

## Tuberculosis Drug Development Ensuring People Living with HIV Are Not Left Behind

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An unprecedented number of new tuberculosis (TB) medications are currently in development, and there will be great pressure to deploy these new drugs among all populations after their efficacy is demonstrated. People living with HIV experience a large burden of TB and have a particularly pressing need for TB treatments that are shorter and less toxic. In addition, all people living with HIV now require antiretroviral therapy during TB treatment. A roadmap of the research, programmatic, and regulatory considerations includes the following: (1) inclusion of people living with HIV early in clinical trials for treatment and prevention using new TB medications, (2) prioritization of key studies of HIV–TB drug interactions and interactions between new TB agents, and (3) optimization of clinical trial infrastructure, laboratory capacity, and drug susceptibility testing.

**Keywords:** tuberculosis; HIV/AIDS; drug development

After a 40-year hiatus in the development of novel antimycobacterial agents, numerous new tuberculosis (TB) compounds are in the pipeline, generating renewed optimism for the control and eventual elimination of TB. Several of these agents are already in phase II clinical trials (Table 1), and many additional agents are in earlier animal and phase I human studies (1). However, despite the enormous burden of TB among people living with HIV, this population is poised for delayed access to these agents. Patients with TB with advanced HIV and those taking antiretroviral therapy (ART) are often excluded from clinical evaluations of new TB medications or treatment strategies, in part to avoid the issues of overlapping drug toxicities and drug–drug interactions (Table 2).

People living with HIV are at the highest risk of TB disease and mortality and have a dire need for less toxic, shorter TB regimens that can be taken with ART (2). ART should be given during TB treatment regardless of CD4<sup>+</sup> cell count for all HIV–TB coinfecting patients to reduce mortality (3), and three recent studies support immediate initiation of ART for those with very low CD4<sup>+</sup> counts (<50 cell/μl in two studies) to reduce death and AIDS progression (4–6). Therefore, ART has become

a necessity during TB treatment, including during the intensive phase of TB treatment in advanced HIV. ART–TB drug interaction studies and HIV-infected persons on ART must be included early in the TB drug development process to ensure new TB medications can be safely used in the HIV-infected population. Restricting studies of new TB strategies to HIV-uninfected populations will either put many with HIV infection at risk for unanticipated side effects or suboptimal efficacy when new TB drugs become available or result in unnecessary delays in use of novel TB therapies if a sequential approach in evaluation is required. In this viewpoint, we argue that unnecessary delays in HIV-coinfecting patients accessing new TB agents can be averted if research, regulatory, and public health bodies proactively plan for necessary HIV–TB drug–drug interaction studies, inclusion of HIV-infected individuals in clinical trials, and expedited access to effective agents.

### RATIONALE TO INCLUDE PEOPLE LIVING WITH HIV IN EARLY STAGES OF TB DRUG DEVELOPMENT

The tremendous burden of TB in HIV-infected patients alone merits evaluation of new TB agents in this group. TB is the leading cause of death in HIV infection worldwide, accounting for almost one quarter of estimated HIV deaths in 2009 (7). Death rates in people living with HIV with drug-resistant TB remain shockingly high, with 1-year mortality rates of 71% for multidrug-resistant TB (MDRTB) and 83% for extensively drug-resistant TB (XDRTB) in a recent South African series (8). Some 15 to 35% of patients with MDRTB fail to achieve sputum sterilization despite appropriate therapy (9–11), underscoring the need for more potent MDRTB regimens. Acknowledging that many factors contribute to the high mortality rate in HIV–TB coinfection, such as other AIDS-related illnesses, delays in TB diagnosis, and failure to use ART, inadequate TB drug potency and the complexity of delivering HIV–TB care to millions of patients are also major contributors to the high mortality rate (12). Shorter, more potent regimens will be key to reducing HIV–TB mortality in drug-resistant TB and to ease the burden on already overwhelmed healthcare systems, improve efficacy, and lessen TB–ART drug interactions in drug-sensitive TB.

Another reason to include people living with HIV early in TB drug development is that HIV infection, independent of ART coadministration, causes physiologic alterations that impact the safety and efficacy of TB drugs. For example, intermittent rifapentine and rifabutin are associated with treatment failure due to acquired rifampin resistance in HIV-infected patients with TB but not HIV-uninfected patients (13, 14), attributable in part to lower rifamycin levels attained in HIV infection (15–17). Conversely, the combination of pyrazinamide and rifampin for treatment of latent tuberculosis infection (LTBI) was well

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**TABLE 1. TUBERCULOSIS DRUGS IN CLINICAL DEVELOPMENT**

Classes of TB Agents	Drug Target	Examples
Diarylquinolines	ATP synthase	TMC207
Ethambutol derivatives	Mycobacterial cell wall	SQ109
Fluoroquinolones	DNA gyrase	Moxifloxacin, gatifloxacin
High-dose rifamycins	RNA polymerase	Rifampin, rifapentine
Nitroimidazoles	Lipid and protein synthesis	OPC67683, PA824
Oxazolidinones	Protein synthesis	PNU100480, linezolid, AZD5847

Data from References 33 and 57.

tolerated in HIV-infected patients but associated with two to three times higher rates of severe hepatotoxicity in the HIV-uninfected persons (18).

Promising TB regimens should be evaluated early in people living with HIV on ART to ensure compatibility with commonly used HIV medications. ART interactions with current TB drugs are a major limitation to effective HIV-TB treatment. Coadministration of rifampin with nevirapine (NVP), the most commonly used nonnucleoside reverse transcriptase inhibitor worldwide, reduces NVP levels (19) and leads to inferior HIV suppression in TB coinfecting compared with TB-uninfected people living with HIV (20). Although the nonnucleoside reverse transcriptase inhibitor efavirenz can be given with rifampin effectively (20), many HIV-infected persons cannot take either efavirenz or NVP due to drug resistance or intolerance and require protease inhibitors (PIs). Unfortunately, rifampin drastically reduces PI concentrations, and increasing the dosage of the PI and/or accompanying ritonavir to overcome the effect of rifampin is poorly tolerated and can cause hepatotoxicity (21, 22). Thus TB agents that can safely be given with PIs and other frequently used ART are urgently needed.

## ROADMAP TO ENSURE TIMELY ACCESS TO NEW TB DRUGS

### Early TB-ART Interaction Studies Essential

All patients with TB living with HIV require ART initiation before completion of TB treatment, and those with CD4<sup>+</sup> cell counts of less than 50 cells/mm<sup>3</sup> should be started as early as 2 weeks after TB treatment initiation (4–6, 23). Thus, it is critical to conduct pharmacokinetic studies of new TB agents and several key HIV medications early in the drug development process. Patients with M/XDR TB living with HIV have better outcomes when on ART (24), reinforcing the need for concomitant HIV and TB treatment in this vulnerable population.

The development of new oral agents for hepatitis C virus (HCV) treatment provides an important cautionary tale. Two oral HCV protease inhibitors, boceprevir and telaprevir, received U.S. Food and Drug Administration (FDA) approval (25, 26) in May 2011 with little to no drug–drug interaction or efficacy data available at the time of market availability (27, 28). These data are needed to guide safe usage in the HIV population, which bears a large burden of HCV coinfection and has a pressing need for better HCV treatment given the more rapid progression of HCV in patients with HIV (29).

Strategic evaluation of frequently used ART agents that typically incur drug–drug interactions should be prioritized. For example, efavirenz- and ritonavir-boosted PIs such as lopinavir are commonly used in HIV-TB treatment worldwide and can be anticipated to respectively induce or inhibit TB drugs metabolized by cytochrome P450, such as rifamycins. Impact of TB drugs on ART levels must also be evaluated, acknowledging that with agents like efavirenz there can be genetically determined heterogeneity in plasma levels (30, 31). Evaluation of key

TB-ART drug interactions will need to anticipate the continued evolution of the ART arsenal with early studies of well-tolerated, potent ART agents such as integrase inhibitors.

Early conduct of drug interaction studies for compounds in phase I and II development has drawbacks that must be acknowledged. Many medications in development will never make it to market due to lack of efficacy or toxicity, and phase II studies may alter the ideal dose, necessitating additional drug interaction studies. Given this, pharmaceutical companies may be reluctant to invest resources in early drug interaction studies. However, partnering with publically funded clinical trial networks and initiatives, such as Global Alliance for TB Drug Development (TB Alliance) and the Critical Path to TB Drug Regimens, would reduce expenditures born solely by the company and provide opportunities to conduct these essential early drug–drug interaction studies, as has been done with ART interaction studies with TMC-207 (32).

### How and When to Include People Living with HIV in Clinical Trials of Novel TB Regimens

The TB regimen development pathway proposed by the TB Alliance and others starts with short early bactericidal activity studies, first in single drugs and then in drug combinations (33). These are followed by phase II studies of up to 8 weeks that evaluate promising combinations with surrogate markers of sterilizing activity, such as serial sputum colony count and time to culture conversion (34). These studies establish the combinations that will merit evaluation in much larger phase III studies powered for TB cure and relapse (35, 36). At what point in this drug development pathway is it most appropriate to include people living with HIV, once preliminary drug interaction data are available to advise appropriate dosing of both HIV and TB agents?

HIV infected persons should be included systematically in phase II studies to ensure TB regimens are not performing differently in the HIV-infected population (Figure 1). One approach to facilitate early inclusion of people living with HIV is to conduct early combination drug early bactericidal activity studies of several TB drugs in HIV-TB coinfecting patients with CD4<sup>+</sup> greater than 200 who can safely defer initiation of ART during the intensive phase of TB therapy (4, 6). Subsequent 8-week phase II studies of promising combinations would then include patients on compatible ART to ensure that commonly used HIV medications can be safely coadministered and that these regimens perform well in both HIV-infected and -uninfected participants. This approach will ensure that data are available to guide use in HIV-TB coinfection when new TB drugs become available. Deferring participation of people living with HIV until phase III studies is not advisable as this will delay identification of regimens that do not perform well in HIV infection or, conversely, even result in dismissing TB treatments that are particularly promising in HIV infection on the basis of poor performance in HIV-uninfected population.

TABLE 2. PHASE II AND III TRIALS OF NOVEL TUBERCULOSIS MEDICATIONS

Study	Phase	TB Medications	HIV-Related Exclusion Criteria	ART Permitted	% HIV Coenrolled
TMC207-TiDP13-C202 (34)	Ila	7 d multiple doses of TMC207 + HZ	No	No	21/67 (31%)
TMC207-TiDP13-C208 (57)	II	TMC207 vs. placebo, with MDRTB OBR	CD4 <sup>+</sup> < 300	No	6/47 (13%) (Stage I) stage II ongoing
TMC207-TiDP13-C209 (58)	II	TMC207 with MDRTB regimen	No	No	Study ongoing
TB Alliance EBA Study TMC207 (59)	II	14 d of multiple doses of TMC207 vs. RHZE	CD4 <sup>+</sup> < 300 Cells or HIV-related OI/malignancy	No	Not available
TB Alliance EBA Study TMC207 & PA824 (60)	II	14 d of TMC207 vs. TMC207/Z vs. PA824/Z vs. PA824/Z/M vs. TMC207/PA824 vs. RHZE	CD4 <sup>+</sup> < 300	No	Study ongoing
TB Alliance PA-824 EBA (61)	II	14 d of multiple doses of PA824 vs. RHZE	CD4 <sup>+</sup> < 300	No	10/65 (14.5%)
PNU100480 and linezolid EBA study (62)	Ila	14 d of 600mg PNU vs. 1,200 mg PNU vs. linezolid 300 mg. vs. RHZE	CD4 <sup>+</sup> < 350	Not known	Study ongoing
OPC 67683 EBA study (Trial 242-06-101) (63)	II	14 d of multiple doses of OPC 67683 vs. RHZE (control)	CD4 <sup>+</sup> < 350	No	Not available
OPC 67683 in MDR TB (64)	II	OPC 100 mg vs 200 mg vs. placebo + MDRTB OBR	CD4 <sup>+</sup> < 350	No	Study ongoing
OPC 67683 in MDR TB (65)	II	Dose escalation of OPC in MDRTB	CD4 <sup>+</sup> < 350	No	Study ongoing
SQ109 EBA study (66)	Ila	14 d of multiple doses of SQ109 vs. RHZE (control)	CD4 <sup>+</sup> < 250	No	Study ongoing
OFLOTUB/Gatifloxacin for TB (67, 68)	II	2MHRZ/4HR vs. 2GRHZ/4HR, vs. 2ORHZ/4HR vs. 2RHZE/4HR	WHO stage 4 HIV	No	126/217 (58%)
	III	2GHRZ/2GHR vs. 2RHZE/4HR	WHO stage 3/4 HIV	No	Study ongoing
Moxifloxacin vs. ethambutol (Conde et al.) (69)	II	2MHRZ/4HR vs. 2RHZE/4HR	CD4 <sup>+</sup> < 200	No	5/146 (3%)
Moxifloxacin vs. ethambutol (TBTC 27) (70)	II	2MHRZ/4HR vs. 2RHZE/4HR	No	Not for first 2 mo	60/277 (22%)
REMOX TB (71)	III	2MHRZ/2MHR vs. 2MHR/4HR vs. 2RHZE/4HR (control)	CD4 <sup>+</sup> < 250	No	Study ongoing
Moxifloxacin substitution for INH (TBTC 28) (72)	II	2MRZE/4HR vs. 2RHZE/4HR	No	Not for first 2 mo	35/328 (11%)
Levofloxacin vs. moxifloxacin in MDRTB (73)	III	Levofloxacin vs. moxifloxacin × 3 mo	No HIV+	n/a	n/a
Rifapentine + moxifloxacin for pulmonary TB (74)	II	2MHPZ/4HR vs. 2RHZE/4HR	CD4 <sup>+</sup> < 200 or HIV-related OI/malignancy	Not for first 2 mo	Study ongoing
RIFAQUIN (75)		2MRZE/4MP(1 × wk) vs MRZE/4MP(2 × wk) vs. 2RHZE/4HR (control)	CD4 <sup>+</sup> < 200	No	Study ongoing
Rifapentine vs. rifampin (TBTC 29) (76)	II	2PHZE vs. 2RHZE (control)	No	Not for first 2 mo	Study ongoing

*Definition of abbreviations:* ART = antiretroviral therapy; E = ethambutol; EBA = early bactericidal activity; G = gatifloxacin; H = isoniazid; MDRTB = multidrug-resistant tuberculosis; O = ofloxacin; OBR = optimized background therapy; OI = opportunistic infection; P = rifapentine; R = rifampin; TB = tuberculosis; TBTC = Tuberculosis Clinical Trials Consortium; WHO = World Health Organization; Z = pyrazinamide.

### Addressing Challenges of HIV–TB Coinfected Study Populations

Facilitating evaluation of new TB agents in people living with HIV will require attention to several inherent challenges of enrolling and caring for this population.

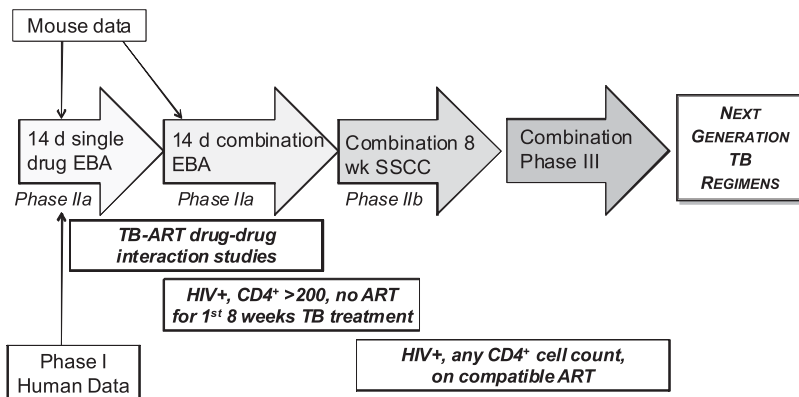
First, diagnosis of TB is more difficult in people living with HIV than in HIV-uninfected persons due to a higher frequency of acid-fast bacillus (AFB) smear-negative and extrapulmonary forms of disease. Fortunately, the expanding availability of rapid molecular TB diagnostics, such as World Health Organization (WHO)-endorsed Xpert MTB/RIF real-time polymerase chain reaction (37), will allow quicker and more accurate identification of TB in HIV-infected persons compared with currently available diagnostics (38). Recent studies demonstrate Xpert MTB/RIF can improve the ability to promptly identify smear-negative TB and provide a rapid screen for rifampin resistance, which is critical for patients at risk for M/XDRTB (39, 40).

Second, people living with HIV may be ill not only from TB but also from other serious HIV-related opportunistic infections and cancers. However, large randomized studies of HIV–TB coinfecting patients with low CD4<sup>+</sup> cell counts demonstrate that this population can be recruited and retained in rigorously conducted clinical studies in which site staff are experienced in management of HIV disease (4, 6). Third, TB immune reconstitution syndrome (IRIS) adds another layer of complexity when studying new TB agents in people living with HIV. A high frequency of TB paradoxical reactions or IRIS has been reported in patients with TB/HIV when compared with HIV-

uninfected patients (41). TB IRIS is more common among patients with low CD4<sup>+</sup> cell counts who require ART within 2 weeks of starting TB therapy (4–6). TB IRIS is challenging to appropriately identify and manage and can be confused with drug toxicity. Sufficient laboratory and diagnostic capacity must be available to exclude alternate diagnoses. Staff experienced with the complex care of HIV–TB coinfection is needed at clinical trial sites to permit safe and efficient study conduct. Planning ahead for the expected challenges presented by care of HIV–TB coinfecting study participants is key to ensuring success of clinical trials of new TB regimens.

### Ensuring Adequate Clinical Trial Capacity

The development of novel TB regimens will require extensive clinical trial capacity to conduct the necessary studies in populations with high TB prevalence (42). Current TB drug regimens were developed as the result of years of enormous coordinated efforts by the British Medical Research Council and others (43), and a similar series of sequential clinical trials will be required now to revolutionize TB care in light of newly developed TB drugs. Experienced clinical trial sites with expertise in HIV and TB already exist through clinical trials networks like the Tuberculosis Trials Consortium, AIDS Clinical Trials Group, and Agence Nationale de Recherche sur le Sida, as well as through an extensive industry clinical trials infrastructure. Efforts by the Critical Path to TB Regimens Initiative and others to leverage and coordinate the resources of existing trial networks and streamline communication among the many stakeholders in TB



**Figure 1.** Timeline for inclusion of people living with HIV in TB drug development. ART = antiretroviral therapy; EBA = early bactericidal activity study; SSCC = serial sputum colony counting study; TB = tuberculosis. Adapted from Ginsberg and colleagues (33).

drug development (44) will be key to ensure the timely conduct of numerous necessary clinical trials. Expansion of TB laboratory capacity is required to support future clinical trials. Study participants will need rapid screening with molecular methods to detect TB and potential TB drug resistance and frequent evaluation while on study with solid and liquid cultures, including labor-intensive methods such as serial sputum colony counting. Use of shared resources, such as specimen banks and databases, may help facilitate needed research. Increased funding will be essential to coordinate and support this necessary laboratory and clinical trial infrastructure.

#### Clinical Trials of Novel TB Regimens in Special Populations

Special HIV-infected populations, such as those with M/XDRTB, children, pregnant women, and injection drug users (IDU), will present additional complexity to the conduct of clinical trials of new TB drugs. Drug-resistant TB has been particularly lethal in people living with HIV, and transmission is known to occur both nosocomially and in the community (45). Therefore, sites with elevated rates of resistant TB will need to be able to quickly identify drug-resistant TB with rapid diagnostic methods, and studies of M/XDRTB regimens will require special attention to infection control. Laboratory capacity must be available to fully characterize drug resistance patterns of TB isolates to properly evaluate efficacy of new regimens. Drug–drug interaction studies evaluating combinations of new MDRTB agents should be prioritized; deferring these pharmacokinetic studies until licensure of new TB agents will lead to unnecessary delay in development of better regimens for drug-resistant TB and put patients with MDRTB at risk for drug toxicity if unstudied combinations are used after new drug approval. To allow timely conduct of these drug–drug interaction studies and development of drug resistance assays for new drugs, pharmaceutical companies should be encouraged to provide research collaborators with access to MDR agents before completion of phase III studies and licensure.

Children and pregnant and lactating women bear a considerable burden of TB in the HIV-infected population (46), and studies should include these groups as soon as is feasible. Diagnosing TB in young children is difficult (47), and inclusion criteria for pediatric clinical trials must often permit entry of those with suspected TB until TB diagnostics are sufficiently improved to allow confirmation of TB. Pharmacokinetic and drug–drug interaction studies are needed evaluating ART most frequently administered to HIV-infected young children as well as pregnant and breastfeeding women, such as nevirapine and lopinavir/ritonavir, with attention to appropriate dosing throughout childhood, pregnancy, and lactation.

IDU bear a disproportionate proportion of the TB burden. New TB agents should be evaluated for drug interaction with

ART and commonly used opiate replacement treatments, such as methadone and buprenorphine, to inform the safe use in IDU (48). Attention to identifying IDU with HIV–TB coinfection early is important, as mortality in this population is high in the presence of advanced HIV (49).

#### Improved Regimens for TB Prevention in HIV-Infected Population

Prevention of TB reactivation and reinfection is also a high priority in people living with HIV (50). Shorter, more effective regimens for LTBI may improve uptake of preventative therapy, decrease overlapping toxicity, and reduce the burden on the healthcare system. New drugs must be evaluated as options for LTBI due to both drug-sensitive and drug-resistant TB, recognizing that needs of TB prevention in HIV-infected persons are different from those without HIV infection. Also, with the recent shift toward extended or even lifelong isoniazid treatment in high-prevalence TB settings (50), different clinical trial designs will be needed to evaluate TB prevention strategies with new agents in people living with HIV.

#### REGULATORY AND PROGRAMMATIC CONSIDERATIONS

Once potent new TB drugs are identified, it will be crucial to ensure that the regulatory approval process does not impede access to these agents. Accelerated approval by regulatory bodies, such as the FDA and the European Medicines Agency, based on surrogate markers of new drug efficacy should be strongly considered to ensure that access to life-saving TB medications is not delayed, particularly in the HIV-infected population. In addition, TB control programs will need to begin capacity building now to prepare for an expanded and evolving arsenal of new TB agents as well as new treatment regimens for both drug-sensitive and MDRTB and for potentially radical changes in the way TB treatment and prevention are delivered. This preparation should include ensuring that programs have the financial and personnel resources necessary to provide timely national approval and to rapidly scale up delivery of new drugs for sensitive and resistant TB.

The WHO must play a crucial role facilitating dialogue with drug developers to agree on the evidence required to recommend introduction of new drugs/regimens for treatment of TB and MDRTB, including for people living with HIV. The WHO will need to build evidence-based strategies for post-approval introduction of drugs to ensure affordability and access while preserving drug efficacy. Programmatic implementation should be aligned with ongoing efforts, such as the Treatment 2.0 initiative, coordinated by the Joint United Nations Program on AIDS and

WHO, that aims to maximize the efficiency and effectiveness of HIV treatment by optimizing drug regimens, advancing point-of-care and other simplified platforms for diagnosis and monitoring, reducing costs, adapting delivery systems, and mobilizing communities (51).

### Lessons from HIV Drug Development

FDA acceptance of the surrogate marker of HIV RNA in lieu of clinical AIDS endpoints in 1997 allowed the transformation of a traditionally decade-long drug approval process to accelerated approval based on 24-week HIV RNA data under Subpart H of 21CFR314 (52). This change led to unprecedented early access to HIV medications and was lifesaving for thousands with AIDS who could not afford delayed access to highly effective drug combinations. Despite accelerated approval and pharmaceutical company-sponsored expanded access programs that provided access to drugs before approval, key ART trials were still able to be completed, providing the necessary definitive long-term data and confirmation of drug efficacy with validated endpoints.

As with HIV drug development, the case for accelerated approval of TB drugs in people living with HIV is founded on saving lives in a vulnerable population that cannot afford to wait years for new TB medications. Currently, TB endpoints required for drug approval are based on the presence of a relapse-free cure for a duration of at least 24 months after treatment, which requires large clinical trials and many years to complete. The FDA and the European Medicines Agency have indicated that culture conversion may be considered as an acceptable surrogate endpoint in conjunction with clinical response to therapy as a basis for accelerated approval for M/XDR TB medications (53, 54).

Research must be prioritized to identify additional appropriate surrogate markers of drug-sensitive TB treatment efficacy in addition to 2-month culture conversion, a valuable marker that nonetheless has limitations in predicting efficacy of drug-sensitive regimens (55, 56). Regulatory agencies should strongly consider expedited approval of new agents for drug-sensitive TB on the basis of appropriate surrogate markers as these emerge. Last, it is important to note that particularly in resource-limited settings, reliance on pharmaceutical company-administered expanded access programs will not be feasible on the scale required to provide timely pre-approval access to new TB drugs.

### CONCLUSIONS AND NEXT STEPS

A promising new era in TB drug development has begun. It is critical to act now to ensure that people living with HIV, a group in need of more effective, shorter, and less-toxic TB treatment, do not become the least likely to have access to these potentially life-saving medications.

To ensure that patients with TB living with HIV have timely and safe access to new TB regimens, the following steps are recommended:

- Prioritize drug–drug interaction studies of novel TB agents and combinations of TB agents with commonly used first- and second-line ART early in the TB drug development process. Novel HIV medications with potential for less ART–TB drug–drug interactions should also be evaluated.
- Promote systematic and standard inclusion of people living with HIV in early phase II clinical trials to identify potential differential performance of regimens in HIV-infected and -uninfected participants.
- Promote validation of better surrogate markers of efficacy in drug-sensitive TB as well as development of novel clinical trial design to shorten time to drug approval.
- Optimize clinical trial infrastructure by improved communication between research programs developing novel TB regimens, creation of shared resources such as specimen banks and databases, and efficient use of existing clinical trial networks.
- Expand TB laboratory capacity to allow rapid identification of TB disease and drug resistance and to permit intensive monitoring of patients on new regimens with methods including quantitative and liquid cultures.
- Develop accelerated approval processes for drug-resistant and drug-sensitive TB medication, based on appropriate surrogate markers of regimen efficacy.
- Strengthen capacity-building of national regulatory bodies in countries with high prevalence of HIV–TB coinfection for expedited evaluation and distribution of numerous promising drugs in development.

We believe that taking these proactive steps now will help to ensure timely and responsible access to the long-awaited new TB regimens that are on the horizon for people living with HIV.

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