



# R&D Pipeline for TUBERCULOSIS

## DISEASE IMPACT

Tuberculosis (TB) is caused by bacteria (*Mycobacterium tuberculosis*) that most often affect the lungs, but may also attack any part of the body such as the kidney, spine, and brain. Not everyone infected with TB bacteria becomes sick, hence two TB-related conditions exist: latent TB infection (LTBI) and TB disease. TB is curable and preventable, yet without treatment, the disease can be fatal. Common symptoms of active lung TB are cough with sputum and blood at times, chest pains, weakness, weight loss, fever and night sweats. Another form of the disease is multidrug-resistant tuberculosis (MDR-TB), which emerges when bacteria that causes the illness do not respond to the two most powerful, first-line anti-TB drugs (isoniazid and rifampicin). MDR-TB is treatable and curable by using second-line drugs, however treatment success rates are low given the complexity of managing the disease.

## KEY FACTS

- Globally, TB incidence is falling at about 2% per year. This needs to accelerate to a 4–5% annual decline to reach the 2020 milestones of the End TB Strategy.
- In 2016, 10.4 million cases (estimated 1 million children) and 1.7 million deaths (estimated 250,000 children died of TB, including children with HIV associated TB) occurred from the disease, 490,000 people developed MDR-TB worldwide.
- TB is one of the top 10 causes of death worldwide, it is a leading killer of HIV-positive people with 40% of HIV deaths occurring due to TB in 2016.
- In 2016, seven countries accounted for 64% of the total cases, with India bearing the brunt, followed by Indonesia, China, Philippines, Pakistan, Nigeria and South Africa.
- Worldwide, only 54% of MDR-TB patients and 30% of XDR-TB are currently successfully treated.

ABBREVIATIONS	PARTNER'S FULL NAME
Aeras	Aeras Global TB Vaccine Foundation
Aurum Inst	Aurum Institute
Broad Inst	Broad Institute
BHAM	Birmingham University
BMGF	Bill & Melinda Gates Foundation
British Columbia Uni	University of British Columbia
Chicago Uni	University of Chicago
Colorado Uni	Colorado State University
Cornell Uni	Cornell University
CS Uni	Colorado State University
Dundee Uni (DDU)	Dundee University (Drug Discovery Unit)
GHIT	Global Health Innovative Technology Fund
HMS	Harvard Medical School
IMTECH	Institute of Microbial Technology
Illinois Uni	University of Illinois
IDRI	Infectious Disease Research Institute
IMI	The Innovative Medicines Initiative
ISB	Institute for Systems Biology
JHU	Johns Hopkins University
Korean Health Technology R&D Project	Ministry of Health & Welfare, Republic of Korea
KNCV	KNCF Tuberculosis Foundation
Leicester Uni	University of Leicester
LSHTM	The London School of Hygiene & Tropical Medicine

ABBREVIATIONS	PARTNER'S FULL NAME
MLU	Martin Luther Universität Halle-Wittenberg
MM4TB	More Medicines for TB
NIAID	National Institute of Allergy and Infectious Diseases
NIH	National Institutes of Health
NMRC	National Medical Research Council Singapore
OOPD	The FDA Office of Orphan Products Development
PHRI	Public Health Research Institute
RIT/JATA	Research Institute of Tuberculosis
RTI	RTI International
SAMRC	South African Medical Research Council and the South African Department of Health
SSI	Statens Serum Institute
TAMU	Texas A&M University
TB A	Global Alliance for TB Drug Development
TBDA	TB Drug Accelerator
TBTC	Tuberculosis Trials Consortium
TCOLF	Tres Cantos Open Lab Foundation
UAB	The University of Alabama at Birmingham
UCT	University of Cape Town
UCSF	The University of California, San Francisco
University College London MRC	University College London, Medical Research Council
Washington Uni	University of Washington
Weill Cornell	Weill Cornell Medical College
Wellcome	Wellcome Trust

## CURRENT R&D PROJECTS

COMPANY	PARTNERS	PROJECT	PHASE	TYPE
AbbVie	TB A	Technical consulting and preclinical support	Preclinical	Medicine
	BMGF TBDA	Whole-cell screening program, collaborative, drug discovery	Lead identification	Medicine
Bayer	BMGF TBDA, Dundee Uni, UCT	Whole-cell screening program	Lead identification	Medicine
	Weill Cornell	Development of treatments	R/NR screening	Medicine
Celgene	UCT	Development of treatments	Hit-to-lead and structure activity relationship (SAR)	Medicine
	BMGF/Aurum Inst	Clinical Trial for Host Directed Treatment	Phase 1b/2 Randomized/controlled study	Medicine
Daiichi Sankyo	TB A, GHIT	Screening program (Natural Products Library)	Hit identification	Medicine
	BMGF TBDA	Whole-cell screening program	Lead identification	Medicine
Eisai	Broad Inst, Colorado Uni, Chicago Uni, GHIT	Compound identification from Diversity-Oriented Synthesis chemical library for designing inhibition of tryptophan synthase	Hit identification	Medicine
	Company	GSK 656 (Benzoxaborole Mtb LeuRS inhibitor)	Phase I	Medicine
GlaxoSmithKline	Company	Sanfetrinem	Phase I	Medicine
	BMGF	GSK286 (Mtb cholesterol dependant inhibitor)	Preclinical	Medicine
	BMGF TBDA	Whole-cell screening program	Lead identification	Medicine
	TB A	Whole-cell hit to lead screening program	Lead identification	Medicine
	Wellcome (SDD), BioVersys	GSK038 and GSK098 Ethionamide Boosters	Preclinical	Medicine
	Wellcome (SDD), GSK	GSK839 (Mtb Tryptophan Synthase Inhibitor, Tetrazole series)	Preclinical	Medicine
	TB A	Mtb Tryptophan Synthase Inhibitor (Aryl Sulfonamides series)	Lead optimization	Medicine
	TB A	Mtb KasA inhibitors	Lead optimization	Medicine
	Aeras	Vaccine (GSK M72)	Phase II	Vaccine
	Dundee Drug Discovery	Mtb Phenotypic and target based projects	Lead optimization	Medicine
	TCOLF, UAB	Self-poisoning of Mycobacterium tuberculosis by inhibiting siderophore secretion	Discovery (tool)	Medicine
	TCOLF, BHAM	Exploring TB Space: Optimization of novel, high quality phenotypic hit	Discovery (tool)	Medicine
	TCOLF, ISB	Biochemi, and Struct Characterization of Mtb ClpC1P1P and ClpXP1P2 inhibitors	Discovery	Medicine
	TCOLF, BHAM	Chemical Proteomics	Discovery	Medicine
	TCOLF, BHAM, TAMU	Whole cell protein synthesis inhibition assay for high-throughput	Discovery	Medicine
	Company	Diarylquinoline bedaquiline (SIRTURO®) for treatment of MDR-TB	Phase III	Medicine
	TB A	Diarylquinoline, bedaquiline for treatment of drug sensitive TB	Phase II	Medicine
	TB A	Next generation diarylquinoline	Preclinical	Medicine
	IMTECH	Explore potentially more effective, safer, all-oral treatment regimens to tackle MDR-TB, and new molecular entities to treat TB	Discovery	Medicine
	Company	Bedaquiline for treatment of pediatric MDR-TB	Phase II	Medicine
Company	MDR TB registry	Phase IV	Medicine	
Janssen (J&J)	ThermoFisher, Becton Dickinson	Collaboration to develop drug sensitivity testing devices	Phase II	Device
	BMGF TBDA	Cytochrome bd BU inhibitors	Discovery	Medicine
	IDRI	TB vaccine mouse study	Discovery	Vaccine
	NIAID	Screening of Janssen's molecular library for TB drug candidates	Discovery	Medicine
	Genoscreen	Sequencing of cytochrome bc resistant mutants	Discovery	Medicine
	JHU	Assessing bedaquiline long acting formulation against latent TB in the mouse model	Discovery	Medicine
	Leicester Uni	Mechanistic study of TB compounds	Discovery	Medicine
	Colorado Uni	<i>in vivo</i> testing of TB compounds	Discovery	Medicine
	IDRI, NIH, RTI	CPZEN-45	Preclinical	Medicine
	IDRI, NIH, AbbVie	TBDA Screening program	Discovery	Medicine
Lilly	IDRI, NIH, Abbvie	TBDA Lead generation/optimization portfolio	Discovery	Medicine
	BMGF TBDA	Whole-cell screening program	Lead identification / optimization	Medicine
	IDRI, BMGF TBDA	pH screening program / Lead generation	Discovery / lead identification	Medicine
	IDRI, BMGF TBDA	LepB screening program	Discovery	Medicine
	TB A, HMS, Illinois Uni	ClpC1 ATPase screening program	Discovery	Medicine
	BMGF TBDA, NIAID, CS Uni, PHRI	Protein synthesis inhibitor	Lead optimization	Medicine
MSD	BMGF TBDA, TAMU	Compound screening ALIS (MOA)	TID / lead identification	Medicine
	TB A	ATP Synthase inhibitor 1 mo GLP safety studies	Preclinical	Medicine
	JHU	In vivo preclinical PK / PD dose ranging	Preclinical	Medicine
Novartis	TB A	Exclusive worldwide licensing agreement	N/A	Medicine
	Company	Lamprene® (clofazimine) in MDR-TB	Phase III	Medicine
	Company	Deltyba® (Delamanid) for the treatment of MDR-TB in adults	Phase IV	Medicine
	Company	Deltyba® (Delamanid) for the treatment of MDR-TB in children	Phase II	Medicine
Otsuka	BMGF	OPC-167832 for the treatment of TB and MDR-TB	Phase Ib/IIa	Medicine
	BMGF	Deltyba® (Delamanid) for the treatment of TB and MDR-TB	Phase Ib/IIa	Medicine
	CPTR	LAM for tuberculosis treatment monitoring	N/A	Drug Development Tool
Pfizer	Washington Uni	Evaluation of the impact on Azithromycin on mortality in Kenyan children discharged from the hospital (Azithromycin)	Phase II	Medicine
	Korean Health Technology R&D Project	Evaluation of the use of linezolid in South Korea to shorten the duration of MDR-TB treatment (Linezolid)	Phase II	Medicine
	Aurum Inst	Effort to define an oral regimens for MDR-TB in South Africa (Rifabutin)	Phase II	Medicine
	University College London MRC, Wellcome, NMRC	Two-month regimens to treat drug-sensitive TB in Singapore (Linezolid)	Phase II	Medicine
	OOPD	Short-course therapy options to treat drug-sensitive TB in South Africa (Rifabutin)	Phase II	Medicine
	Korean Health Technology R&D Project	Evaluation of treatment options for Korean patients with drug sensitive-TB (Linezolid)	Completed	Medicine
	SAMRC	New treatment regimens for African patients with MDR- and XDR-TB (Linezolid)	Completed	Medicine
	IMI	Operations research	Basic research	Medicine
	CDC- TBTC	Rifapentine (new regimen development for active TB)	Phase III	Medicine
	Company	Rifapentine (new 3HP regimen development for latent TB)	Registration	Medicine
Sanofi	SSI, Aeras, Intercell	Vaccine HyVac4 IC31 (AERAS-404) adjuvanted subunit TB vaccine	Phase II	Vaccine
	NIAID	Rifapentine, new ultra-short course regimen for LTBI - PLHIV	Phase III	Medicine
	UCSF	Rifapentine for LTBI, periodic 1 HP for PLHIV	Phase III	Medicine
	UCT	Rifapentine 3HP for LTBI, correlate of risk intervention	Phase II/III	Medicine
	NIAID	Rifapentine 3HP for LTBI, pregnancy/postpartum	Phase I/II	Medicine
	KNCV	Rifapentine for LTBI, periodic 3HP for PLHIV	Phase III	Medicine
	Company	Rifapentine-based new formulation	Phase I	Medicine
	LSHTM	High dose rifampicin for TB meningitis	Phase II	Medicine
	Regeneron	Operations research	Basic research	Medicine
	Company	Antimycobacterial screening program	Discovery	Medicine
Sanofi/EVOTEC	Cornell Uni	Screening on non growing TB phenotypes	Lead identification	Medicine
	TB A	Lead to candidate portfolio	Lead optimization	Medicine
	BMGF TBDA	Whole-cell screening program, hit-to-candidate portfolio	Lead identification/optimization	Medicine
Shionogi	Company	S-004992	Preclinical	Medicine
Takeda	GHIT, TB A	Hit-to-lead	Lead identification	Medicine

Total R&D projects for Tuberculosis: 82