

Status of the TB Drug Pipeline

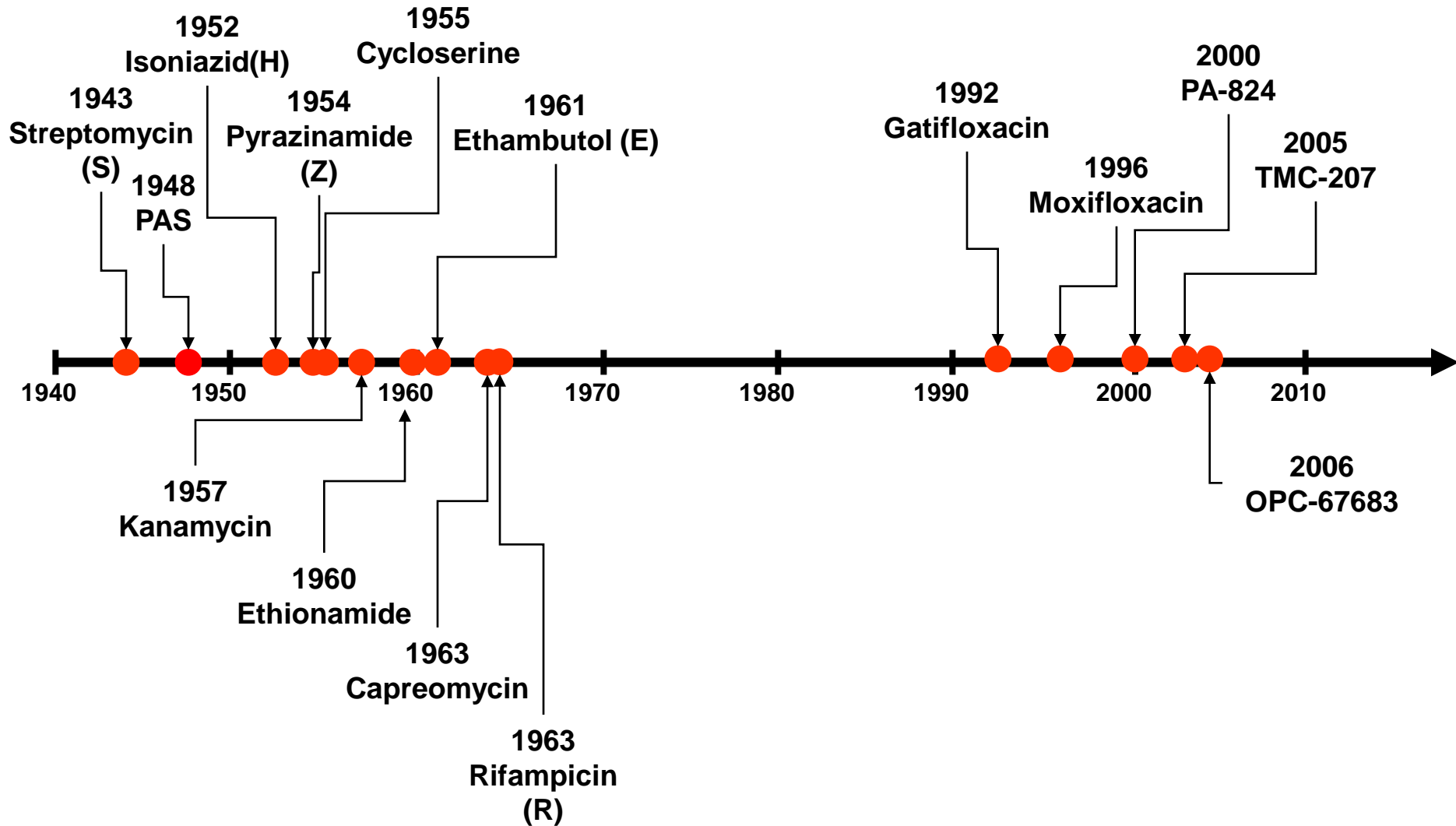
Chair: *Dr. Barbara Laughon, NIAID, NIH*

- ***Discovery/Preclinical*** - *Dr. Tanjore Balganes, AstraZeneca**
- ***Clinical Development*** - *Dr. Ngozi Erond, TB Alliance*
- ***Community Perspective on Need for a Robust Pipeline and Challenges with Current Regimens*** - *Francis George Alpina, patient representative*

The Global Discovery / Preclinical Pipeline for New TB Drugs

Barbara E Laughon, PhD
Senior Scientist for TB Drug Development Partnerships
Division of Microbiology and Infectious Diseases
NIAID, NIH, DHHS

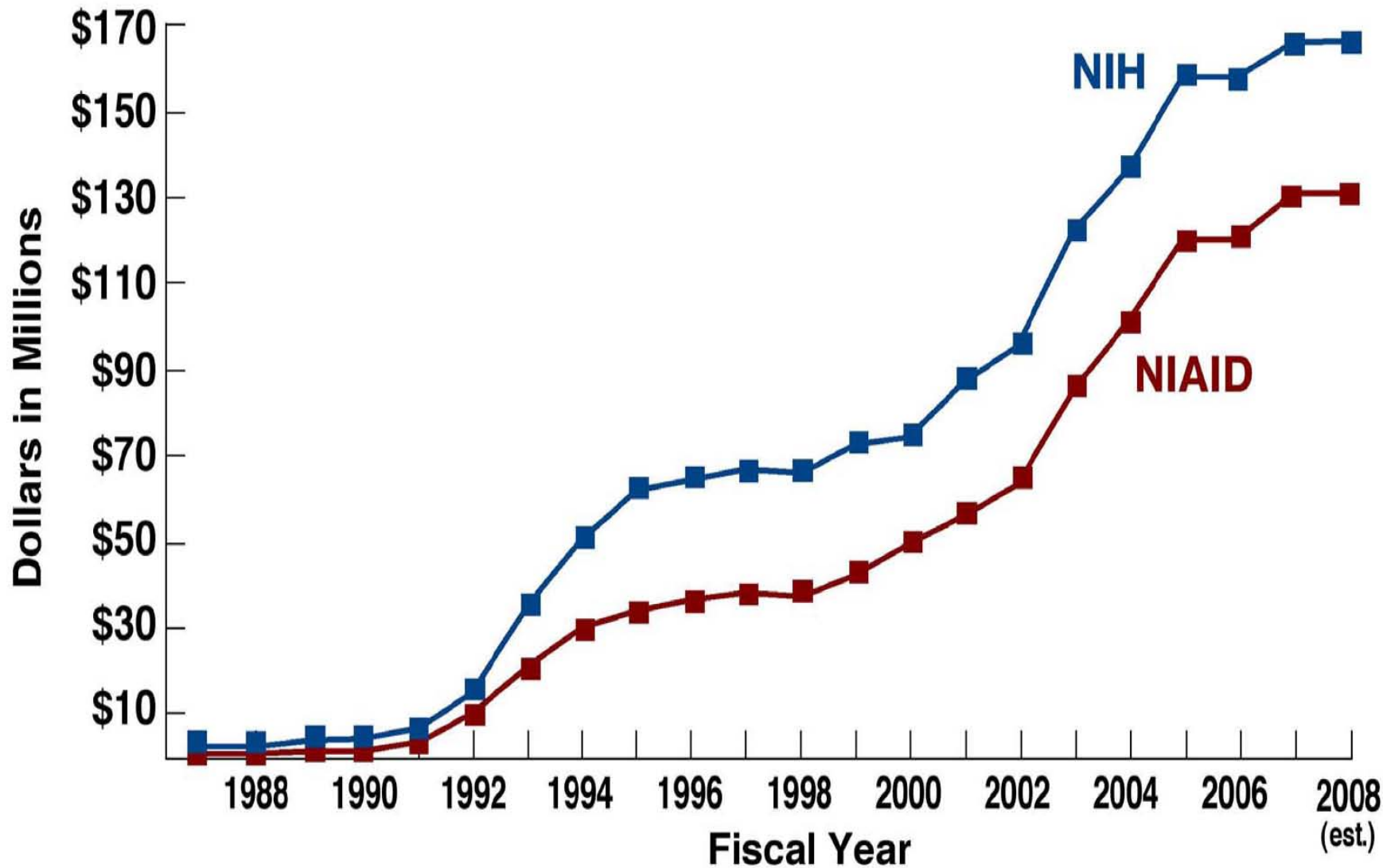
Discovery of TB Drugs



TB ALLIANCE

GLOBAL ALLIANCE FOR TB DRUG DEVELOPMENT

Tuberculosis: NIH and NIAID Funding



2008 TB R&D Funders

2008 Rank	Institute	Total
1	Bill & Melinda Gates Foundation (BMGF)	147,827,264
2	US NIAID, NIH	104,645,069
3	Otsuka Pharmaceutical Company	31,769,216
4	European Commission Framework 6/7	26,744,573
5	US other institutes & centers, NIH	26,472,839
6	US Centers for Disease Control & Prevention (CDC)	19,097,813
7	UK Medical Research Council (MRC)	14,941,234
8	USAID	10,925,000
9	Company X	10,640,454
10	US NHLBI, NIH	10,439,385
11	AstraZeneca	8,300,000
12	Company Z	7,050,000
13	Institut Pasteur	5,665,271
14	UK Department for International Development (DFID)	5,583,287
15	Wellcome Trust	5,446,998
16	Sequella, Inc	5,157,298
17	Netherlands Ministry of Foreign Affairs (DGIS)	5,140,858
18	Brazil (aggregate)	3,940,014
19	India (aggregate)	3,907,318
20	Canadian Institute of Health Research	3,766,005

Global TB Research Partnerships

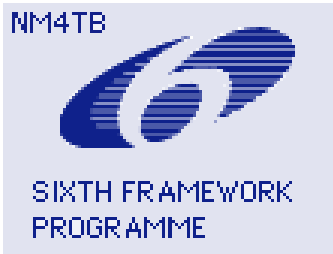
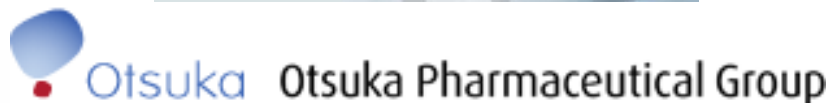
- **Governments**
- **Academic Consortia**
- **Global Alliance for TB Drug Development**
- **STOP TB Partnership / WHO**
- **Multinational Research Organizations**
- **Philanthropic Efforts**
- **Pharmaceutical Companies**



Stop TB Partnership



The Lilly TB Drug Discovery Initiative



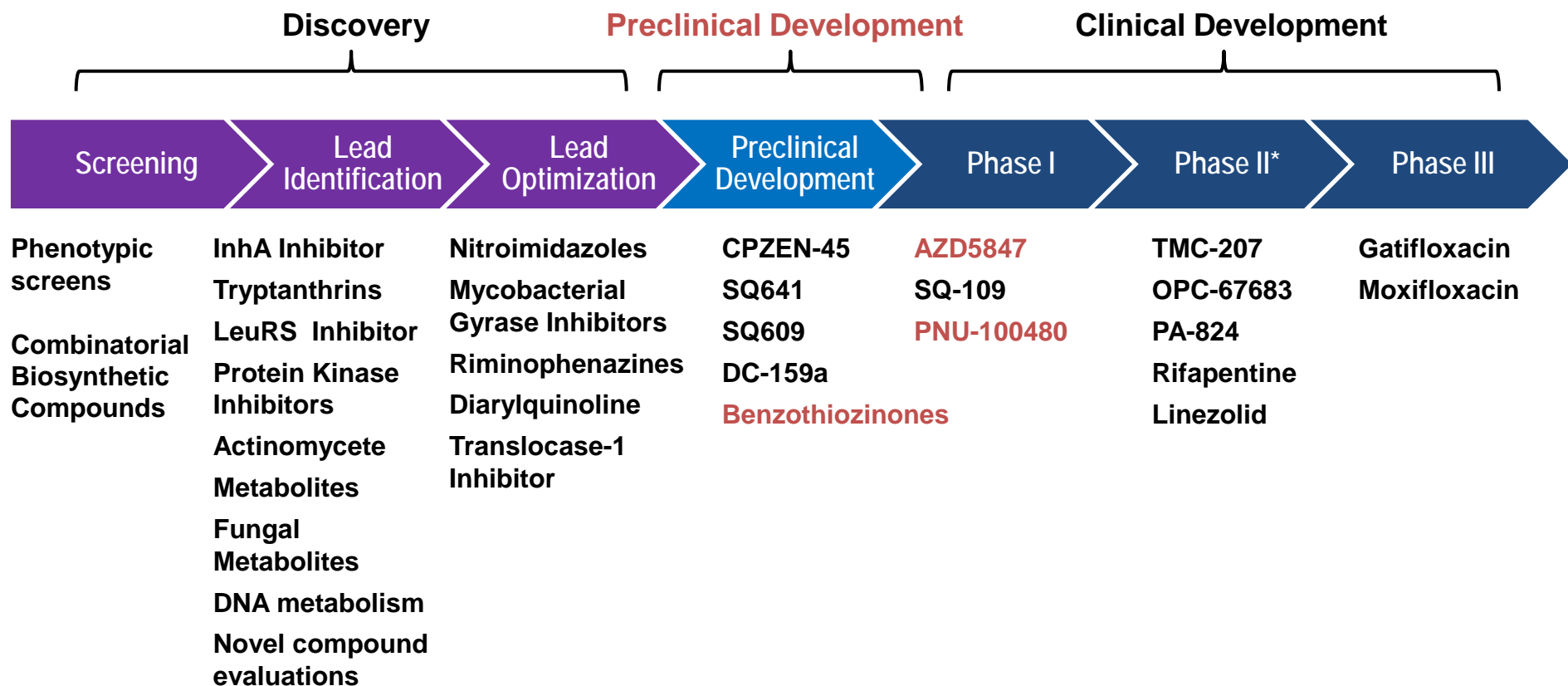
NIAID



International Union Against Tuberculosis and Lung Disease



Global TB Drug Pipeline, 2010





Tuberculosis drug discovery- a decade of learning

Tanjore S Balganesch
Vice President Discovery
Head of Research
AstraZeneca India Pvt Ltd.



AstraZeneca India in Bangalore

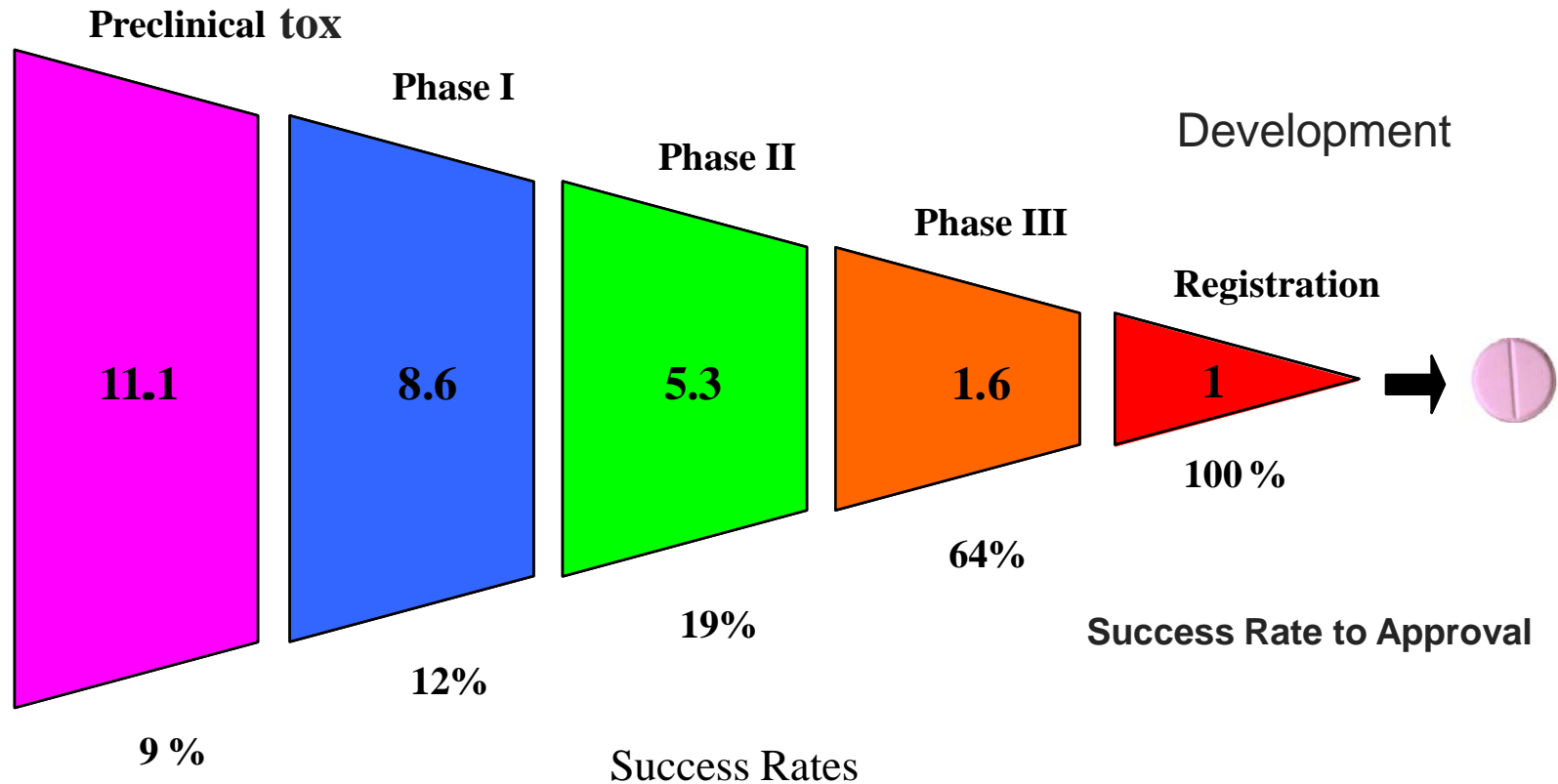
- **Unit devoted to the discovery of novel molecules for the treatment of Tuberculosis**
- **Mandate given in 2002**
- **110 researchers**
- **Integrated into the global R and D of AZ**
- **Access to all the technologies, compound libraries of AZ corporate**
- **Delivered first compound for development in 2009**

- **Multiple drugs / compounds are needed to allow new combinations**
 - **Introducing one new drug at a time into the existing regimen is the worst possible scenario- and thus the challenge for MDR regimen.**
 - **Compounds with different attributes needed to treat the heterogeneity in the infecting microbial population.**
 - **Need a portfolio of projects to deliver this.**

Success rates



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Based on the most recent success rate data, major pharmas must enter 11.1 FGLPs in order to achieve one new drug approval.

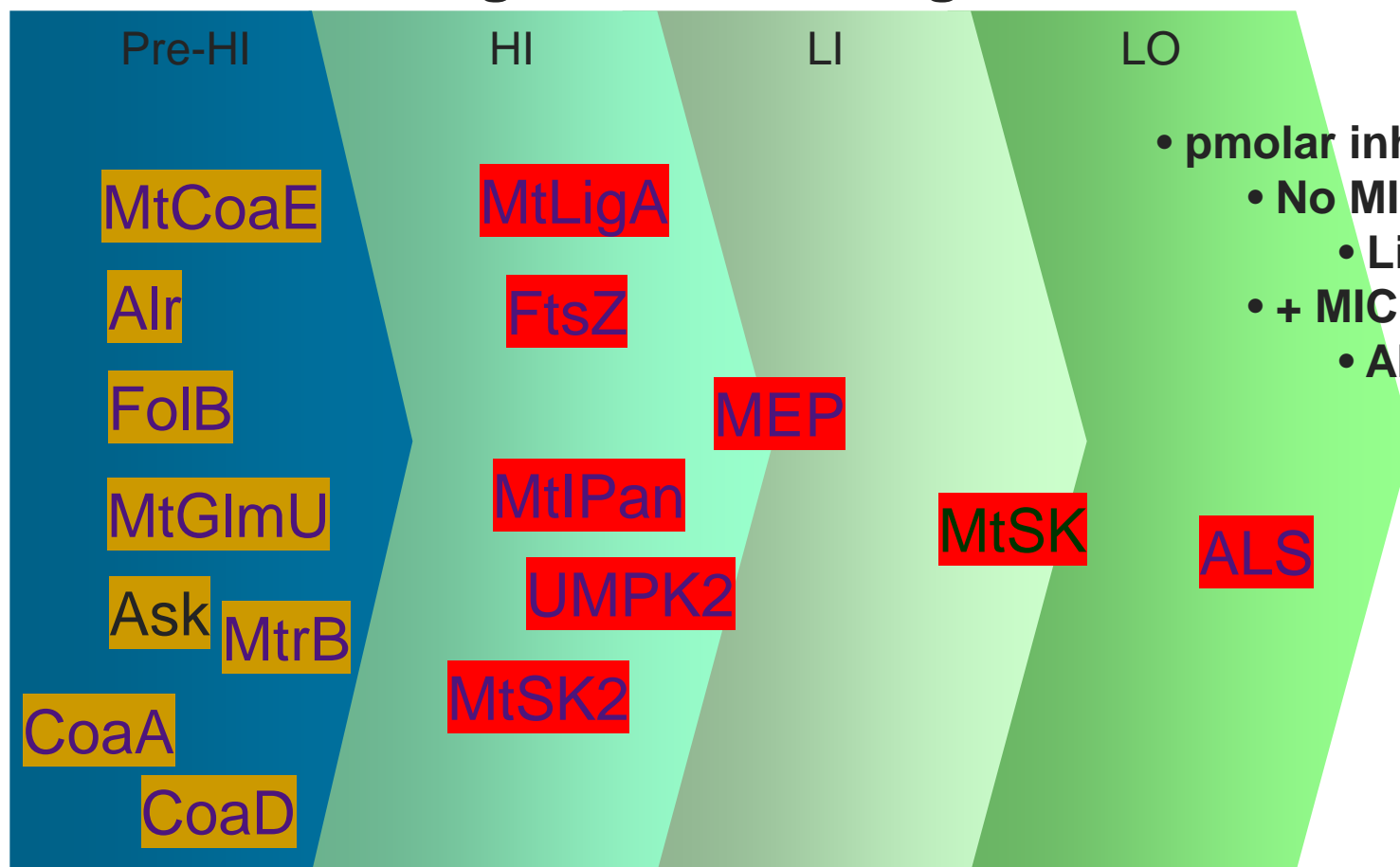
AZI 2006-07 Portfolio




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Screening

Lead generation



- pmolar inhibitors
 - No MIC
 - Lig A, Umpk
 - + MIC no MBC
 - ALS, Mtsk

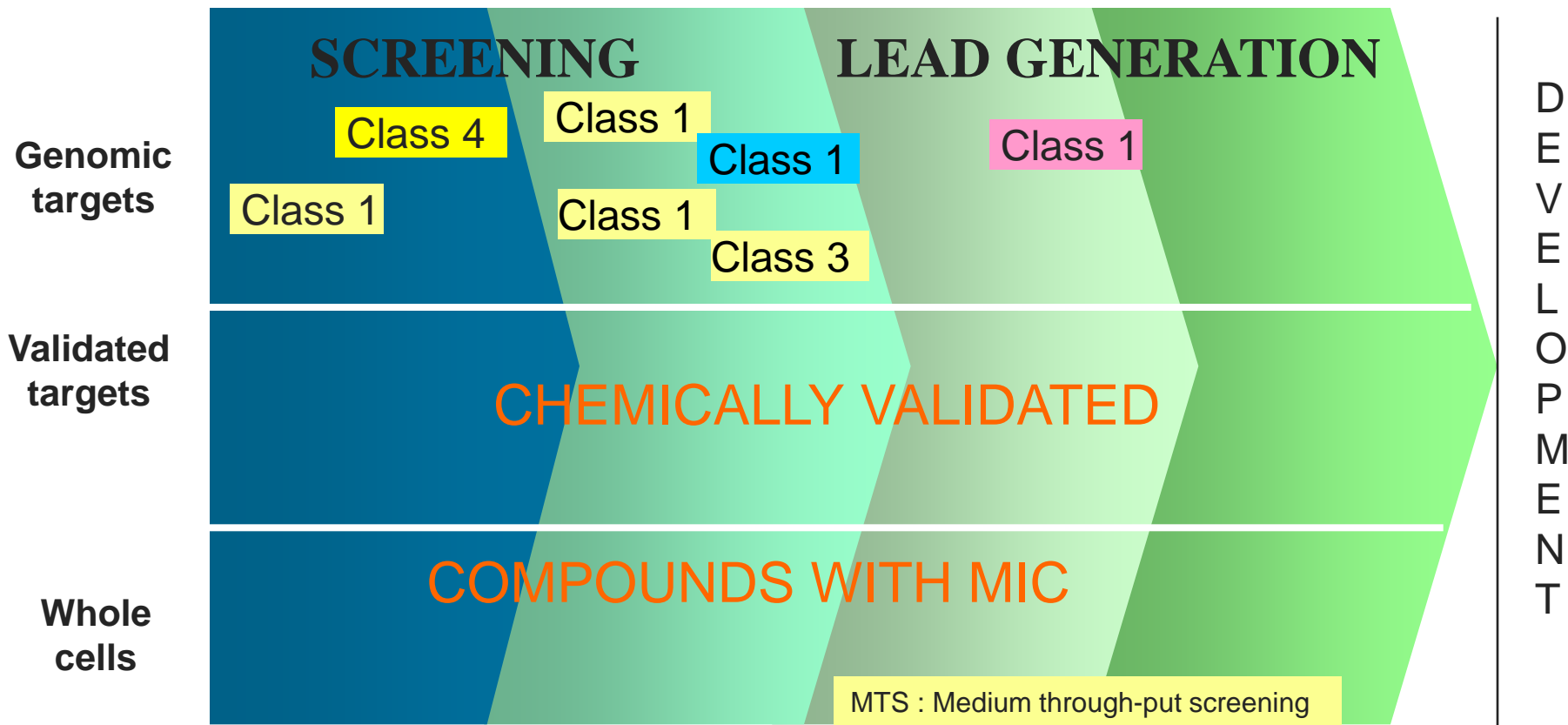
 Genomic targets

- Most programmes genome target based
- No validated (clinically proven) targets in portfolio

Diversity of approaches



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- Class 1: Macromolecular synthesis and repair
- Class 2: Energy metabolism
- Class 3: Cell wall
- Class 4: Whole cell screening

TB Alliance Portfolio

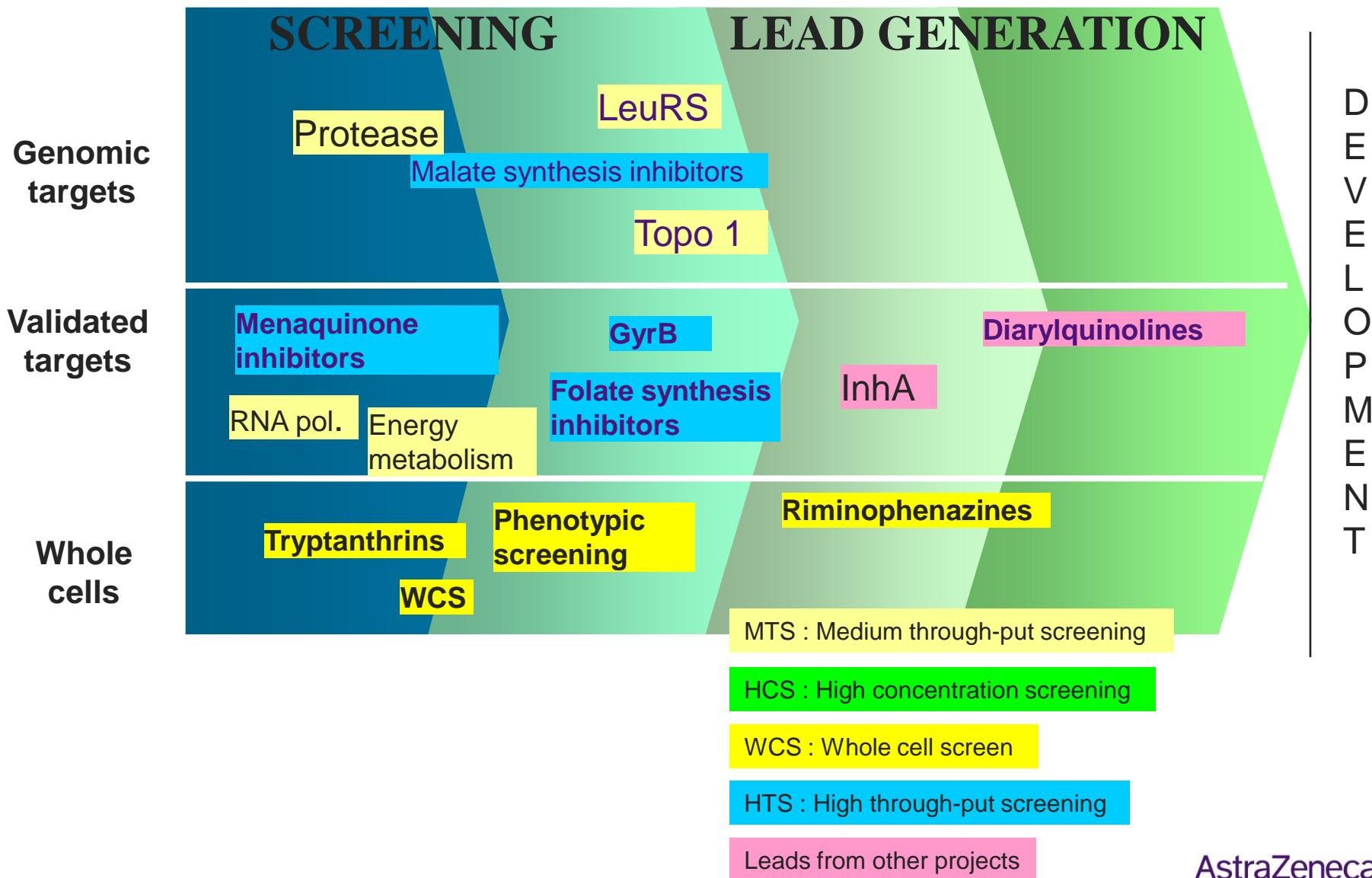


TB ALLIANCE PROGRAMS	DISCOVERY			CLINICAL DEVELOPMENT		
	Lead Identification	Lead Optimization	Preclinical	Phase I	Phase II	Phase III
Moxifloxacin						Bayer
TMC-207					Tibotec	
PA-824					Novartis	
Nitroimidazoles				University of Auckland		
Mycobact. Gyrase Inhibitors				GlaxoSmithKline		
Riminophenazines				Inst. of Materia Medica, Chinese Academy of Medical Sciences		
InhA Inhibitors				GlaxoSmithKline		
Diarylquinolines				Tibotec		
Tryptanthrins				Korea Research Inst. of Chem. Tech. and Yonsei University		
LeuRS Inhibitors				Anacor Pharmaceuticals		
Phenotypic Screening (H2L)				University of Illinois		
GyrB Inhibitors				AstraZeneca		
Folate Biosynthesis Inhibitors				AstraZeneca		
AZ Whole-Cell Screening (H2L)				AstraZeneca		
GSK Whole-Cell Screening (H2L)				GlaxoSmithKline		
Malate Synthase Inhibitors				GlaxoSmithKline		
Menaquinone Syn Inhibitors				Colorado State University		
Natural Products				Institute of Microbiology, Chinese Academy of Sciences		
RNA Polymerase Inhibitors				Rutgers, State University of New Jersey		
Energy Metabolism Inhibitors				AstraZeneca and University of Pennsylvania School of Medicine		
Protease Inhibitors				Infectious Disease Research Institute		
Topoisomerase I Inhibitors				AstraZeneca and New York Medical College		
NITD Portfolio				Novartis Institute for Tropical Diseases		

Aligning the portfolio



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The Lilly TB Drug Discovery Initiative

www.tbdrugdiscovery.org

Lilly's Commitment in TB



The Lilly TB Drug Discovery Initiative



www.tbdrugdiscovery.org

In 2007, Lilly announced **The Lilly TB Drug Discovery Initiative**.

A not-for-profit, public-private partnership focused on accelerating early-stage drug discovery in TB

Lilly grants access to its library of 800,000 compounds and contributes drug discovery technology and expertise.

Founding members include the Infectious Disease Research Institute in Seattle, the U.S. National Institutes of Health, and Lilly.

New members include Jubilant Biosys and Academia Sinica.

Together, the MDR partnership and the Drug Discovery initiatives represent Lilly's comprehensive approach and a \$135 million commitment

STOP TB Partnership
Working Group on New Drugs
TB Drug R&D Portfolio, 2009

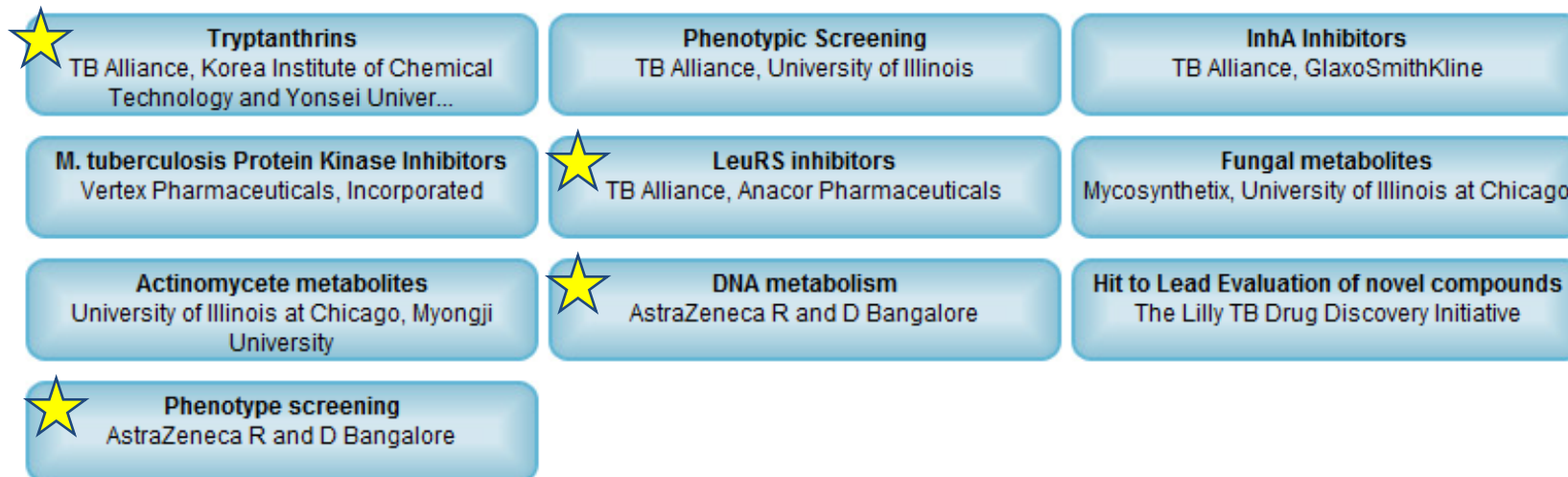
www.newTBdrugs.org

Global TB Drugs Pipeline 2009

more project information at www.newtbdrugs.org



Hit To Lead



Lead Optimization

