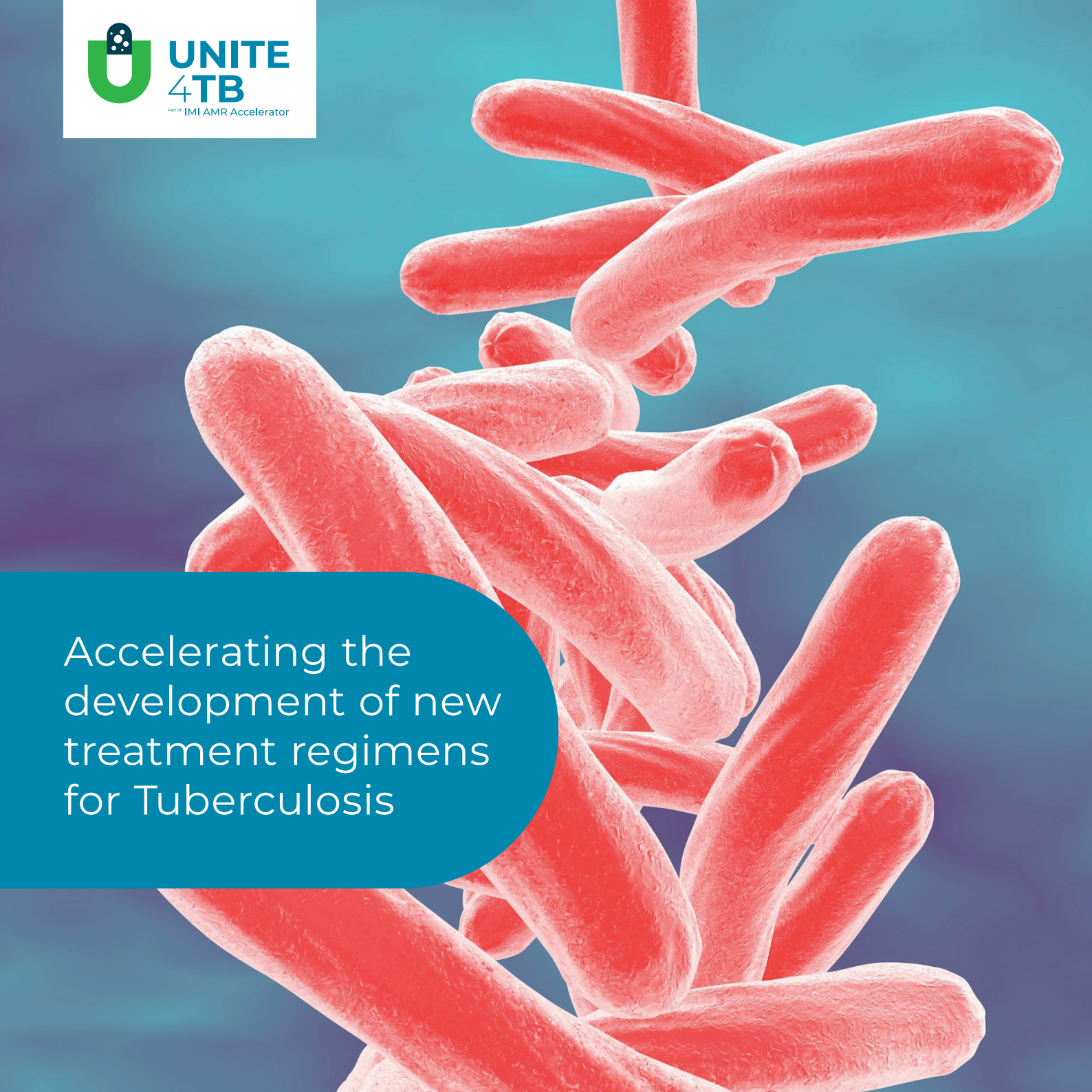
UNITE 4TB

Part of IMI AMR Accelerator



Accelerating the development of new treatment regimens for Tuberculosis

Tuberculosis is among the leading causes of death worldwide

THE TB CHALLENGE

With 1.5 million people dying and 10 million being affected every year worldwide, tuberculosis (TB) is, by far, the leading cause of death from a single infectious agent. According to a 2021 report by the World Health Organization (WHO), the COVID-19 pandemic has reversed years of global progress in tackling TB with TB deaths increasing for the first time in over a decade[1].

Over the last three decades, the public health challenge of multidrug-resistant TB (MDR-TB) – the largest concern in the control of antimicrobial resistance (AMR) globally – has triggered renewed scientific efforts in anti-TB drug research and development (R&D)[2].

An integrated approach to anti-TB drug R&D is still lacking with the recent clinical trial designs generally focused on developing single drugs rather than drug combinations. With current methodology, it is estimated it will take 15-20 years to develop a new 3-4 drug combination regimen to treat all forms of TB, including the most drug-resistant ones[3].

Consequently, new drugs and shorter regimens for the treatment of TB infection and active disease, and their rapid uptake, are urgently required by 2025 to reach the ambitious targets of 95% death reduction and 90% incidence decline set by the WHO in its global strategy to end TB[4].

[1] WHO 2021 Global TB report: https://www.who.int/publications/i/item/9789240037021
[2] WHO Consolidated Guidelines on Tuberculosis, Module 4: Treatment - Drug-Resistant Tuberculosis Treatment, available in https://www.who.int/publications/i/item/9789240007048
[3] Gler MT, Skripconoka V, Sanchez-Garavito E, Xiao H, Cabrera-Rivero JL, Vargas-Vasquez DE, et al. Delamanid for multidrug-resistant pulmonary tuberculosis. N Engl J Med. 2012;366(23):2151-60.
[4] Implementing the end TB strategy: the essentials. Geneva: World Health Organization, 2015 https://apps.who.int/iris/rest/bitstreams/916192/retrieve

UNITE4TB aims to deliver more effective and shorter regimens through innovative clinical trial designs that conform to the highest regulatory standards.

Available clinical trial sites worldwide

This map shows the countries where studies will potentially be performed

Bringing together key stakeholders in the field of TB to tackle this growing global challenge.

UNITE4TB is a public-private partnership with representation from academic institutions, small- and medium-sized enterprises (SMEs), patient-led organisations, and pharmaceutical companies.

With 30 partners from 13 countries, UNITE4TB aims to accelerate and improve the clinical evaluation of novel compounds and drug combinations to develop new and effective anti-TB treatments for drug-resistant (DR) and drug-sensitive (DS) TB.

Over a project term of 7 years, UNITE4TB will be active in four WHO regions (Europe, Asia, Africa and South America), with the goal of delivering novel phase 2 clinical trials that will accelerate the development of new anti-TB drugs and regimens.

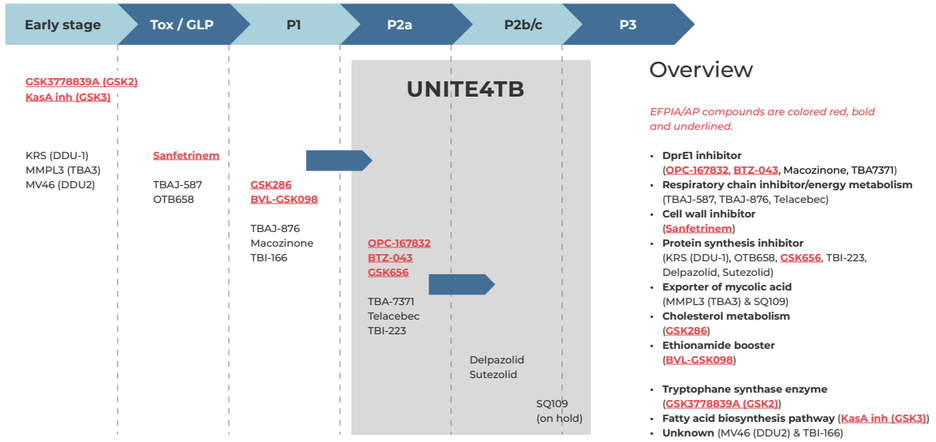
Achieving this goal will facilitate fulfilment of one of the main unmet needs in the TB field: well-tolerated drug regimens of shorter duration that can be deployed to tackle TB across various DR patterns and co-morbidities.

CONCEPT & METHODOLOGY

To address the challenge of developing new anti-TB treatment regimens, UNITE4TB follows a concept that is analogous to a car racetrack.

UNITE4TB will ensure access to the most innovative anti-TB compounds (the key *car parts*) tested during phases 1 and 2A (the *pitstop*) before being assembled into a new treatment regimen (the *race car*) to be launched into a clinical trial platform covering four continents (the *racetrack*).

New *car parts* (drugs) and *cars* (regimens) may enter the race when ready, making this a state-of-the-art adaptive trial design with conventional and new biomarkers of treatment success. Advanced pharmacokinetic and pharmacodynamic modelling techniques as well as artificial intelligence and machine learning techniques will be employed to select, test and deliver novel combination regimens with a high probability of success in subsequent phase 3 clinical trials.



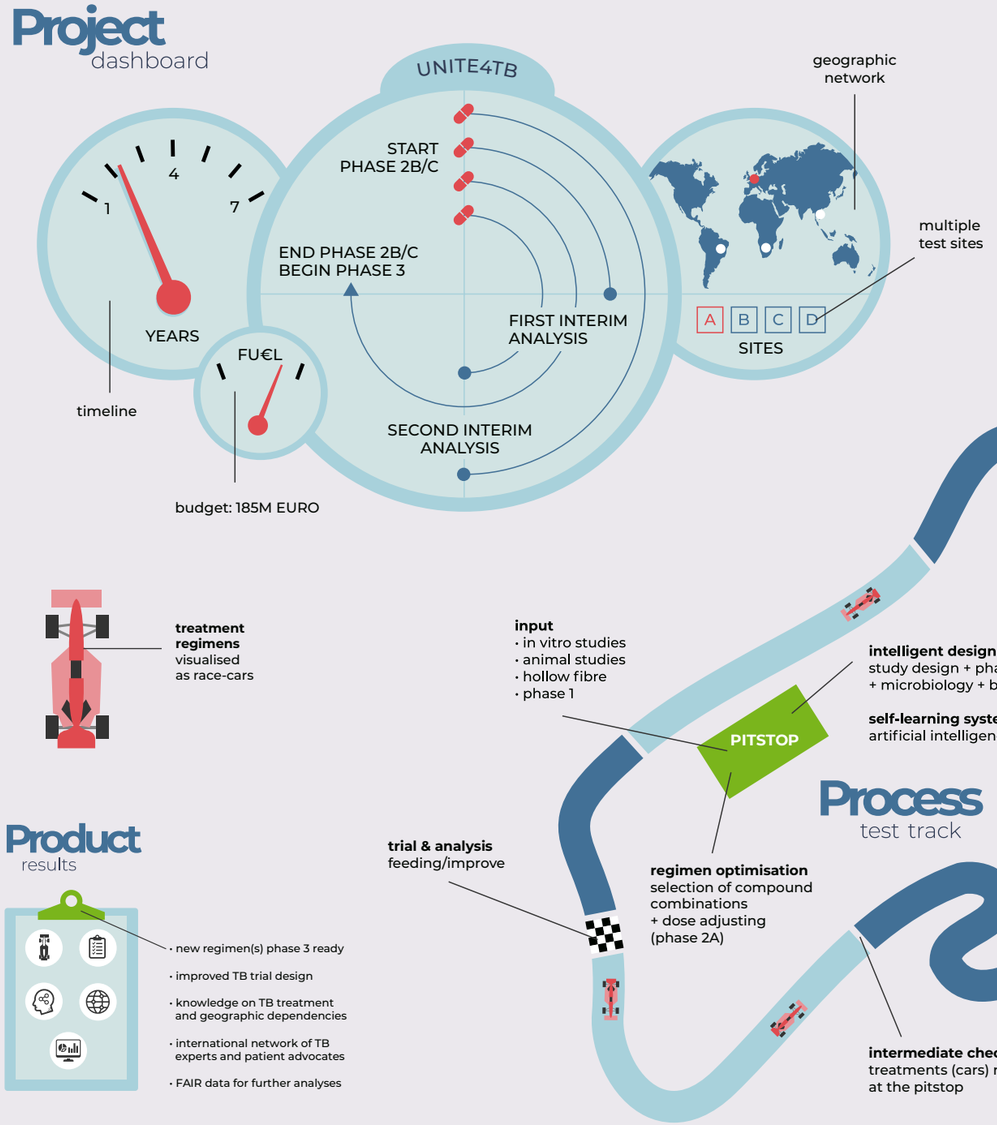
Global TB drug pipeline (October 2020), with UNITE4TB EFPIA/AP drug candidates in red (EFPIA/AP = European Federation of Pharmaceutical Industries and Associations/Associated Partners).

Overview

EFPIA/AP compounds are colored red, bold and underlined.

- **DprE1 inhibitor** (OPC-167832, BTZ-043, Macozinone, TBA7371)
- **Respiratory chain inhibitor/energy metabolism** (TBAJ-587, TBAJ-876, Telacebec)
- **Cell wall inhibitor** (Sanfetrinem)
- **Protein synthesis inhibitor** (KRS (DDU-1), OTB658, GSK656, TBI-223, Delpazolid, Sutezolid)
- **Exporter of mycolic acid** (MMPL3 (TBA3) & SQ109)
- **Cholesterol metabolism** (GSK286)
- **Ethionamide booster** (BVL-GSK098)

- **Tryptophane synthase enzyme** (GSK3778839A (GSK2))
- **Fatty acid biosynthesis pathway** (KasA inh (GSK3))
- **Unknown** (MV46 (DDU2) & TBI-166)



The consortium intends to have an impact on a number of critical issues within TB drug development by:

Providing **new tools and knowledge** of how to progress TB science

Enabling the **progression** of new, safe and affordable treatment solutions that are well-tolerated, shorter in duration and highly effective

Developing an innovative clinical trial design

Contributing to the development of a vibrant TB research environment

Improving current practices through contributing to new **policy recommendations**

Collaborating with other consortia to accelerate the development of new anti-TB drug regimens

Improving the lives of people living with TB

The ambition of UNITE4TB is to connect with policymakers, funders, and agencies at both national and international levels to ensure that all necessary viewpoints are collected. By doing so, we aim to progress the development and implementation of new and better drug regimens to treat TB.

With your collaboration we can:

1. Share state-of-the-art knowledge and expertise to progress new TB treatment innovations
2. Ensure engagement of civil society, decision-makers, and other key stakeholders, so that the people affected by TB are at the heart of the project
3. Support affected communities with easier, faster, more effective regimens

> The UNITE4TB consortium has the expertise, capacity, and influence to change the paradigm of clinical TB drug R&D.

We have a vision for UNITE4TB to be the start of a major enterprise, in collaboration with centres of excellence around the world, that ensures there is sustained investment in TB drug development in the years to come so that the elimination of TB as a public health problem is finally achieved.

For more information, visit the UNITE4TB website:

www.unite4tb.org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every breath counts


TBnet


LMU KLINIKUM

Contact information

If you have general questions about the project, please send an email to: office@unite4tb.org

For more information, visit the UNITE4TB website: www.unite4tb.org

Facts & figures

Who's involved?	30 partners from 13 countries
Participating countries	Belgium, France, Germany, Ireland, Italy, Netherlands, Portugal, South Africa, Spain, Sweden, Switzerland, United Kingdom, USA
Start date	1 June 2021
End date	31 May 2028

Project coordinator	RadboudUMC
Project lead	GSK
Scientific lead	LMU
Clinical lead (rotating representatives)	UOXF; FZB; LSHTM
Total budget	185M Euro

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