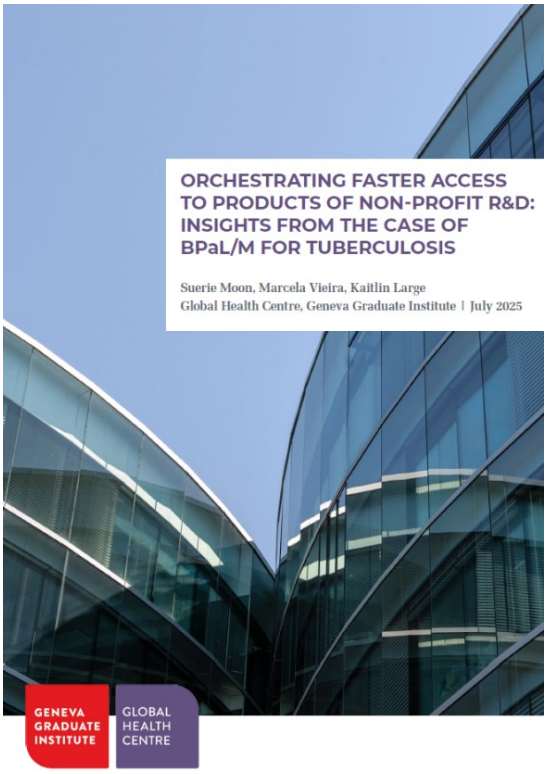
REPORT SUMMARY

Accelerating Access through Product Development Partnerships

TB ALLIANCE'S RAPID ROLLOUT OF MODERN DR-TB CURES HIGHLIGHTS OPPORTUNITIES FOR DONORS TO MAXIMIZE IMPACT

Summary of the Geneva Graduate Institute Global Health Centre report, *Orchestrating Faster Access to Products of Non-Profit R&D: Insights from the Case of BPaL/M for Tuberculosis*.

In global health, translating scientific breakthrough to real-world patient benefit is often where progress stalls. A case study by Geneva Graduate Institute (GHC) on TB Alliance (TBA), a non-profit product development partnership (PDP), shows how a PDP can orchestrate the many moving parts needed to turn an innovation into widespread access within a short time. In this case, it was the new drug, pretomanid, and the new treatment it was part of, BPaL/M, for drug-resistant tuberculosis (DR-TB) which was scaled up within two years of World Health Organization (WHO) programmatic recommendation, or five years from initial stringent regulatory approval. That speed is unusually fast in global health and holds lessons for donors seeking timely, equitable impact.



Prior to pretomanid and BPaL/M, the subject of this case study, innovations in DR-TB such as the new drug, bedaquiline, had taken 9 years or longer from initial approval to achieve widespread programmatic use, which we defined as achieving over 50% market reach.

In contrast, more than 150,000 treatments of pretomanid had been shipped to over 100 countries by Dec-2024 in two years since WHO's recommendation, representing over 85% of market need.

This is important because prior to BPaL/M, DR-TB was characterized by treatment success rates of 43-55% in programmatic settings and included debilitating toxicities. BPaL/M, with 90% success rates in trials and implementation research, presented a lifeline for people with DR-TB. Getting new and improved treatments to people with DR-TB was literally a matter of life and death; the faster BPaL/M reached those in need, the more lives would be saved.

How TB Alliance Rapidly Orchestrated Effective Access

TB Alliance has an organizational mandate to ensure its products are affordable, adopted, and available. The case study clusters TBA's access interventions that helped achieve that mandate into three mutually reinforcing tracks: (i) Regulatory & Normative Guidance, (ii) Market-Shaping for Affordability & Availability, (iii) Country-Level Implementation & Knowledge-Sharing.

Regulatory & Normative Guidance

TB Alliance sought U.S. Food and Drug Administration (FDA) approval for pretomanid as part of the BPaL regimen and simultaneously worked toward inclusion in WHO guidelines. While U.S. FDA approval was important to build confidence in quality of evidence from clinical trials and the manufactured product, inclusion in WHO guidelines was important to enable adoption in most low- and middle-income countries (LMICs) which usually follow WHO guidelines.

The U.S. FDA approved pretomanid in late 2019. The European Medicines Agency approved pretomanid in 2020. By mid-2020, WHO conditionally recommended it for use, but this guidance was limited to operations research and in the XDR-TB and pre-XDR-TB patient populations, a subset of the DR-TB population numbering about 10-12,000 people annually. TB Alliance continued further trials for BPaL while continuing to engage with WHO, as well as with Medicines sans Frontieres, which also generated additional evidence on BPaL and BPaLM from another study. These efforts resulted in WHO upgrading Its recommendation in late 2022. The new recommendation was for programmatic use of pretomanid and the BPaL/M regimens in almost all people with DR-TB (about 175,000 treatments annually). This shift set the stage for wider scale-up.

Market-Shaping for Affordability & Availability

Licensing: To ensure sustainable global supply and encourage competition in LMICs, TB Alliance granted five non-exclusive licenses to manufacturing partners: Viatris, Macleods, Lupin, Hongqi, and Remington.

Pricing: TB Alliance negotiated an LMIC launch price of $364/treatment for pretomanid with Viatris. This price was 60-80% below access prices for bedaquiline and delamanid at the time of those product launches but, pretomanid was only approved for use in a smaller subset of the DR-TB market – those with highly drug-resistant TB. In advance of WHO expanded guidelines for programmatic use in nearly all DR-TB, TB Alliance worked with MedAccess to provide Viatris a volume guarantee resulting in a price drop of 34% to $240 per treatment. This brought the cost of the full BPaL/M regimen substantially closer to the $500 price point long desired by the TB community.

Economic Evidence: Price reductions were complemented with robust pharmacoeconomic evidence. TB Alliance and partners published studies on feasibility, cost-effectiveness, and budget impact to demonstrate to country decision makers that adopting BPaL/M was financially advantageous in diverse country settings. TB Alliance also created SLASH-TB, a free software tool that enabled countries to estimate their own cost savings and reduce budget uncertainty when transitioning to the new regimen – without investing in expensive and time-consuming Health Technology Assessment exercises.

Country-Level Implementation & Knowledge-Sharing

TB Alliance engaged several countries during clinical development of BPaL to understand local requirements and pre-requisites for implementation, including through landscaping, feasibility and acceptability studies in several representative high-burden countries. This allowed identification of potential early-adopters and influencer countries.

Following WHO guidance for operational research in May 2020, TB Alliance kicked off the LIFT-TB project within five months, in October 2020, to carry out operational research (OR) in seven high-burden countries to prove replicability of clinical trial results and feasibility in real-world settings. Immediately following updated WHO programmatic use guidelines in December 2022, the OR programs concluded, and countries supported national guideline changes and transitioned to scale-up. Two months later, in February 2023, the first country, Ukraine, updated its guidelines and other countries followed soon after.

TB Alliance enabled or launched a series of initiatives to support global advocacy and scale-up: A call-to-action by WHO and partners rallying countries and stakeholders to switch to BPaL; the BPaLM Accelerator by WHO that brought all countries and key partners into monthly meetings to take stock of and discuss BPaL/M roll-out; Fast Track the Cure, a community-led program in collaboration with the Stop-TB Partnership that mobilized communities for demand creation; and later, the PeerLINC Knowledge Hub that trained National TB programs and experts on BPaL/M worldwide.

The consistent approach was to plan long ahead, execute rapidly, and adapt to changes.

GHC identified **five attributes** that enabled TBA to orchestrate the above effectively:

1. Deep product/regimen knowledge and evidence generation,
2. Non-profit legitimacy,
3. Ability to mobilize resources for access,
4. Collaborative relationships with countries, WHO, funders, manufacturers, communities,
5. Mission-driven motivation to ensure the product reaches people who need it.

Lessons Learned and Implications for Donors

The speed and scope of pretomanid and BPaL/M access was substantially greater than historical norms in the field, and some key takeaways emerged providing insight into how future new product access efforts could get life-saving technologies to those who need them even faster and more efficiently.

- **Synchronize evidence needs earlier.** Despite U.S. FDA approval in 2019, WHO's initial operations research-only guideline and need for more evidence before the eventual 2022 programmatic guidance underscores the need for earlier, larger, multi-country pivotal trials designed to meet both regulatory and WHO standards. This would require greater financing but could reduce the time to global policy development and speed impact.
- **De-risk supply sooner.** Despite TB Alliance having licensed a second supplier early on, WHO Prequalification (PQ), an essential process to ensure highest quality product, took two years for approval, resulting in supply bottlenecks during rapid scale-up in early 2023. Funding and planning for multi-supplier PQ earlier could prevent such bottlenecks and more quickly induce price competition. Thankfully, the volume guarantee announced in December 2022 mitigated the lack of generic competition.
- **Resource the access phase, not just R&D.** Typically PDP donors fund research and development. But PDPs are also uniquely positioned to drive the access work that turns scientific breakthroughs into lives saved and improved. This access work also needs explicit, predictable funding, so future product introductions can continue to be rapid and global.

How to Ensure PDPs are Engines of Access and Impact and Maximize ROI

The BPaL/M experience supports a straightforward investment thesis: *When PDPs are resourced to orchestrate access across global policy and implementation, they can drive rapid, widescale, and efficient product uptake*. This requires:

1. Organizational mandates that include access as a core commitment and function,
2. Flexible funding to implement access work early and in parallel (not sequentially),
3. Dedicated budgets for country readiness, evidence generation, and supply diversification, well before guideline changes happen.

The three ingredients would dramatically reduce the gap between scientific breakthroughs and life-saving impact, as well as ensure that return on investment for funders is realized more quickly and maximized.