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Agenda item 8

Area for Intervention:

Accelerate and promote responsible introduction of new DR-TB drugs and regimens

TB programmatic priority: Accelerate access to new drugs and regimens

For Information ☐ **For Review and Advice** ☐ **For Decision** ☒

Contents

1. Purpose of this document

This Area for Intervention (AfI) outlines a priority investment opportunity for accelerating and promoting responsible introduction of new drug-resistant tuberculosis (DR-TB) drugs and regimens, for Executive Board endorsement.

2. Introduction

Newly recommended and pipeline regimens could fundamentally change drug-resistant (DR) TB care. One regimen, BPaL/M[1], was recommended by WHO in late 2022, cutting treatment time by 50%. Additional pipeline regimens include those investigated in Unitaid's endTB project, for which evidence is anticipated to be available as early as Q3 of 2023. Key drugs in these new and pipeline regimens include bedaquiline, pretomanid, and delamanid.

Responsible, equitable access to these drugs is essential to realizing their lifesaving potential, while guarding against the rise of drug resistance. With introduction efforts already underway in major high-burden countries, governments and other stakeholders involved in the global response are joining with WHO in supporting a Call to Action to accelerate the implementation of the novel, 6-month all-oral regimen for the treatment of drug-resistant tuberculosis.[2] The drugs included in this new regimen will feature increasingly in the next generation of TB regimens. Although Unitaid and partners such as the Global Fund and USAID are engaging and discussing the strategies for timely and broad access to the regimen, several gaps and challenges remain.

As outlined in this AfI, Unitaid is in a strong position to lead specific efforts to address some of these gaps in the response. During the development of Unitaid's new strategy, consultations with country stakeholders, community and civil society representatives, funders, and other partners informed Unitaid priorities in TB. The resulting three programmatic priorities focus on: enabling TB prevention tools, accelerating TB detection tools, and accelerating the adoption of new drugs and regimens.

Despite modest gains in the last decade, DR-TB treatment has remained arduous with patients having to endure high burden of pills and, in some cases, injections for up to 24 months. Mortality has remained high with 191 000 deaths in 2021 (among an estimated 450 000 incident cases).

The first new TB drug to reach the market in seven years, pretomanid received its first marketing authorization from the US FDA in 2019. BPaL/M has proven to be an effective cure with 6 months of treatment, with fewer pills and no injections. Based on growing evidence, in December 2022 the WHO broadened its recommendations for BPaL/M to be the primary treatment for DR TB, noting that "*the newly recommended BPaLM regimen offers better outcomes, remarkably shortens the duration of treatment, and thus significantly improves quality of life for people with MDR/RR-TB*".[3]

Interventions to reduce the price of key TB medicines will be key to timely, equitable access – but should be accompanied by efforts to grow demand responsibly with linkages to vital adherence and drug-susceptibility

[1] Pretomanid, combined with bedaquiline, linezolid, and/or moxifloxacin
[2] WHO CALL TO ACTION: Shorter and more effective treatment for all people suffering from drug-resistant TB, 21 March 2023. https://cdn.who.int/media/docs/default-source/hq-tuberculosis/call-to-action_shorter-and-more-effective-regimens-for-all-people-suffering-from-drug-resistant-tb.pdf?sfvrsn=30dbefbe_6&download=true
[3] WHO consolidated guidelines on tuberculosis. Module 4: treatment - drug-resistant tuberculosis treatment, 2022 update, 15 December 2022. https://www.who.int/publications/i/item/9789240063129

testing (DST) support, to avoid losing these drugs to resistance before they can reach their full, lifesaving potential. This is all the more important given the setbacks in TB as a result of the COVID-19 pandemic, as well as the use of novel drugs in other, ongoing clinical trials for other shorter TB regimens.

3. Public health challenge and key access issues

During the COVID-19 pandemic, the TB burden reached an estimated 10.6 million cases in 2021, with an increase in incidence and mortality rates, reversing 20 years of progress. The burden of drug-resistant TB (DR-TB) is also estimated to have increased in 2021, reaching 450,000 new cases of rifampicin-resistant TB. Despite the introduction of bedaquiline in 2012 and delamanid in 2014, and an expectation of rapid adoption of shorter, less toxic and more effective treatments for DR-TB, broad coverage with the best available treatments is still suboptimal. Key access barriers include unaffordable prices, delays in revision and adoption of global and national guidelines, IP-related barriers to generic entry, limited registration in LMICs and procurement. Combined with low rates of diagnosis, these factors result in continued small volumes and demand.

The pandemic has had a major impact on TB, decreasing case detection and reducing the number of people on treatment. TB continues to be one of the largest contributors to the crisis in antimicrobial resistance (AMR). To reverse setbacks and to address the growing problem of drug resistance, improving detection tools and accelerating responsible adoption of new drugs have become high priority. In 2022, Unitaid invested in two new projects to accelerate access to detection tools, helping ensure that those diagnosed with TB – including drug-resistant forms – can receive the care they need and access the best possible treatment. Now, Unitaid is well positioned in alignment with other partners, including key scale-up partners such as the Global Fund and USAID, to leverage its investments across the TB portfolio and to address specific gaps in the response as it relates to the new DR-TB regimens being introduced and ensuring all key populations are considered and included.

4. Potential opportunities to accelerate adoption of new TB drugs and regimens

In February 2023, the WHO Global TB Programme launched the BPaL/M Accelerator Platform to facilitate coordination amongst partners and included the subsequent launch of a Call to Action for World TB Day on March 24. Efforts to enable roll-out and scale-up of the new regimen are just getting underway with an acknowledgement amongst Unitaid, partners, and other stakeholders that there are several gaps that need to be addressed if the coordinated response will be successful including the consideration of conditions that will also support other new regimens emerging from the pipeline.

4.1. Opportunities for responsible scale-up efforts with expansion of quality of care

Near-term opportunities exist to close gaps in the response, notably: reducing pricing to meet affordability targets set by the global TB community; securing adequate and sustainable supply; introducing the new regimen as part of a comprehensive care package; ensuring efficient and effective coordination on supporting implementation efforts in LMICs; linking TB detection and treatment efforts to enable adequate testing and resistance monitoring; and providing evidence to ensure alternative treatment options for those patients not eligible for BPaL/M.

Along with its issuance of new recommendations for BPaL/M, WHO stated that it "*welcomes new initiatives by the public and private sectors to reduce the pricing of pretomanid and potentially other component medicines – that will lower the cost of the new BPaL/BPaLM treatment regimen and make it more accessible*."

According to Médecins Sans Frontières (MSF)'s Access Campaign in their *8th edition of the DR-TB Drugs Under the Microscope* report[4], market interventions to date are insufficient to reduce price for the key components of the new regimens to achieve affordability targets of at or below US$500 to foster rapid uptake. Fair price targets are informed by estimated costs of active and inactive pharmaceutical ingredients, formulation, packaging, and a cost-plus model, which includes a reasonable profit margin. Further engagement with country stakeholders and scale-up partners can be undertaken to validate willingness to pay if fair price targets are achieved.

Price drivers for the newly recommended DR-TB regimen are pretomanid and bedaquiline – and delamanid for childhood TB treatment and emerging alternative regimens. For reference, the current prices for these drugs were those listed on the Stop TB Partnership' Global Drug Facility Catalogue. Bedaquiline, at US$270 for a 6-month treatment course, is almost three times more expensive than it could be (US$ 102 considering a cost-plus model as outlined above). Also, access to bedaquiline at a fair price is hindered by intellectual property barriers. Even though bedaquiline will go off patent in 2023, secondary patents in several countries, as well as inaccessibility of originator samples for studies needed for quality generics hinder generic entry and competition. Pretomanid has had recent reduction in price negotiated between TB Alliance, Viatris and MedAccess but the agreement is not yet executed, and its price still exceeds the potential cost-plus target of US$ 180. For delamanid, access is hindered by lack of affordability, restricted registration and access in LMICs. Generics are poised to enter the market but may require incentives and demand-side interventions.

Many country programmes have indicated interest in adopting the newly recommended BPaL/M regimen into national TB programs, although many of the high burden countries that could benefit most lack some of the infrastructure or key tools that could support effective introduction and scale. There is a real concern that not ensuring appropriate stewardship and not guarding against the development of resistance against the drugs in the new regimens could give rise to AMR. Modelling efforts and clinical research (in the process of publication) are more and more demonstrating the link between adherence and proper DST to positive outcomes and informing treatment strategies. These concerns could be addressed in part by implementing tools such as digital technologies for adherence, diagnostics including DST to define the best regimen for an individual, and safety monitoring to optimize use of the drugs and give health providers more confidence in administering the medications.

An additional opportunity is to ensure improvements in DR-TB treatment for all people with DR-TB. Only 50% of those with DR-TB are anticipated to be eligible to receive BPaL/M. Notably, this regimen excludes key populations such as children, adolescents, pregnant and breastfeeding women, and people with bedaquiline resistance and allergies. To address these subgroups, further support is needed for evidence to support WHO guidelines that would provide alternatives to BPaL/M such as delamanid-containing or linezolid-sparing regimens.

Overall, there is a recognition that these efforts require strategic partnering and coordination at the global, reginal, and national levels. To underpin all these interventions and efforts, it is pertinent to ensure that civil society and communities are taking the lead to raise awareness, educate across providers and users, and generate demand for the treatments and supportive tools.

[4] New MSF report warns that major opportunity to increase access to newer, safer DR-TB drugs is at risk, November 8, 2022. https://msfaccess.org/new-msf-report-warns-major-opportunity-increase-access-newer-safer-dr-tb-drugs-risk

5. Partner engagement

Unitaid is a key thought partner in this area and is actively involved in the WHO BPaL/M Accelerator Platform, and other coordinating efforts like the TB Procurement and Market-Shaping Action Team (TPMAT) led by the Stop TB Partnership Global Drug Facility. In addition, Unitaid has held several consultations and received inputs from key partners on the areas in most need of intervention related to the roll-out of the new 6-month regimen including the Global Fund, USAID, Bill and Melinda Gates Foundation (BMGF), Stop TB Partnership, TB Alliance, MedAccess, Medicines4All, community delegations and representatives, and generic manufacturers. All have been supportive of potential Unitaid work in the areas outlined below and indicated alignment with their own efforts in the response.

6. High potential opportunities for Unitaid investment

The BPaL/M regimen is poised to be a transformative treatment for DR-TB and contains two new drugs, bedaquiline and pretomanid, that may form the 'backbone' of new regimens in development for all forms of active TB. Complementarily, delamanid, a drug in the same class as pretomanid, has proven vital to DR-TB treatment in children and as the potential to offer alternatives where BPaL/M is not indicated. On each of the identified areas of opportunity - market shaping, implementation, and demand creation - Unitaid is poised to intervene, leveraging its existing investments and undertaking new work as required.

The intervention needed for timely introduction and access to better shorter regimens for DR-TB is three-pronged: 1) Market-shaping: Reduce price of component drugs of BPaL/M and other shorter regimens and secure adequate supply 2) Implementation: Expand geographical scope of adoption and uptake efforts including expansion of better regimens for key populations excluded from BPaL/M and 3) Demand creation: Support efforts to catalyse scale-up including responsible product introduction and a comprehensive care package.

6.1 Market-shaping: Reduce price of component drugs of BPaL/M and other shorter regimens and secure adequate supply

Alongside the WHO guidelines update announcement in December 2022, the TB Alliance, Viatris and MedAccess announced a price reduction[5] for pretomanid 200mg tablets, one of the constituent medicines in the new regimen. With this price reduction, the price for the new BPAL/M regimen ranges from US$588 – US$650 (EXW) per patient's 6-month regimen (see Table 1 below).

[5] https://medaccess.org/news/price-reduction-paves-the-way-for-expanded-access-to-highly-effective-multidrug-resistant-tuberculosis-treatment/

Table 1: Price Breakdown of different options for the BPAL-M regimen (Source GDF and WHO)

Current Prices							
						Cost/patient (US$)	
	daily dose (mg)	tabs	weekly	duration	Total tabs	Low	High
Bedaquiline, 100 mg tabs	400	4	7	2			
	200	2	3	24	200	$ 289.36	$ 361.70
OR							
Bedaquiline, 100 mg tabs	200	2	7	8			
	100	1	7	18	238	$ 344.34	$ 430.43
Pretomanid, 200 mg tabs	200	1	7	26	182	$ 240.03	$ 240.03
Linezolid 600mg tabs	600	1	7	26	182	$ 30.99	$ 38.29
Moxifloxacin 400mg tabs	400	1	7	26	182	$ 27.30	$ 29.12
B-PALM Regimen 1 (Bedaquiline 3ce weekly)					**746**	**$ 587.69**	**$ 669.14**
B-PALM Regimen 2 (Bedaquiline daily)					**784**	**$ 642.67**	**$ 737.87**

While the price reduction of pretomanid was an important step, barriers to access persist. The affordability target has still not been met based on MSF Access report and targets referenced earlier. Related to this is the lack of generic competition; for example, limited scope of voluntary licenses, and secondary patents filed by the originator of bedaquiline (and delamanid) that prevent generic manufacturers from entering the market when the primary patent expires in 2023. Reducing the dependency on originators, and the barriers to generic entry, will allow for a diverse, competitive supply base that will stabilize the market for these key drugs (bedaquiline, pretomanid, and delamanid) and subsequently lead to more affordable, fair pricing.. This will not only impact and support scale-up of BPaLM but any emerging regimen in the short- or long-term using these drugs, which are considered the backbone of many regimens in the pipeline.

In line with the above conclusions, a combination of the following interventions could be done:

1. Validation exercise of demand and supply for the newer shorter regimens and component drugs to inform the market interventions.

2. An early market access vehicle such as a demand-driven catalytic procurement to bring generics into the market to achieve a price target of US$1 per day or below for pretomanid and possibly bedaquiline, while ensuring a healthy market of at least two quality assured suppliers of the product.

3. Collaboration with civil society and complementary Unitaid projects to address IP-related barriers and encourage voluntary licensing or nonenforcement of patents, supporting generic entry and competition for bedaquiline and delamanid.

4. Additional cost-reductions through enabling more optimized and/or ecologically friendly manufacturing processes for the component drugs of newer shorter regimens.

These interventions could be informed in collaboration with actors such as the TB Procurement and Market-Shaping Action Team (TPMAT) members, the Global Fund, and key governments like South Africa and Brazil, and through Unitaid's existing grantees such as KNCV, Aurum and CHAI.

6.2 Implementation: Expand geographical scope of adoption and uptake efforts

There are already key efforts underway that could be leveraged and further enabled to support the objectives of successful, responsible and broad-scale implementation of the BPaL/M regimen in high burden countries.

- The LIFT-TB study, which is an operational research study funded by Korea International Cooperation Agency (KOICA) and TB Alliance, has already worked to create evidence to support BPaL/M adoption in several countries with partners KNCV, PATH, International Tuberculosis Research Center, and other in-county stakeholders.

- The Unitaid-funded ASCENT TB Project led by KNCV is leveraging today's smart information and (mobile) communication technologies to support TB patients with their treatment in a modern and more effective way through the use of digital adherence technologies such as smart pill boxes, medication sleeves and video supported treatment. The project is generating evidence, establishing a global market, and engaging stakeholders to make future scale up possible so that these digital innovations can be available to all TB patients worldwide.

- The Unitaid-funded Seq&Treat Project led by FIND is enabling the use of next-generation sequencing to ensure the appropriate data on resistance is available to facilitate clinical decision making and assignment of the best treatment regimen.

- The Unitaid-funded endTB Project led by Partners In Health and MSF is generating clinical evidence on bedaquiline and/or delamanid-containing regimens that could offer alternative regimens including for those not indicated to receive the BPaL/M regimen.

- Other notable and relevant Unitaid-funded work – 1) BENEFIT Kids Project led by Stellenbosch University which is optimizing dosing and developing child-friendly formulations and approaches to treat children with DR-TB and 2) DriveDx4TB led by FIND and START4ALL led by Liverpool School of Tropical Medicine which is improving TB detection by bringing key diagnostic solutions to the primary and community level.

There is an opportunity to leverage some of this work to bring the additional linkages and support required for the adoption and scale-up of the new regimens in **6-7 countries who would be targeted for direct intervention related to the new regimens linked with a supportive care package of adherence and diagnostic/DST support**. The specific countries would be chosen based on being 1) where ASCENT TB, Seq&Treat, and/or LIFT-TB coincide 2) priority as a high-burden DR-TB country 3) motivated to introduce the new regimens alongside adherence support, and DST and/or 3) influential to drive markets and volumes (see Annex). In addition, even though Brazil is not a high-burden country for DR-TB, there is the opportunity to use its positioning and its ongoing partnership with Unitaid to enable the roll-out of BPaL/M along with adherence and DST in the country and the priority countries it supports (i.e., Angola, Mozambique).

In addition, given the excluded groups for whom BPaL/M is unable to be an option, there is opportunity to support the adoption and integration of any additional recommendations (resulting from the data from endTB for example), expanding ASCENT TB work in target countries to address these groups. For children, there is also an opportunity to generate evidence to allow for an equivalent 6-month regimen for DR-TB that could leverage the experience and work of the BENEFIT Kids Project. There could be partnering with USAID's SMART4TB[6] on this additional evidence generation.

[6] In August 2022, USAID announced an up to US$200 M 5-year initiative called SMART4TB to enable research that identifies more effective methods and tools for finding, treating, and preventing TB. KNCV (also EGPAF and TAG) is part of the consortium.

6.3 Demand Creation: Catalyse scale-up ensuring responsible product introduction

To further catalyse efforts around BPaL/M and other shorter regimens in the pipeline there is agreement on the need to introduce the regimen as part of a quality package of care. This suite of tools could be outlined in guidance to countries indicating best practice in operationalization of the treatment, links to diagnosis and DST, adherence support and safety and treatment monitoring. In addition, there is a continued gap in demand creation to complement the market shaping interventions. Through engagement with partners, the Unitaid Secretariat has mapped many synergies in partner activities that could be coordinated and leveraged through Unitaid-funded efforts.

As indicated, Unitaid could expand not only the work of the ASCENT TB project, but to also efforts of our diagnostic work specifically the Seq&Treat Project, which could add the capacity to test for resistance to the drugs pretomanid and delamanid for which no rapid DST is available. In addition, partner coordination and collaboration is essential so that partners are providing the same message and package of care to all implementing countries. This can be done through various existing coordinating mechanisms as well as partnering on technical communications and convening at the regional and national levels.

Engagement of civil society and communities will be key for overall roll-out success and demand creation. The work of initiatives like IMPAACT4TB[7] and the community advisory boards[8] of ASCENT TB could be engaged on demand generation activities and community engagement to further timely access and responsible scale-up. As part of demand creation activities and building on existing community efforts, Unitaid and its partners (i.e., USAID, Stop TB Partnership, Global Coalition of TB Advocates) could incorporate and leverage approaches such as small grants, community led monitoring, and tools to inform advocacy and other activities to address issues around regaining momentum on TB targets, combating drug resistance, overcoming stigma while supporting the TB community to engage in their own health.

Another group to work with in this regard is the WHO's Civil Society Task Force on TB, a collaboration mechanism to mainstream and amplify civil society and affected communities' voices in decision making, policy, programmes and activities at global, regional and country levels, advocate for increases in domestic funding, sharpen focus on vulnerable populations, engage in TB research, and identify social, legal and gender barriers to care and define solutions.

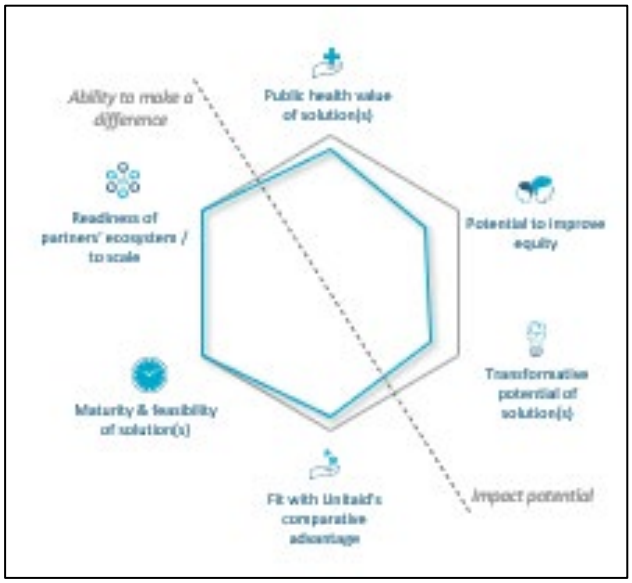
In summary, there are actionable opportunities with high potential for Unitaid investment. Much is in motion to ready the way for a full scale-up of BPaL/M although many unaddressed gaps threaten success. This year 2023 is critical for initiating and moving swiftly to ensure Unitaid's involvement, so many opportunities will not be missed to ensure responsible roll-out of this regimen and pave the way for new TB regimens and drugs emerging from the pipeline. Given the success and impact that could be leveraged from the ASCENT TB and the Seq&Treat projects, as well as strategic and operational relevance to the work required, these investment vehicles could move on some of the opportunities presented with costed extensions for implementation, responsible product intro and some demand creation. The Unitaid Secretariat could also be positioned to intervene directly and indirectly (i.e., market interventions, coordination efforts) through these projects to ensure key short-term objectives in the response are met. To be most effective, these investments would be best initiated by end of Q2 2023 with close coordination

[7] The IMPAACT4TB led by the Aurum Institute is catalyzing scale-up of new TB prevention (3HP and 1HP) and are building significant community engagement networks around demand creation.
[8] https://www.digitaladherence.org/the-community-advisory-board-for-the-ascent-project-is-established/

on transition and planned hand-offs to allow for further implementation and scale-up by partners such as Global Fund and USAID, and involved governments. For other objectives still within the scope of the response for the initial roll-out, there is opportunity to address evidence gaps and support civil society and communities in demand creation through a competitive call for proposals to be launched later in 2023.

7. Assessment of the opportunity

7.1. High impact potential, including public health value of the solution, potential to improve equity, and the transformative potential of the solution



Effective treatment of DR-TB requires use of several drugs in combination for an adequate period. Newer, shorter, less toxic BPaL/M and alternative regimens have the greatest potential for impact at present and will transform the TB response. There already exist WHO recommendations on BPaL/M, but these recommendations exclude the use for pregnant and breastfeeding women, children and adolescents and people with bedaquiline resistance. Alternatives to the new regimen can allow access to similarly effective treatment in these groups.

Public health impact: The primary impact of the project is to reduce DR-TB cases and deaths by effectively treating DR-TB disease and breaking the chain of transmission. Rapid and responsible introduction and scale up of BPaL/M and better outcome of treatment are the key drivers of impact. Between 2023-2030, Unitaid's investment in DR-TB treatment has the potential to enable access to BPaL/M to 281,500 [161,000 – 421,000] additional people, mostly as a result of proposed market shaping and country engagement activities. Use of adherence technologies along with scale up of BPaL/M and alternative regimens could result in successful treatment of up to 8% of the global estimated cases and avert close to 65,000 person-to-person DR-TB infections at scale in 2030. A quality of care package has the potential to increase the treatment adherence and therefore treatment success by 20%, resulting in additional 221,500 [192,000 – 237,000] people successfully treated by 2030.

Economic impact: With successful market interventions to bring the price of the BPaL/M regimen down to a total of $450 per patient course ($400 for BPaL/M and $50 for digital adherence technologies), there is a potential to save up to $172m by 2030. Further, substantial savings are expected from reduction in infections and higher treatment success rates. These savings could be repurposed for furthering responsible treatment of the DR-TB cases. Eliminating catastrophic costs faced by TB-affected households by 2030 is a key target of WHO's End TB Strategy. WHO's Global TB Report 2021 shows that 45% of TB-affected households and 87% of DR-TB affected households incur catastrophic costs.[9] It is anticipated that increased access to new

[9] Catastrophic costs are defined as total TB-related out-of-pocket costs plus lost income equating to more than 20% of a household's annual income.

favourably priced and more effective DR-TB treatment regimens have the potential to substantially reduce the cost of treatment and care for households.

Equity: The equity argument for the investment in DR-TB regimens is strong. MDR-TB affects the most vulnerable people in society who have a very high risk of death without access to treatment and treatment adherence support. The risk of death increases by 92% among HIV-positive patients and in poor populations, with undernutrition and low body weight raising the risk of death by more than 300%.

The proposed interventions contribute directly and indirectly to the fight against AMR. It is estimated that drug-resistant strains of TB will account for 25% of the AMR-related deaths and cost the global economy $16.7 trillion by the year 2050.[10] The work and learning resulting from this AfI could therefore have substantial direct impact by reducing DR-TB – but also act as a bellwether to better tackle and find solutions to emerging resistance to antibiotics.

7.2. Ability to make a difference, including fit Unitaid's comparative advantage, maturity and feasibility of the solution and readiness of partner ecosystem

Unitaid is strongly positioned to make a difference and planned efforts strongly fit Unitaid's comparative advantage, given Unitaid's extensive experience funding multi-country implementation pilots for TB diagnostics, prevention, and treatment. There exists already strong partner and community engagement directly with the Secretariat and through our implementers. The timing also aligns with the short-term interventions included in Unitaid's programmatic priority on TB treatment, fitting with Unitaid's overall planned investments to accelerate adoption of new TB drugs and regimens. This work builds on Unitaid's previous and active investments in accelerating tools to drive TB detection, enabling preventive TB treatment in high-risk groups, and enabling new, better, shorter treatments for MDR-TB.

7.3. Risk

The opportunity has a low to moderate risk profile. The strategic risks are low, given the opportunity's high relevance to public health, the maturity and viability of the new regimen and the readiness of partners and countries to adopt and scale new regimes in a programmatic approach. A moderate investment is needed to add value to the response and address identified gaps. Our existing grants can be leveraged for much of the work. There is a moderate implementation risk, given barriers to affordability and supply; also it is unclear how much consensus we can achieve on the supportive package needed for implementation despite significant partner buy-in. For scalability, while the intervention is linked to WHO and partner activities, price and user and/or provider hesitancies related to perceptions of the regimens may impede or slow uptake.

7.4. Cost and level of effort

The intervention as proposed is estimated to cost approximately US$30 million based on this type of product introduction work, with approximately 50% of the investment anticipated to be committed in 2023 to support country implementation of BPaL/M in 6-7 countries through costed extensions of ASCENT and Seq&Treat and any market interventions, and the balance to be committed in 2024 to support additional evidence generation and demand creation activities solicited through a call for proposals.

[10] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6361324/#R3

Annex: Table 2: Points of leverage and considerations for country selection based on work of Unitaid-funded projects

Country	On 30 HBCs list DR-TB	KNCV (ASCENT)	KNCV (Via LIFT-TB)	FIND Seq&Treat	endTB
Armenia					X
Bangladesh	X				X
Belarus					X
DPR Korea	X				X
Ethiopia		X	X		X
Georgia					X
Haiti					X
India	X			X	X
Indonesia	X		X		X
Kazakhstan	X		X		X
Kenya				X	X
Kyrgyzstan	X		X		X
Lesotho					X
Mozambique	X		X		
Myanmar	X		X		X
Nigeria	X		X		
Pakistan	X				X
Peru	X				X
South Africa	X	X			X
Tanzania		X			
Philippines	X	X	X		
Ukraine	X	X	X		
Uzbekistan	X		X		
Viet Nam	X		X	X	X