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R&D Pipeline for TUBERCULOSIS

DISEASE IMPACT^{1,2}

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^{3,4}

- From 2000 to 2015, TB incidence has fallen by an average of 1.5% per year, with 49 million lives saved through effective diagnosis and treatment.
- In 2015, 10.4 million cases (estimated 1 million children) and 1.8 million deaths (estimated 170,000 children, not including those with HIV) occurred from the disease, 480,000 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 35% of HIV deaths occurring due to TB in 2015.
- In 2015, six countries accounted for 60% of the total cases, with India bearing the brunt, followed by Indonesia, China, Nigeria, Pakistan and South Africa.
- Only 52% of the multidrug-resistant TB (MDR-TB) and rifampicin-resistant TB (MDR/RR-TB) patients who started treatment in 2013 were successfully treated.

ABBREVIATIONS	PARTNER'S FULL NAME
Aeras	Aeras Global TB Vaccine Foundation
BHAM	Birmingham University
BMGF	Bill & Melinda Gates Foundation
British Columbia Uni	University of British Columbia
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
IDRI	Infectious Disease Research Institute
IMI	The Innovative Medicines Initiative
JHU	Johns Hopkins University
KNCV	KNCF Tuberculosis Foundation
MLU	Martin Luther Universität Halle-Wittenberg
MM4TB	More Medicines for TB
NIAID	National Institute of Allergy and Infectious Diseases

ABBREVIATIONS	PARTNER'S FULL NAME
NIH	National Institutes of Health
OOPD	The FDA Office of Orphan Products Development
PHRI	Public Health Research Institute
RIT/JATA	Research Institute of Tuberculosis
SAMRC	South African Medical Research Council
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
Weill Cornell	Weill Cornell Medical College
Wellcome	Wellcome Trust

1 <http://www.who.int/mediacentre/factsheets/fs104/en/>
 2 <https://www.cdc.gov/tb/>

3 <http://www.who.int/tb/en/>
 4 <http://www.who.int/mediacentre/factsheets/fs104/en/>

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
AstraZeneca	TB A	Joint research collaboration agreement	Lead identification/optimization	Medicine
	BMGF TBDA	Whole-cell screening program	Lead identification	Medicine
	NIAID	AZD5847	Phase II	Medicine
Bayer	BMGF TBDA, Dundee Uni, UCT	Whole-cell screening program	Lead identification	Medicine
	Weill Cornell	Development of treatments	R/NR screening	Medicine
Celgene	Weill Cornell	Development of treatments	Host-directed screening	Medicine
	UCT	Development of treatments	Hit-to-lead and structure-activity relationship (SAR)	Medicine
Daiichi Sankyo	TB A, GHIT	Identification of lead compounds as novel anti-TB agents	Lead identification	Medicine
	TB A, GHIT	Screening program (Natural Products Library)	Hit identification	Medicine
Eisai	BMGF TBDA	Whole-cell screening program	Lead identification	Medicine
	Company	GSK 070	Phase I	Medicine
GlaxoSmithKline	BMGF TBDA	Whole-cell screening program	Lead identification	Medicine
	TB A	Whole-cell screening program	Lead optimization	Medicine
	TB A	Whole-cell hit to lead screening program	Lead identification	Medicine
	Wellcome, BioVersys	(SDD) Ethionamide Boosters	Lead optimization	Medicine
	TB A	Mtb DprE1 inhibitors	Lead optimization	Medicine
	Aeras	Vaccine (GSK M72)	Phase II	Vaccine
	TCOLF, Dundee Uni (DDU)	Tuberculosis InhA focused fragment based drug discovery	Discovery	Medicine
	Weill Cornell	Whole-cell assays for the identification and classification of Mtb growth inhibitors	Discovery (tool)	Medicine
	UBC	Intra-macrophage driven optimization of confirmed hit GSK421197A	Discovery	Medicine
	BHAM	Optimisation of Fidaxomicin analogs	Lead optimization	Medicine
	UAB	Self-poisoning of Mycobacterium tuberculosis by inhibiting siderophore secretion	Discovery (tool)	Medicine
Janssen (J&J)	BHAM	Exploring TB Space: Optimization of novel, high quality phenotypic hits	Discovery (tool)	Medicine
	BHAM, TAMU	Whole cell protein synthesis inhibition assay for high-throughput	Discovery	Medicine
	TCOLF, Weill Cornell	Studies towards the identification of orally available beta-lactams with efficacy against M. tuberculosis	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
Lilly	TB A	Next generation diarylquinoline	Preclinical	Medicine
	IDRI, NIH	CPZEN-45	Preclinical	Medicine
	IDRI, NIH, TB A	Screening program	Discovery	Medicine
	IDRI, NIH, TB A	Lead generation/optimization portfolio	Discovery	Medicine
MSD	BMGF TBDA	Whole-cell screening program	Lead identification	Medicine
	BMGF TBDA, NIAID, CS Uni, PHRI	Protein synthesis inhibitor	Lead optimization	Medicine
	BMGF TBDA, TAMU	Compound screening ALIS (MOA)	TID / Lead identification	Medicine
	TB A	Protein synthesis	Phase I	Medicine
Novartis	JHU	In vivo preclinical PK / PD dose ranging	Preclinical	Medicine
	TB A	Exclusive worldwide licensing agreement	NA	Medicine
	Company	Lamprene® (clofazimine) in MDR-TB	Phase III	Medicine
Otsuka	Company	Deltyba® (Delamanid) for adult patients with pulmonary MDR-TB: evaluation of the safety and efficacy	Phase III	Medicine
	Company	Deltyba® (Delamanid) for pediatric patients with pulmonary MDR-TB: evaluation of long-term safety, tolerability, and pharmacokinetics	Phase I & II	Medicine
Pfizer	South Korean Ministry of Health & Welfare	Linezolid	Phase II	Medicine
	SAMRC	Linezolid, Oxazolidinone antibiotic	Phase II	Medicine
	OOPD	Rifabutin & Rifampin	Phase II	Medicine
	Pfizer Foundation	Linezolid, Oxazolidinone antibiotic	Phase II	Medicine
Sanofi	IMI	Operations research	Basic research	Medicine
	Regeneron	Operations research	Basic research	Medicine
	TBTC	Rifapentine (new regimen development for active TB)	Phase III	Medicine
	Company	Rifapentine (new 3HP regimen development for latent TB)	Registration	Medicine
	Company	Antimycobacterial screening program	Discovery	Medicine
	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
	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
Shionogi	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
	GHIT, TB A, RIT/JATA	Hit-to-lead development of anti-TB phenotypic screening hits	Drug discovery	Medicine
	Takeda	Hit-to-lead	Lead identification	Medicine
	TB A, GHIT	Hit-to-lead	Lead identification	Medicine

Total R&D projects for Tuberculosis: 62