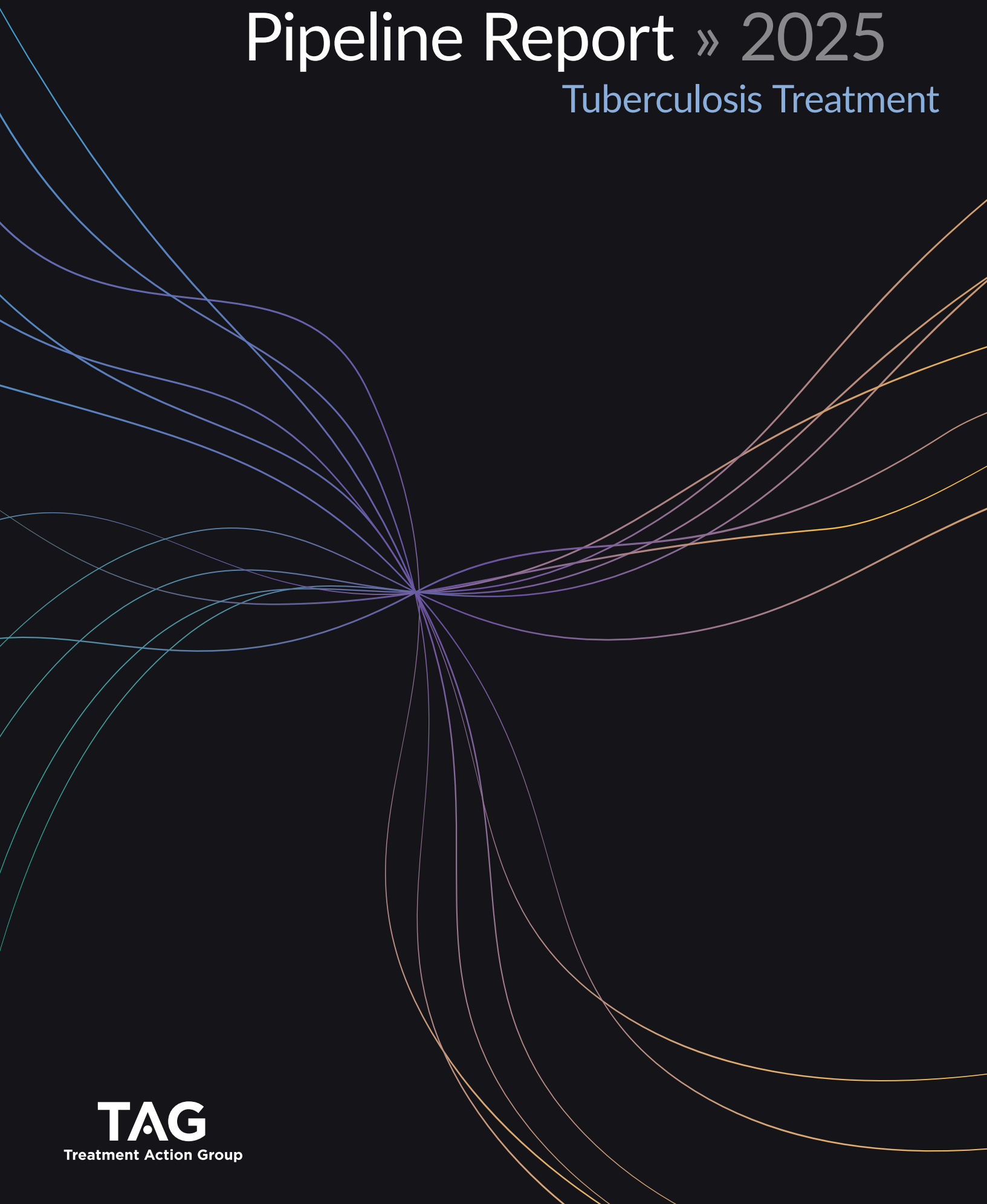
Pipeline Report » 2025

Tuberculosis Treatment



TAG
Treatment Action Group

2025 Tuberculosis Treatment Pipeline Report

By Lindsay McKenna

Introduction

The slew of United States Government (USG) research funding cuts, suspensions, and interruptions that began in January 2025 couldn't be happening at a worse moment for tuberculosis (TB) treatment research and development. Unfinished business from advances made in the past two decades, as well as ongoing work in mid-development critical to advance the next generation of new TB drugs (see Figure 1) and regimens and to aid further breakthroughs, are at risk.

The 2025 Tuberculosis Treatment Pipeline Report covers recent trial results and provides an overview of the state of the clinical TB treatment research pipeline in four tables. Table 1 reviews results from one phase III trial (**endTB-Q**) and two phase IIb/c trials completed (**Trial 323-201-00006**) or discontinued (**Gates MRI-TBD06-201**) in 2024. Table 2 covers ongoing and planned trials of regimens composed of existing drugs. Table 3 lists new drugs in clinical development for TB. Table 4 covers trials of investigational regimens that advance these new drugs. Highlights include new trials targeting asymptomatic TB (**RADIO-TB**) and bedaquiline-resistant TB (**BacTR, EX-DR, CLOBBER-TB**), the first long-acting formulation of a TB medicine to enter clinical development (bedaquiline), and the first new drug from a new class since bedaquiline and delamanid to approach phase III (quabodepistat).

Figure 1. Global Pipeline of Medicines in Clinical Development for TB

Phase 1	Phase 2	Phase 3	Regulatory Market Approvals
LA-Bedaquiline	Sorfequiline (TBAJ-876)	Sudapyridine (WX-081)	Bedaquiline
TBAJ-587	TBI-223	Sitafloxacin	Delamanid
TBD09 (MK-7762)	Delpazolid	Contezolid	Pretomanid
SPR720	Sutezolid		Linezolid
TBD11 (CLB073)	Tedizolid		Clofazimine
	BTZ-043		Moxifloxacin
	Macozinone (PBTZ-169)		Levofloxacin
	TBA-7371		
	Quabodepistat (OPC-167832)		
	Pyrifazimine (TBI-166)		
	Ganfeborole (GSK-656)		
	Telacebec (Q203)		
	Alpibectir (BVL-GSK098)		
	Sanfetrinem		
	SQ-109		

Figure adapted from Stop TB Partnership Working Group on New Drugs.
Diarylquinoline; Oxazolidinone; DprE1 inhibitor; Riminophenazine Nitroimidazole; Fluroquinolone.
Drugs that appear in black font are from classes and/or with mechanisms of action not otherwise represented by the other colors.

Results from Recently Completed TB Treatment Trials

endTB-Q is the only randomized controlled trial (RCT) to date focused on pre-extensively drug-resistant TB (pre-XDR-TB). Results of the study raise concerns about whether we know how to optimally treat TB in the presence of fluoroquinolone resistance, especially among people with more extensive disease. The endTB-Q trial evaluated six or nine months of bedaquiline, delamanid, linezolid, and clofazimine against longer, individualized regimens. The choice between six or nine months of the experimental regimen was determined by baseline disease severity and initial microbiological response on treatment. The experimental regimen failed to demonstrate noninferiority to the longer, individualized regimens that comprised the control arm (see Table 1).[1] Although outcomes overall weren't good enough to achieve noninferiority, the experimental regimen was safe and outcomes were good among participants with limited disease (defined by a negative or scanty smear irrespective of cavitation or smear grade 1+ in the absence of cavitation): 93.1% of participants with limited disease in the experimental arm compared to 87.5% in the control arm had a favorable treatment outcome (risk difference: 5.6% [95% confidence interval: −7.6% to 18.8%]).[2] The World Health Organization (WHO) currently recommends six-month regimens composed of bedaquiline, pretomanid, and linezolid (the BPaL or Nix-TB regimen) or bedaquiline, delamanid, linezolid, and clofazimine (the BEAT Tuberculosis regimen), and an 18- to 20-month individualized regimen for the treatment of pre-XDR-TB, but it will revisit this section of its guidelines while reviewing endTB-Q and other data submitted in response to a public call for individual patient data issued earlier this year.[3]

Results from Otsuka's phase IIb/c study of quabodepistat and from stage one of the first wave of regimens to be evaluated through the Gates Medical Research Institute's PAN-TB collaboration were presented at the 2024 Union Conference. Findings from both studies encourage the continued advancement of quabodepistat, but the combination regimen with quabodepistat required to enable treatment shortening to four months or less is not yet determined. In **Trial 323-201-00006**, Otsuka found four months of quabodepistat given together with bedaquiline and delamanid noninferior to the six-month standard of care for drug-sensitive TB based on rates of sputum culture conversion at the end of treatment (primary endpoint).[4] But after six months of follow-up, there were more favorable outcomes and fewer relapses (exploratory endpoints) observed among participants in the control arm (see Table 1).[5] This indicates that the addition of a fourth, more powerful drug to the regimen will be required to shorten treatment. Stage one of **Gates MRI-TBD06-201** was designed to evaluate four months of quabodepistat given together with bedaquiline, delamanid or pretomanid, and a fourth drug, sutezolid, from the oxazolidinone class. The trial was discontinued early after an interim analysis revealed that rates of sputum culture conversion in the experimental arms were inadequate to support treatment shortening down to three months (see Table 1).[6] In this case, the study population was enriched with participants with more severe disease (59.6% of participants had a smear grade of 2+ or 3+) and sputum culture conversion was determined from six cultures performed at each timepoint.[7] The PAN-TB collaboration is continuing its efforts to identify the next wave of regimens for clinical evaluation based on the ongoing generation of preclinical and clinical data and use of translational tools.

Table 1. Key Findings from Recently Completed Treatment-Shortening Trials

<table>
<tr><th>Study Name
(Type of TB; Sample Size)</th><th>Study Arms
Experimental Regimens
[Control Regimen]</th><th>Key Findings</th></tr>
<tr><td rowspan="8">endTB-Q
NCT03896685
(pre-XDR-TB, N=324)</td><td rowspan="8">(a) 6–9BDLzC
(b) [18–20mo SOC]</td><td>Primary Efficacy Outcome:
The experimental endTB-Q regimen failed to demonstrate non-inferiority to the SOC (mITT analysis). The NI margin was −12%.</td></tr>
<tr><td><table>
<tr><td>Favorable outcomes (mITT):</td><td></td><td>Risk difference (95% confidence interval)</td><td colspan="2">Favorable outcomes, risk difference stratified by extent of disease</td></tr>
<tr><td rowspan="2">(a)</td><td rowspan="2">141/163 (86.5%)</td><td rowspan="2">0.2 (−9.1, 9.5)</td><td>Limited:</td><td>54/58 (93%)
5.6 (−7.6, 18.8)</td></tr>
<tr><td>Extensive:</td><td>87/105 (83%)
−7.5 (−18.3, 3.2)</td></tr>
<tr><td rowspan="2">(b)</td><td rowspan="2">75/84 (89.3%)</td><td rowspan="2">Not applicable</td><td>Limited:</td><td>28/32 (88%)</td></tr>
<tr><td>Extensive:</td><td>47/52 (90%)</td></tr>
</table></td></tr>
<tr><td>Primary Safety Outcome:
Adverse events (AEs) occurred more often with the SOC compared to the endTB-Q regimen. A higher proportion of participants permanently discontinued one or more drugs due to AEs (predominantly hematologic toxicity and peripheral neuropathy) in the control arm (53.3 vs. 14.1%).</td></tr>
<tr><td><table>
<tr><td></td><td>Any grade 3 or higher AEs</td><td>Any serious AEs</td><td>Deaths</td></tr>
<tr><td>(a)</td><td>145 (68.1%)</td><td>42 (19.7%)</td><td>9 (4.2%)</td></tr>
<tr><td>(b)</td><td>77 (73.3%)</td><td>23 (21.9%)</td><td>2 (1.9%)</td></tr>
</table></td></tr>
<tr><td colspan="3">Guglielmetti L, Khan U, Velásquez GE, et al. Bedaquiline, delamanid, linezolid, and clofazimine for rifampicin-resistant and fluoroquinolone-resistant tuberculosis (endTB-Q): an open-label, multicentre, stratified, non-inferiority, randomised, controlled, phase 3 trial. Lancet Respir Med. 2025 Jul 16:S2213-2600(25)00194-8. doi: 10.1016/S2213-2600(25)00194-8.</td></tr>
</table>

<table>
<tr><th>Study Name
(Type of TB; Sample Size)</th><th>Study Arms
Experimental Regimens
[Control Regimen]</th><th>Key Findings</th></tr>
<tr><td rowspan="11">Trial 323-201-00006
NCT05221502
(DS-TB; N=122)</td><td rowspan="11">(a) 4BDQ₁₀
(b) 4BDQ₃₀
(c) 4BDQ₉₀
(d) [2HRZE/4HR]</td><td>Efficacy Outcomes:
The trial was powered to evaluate sputum culture conversion (SCC) at the end of treatment. While the experimental regimens demonstrated noninferiority for SCC, there were more favorable outcomes and fewer relapses (exploratory endpoints) among participants in the control arm.
<table><tr><th></th><th>Favorable outcomes six months after treatment</th><th>Relapses six months after treatment</th></tr><tr><td>(a)</td><td>17/20 (85%)</td><td>0/20 (0%)</td></tr><tr><td>(b)</td><td>37/42 (88.1%)</td><td>2/42 (4.8%)</td></tr><tr><td>(c)</td><td>31/38 (81.6%)</td><td>5/38 (13.2%)</td></tr><tr><td>(d)</td><td>20/21 (95.2%)</td><td>1/21 (4.8%)</td></tr></table>Primary Safety Outcome:
The experimental regimens had similar safety to the SOC.
<table><tr><th></th><th>Any grade 3 or higher AEs</th><th>Any serious AEs</th><th>Deaths</th></tr><tr><td>(a)</td><td>3 (15%)</td><td>2 (10%)</td><td>0 (0%)</td></tr><tr><td>(b)</td><td>5 (11.9%)</td><td>3 (7.1%)</td><td>1 (2.4%)</td></tr><tr><td>(c)</td><td>2 (5.3%)</td><td>0 (0%)</td><td>0 (0%)</td></tr><tr><td>(d)</td><td>1 (4.8%)</td><td>0 (0%)</td><td>0 (0%)</td></tr></table></td></tr>
<tr><td colspan="3">Dawson R, Diacon AH, Variava E, et al. A 4-month regimen of quabodepistat, delamanid, and bedaquiline for drug-susceptible pulmonary tuberculosis [TBS4B-25]. Oral abstract presented at: Union Conference during Pharmacological considerations for optimizing new regimens. 2024 November 16; Bali, Indonesia. https://unionconf2024.abstractserver.com/programme/#/details/presentations/2456.</td></tr>
<tr><td rowspan="11">Gates MRI-TBD06-201
NCT05971602
(DS-TB; N = 93/514*)
*The trial was stopped early after an interim analysis.</td><td rowspan="11">(a) 4PaBQ₃₀S
(b) 4DBQ₃₀S
(c) [2HRZE/4HR]</td><td>Efficacy Outcomes:
The trial was stopped early after an interim analysis revealed poor rates of sputum culture conversion in the experimental arms, making the trial aim to shorten treatment to three months or less impracticable.
<table><tr><th></th><th>Sputum culture conversion at month two</th><th>Sustained culture conversion at end of treatment</th></tr><tr><td>(a)</td><td>5/18 (27.8%)</td><td>7/16 (43.7%)</td></tr><tr><td>(b)</td><td>5/16 (31.3%)</td><td>10/14 (71.4%)</td></tr><tr><td>(c)</td><td>6/17 (35.5%)</td><td>7/11 (63.6%)</td></tr></table>Primary Safety Outcome:
No safety concerns were identified for the experimental regimens.
<table><tr><th></th><th>Any grade 3 or higher AEs</th><th>Any serious AEs</th><th>Deaths</th></tr><tr><td>(a)</td><td>5 (18.5%)</td><td>3 (11.1%)</td><td>0 (0%)</td></tr><tr><td>(b)</td><td>2 (7.1%)</td><td>1 (3.6%)</td><td>0 (0%)</td></tr><tr><td>(c)</td><td>2 (7.1%)</td><td>2 (7.1%)</td><td>1 (5.6%)</td></tr></table></td></tr>
<tr><td colspan="3">Holtzman, David. Challenges in TB drug development: A partnership perspective – including an update from the PAN-TB trial [SS11]. Presented at: Union Conference during Trials and tribulations in TB drug development: A UNITE4TB and PAN-TB perspective. 2024 November 14; Bali, Indonesia. https://unionconf2024.abstractserver.com/programme/#/details/presentations/2131.</td></tr>
<tr><td colspan="3">DS-TB = drug-sensitive TB, mITT = modified intention to treat, NI = non-inferiority, pre-XDR-TB = multidrug-resistant TB (MDR-TB) with additional resistance to the fluoroquinolones, SOC = standard of care
Numbers at the beginning of each regimen or after the forward slash (for regimens with intensive and continuation phases) represent the duration of treatment in months; subscripts indicate dosing in mg; letters represent the individual drugs comprising each regimen:
B = bedaquiline, C = clofazimine, D = delamanid, E = ethambutol, H = isoniazid, Lz = linezolid, Pa = pretomanid, Q = quabodepistat, R = rifampicin, S = sutezolid, Z = pyrazinamide</td></tr>
</table>

Trials evaluating treatment-shortening regimens composed of *existing drugs* (see Table 2) can be sorted into three notable categories: 1) trials that fill data gaps or iterate on existing regimens, including to improve accessibility and tolerability (in green); 2) trials of asymptomatic TB treatment (in pink); and 3) trials for bedaquiline-resistant TB (in blue). Ongoing and planned trials that fill data gaps for existing regimens are focused on the four-month rifapentine- and moxifloxacin-containing regimen (HPMZ) and six-month bedaquiline- and pretomanid-containing regimen (BPaLM) endorsed by the WHO for use in adults and adolescents in 2021 and 2022, respectively. Trials designed to iterate on these treatment-shortening advances are evaluating approaches that swap in high-dose rifampicin for rifapentine or alter the dose of rifapentine and/or moxifloxacin. They will also test the application of a stratified medicine approach to further shorten treatment duration for HPMZ and BPaLM. Exploring approaches to improving the accessibility and tolerability of recent treatment advances are important research objectives.
For the first time, the pipeline includes trials focused on asymptomatic TB, defined as TB apparent on chest X-ray but microbiologically unconfirmed (**RADIO-TB**), and bedaquiline-resistant TB. The experimental regimen under evaluation in the bedaquiline-resistant TB-focused trial listed in Table 2 (**BacTR**) is composed of existing drugs, whereas the experimental regimens under investigation for bedaquiline-resistant TB listed in Table 4 are composed of new drugs (**CLOBBER-TB, EX-DR**).

Table 2. Trials of Treatment-Shortening Regimens Composed of Existing Drugs

Study Name	Experimental Arms [Control]	For Treatment of	Number of Participants	Phase	Status [Est. Completion Date]
Drug-Sensitive TB					
RADIO-TB	2HRZE 2HRZE/1HR 2HRZE/2HR 2HRZE/3HR [2HRZE/4HR – immediate] [2HRZE/4HR – deferred]	aTB	784	III	Not yet recruiting [Dec 2028]
2021010 NCT05047055	2HRZEM/2HREM [none]	DS-TB	550	III	Active, not recruiting [Mar 2025]
STEP2C-01 NCT05807399	$4R_{Hd}HZM_{600}$ $3R_{Hd}HZ_{Hd}M_{600}$ [2HRZE/4HR]	DS-TB	270	IIb/c	Active, not recruiting [Jan 2026]
PORT NCT06057519	$2HR_{Hd}ZE/4HR_{Hd}$ [2HRZE/4HR]	DS-TB	164	III	Recruiting [Dec 2025]
OptiRiMoxTB NCT05575518	$4HR_{Hd}ZE$ $4HR_{Hd}MZ$ [2HRZE/4HR]	DS-TB	414	III	Recruiting [Mar 2026]
RIFAstrat	$2HR_{Hd}ZE/2HR_{Hd}$ [2HRZE/4HR]	DS-TB (nonsevere)	1,080	III	Not yet recruiting
A5406 NCT05630872	PK and DDI study of DTG given BID with HPMZ	DS-TB	30	II	Active, not recruiting [Sept 2025]
ORIENT NCT05401071	$2HP_{600}MZ/2HP_{600}M$ $2HP_{900}MZ/2HP_{900}M$ $2HP_{1200}MZ/2HP_{1200}M$ [2HRZE/4HR]	DS-TB	2,442	II/III	Recruiting [Nov 2027]

Study Name	Experimental Arms [Control]	For Treatment of	Number of Participants	Phase	Status [Est. Completion Date]
A5414 / SPECTRA-TB	10wkHP$_{1500}$MZ 12wkHP$_{1500}$MZ 14wkHP$_{1500}$MZ 16wkHP$_{1500}$MZ 18wkHP$_{1500}$MZ 26wkHP$_{1500}$MZ [2HRZE/4HR] Duration assigned depending on risk score (lower risk: 10-18wk; higher risk: 26wk).	DS-TB	900	IIc	Protocol in development
SMILE-TB NCT06253715	2HPMZ [SOC]	DS-TB (children)	860	III	Recruiting [Sept 2027]
Radiant-Kids / Formerly TBTC Study 39	Pediatric PK and safety study of 4HPMZ	DS-TB (children)	60	I/II	Protocol in development – seeking funding
IMPAACT 2047 / RADIANT-MOMS	2HPMZ/2HPM [2HRZE/4HR]	DS-TB (pregnant women)	TBD	II	Protocol in development
TBTC Study 38 / CRUSH-TB NCT05766267	2BMZRb/BMRb 2BMZD/2BMD [2HRZE/4HR]	DS-TB	288	IIc	Recruiting [Dec 2027]
PRESCIENT NCT05556746	3BDZC [2HRZE/4HR]	DS-TB	156	IIc	Recruiting [Jan 2027]
SURE ISRCTN40829906	6HR$_{Hd}$ZLx ± aspirin [2HRZE/10HR ± aspirin]	TBM (children)	369	III	Active, not recruiting [Mar 2026]
INTENSE-TBM NCT04145258	2HR$_{Hd}$ZELz/7HR ± aspirin [2HRZE/7HR ± aspirin]	TBM	768	III	Recruiting [Apr 2026]
A5384 / IMAGINE-TBM NCT05383742	2HR$_{Hd}$ZLz/4HR$_{Hd}$ [2HRZE/7HR]	TBM	330	II	Temporarily suspended
INSHORT NCT05917340	2HR$_{Hd}$ZM/4HRZ + aspirin, steroid 2HR$_{Hd}$ZM/4HRZ + steroid [2HRZE/7HR]	TBM	372	III	Recruiting [Sept 2028]
Drug-Resistant TB					
TMC207-C211 NCT02354014	Pediatric PK and safety study of bedaquiline	MDR-TB (children)	60	II	Recruiting [Nov 2027]
IMPAACT 2005 NCT03141060	Pediatric PK and safety study of delamanid	MDR-TB (children)	37	I/II	Completed [May 2025]
IMPAACT 2034 NCT05586230	Single-dose pediatric PK and safety study of pretomanid	MDR-TB (children)	72	I	Temporarily suspended
PRISM-TB NCT06441006	3BPaLM 4BPaLM 6BPaLM [SOC] Duration assigned depending on risk score.	MDR-TB	400	II/III	Protocol in development

Study Name	Experimental Arms [Control]	For Treatment of	Number of Participants	Phase	Status [Est. Completion Date]
BacTR	6-18B_{Hd}PaLz + AmCpmLx_{Hd}Cs* [none] *Referred to as "BPaLL*plus*" – depending on resistance, other group B and C drugs swapped in until at five-drug regimen.	At risk of or confirmed BDQ-R TB	125	III	Protocol in development
K21-024 NCT05278988	6–9BDCZ [9–20mo SOC]	MDR-TB	60	IV	Completed [Oct 2024]
mBPaL NCT05040126	2BPaLz_{600}/4BPaLz_{300} 3BPaLz_{600}/3BPaLz_{300} [6BPaLz_{600}]	Pre-XDR-, TI-NR-MDR-TB	400	III	Results published, CID Dec 2024[8]
ACTG A5356 NCT05007821	1BDC$Lz_{1200\ QD}$/5BDC$Lz_{1200\ TIW}$ 6BDC$Lz_{600\ QD}$ [none]	RR-, MDR-, pre-XDR-TB	138	II	Active, not recruiting [Mar 2026]
DRAMATIC NCT03828201	16wkBDCLxLz$_{8wk}$ 24wkBDCLxLz$_{8wk}$ 32wkBDCLxLz$_{8wk}$ 40wkBDCLxLz$_{8wk}$ [none]	MDR-TB	161	IIc	Active, not recruiting [May 2027]

Post-2021 definitions for pre-extensively drug-resistant TB (pre-XDR-TB) and extensively drug-resistant TB (XDR-TB) are used in Table 2, i.e., pre-XDR-TB: multidrug-resistant TB (MDR-TB) with additional resistance to the fluoroquinolones; XDR-TB: MDR-TB with additional resistance to the fluoroquinolones and other group A drugs (bedaquiline or linezolid)

aTB = asymptomatic TB – radiographically apparent but bacteriologically unconfirmed TB, BDQ-R = bedaquiline-resistant, DDI = drug-drug interaction, DTG = dolutegravir, DS-TB = drug-sensitive TB, RR-TB = rifampicin-resistant TB, PK = pharmacokinetics, SOC = standard of care, TBM = tuberculous meningitis, TI-NR-MDR-TB = treatment-intolerant or nonresponsive MDR-TB

Numbers at the beginning of each regimen or after the forward slash (for regimens with intensive and continuation phases) represent the duration of treatment in months, unless otherwise specified (i.e., wk = weeks); letters represent the individual drugs comprising each regimen

Subscripts indicate dosing in mg; Hd = high dose, BID = twice daily, QD = once daily, TIW = thrice weekly

Letters indicate TB drugs: Am = amikacin, B = bedaquiline, C = clofazimine, Cpm = carbapenem, Cs = cycloserine, D = delamanid, E = ethambutol, H = isoniazid, Lx = levofloxacin, Lz = linezolid, M = moxifloxacin, P = rifapentine, Pa = pretomanid, R = rifampicin, Rb = rifabutin, S = sutezolid, Z = pyrazinamide

Pediatric Investigations of TB Drugs

Several ongoing and planned TB treatment studies in children have been interrupted or otherwise thrown into uncertainty by an executive order prohibiting USG financial assistance to South Africa, a pause on foreign subawards at the US National Institutes of Health (NIH) pending a new award structure, and funding suspensions targeting specific universities.[9] While the NIH has since lifted a hold on payments for some existing grants and issued updated guidance for renegotiating the structure of projects with foreign subawards active or submitted before May 2025[10,11], TB treatment studies in children have yet to resume. Pediatric TB trials at risk include:

- **IMPAACT 2034:** This single-dose pediatric pharmacokinetic (PK) and safety study of pretomanid sponsored by the NIH-funded International Maternal Pediatric Adolescent AIDS Clinical Trials (IMPAACT) network opened in 2023 and enrolled 27 of 36-72 children before being temporarily paused in May 2025.

- **IMPAACT 2005:** An important study for refining delamanid dosing in children under two years of age and weighing less than 10 kg was closed early to long-term follow-up. Participants were followed for 30 weeks rather than 90 weeks so PK and safety data while on treatment will be available, but not longer-term safety or outcomes data as was originally planned.
- **IMPAACT 2020:** Protocol development was discontinued for this study to evaluate a six-month bedaquiline- and delamanid-containing regimen that includes levofloxacin or clofazimine (depending on fluoroquinolone resistance) and linezolid for the first eight weeks with all medications given once daily.
- **Radiant Kids:** A pediatric PK and safety study of the four-month rifapentine- and moxifloxacin-containing regimen for drug-sensitive TB (HPMZ) was being developed as Study 39 by the U.S. Centers for Disease Control and Prevention (CDC) Tuberculosis Trials Consortium (TBTC) but is now looking for a new home.

Interruptions of IMPAACT 2034 and Radiant Kids are especially problematic given that these trials are necessary for children to benefit from access to the full suite of short-course regimens the WHO currently recommends for the treatment of drug-sensitive and drug-resistant TB in adults and adolescents. The one USG-sponsored pediatric TB trial that has been able to resume following a brief interruption is **SMILE-TB**. Sponsored by Johns Hopkins University under the USAID-funded SMART4TB Project, SMILE-TB evaluates the HPMZ regimen given for just two months to children under ten years old.

Thanks in large part to proactive engagement by CHEETA (CHasing Expedited and Equitable Treatment Access for Children), a global consortium comprised of pediatric TB treatment research experts, several sponsors of new TB drugs have begun developing pediatric investigational plans. CHEETA has proposed a platform trial approach and other cross-cutting solutions to close the current 8- to-13-year gap between when new TB medicines are indicated for use in adults and children.[12,13]

Updates on New Drugs in Clinical Development for TB

The pipeline contains a total of 22 new or repurposed drugs in clinical development for TB. This is the same number of drugs reported previously because as one new drug entered clinical development in 2025, another fell out of the pipeline. The new entry to the pipeline is TBD11, a new drug with a novel mechanism of action, which entered phase I in December 2024. The drug that has been removed from the pipeline is GSK-286. GSK discontinued further development of GSK-286 after adverse events were observed in the phase I trial.[14] A long-acting formulation of bedaquiline entered phase I (TMC207TBC1006); it is the first long-acting formulation of a TB drug to enter clinical development. Long-acting formulations of other TB medicines (e.g., rifapentine, isoniazid, macozinone, pretomanid, sorfequiline (TBAJ-876), TBAJ-587, and telacebec) are in preclinical development.[15,16,17] Further down the pipeline, quabodepistat is the first among the novel class of DprE1 inhibitors that will advance to phase III. Otsuka plans to conduct its phase III trial of quabodepistat in people with drug-resistant TB and seek licensure for this indication.

Table 3. New (and Repurposed) Drugs in Clinical Development for TB

Drug	Class	Mechanism of Action	Sponsor	Phase	Clinical Trial(s)
Energy Production					
NEW → **TBD11 (CLB073)**	Not available	Inhibits cholesterol metabolism (adenyl cyclase activation)	GMRI	Ia/Ib	NCT06707142
pyrifazimine (TBI-166)	Riminophenazine	Inhibits ion transport and bacterial respiration	IMM/CAMS/ PUMC	IIa	ChiCTR1800018780 NCT04670120
sudapyridine (WX-081)	Diarylquinoline	Inhibits ATP synthase	Shanghai Jiatan Pharmatech Co.	III	NCT06117514 NCT06701110 NCT06701136 NCT04608955 NCT05824871
TBAJ-587	Diarylquinoline	Inhibits ATP synthase	TB Alliance/ ERA4TB	Ia/Ib	NCT04890535
sorfequiline (TBAJ-876)	Diarylquinoline	Inhibits ATP synthase and bacterial respiration	TB Alliance	IIb	NCT04493671 NCT05526911 NCT06058299
telacebec (Q203)	Imidazopyridine	Inhibits ATP synthesis (QcrB) and bacterial respiration	Qurient/TB Alliance/Infectex	IIa	NCT02530710 NCT02858973 NCT03563599
Cell Wall Synthesis					
BTZ-043	Benzothiazinone	Inhibits cell wall synthesis (DprE1)	University of Munich/DZIF	IIb/c	NCT03590600 NCT04044001 NCT04874948 **NCT05382312** ← NEW NCT05926466 NCT06114628 **NCT05807399** ← NEW
alpibectir (BVL-GSK098)	Amido-piperidine	Inhibits cell wall synthesis via boosting ethionamide	BioVersys/GSK	IIa	NCT04654143 NCT05473195 **NCT06748937** ← NEW
macozinone (PBTZ169)	Benzothiazinone	Inhibits cell wall synthesis (DprE1)	iM4TB/ Nearmedic	Ib/IIa	NCT03036163 NCT03423030 NCT04150224 NCT03776500 NCT03334734
quabodepistat (OPC-167832)	Carbostyril	Inhibits cell wall synthesis (DprE1)	Otsuka	IIb/c	NCT03678688 NCT05221502 NCT05971602
sanfetrinem cilexetil	Carbapenem	Inhibits cell wall synthesis	GSK	IIa	NCT05388448
SQ109	Ethylenediamine	Inhibits cell wall synthesis (MmpL3)	Sequella	IIb	NCT01585636 NCT00866190 NCT01358162 NCT01218217 NCT01785186
TBA-7371	Azaindole	Inhibits cell wall synthesis (DprE1)	TB Alliance	IIa	NCT03199339 NCT04176250

Drug	Class	Mechanism of Action	Sponsor	Phase	Clinical Trial(s)	
Protein Synthesis						
contezolid	oxazolidinone	Inhibits protein synthesis (23S ribosome)	MicuRx	III	NCT03033342 NCT03033329 NCT03747497 **NCT06811012** **NCT06811025** NCT06081361	← NEW
delpazolid (LCB01-0371)	Oxazolidinone	Inhibits protein synthesis (50S ribosomal subunit)	LegoChem Biosciences	IIb	NCT01554995 NCT01842516 NCT02540460 NCT02836483 NCT04550832	
sutezolid (PNU-100480)	Oxazolidinone	Inhibits protein synthesis (50S ribosomal subunit)	Sequella/TB Alliance	IIb/c	NCT00871949 NCT00990990 NCT01225640 NCT03199313 NCT03959566 NCT06192160 NCT05971602 NCT05686356 NCT06192160	
tedizolid*	Oxazolidinone	Inhibits protein synthesis (50S ribosomal subunit)	Assistance Publique – Hôpitaux de Paris	IIa	NCT05534750	
TBI-223	Oxazolidinone	Inhibits protein synthesis (50S ribosomal subunit)	TB Alliance/IMM	IIa	NCT03758612 NCT04865536 NCT06192160	
TBD09 (MK-7762)	Oxazolidinone	Inhibits protein synthesis (50S ribosomal subunit)	GMRI/Merck	Ia/b	NCT05824091	
ganfeborole (GSK-656)	Oxaborole	Inhibits protein synthesis (LeuRS)	GSK	IIb	NCT03075410 NCT03557281 NCT05382312 NCT06114628 **NCT06354257**	← NEW
DNA Synthesis						
SPR720	Benzimidazole	Inhibits bacterial DNA synthesis (GyrB)	Spero Therapeutics	Ia/Ib	NCT03796910	
Sitafloxacin*	Fluoroquinolone	Inhibit bacterial DNA synthesis	Daiichi Sankyo/ Zhejiang University	III	NCT05454345	

*Repurposed
Phase listed represents the most advanced trial that is ongoing/completed.

ATP = adenosine triphosphate
CAMS = Chinese Academy of Medical Sciences
DprE1 = decaprenylphosphoryl-β-d-ribose 2′-epimerase, an enzyme involved in cell wall synthesis
DZIF = German Center for Infection Research
GMRI = Bill & Melinda Gates Medical Research Institute
GSK = GlaxoSmithKline
GyrB = DNA gyrase subunit B, an enzyme involved in DNA synthesis
iM4TB = Innovative Medicines for Tuberculosis
IMM = Institute of Materia Medica, China
LeuRS = leucyl-tRNA synthetase, an enzyme involved in protein synthesis
MmpL3 = mycobacterial membrane protein large 3, mycolic acid and lipid transporter required for cell growth and viability
PUMC = Peking Union Medical College, China
QcrB = cytochrome b subunit of the cytochrome bc1 complex, an essential component of the respiratory electron transport chain required for ATP synthesis

Ongoing and planned trials of investigational regimens that advance new drugs (see Table 4) are poised to provide complementary information that will inform what regimens progress to evaluation in phase III as well as the next wave of regimens to be evaluated in phase IIb/c trials. These trials are designed to replace bedaquiline with a next-generation diarylquinoline, replace linezolid with a next-generation oxazolidinone or other new drug, select between the two nitroimidazoles (pretomanid and delamanid), and figure out the optimal combination of these with new drugs with novel mechanisms of action for shortening and improving treatment. And finally, trials are being designed to inform how we might use new drugs in combination to treat bedaquiline-resistant TB.

Table 4. Trials of Investigational Regimens That Advance New Drugs

Study Name	Experimental Arms [Control]	For Treatment of	Number of Participants	Phase	Status [Est. Completion]
NC-009 NCT06058299	2J_{25}PaL/2–4HR 2J_{50}PaL/2–4HR 2J_{100}PaL/2–4HR 6BPaL [2HRZE/4HR]	DS-TB	309	IIb	Active, not recruiting [June 2026]
A5409/RAD-TB NCT06192160	2BPaS_{800}/4HR 2BPaS_{1600}/4HR 2BPa**TBI-223**$_{1200}$/4HR 2BPa**TBI-223**$_{2400}$/4HR 2BPaL/4HR [2HRZE/4HR]	DS-TB	315	IIa+	Temporarily suspended
SUDOCU NCT03959566	3BDMS_{600}/3HR 3BDMS_{1200}/3HR 3BDM$S_{600\ BID}$/3HR 3BDM$S_{800\ BID}$/3HR [3BDM/3HR]	DS-TB	75	IIb	Results published, Lancet ID 2025[18]
DECODE NCT04550832	4BDM**Dzd**$_{400}$ 4BDM**Dzd**$_{800}$ 4BDM**Dzd**$_{1200}$ 4BDM**Dzd**$_{800\ BID}$ [4BDM]	DS-TB	76	IIb	Results published, Lancet ID 2025[19]
DECISION/ UNITE4TB-02 NCT05926466	4BDT_{500}/2HR 4BDT_{1000}/2HR 4BDT_{1500}/2HR [4BDM/2HR]	DS-TB	90	IIb	Results forthcoming, Union 2025
STEP2C-02 NCT05807399	4RHZT/2HR [2HRZE/4HR]	DS-TB	270	IIb/c	Active, not recruiting [Jan 2026]
STEP2C-03	6PG**TDzd** 2RZE**Eto-Alp**/4HR [2HRZE/4HR]	DS-TB	120	IIb/c	Not yet recruiting
Trial 323-201-00006 NCT05221502	4BDQ_{10} 4BDQ_{30} 4BDQ_{90} [2HRZE/4HR]	DS-TB	122	IIb/c	Results presented, Union 2024
Gates MRI-TBD06-201 NCT05971602	2–4PaB**QS** 2–4DB**QS** [2HRZE/4HR]	DS-TB + RR/MDR obs. cohort	514	IIb/c	Terminated; results presented, Union 2024

Study Name	Experimental Arms [Control]	For Treatment of	Number of Participants	Phase	Status [Est. Completion]
PARADIGM4TB / UNITE4TB-01 NCT06114628	2–4BD**G**M 2–4BPa**G**M 2–4BD**G**Z 2–4BD**G**L* 2–4BD**T**M 2–4BPa**T**M 2–4BD**T**Z 2–4BD**T**L* 2–4BD**G****T** 2–4BM**T**Z 2–4BDM [2HRZE/4HR] *L for the first 8 weeks only.	DS-TB	2,500	IIb/c	Recruiting [Aug 2027]
panTB-HM NCT05686356	4BPaS_{1200} 4BPaS_{1600} 4BPaS_{1600} + $NAC_{1800\ BID}$ [2HRZE/4HR]	DS-TB	352	II/III	Active, not recruiting [Jan 2026]
INSPIRE-CODA NCT06081361	6BD**Czd** (Lx or Cz) [6BLzCsCzLx/12CsCzLx]* *For FQ-R, Lx will be replaced by Pto, Z, PAS, or E.	MDR-TB, pre-XDR-TB	186	III	Active, not recruiting [Dec 2026]
WISH NCT05824871	6**W** + OBR [6B + OBR] OBR given for up to 18 months.	MDR-TB	450	III	Recruiting [Oct 2026]
yzhang207 NCT05454345*	1.5HP**Sx**Z/1.5HP**Sx**+SMZ/TMP 3HP**Sx**Z [2HRZE/4HR] [2HPMZ/2HPM]	DS-TB	620	III	Not yet recruiting [June 2026] *Entry last updated 2022.
QUANTUM	4BPa**Q**M 6BPa**Q** [6BPaL/M]	MDR-TB, pre-XDR-TB	532	III	Protocol in development
CLOBBER-TB	6–9Pa**G****QS**+**TBAJ-587** [18- to 20-month individualized regimen]	XDR-TB	120	III	Protocol in development – seeking funding
EX-DR	9Pa**G****TDzd** 6Pa**G****TSDzdJ** [SOC]	XDR-TB	400	III	Protocol in development

DS-TB = drug-sensitive TB, FQ-R = fluoroquinolone-resistant TB, MDR-TB = multidrug-resistant TB, RR-TB = rifampicin-resistant TB, XDR-TB = extensively drug-resistant TB

Numbers at the beginning of each regimen or after the forward slash (for regimens with intensive and continuation phases) represent the duration of treatment in months, unless otherwise specified; letters represent the individual drugs comprising each regimen

Subscripts indicate dosing in mg; BID = twice daily; TIW = thrice weekly

NAC = N-acetyl cysteine (a repurposed host-directed therapy)

OBR = optimized background regimen

Letters indicate TB drugs: B = bedaquiline, Cs = cycloserine, Cz = clofazimine, Czd = contezolid, D = delamanid, Dzd = delpazolid, E = ethambutol, Eto-Alp = ethionamide + alpibectir, G = ganfeborole, H = isoniazid, J = TBAJ-876, TBAJ-587 = TBAJ-587, L = linezolid, Lx = levofloxacin, M = moxifloxacin, Pa = pretomanid, PAS = para-aminosalicylic acid, Pto = prothionamide, Q = quabodepistat, R = rifampicin, S = sutezolid, SMZ/TMP = sulfamethoxazole/ trimethoprim, Sx = sitafloxacin, T = BTZ-043, TBI-223 = TBI-223, W = WX-081, Z = pyrazinamide

Conclusion

The TB treatment pipeline is fuller than it's ever been in the 88 years since the original streptomycin study[20], but work important to closing research gaps for priority populations (children, pregnant women) and to delivering a new wave of treatment advances is direly threatened by funding and organizational changes. As the leading global funder of TB R&D, shifts in USG policies and priorities can be expected to have major ripple effects across the entire ecosystem for TB drug development and treatment research. Other governments and research funders will need to increase their investments to preserve scientific advances underway and to bolster TB research infrastructure that has been jeopardized by the current US administration.

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