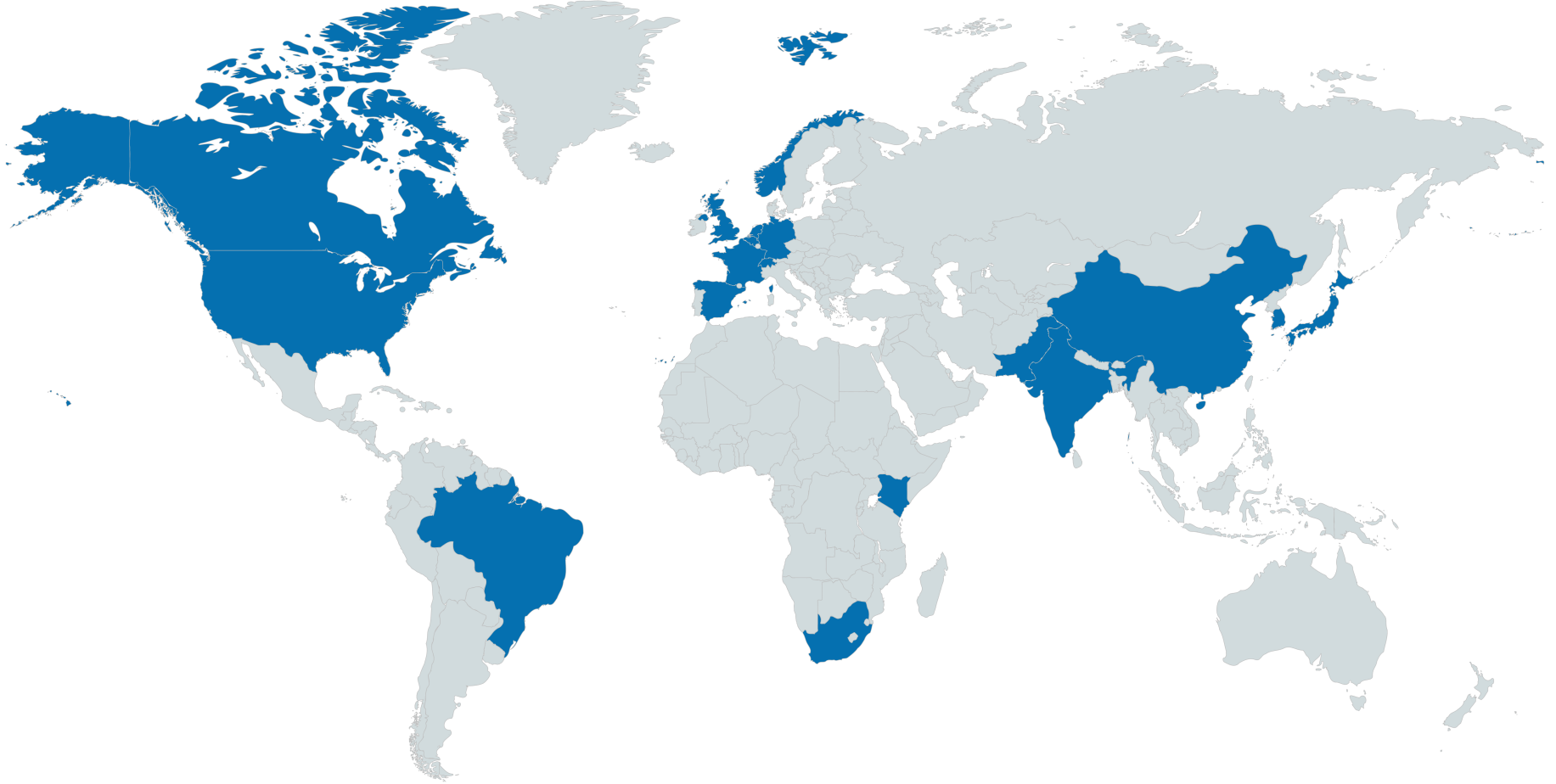
CPTR MODELING AND SIMULATION PROGRAMS
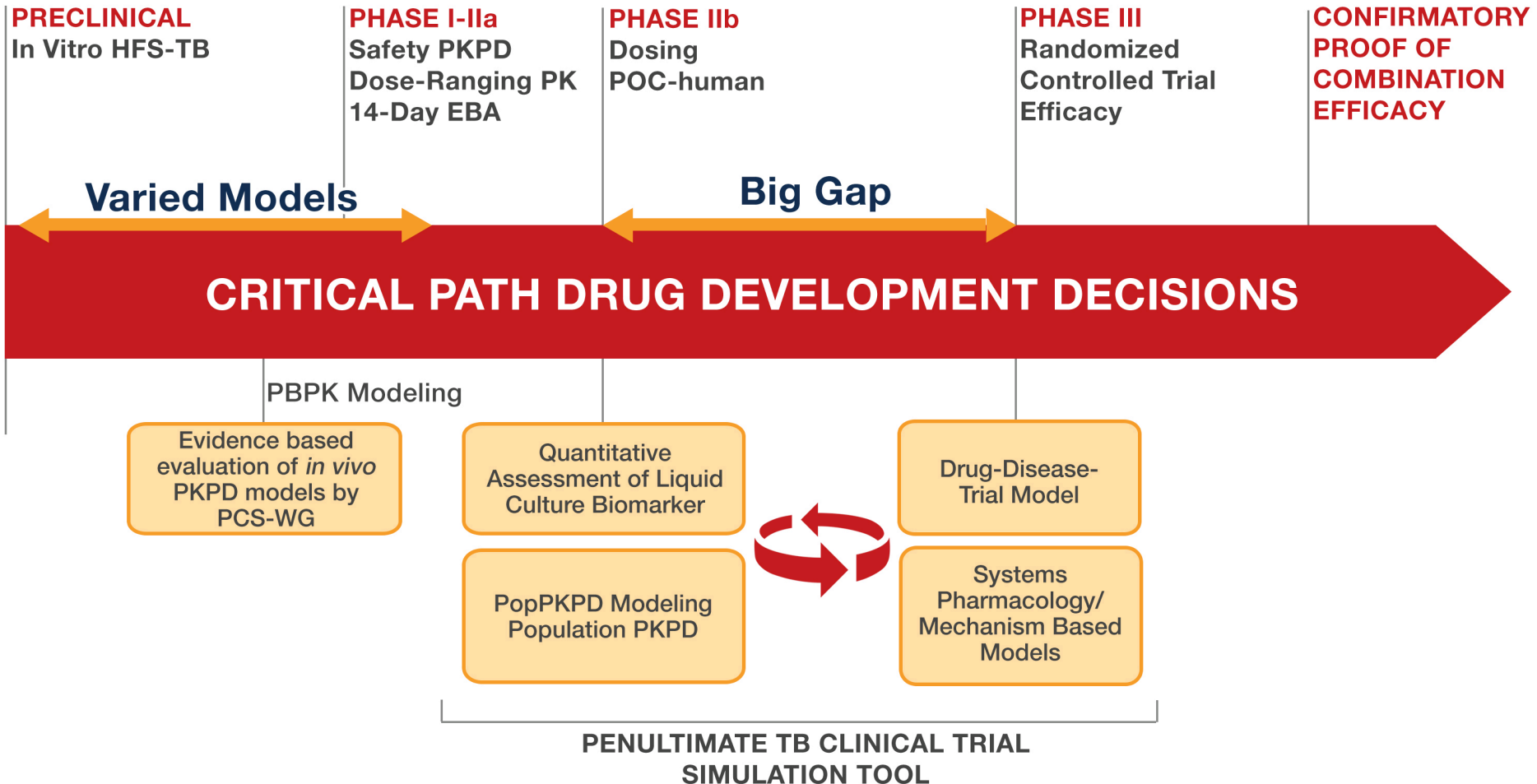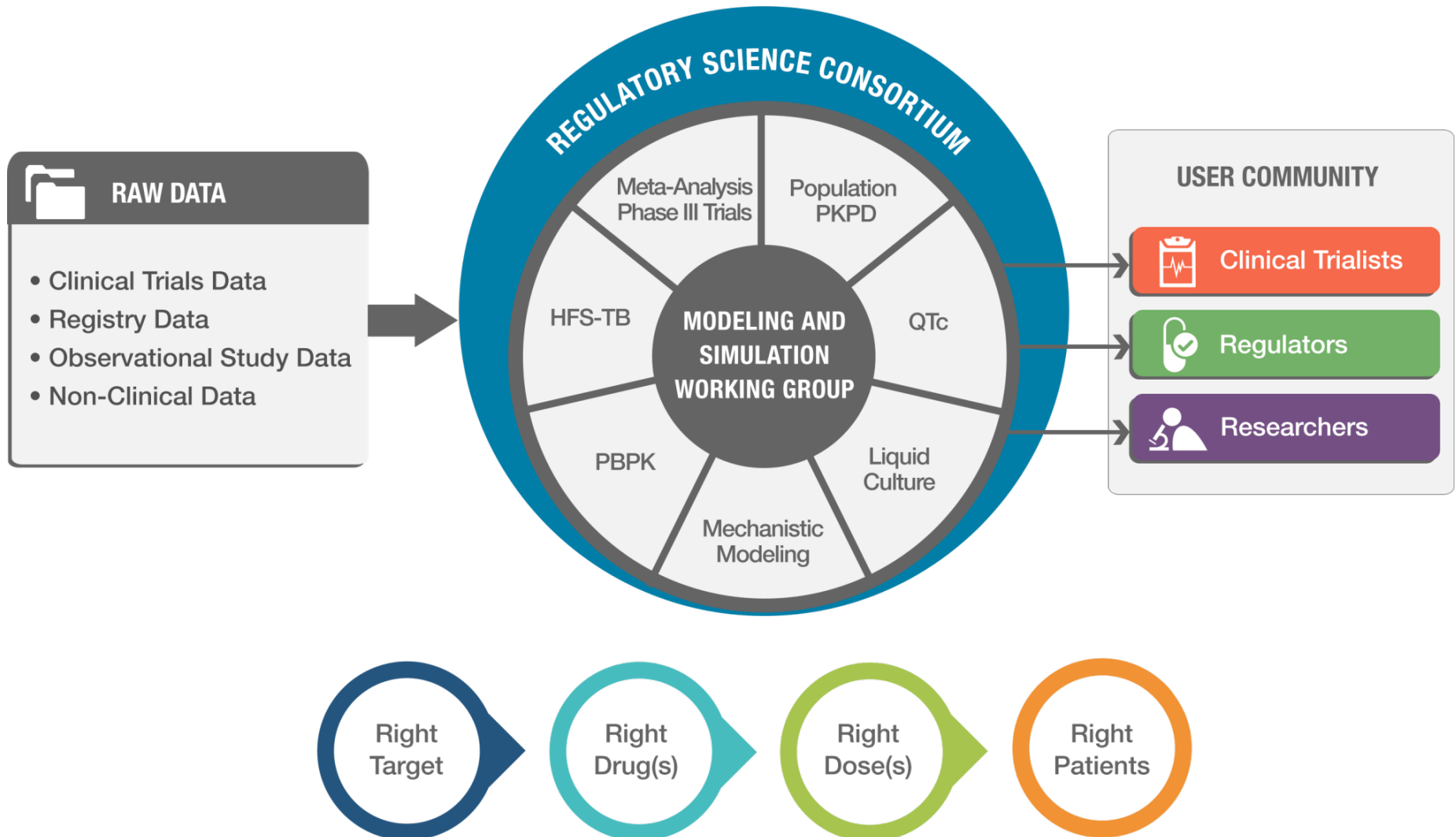
REGULATORY & POLICY SUCCESSES

Critical Path to TB Drug Regimens

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EUROPEAN MEDICINES AGENCY — SCIENCE MEDICINES HEALTH

FDA

World Health Organization

	European Medicines Agency	FDA	World Health Organization
Hollow Fiber System Model	Qualified as a translational drug development tool	Inserted into Draft Guidance on Drug Development for Pulmonary TB	
Physiologically Based Pharmacokinetic Model	Submitted Letter of Intent and Briefing book for Scientific Advice Qualification	Pursue Critical Path Innovation Meeting 1Q2018	
LAM Biomarker	Pursue Innovation Task Force Meeting 1Q2018	Letter of Intent accepted into the biomarker qualification program	
TB-ReFLECT			Inform programmatic decisions based on meta-analysis of Phase III clinical trials
TB-PACTS			Sponsored C-Path to aggregate and share TB clinical data
ReSeqTB			Implement as the global srv. platform for TB resistance

HOW WE WORK TOGETHER

CPTR MANAGEMENT AND WORKFLOW