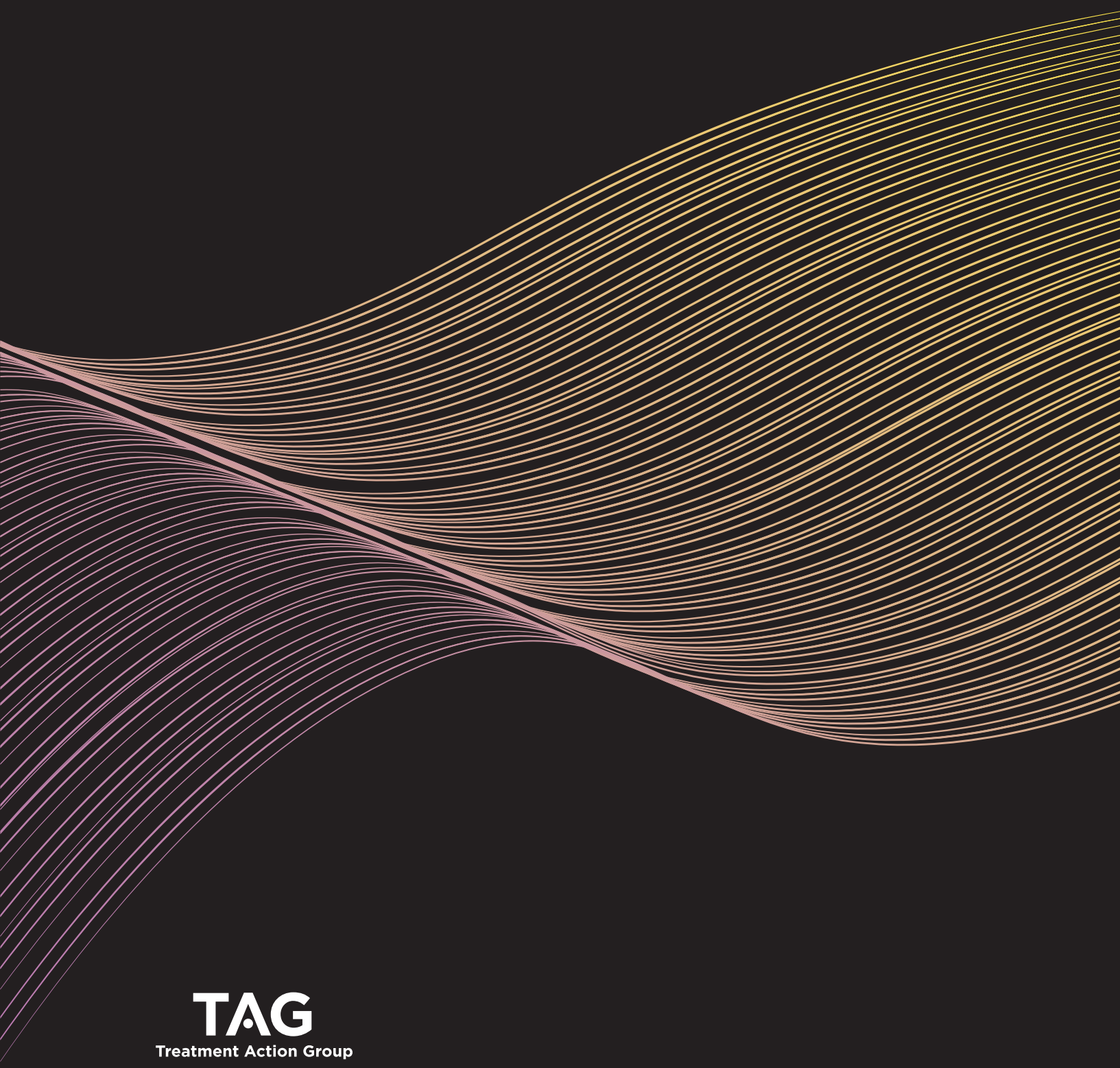
Pipeline Report » 2026

Tuberculosis Long-Acting Technologies



TAG
Treatment Action Group

2026 Tuberculosis Long-Acting Technologies Pipeline Report

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Introduction

This pipeline report represents Treatment Action Group's pioneer effort to track the development of long-acting technologies (LATs) for tuberculosis (TB), an area of increasing interest and activity in the field. LATs for TB treatment and prevention are advancing to clinical trials for the first time in the wake of the excitement generated around new LATs for prevention of HIV — the injectables cabotegravir and lenacapavir. Like the first long-acting technologies for HIV, early efforts for TB are primarily focused on long-acting injectables (LAIs) over alternative formulations (e.g., microneedle patches, implants, antibody infusions or oral pills).

LATs carry unique promises and perils for TB. The use of a LAT for even one component of a TB treatment regimen promises to reduce pill burden. The potential of a single long-acting (LA) injection for TB preventive treatment (TPT) opens the possibility of an entirely pill-free TPT regimen. At the same time, the history of injectable aminoglycosides for the treatment of multidrug-resistant TB, and the hearing loss associated with these drugs, casts a long shadow over the potential acceptability of novel LAIs.[1] Despite past negative experiences with daily, toxic injectable medicines for TB, early acceptability and preference studies have revealed an appetite for novel LAIs and the expansion of treatment and prevention options.[2,3]

The pipeline for LATs for TB is young with just 13 in development, the bulk of which are still in preclinical development (see Table 2). To guide these nascent efforts, the World Health Organization (WHO) has developed *Target Regimen Profiles for Long-Acting Injectables for Tuberculosis Prevention and Treatment* that lay out the optimal requirements for future technologies before they enter clinical trials.[2] The Target Regimen Profiles in tandem with continued robust engagement of communities throughout development will ensure that LATs are designed to meet the needs and preferences of affected communities.[3]

This inaugural *TB Long-Acting Technologies Pipeline Report* offers a bird's eye view of LATs in a moment when only two such technologies for TB have entered clinical trials: Akagera's AKG-100 and Janssen's long-acting form of bedaquiline.[4,5] Future iterations of this report will follow the field with greater detail as LATs enter and progress through clinical development. For information on the pipeline of TB treatment and prevention tools being developed in oral formulations, readers can consult the most recent publications of TAG's Pipeline Reports on *TB Treatment (2026)* and *TB Preventive Therapies (2021)*.

Background

The first LAT was introduced in 1952 with the launch of an outer capsule for oral medicines that allowed for the gradual release of active compounds over a 12-hour period, revolutionizing the administration of medicines for psychiatry and treatment of diabetes.[6] Depo-Provera, the long-acting injectable originally marketed for treatment of endometrial cancer, was introduced in 1967 — later becoming widely used in Africa as the first long-acting contraceptive in the 1970s.[7] The late 1980s and early 1990s welcomed the next significant advancements of LATs with the introduction of injectable drug depot technologies that maintained effective drug concentrations over months or years and opened the field to long-acting injectables and implants.[6] Since the turn of the century, new LATs have been introduced for contraception (e.g., implants), addiction therapy (e.g., microneedle patches), chemotherapy, and more recently LAIs for the treatment and prevention of HIV.[1] As LATs became more common, researchers and developers in the TB field began exploring long-acting solutions for the treatment and prevention of TB. Soon after bedaquiline was introduced to market in 2012, researchers started scoping out long-acting formulations of the drug alongside other anti-TB compounds, though the first clinical trial of long-acting bedaquiline came nearly 12 years later.[5,8] These early efforts have yielded 13 unique LAT products currently under development for the treatment or prevention of TB, including two in clinical trials.

LATs for TB carries unique considerations and challenges stemming from both the shorter duration of treatment administration (i.e., not life-long or chronic) and the reliance on multidrug regimens for the treatment and prevention of TB. Reaping the greatest benefit from LAIs for TB will require tackling novel concerns beyond a single LAI, including:

a) the injection volumes of all LAIs administered as part of a regimen;

b) the co-formulation of unrelated drugs into a single LAI suspension;

c) the pharmacokinetic (PK) tails of each LAI or LAT in a regimen and mitigating the risk of developing drug resistance;

d) the risk of drug-drug interactions with commonly co-administered drugs (e.g., antiretrovirals); and

e) the integration of LATs into existing TB programs and systems.

These challenges reflect considerations far beyond the basic question of if LAIs or other LATs for TB can demonstrate clear advantages over existing low-cost, oral regimens in treatment completion, equity, resistance prevention, or acceptability. If these challenges can be overcome, effective LATs for TB carry the potential to improve TB treatment experiences and find their place among other novel TB interventions billed as game-changing such as new TB vaccines or enhanced community-wide screening programs.

Overview of the Pipeline

LAIs under development can be grouped into two main buckets:

- LA formulations of drugs currently recommended and used for the treatment or prevention of TB
- LA formulations of compounds that are still in clinical trials and not yet recommended or approved for use

The preclinical work required for each of these buckets is largely the same, focused on pharmacokinetic (PK) studies (e.g., duration of sustained drug levels in plasma), early safety signals, and long-acting product stability over time. The key distinction between these two buckets is found in how they intersect with the timeline of development of their oral counterparts. For experimental compounds, the oral formulations are largely serving as the vanguard of the development pathway, providing data to inform future preclinical studies and trials of the LA formulation. The goal of this approach is to support the relatively rapid introduction of LA formulations of novel drugs following the late-stage trials of oral formulations. Running in parallel is the development of LA formulations of drugs currently in use in recommended regimens, e.g., LA bedaquiline or LA isoniazid. For these medicines, the development of LA formulations is in direct conversation with the trove of clinical data from studies of the oral formulations that preceded them. Unlike the development of LA formulations of experimental compounds, LA formulations of drugs currently recommended may benefit from rapid integration into regimens in real world settings, where the LAT formulation may be easily swapped in, potentially lowering pill burdens. As the field advances, additional efficiencies in the development, regulatory, policy making, and implementation processes may emerge to speed LAT introduction.

Existing Drugs

LAI formulations of drugs which are currently part of recommended treatment or TPT regimens make up about half of the early developments in the LAT field, with a significant focus on developing and testing LAI formulations for TPT. Early preference and acceptability data collected to inform the WHO Target Regimen Profiles has shown that there is appetite for an LAI form of TPT, particularly if it can be administered as single-shot or in a single encounter with the health system.[2] LA formulations of isoniazid and rifapentine, alongside a combined isoniazid and rifapentine microneedle array patch, are being investigated by the Unitaid-funded LONGEVITY project for TPT, but have yet to enter phase I. LA bedaquiline, the first LAI for TB to enter clinical trials, is being investigated as a single shot, one-month TPT regimen by Janssen Pharmaceuticals, with a phase III trial in collaboration with Division of AIDS (DAIDS)-funded AIDS Clinical Trials Group (ACTG) in development.[5,9]

- **Rifapentine:** A long-acting formulation of rifapentine developed by the LONGEVITY consortium has shown efficacy comparable to the 1HP (i.e., one month of daily oral isoniazid and rifapentine) regimen in preclinical animal studies. Early studies have shown target exposure is maintained over one month in rats with a longer half-life predicted in humans and further studies ongoing. LONGEVITY has completed animal toxicology studies of LA-rifapentine and is currently developing a phase I clinical trial, with an anticipated start by the end of 2027[10]
- **Isoniazid:** The LONGEVITY consortium has developed an isoniazid prodrug that is currently in preclinical development. A prodrug is metabolized into the target active compound (here: isoniazid) after administration, allowing researchers to leverage the unique chemical properties of prodrugs (e.g., solubility) in developing long-acting formulations. The prodrug's preclinical development lags LA-rifapentine but is also targeting a phase I trial in 2027, pending further studies.[10] LONGEVITY's current intentions regarding co-formulation of LA rifapentine and LA isoniazid in a single injection remain undefined, as both injectables will be advancing through phase I trials as independent injections that could be administered at a single visit.
- **Rifapentine + Isoniazid Microneedle Patch:** In addition to separate LAI versions of rifapentine and isoniazid, LONGEVITY is supporting the preclinical development of a microneedle array to co-administer rifapentine and isoniazid together in a single patch. While the patch is still in early preclinical development, initial studies have demonstrated that target drug exposure can be achieved in animal models.[10]
- **Pretomanid:** TB Alliance is developing a long-acting formulation of pretomanid, the oral form of which is recommended as part of the six-month BPaL(M) (i.e., bedaquiline, pretomanid and linezolid +/- moxifloxacin) regimen for the treatment of drug-resistant (DR) TB.[11] Results from preclinical studies reported at the 2026 Conference on Retroviruses and Opportunities Infections demonstrated that subcutaneous administration of an implant forming injectable version of LA-pretomanid produced a sustained release over two months with drug penetration into the lungs, spleen, and lymph nodes in mouse models.[12]

Early Results from Clinical Trials of Existing Drugs

An injectable long-acting bedaquiline (LA-BDQ) formulation was the first long-acting formulation for TB to enter clinical trials. Bedaquiline was considered a strong candidate for LAI formulation based on its long-half life, solubility in water, and low required concentration in the body.[9] Further, bedaquiline's well-established safety profile as an oral regimen across a wide range of populations and the absence of known drug-drug interactions with common antiretroviral treatment (ART) regimens for HIV make it particularly promising as an LAI on the implementation side.[5, 9, 13]

Beginning in July 2024, Janssen Pharmaceuticals opened a phase I, open-label, single ascending dose study of LA-BDQ in Austria, enrolling 32 healthy volunteers into three arms.[5, 14] Participants were randomized to receive a low-, mid-, or high-dose intramuscular (gluteal, i.e., buttocks) injection to assess PK and safety of the regimen. Translational PK and pharmacodynamic modeling was done to inform dose selection for the phase I study. The doses of LAI-BDQ tested matched the target exposure of bedaquiline achieved in BALB/c mice studies in which bedaquiline performed similarly to 3HP (i.e., twelve weeks of once-weekly isoniazid and rifapentine).[15]

At the 2025 Union Conference in Copenhagen, Denmark, Janssen presented interim results from the phase I trial (Table 1). There were no novel safety concerns associated with the long-acting formulation, providing confidence that LAI-BDQ was well positioned to advance to later stage clinical trials.[5] The trial finished in mid-2026 after following all participants out to 12 months post-injection. Full analysis of trial data is expected in the coming months and will inform the development of future trials of LAI-BDQ.

A phase III trial (A5434, VITAL4ALL) comparing a single-shot LAI-BDQ against the 3HP standard of care in people living with HIV on antiretroviral therapy is under development with an anticipated start in 2028. The study is a collaboration between the DAIDS-funded ACTG and Janssen Pharmaceuticals.[9, 16] If the phase III trial proves successful, and LAI-BDQ obtains regulatory approval, it will likely be the first long-acting TB formulation to enter the market offering single administration TPT. However, TPT trials often take many years due to their large size, pace of enrollment, and the need to follow participants to monitor for development of TB. At the very earliest, results of VITAL4ALL are not expected until 2033. A study called BREACH-TB, sponsored by the SMART4TB Project, is evaluating one-month of oral bedaquiline administered daily for TPT enrolling an estimated 2,530 participants, with results expected no sooner than 2028.[17]

Table 1. Interim Results from LA-BDQ Phase I Trial[5]

Trial 2023-508810-41-00		
Study Arms	**Primary Endpoints**	**Interim Results**
1. Low-dose: 1 x 2.5 mL injection (n=4) 2. Mid-dose: 1 x 5 mL injection (n=8) 3. High-dose: 2 x 5 mL (n=20)	***Safety***	
	1. Adverse events (AE)[a]	All participants experienced one treatment-emergent adverse event (TEAE)[b]; none led to study discontinuation. 72% of participants reported grade 1 or 2 AEs; injection site pain was reported most frequently. Serious adverse events were reported in 4 participants (12.5%), all were considered not related to study drug.
	2. Injection site reactions (ISR)	Injection site pain reported in all participants. Most pain resolved within five days of administration. ISRs were primarily Grade 1 or 2; Grade 3 reactions reported in four participants. ISR were well tolerated with counseling or analgesia.
	3. Adverse events of special interest	Reported in two participants (6.2%) One Grade 1 QTc[c] prolongation; one Grade 1 ALT elevation.[d]
	Pharmacokinetics	
	PK of LA-BDQ and M2 metabolite	BDQ exposure increases with dose, but in a less than dose-proportional way. No evidence of sudden spikes of BDQ concentration following administration. Single mid-dose of LA-BDQ, predicted to be similar or non-inferior to 3HP.

a. Adverse event: any undesirable experience associated with the use of medical or experimental product.[18]

b. Treatment-emergent adverse event: unexpected outcome or event arising during or following treatment with a medical or experimental product that did not appear beforehand or is worsening a pre-existing condition.[18]

c. QTc: The QT interval (and corrected QT, i.e., QTc) measures electrical activity of the heart, an elongated or shortened QT can lead to heart complications such as abnormal rhythms or cardiac arrest. QT is measured in the course of clinical trials to assess if the medical intervention under study is associated with adverse cardiac reactions.[19]

d. ALT Elevation: ALT (alanine aminotransferase) is an enzyme that is released by liver cells when injured. ALT levels are monitored over the course of clinical trials to assess the safety of treatment on liver function.[20]

New Compounds

There is a robust preclinical pipeline of LA formulations of promising new compounds, including AKG-100, which has entered early phase I trials. Aside from AKG-100, the development of LA-formulations of new drugs follows the advancement of their oral counterparts. This approach carries benefits like the potential for faster introduction of LAI formulations following the successful introduction of new drugs and the ability to leverage data and clinical trial resources from the development of oral regimens in applications and investigations of LAIs.

- **AKG-100** represents the first new compound in LA formulation to enter phase I clinical trials. AKG-100 is an oxazolidinone, the same class as linezolid — the powerful but difficult to tolerate drug used to treat DR-TB. Akagera is evaluating AKG-100 given as an intravenous administration for use against both DR- and drug-sensitive (DS) TB. In July 2026, Akagera Medicines reported positive results from the initial cohort of its trial investigating single-dose intravenous AKG-100. The initial results were from a single-ascending-dose study of AKG-100 across 40 healthy participants and a 14-day early bactericidal activity study among 15 people with pulmonary TB. Akagera reported that AKG-100 was well tolerated at every dose studied with no participants dropping out of the study due to adverse events and demonstrated good bactericidal activity. Following these early results, Akagera opened a multiple-ascending-dose study.[4, 21] AKG-100 will be the first LA-TB drug to complete phase I with an indication for the treatment of TB.

- **Sorfequiline (TBA-876)**, a compound in the same class as bedaquiline (a diarylquinoline), is under active development by TB Alliance for the treatment of DS-TB in a long-acting form. In tandem, TB Alliance is developing an oral version of sorfequiline for a DR-TB indication that is expected to enter phase III soon.[22] Sorfequiline is thought to be more potent and safer than bedaquiline, and early preclinical evidence suggests that it may be effective against some bedaquiline resistant strains, which has generated significant excitement. An implant-forming, long-acting formulation of sorfequiline has been designed to reach high initial drug levels with continuous drug release sustained for two months following administration. In preclinical studies, LA sorfequiline sustained release over three months.[12, 23] Early preclinical data provide evidence of LA-sorfequiline's ability to sustain stable release levels in animal models. Future studies will offer insight into the dose, duration of coverage (i.e., the time over which a long-acting drug maintains a safe and effective drug concentration in plasma or at the site of the disease following administration), safety, efficacy, and lay the foundation for clinical trials.

- **Telacebec (Q-203)** is a first-in-class ATP synthesis inhibitor that targets a different site than bedaquiline, offering a potential complement to bedaquiline and possibly reducing the chance of drug resistance.[24] An oral version of telacebec has been under development for several years, undergoing phase IIb trials for treatment of DS-TB.[24,25] TB Alliance is supporting the preclinical development of a long-acting formulation of telacebec. Results from these early animal studies will determine if there is rationale for the continuation of development of LA telacebec.

- **TBAJ-587**, another diarylquinoline compound in the same class as bedaquiline and sorfequiline, is currently in phase IIa studies for its oral formulation. A long-acting formulation of TBAJ-587 is being developed in tandem. Like sorfequiline, early animal studies have demonstrated sustained release levels of the drug three months after administration. However, long-acting TBAJ-587 has only been explored in aqueous solutions where it forms crystals over time — alternative approaches to LA TBAJ-587 (e.g., implant forming injectable) may be required.[26]

- **Macozinone** is a benzothiazinone under development by Innovative Medicines for Tuberculosis (iM4TB), a European foundation developing new TB drugs. iM4TB partnered with Medincell, a French pharmaceutical company specializing in long-acting injectables, to develop a long-acting version of macozinone. iM4TB is currently sponsoring macozinone's phase IIa trials for the oral formulation while the LA macozinone is in early preclinical development.[22, 27]

- Researchers at Rice University are studying ganfeborole — an oxaborole with a novel mechanism of action being developed by GlaxoSmithKline (GSK) — in proof-of-concept studies for **a long-acting hydrogel matrix** that controls release over time.[22, 28, 29] Animal studies have demonstrated that ganfeborole's therapeutic effects are extended to weeks when administered via hydrogel matrix and more effective at clearing bacteria than oral administration.[28] While not actively being developed as a long-acting version of ganfeborole, results from the hydrogel matrix proof-of-concept studies show potential for this technology to be deployed in the treatment or prevention of TB.[28, 30]

- With support from the Gates Foundation, researchers at the University of Southern Denmark and the University of North Carolina are collaborating with Gates Medical Research Institute scientists in investigating the feasibility of reformulating oral TB drug candidates currently under development into long-acting injectables (LAIs), towards the overarching goal of developing an all-LAI regimen for the treatment of active TB infection. Researchers are currently focused on two candidates: **TBD11**, a cholesterol metabolism disruptor, in preclinical development as an LAI and **TBD09**, an oxazolidinone, in discovery as an LAI. Both TBD11 and TBD09 are being explored for the treatment of TB.[31]

Table 2. Long-Acting Formulations in Development for TB

Compound	Class	Technology	Sponsor	Phase and Status	Primary Indication
Existing Drugs					
Bedaquiline	Diarylquinoline	Injectable	ACTG	Phase I (Completed); (Phase III Protocol in Dev.)	Prevention
Isoniazid	Hydrazide	Injectable	Unitaid - LONGEVITY	Preclinical (Phase I Protocol in Dev.)	Prevention
Rifapentine	Rifamycin	Injectable	Unitaid – LONGEVITY	Preclinical (Phase I Protocol in Dev.)	Prevention
Isoniazid + Rifapentine	Coformulation (Hydrazide + Rifamycin)	Microneedle Patch	Unitaid - LONGEVITY	Preclinical	Prevention
Pretomanid[32]	Nitroimidazole	Implant forming injectable	TB Alliance	Preclinical	Treatment
Rifabutin[33-35]	Rifamycin	Implant forming Injectable	Gates & TB Alliance	Preclinical	Treatment
Novel Compounds					
AKG-100[21]	Oxazolidinone	Intravenous (IV)	Akagera	Phase I (Ongoing)	Treatment
Ganfeborole*	Oxaborole	Hydrogel matrix (i.e., implant)	GSK* Rice University*	Preclinical	Treatment
Macozinone	Benzothiazinone	Injectable	iM4TB/ Medincell	Preclinical	Treatment
Sorfequiline	Diarylquinoline	Implant forming injectable	TB Alliance	Preclinical	Treatment
TBAJ-587	Diarylquinoline	Injectable	TB Alliance	Preclinical	Treatment
TBD09	Oxazolidinone	Injectable	Gates Medical Research Institute	Discovery	Treatment
TBD11	Cholesterol metabolism disruptor	Injectable	Gates Medical Research Institute	Preclinical	Treatment
Telacebec (Q-203)	Imidazopyridine	Injectable	Qurient/TB Alliance/Infectex	Preclinical	Treatment

* Ganfeborole has been explored in a novel hydrogel matrix technology by Rice University without input from GSK. GSK is advancing development of the oral version of ganfeborole which is in Phase IIb trials.[22]

Future Questions and Considerations for LAIs

Long-Acting Multidrug Regimens

One of the core challenges for the creation of an all-LA regimen for TB treatment is that regimens can be made from up to two drugs for TB preventive therapy (TPT), up to four drugs for DS-TB and often many more for DR-TB, selected to apply pressure on different targets and minimize the risk of treatment failure and drug resistance. Current LATs in development are focused on single compound LA formulations of existing TB drugs (e.g., LA isoniazid, LA rifapentine). Each of these must be paired with other agents to constitute a complete TB treatment regimen. As researchers and developers eye an *all-LAI or LAT* regimen, they will need to contend with challenges including:

- **Developing LA formulations for all component drugs in a TB regimen:** Most TB regimens are made up of three to five drugs which are necessary to undercut the risk of drug resistance and ensure TB is eliminated. When it comes to an all-LAI regimen, however, this means that *each* of those drugs must have LA formulations as a prerequisite. While a single-drug LAI can replace some parts of a regimen, patients would still need to take daily pills to cover the full suite of a regimen. In the absence of an all-LAI regimen, the full potential of LAIs to eliminate all daily pills as they have for other disease areas will remain out of reach.
- **Co-administration or co-formulation of LAIs:** Creating LA formulations of all component drugs of a regimen is challenging enough, but it is further complicated by the need to co-administer LAIs at the minimum number of appointments and with the minimal number of injections or injection volume for comfort. Co-formulation of LAIs is one pathway to reduce the number of injections and potentially volume but adds complexity to development efforts.
- **Aligning PK:** All-LAI regimens will need to integrate thoughtful design to ensure that all component drugs maintain adequate concentrations in the plasma while also aligning administration schedules. The success of a regimen including one or more LAIs may be undercut by inconvenient dosing schedules that increase the burden of healthcare on communities.

Each of these challenges represents a unique barrier to the realization of an all-LAI regimen for TB treatment. It is important to note that the development of any LAI formulation could be integrated into a combined LAI and oral regimen, which would still carry potential benefits such as reducing the number of times a person has to interact with the healthcare system, reducing the number of daily or monthly pills, or creating an all-long-acting continuation phase of treatment.

The Gates Foundation is leading the way for the early pipeline investments, including suspension formulations for anti-TB compounds and stabilization methods to support a four+ month treatment interval.[36, 37] These investments are largely focused on the innovations necessary to support the development of a multi-drug LAI or an all-LAI regimen. While these technologies are a long way off from generating applications that reach TB affected communities, they do represent the foundational research required to realize a longer-term vision of a long-acting regimen for TB that would precipitously reduce or eliminate the need for oral medicines.

Reactions and Drug-Drug Interactions

Unlike oral medicines, which can be ceased immediately if problems arise, once administered, LAIs remain active in the system for the entire course of coverage. LAIs do not allow for either treatment cessation or dose adjustment. In this context, managing drug-drug interactions and adverse reactions requires thoughtful consideration; trials must be designed to assess risks and implement safety measures to mitigate them.

Researchers are approaching this challenge from two angles. One angle incorporates oral lead-ins for a short period of the treatment regimen (e.g., two weeks, one-month) before administering the LAI — as is done with some LA antiretroviral drugs.[38] This approach allows clinicians to monitor for adverse events and drug-drug interactions while the active drug reaches target concentrations via the oral route. During the oral lead-in phase, cessation of treatment in response to adverse events is still possible. Another approach would deploy LAIs during the continuation phase of treatment, after treatment in the intensive phase with an all-oral regimen. Like an oral lead-in approach, an all-oral intensive phase would allow clinicians to monitor for adverse events and discontinue treatment as needed. The key difference between these two approaches comes down to how long the period of oral treatment is before LAIs are administered and what portion of the treatment timeline LAIs cover. Both approaches can offer a straightforward, effective way to ensure safety, comfort, and greater agency to those affected by TB when it comes to managing their condition and treatment within their lives.

Regulatory and Development Considerations

There are several outstanding regulatory questions for LA formulations given their unique position as long-acting versions of compounds that have or will have already undergone phase II and III clinical studies.

For TPT, the question is whether LAIs can easily skip phase II and move directly from phase I clinical trials to phase III. Oral TPT does not have phase II trials as there is no surrogate marker for the efficacy of TPT and TPT regimens have historically been repurposed TB treatment drugs. An LAI TPT formulated from existing drugs could do the same, as is planned with LA-BDQ moving from phase I to VITAL4ALL (phase III). Additionally, TPT regimens have had to satisfy a high threshold for safety and acceptability because they are taken by people who do not have TB disease and therefore feel healthy. This threshold may be even greater for a LA TPT regimen that cannot be ceased once administered, especially for regimens without an oral lead-in to monitor emergent adverse events. Future LA TPT studies may need to consider new approaches for evaluating the safety of LA formulations in advance of phase III trials in the absence of incorporating oral lead-ins or conducting phase II trials.

For LAI formulations of drugs or compounds with existing data from oral regimens, there is some optimism around the applicability of the United States Food and Drug Administration (FDA) 505(b)(2) mechanism, an FDA abbreviated approval pathway.[10] Under such applications, some of the data required for approval can be taken from studies not directly conducted by or for the applicant. In the case of LAIs, this may allow phase II and phase III safety, dosing, and efficacy data on the oral versions of LAI tools to be submitted for regulatory approval.[39] The LONGEVITY project is exploring this pathway for LA-isoniazid and LA-rifapentine based on early feedback from regulators and may provide a test case for the 505(b)(2) pathway for LAIs.[10]

Early and Continuous Community Engagement

As this report highlights, long-acting injectables for treatment and prevention of TB are very early in development, years out from introduction to communities. While this does mean that communities will need to wait to benefit from the potential advantages associated with LAIs for TB, it also means that advocates have ample latitude to shape the development of LAI products towards the needs and desires of their communities. At this early, preclinical stage, communities are well positioned to demand that all future clinical trials engage community advisory boards, include community members as investigators on trial teams, and interface directly with communities throughout and beyond the clinical trial period.

These long-acting technologies offer an opportunity to develop products with the complete implementation platform in view, with design, access, and feasibility addressed upfront, throughout the development process, and long before products are shipped to communities. The WHO's 2026 Target Regimen Profiles for LAIs for TB define safe, short, affordable, cold-chain-free, and decentralized LAI regimens, shaping the pipeline long before product features are locked in through the clinical development process.[2] Failure to engage communities while there is still ample room for them to shape the final products risks community acceptance and uptake of LAI products and undermines the potential to transform TB treatment and prevention for the better.

The Inclusion of Pregnant Persons and Children

As LA formulations move to clinical trials, researchers should make plans for the early inclusion of populations most vulnerable to TB and most in need of better prevention and treatment options, including children and pregnant and breastfeeding persons. As discussed in previous iterations of TAG's TB Treatment and TB Preventive Treatment Pipeline Reports, pregnant and breastfeeding people have been regularly excluded from clinical trials — dating back to before the introduction of isoniazid. Furthermore, the requisite safety studies for pregnant populations have often lagged significantly behind introduction of new TB tools, historically leaving pregnant persons and their doctors guessing at the risks to parent and child in receiving TB medications. In August 2025, the WHO published *Optimal and early inclusion of pregnant and lactating women in tuberculosis research: consensus statement*, which establishes a new norm for the assumed inclusion of pregnant persons in the absence of safety rationale for exclusion:

> *Pregnant and lactating women should be included in any clinical trials of TB drugs or regimens that are being developed for adult populations […] as the default approach, unless there is a clear and justifiable rationale not to do so.*
>
> *DART studies [should be initiated] as soon as the range of human exposures is available from Phase 1 or early Phase 2 trials, to support the inclusion of pregnant and lactating women in pre-licensure TB treatment and vaccine clinical trials […to] enable the enrolment of already pregnant and lactating women into late phase trials (or parallel substudies) to collect initial PK and safety data.*
>
> *— Optimal and early inclusion of pregnant and lactating women in tuberculosis research: consensus statement*[40]

This position is echoed throughout the recent WHO Target Regimens Profiles.[2] Inclusion in pre-licensure phase III trials would offer researchers the opportunity to conduct pregnancy-specific safety and PK studies to understand if any dose adjustments are necessary in pregnant persons, especially important in view of how dramatically bodies change during and after pregnancy.

All clinical trials investigating LATs for TB will begin protocol development and enrollment under the illuminating assumption of inclusion of pregnant persons, whether researchers will follow the guidance of the consensus statement remains a question. Other outstanding questions as to how we assess exclusion based on safety for new long-acting formulations in which treatment administration cannot be easily stopped remains contentious. Despite this, LAI formulations offer a rare chance to include pregnant persons as innovations are developing, thus accelerating access for people who experience increased risk of TB during pregnancy and the postpartum period. Pregnant and breastfeeding persons also have the advantage of regularly interacting with the health system where an LAI could be administered. This potential could be particularly potent for LAI formulations based on existing drugs and existing indications where safety in pregnancy is well characterized.

As with pregnant persons, children are often excluded from pre-licensure phase III clinical trials of new TB medicines or formulations, despite the increased risk that children face from TB disease. Early LAI preference and acceptability studies have revealed interest in the development of LAI formulations for children, stressing the existing challenges caretakers face in administering daily oral medicines to children.[2] However, data on the use of medicines in children often lag clinical trials for adults, and child-friendly formulations of adult medicines are slow to enter markets — leaving children without access to innovations that they, and their caretakers, may particularly benefit from. While researchers can determine pediatric efficacy of a drug from data in adults, pediatric-specific PK and safety studies are required to for inclusion in any phase III study. Ongoing work from researchers, regulators, and civil society is focused on developing a tool kit to shorten the time required to study the safety and efficacy of LAIs in children and ensure access as quickly as possible.[41] However, children (<12 years of age) are currently excluded from planned phase III trials of LATs. Further consideration of necessary steps to ensure early inclusion of children in phase III trials for novel LAI products is needed — failure to meaningfully weigh their inclusion risks leaving children behind as science advances.

Conclusion

LATs carry immense potential to expand treatment options for TB affected communities, reduce pill burden and engagement with healthcare systems, and even offer greater privacy to those undergoing treatment. While challenges and questions remain, if overcome, effective LAIs for TB carry the potential to reduce or eliminate pill burdens, shorten time under treatment, and reduce engagement with healthcare systems. They also are well positioned to complement TB vaccines, screening programs, and other novel tools and interventions to meaningfully shift the course of TB prevention. Continued investment in this space and early community engagement will determine the extent to which communities can benefit from long-acting technologies and how soon.

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