



# Breaking Through

## 2019 Annual Report

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[www.tballiance.org/annualreport2019](http://www.tballiance.org/annualreport2019)

### About TB Alliance

The world is in desperate need of improved, faster-acting and affordable tuberculosis drug regimens that are available to all who need them. These new cures can bring renewed health, hope and prosperity to millions. Since our inception in 2000, TB Alliance has contributed to the global search for and development of new TB drugs and regimens, catalyzing the field and convening cross-sector partnerships to forge the progress that is urgently needed for better TB treatments.  
[Learn more about TB Alliance here.](#)

## A Message from the CEO and Board Chair

We believe 2019 will prove to be a seminal year for the future of tuberculosis (TB) therapy.

The pathway to our goal of short, simplified treatments for all patients with active TB is clearer than ever. We can more readily envision a world in which all patients with active TB can be treated with the same drugs in a short, simplified regimen. Our commitment to developing new regimens is bearing fruit for patients.

As we celebrate our 20th year, we now have proof that the most highly resistant forms of active TB can be treated for the same period of time that it takes to treat drug-sensitive TB. Our newly approved regimen, containing a novel anti-TB drug along with one presently approved drug for TB and one repurposed antibiotic, has now been approved in the United States for the most highly drug-resistant population of active TB patients. It is now under review in Europe, India and South Africa, with many more regulatory submissions to come.

Our next challenge is to translate this accomplishment into saving lives. This will require an enormous amount of work and the same spirit of innovative partnerships as our approach has been to research and development of novel drugs and regimens.

With respect to our new product, we have quickly reached agreements with three commercial partners within four months of US FDA regulatory approval in August 2019, with a goal of bringing generic competition to the market at a rapid pace. In October, it was listed in the Global Drug Facility catalogue for 150 countries at a lower price than that of any other TB drug approved this century.

This achievement brings us much closer to the day when we can break down the barriers between drug-sensitive and drug-resistant TB therapy, thereby simplifying treatment for everyone. But successfully developing a universal regimen will likely require a significantly larger portfolio of compounds than what is presently available that can be combined into novel regimens that are highly active against all strains of the TB bacillus.

This past year has also been noteworthy in that we have continued to advance three Phase 3 trials, shepherd multiple novel compounds through the translational medicine space, and progress the largest single TB drug discovery portfolio.

None of these accomplishments would have been possible without the generosity of our donors, for which we are profoundly grateful. We are especially thankful that so many of our donors have provided continued support over many years, with a clear appreciation that success in this field demands a sustained commitment of time and resources.

Above all, we are grateful to the patients who participate in our research. No progress can be made without their courage, as they literally put their lives on the line when they volunteer to participate in a clinical trial for which there is never a guarantee of success.

Twenty years ago, the signatories to the Declaration of Cape Town deemed TB “a blot on the consciousness of human kind” and set in motion the creation of TB Alliance. Today, we reinforce our commitment to advancing new cures and meeting the aspirations of those who gathered in Cape Town, demanding a better future for all those who suffer from TB.



Mel Spigelman  
President and CEO, TB Alliance



Bruce Carter  
Chairman of the Board, TB Alliance

## U.S. FDA Approves New Treatment for Highly Drug-Resistant TB

On August 14, 2019, [TB Alliance](#) received approval from the [U.S. Food and Drug Administration \(FDA\)](#) for its anti-TB drug pretomanid in a combination regimen for the treatment of people with highly drug-resistant forms of tuberculosis (TB).<sup>1</sup> The approved indication is for the use of pretomanid as part of a three-drug regimen with bedaquiline and linezolid – collectively referred to as the [BPaL](#) regimen. The new drug was approved under the Limited Population Pathway for Antibacterial and Antifungal Drugs (LPAD pathway) as part of a six-month, all-oral regimen for the treatment of people with extensively drug-resistant TB (XDR-TB) or multidrug-resistant TB (MDR-TB) who are treatment-intolerant or non-responsive.<sup>1</sup>

[Pretomanid](#) is only the third new anti-TB drug approved for use by the FDA in more than 40 years, as well as the first to be developed and registered by a not-for-profit organization.<sup>2,3</sup>

Licensed by TB Alliance in 2002, pretomanid has been evaluated in over 19 clinical trials enrolling more than 1,100 participants.<sup>1</sup> It continues to be studied as part of BPaL and other pretomanid-containing regimens, including the [ZeNix](#) trial, which completed enrollment at the end of 2019.

Please see Full Prescribing Information at [www.tballiance.org/pretomanid](http://www.tballiance.org/pretomanid)

## Historic XDR-TB Treatment vs. BPaL Regimen



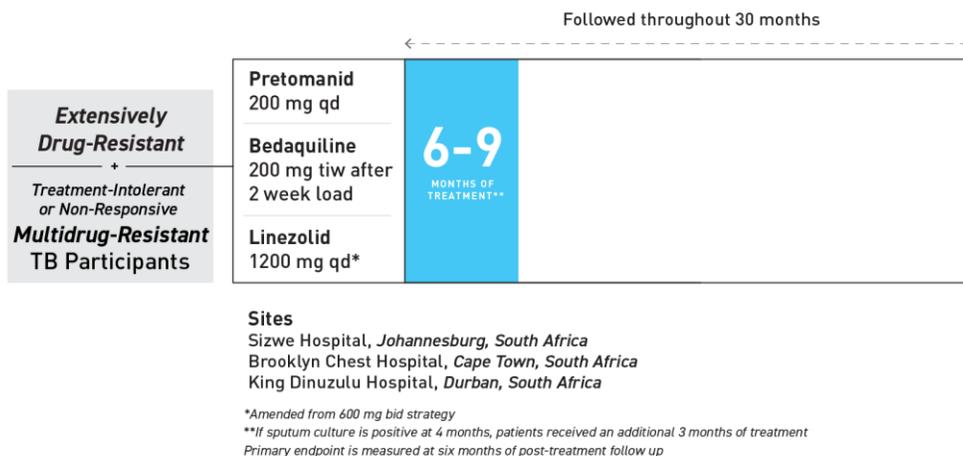
<sup>1</sup> Pretomanid and BPaL. Full Prescribing Information. August 2019.

<sup>2</sup> Fox W. Int J Tuberc Lung Dis. 1999;3(10):S231-S279.

<sup>3</sup> Johnson LA. FDA approves TB pill that cures more hard-to-treat patients. Associated Press. Available at: <https://apnews.com/d1df70cf5dcc41cf9932d6be0a65ee5f>.

## Nix-TB: Phase 3 Clinical Trial

BPaL was studied in the pivotal [Nix-TB clinical trial](#) across three sites in South Africa.<sup>1</sup> The trial enrolled 109 people with XDR-TB, as well as treatment-intolerant or non-responsive MDR-TB. As documented in the *New England Journal of Medicine*, Nix-TB data have demonstrated a successful outcome in 90 percent of patients who were treated with the BPaL regimen.<sup>4</sup>



## Spotlight: Tsholofelo Msimango

“I cried the whole way in the ambulance,” Tsholofelo Msimango recalled recently. “They said . . . there was no way I would come back. They told my parents to fix the insurance because I would die.”

Five years later, Ms. Msimango, 25, is now tuberculosis free. She is healthy and has a young son.

Tsholofelo participated in the Nix-TB clinical trial of the BPaL regimen. Read more of her story in *The New York Times* [here](#).

## Ensuring Access around the World

TB Alliance announced licensing agreements with multiple manufacturers to secure an affordable and sustainable market for pretomanid as part of the BPaL regimen. In April 2019, TB Alliance and Mylan announced a [global commercialization partnership](#), giving Mylan a license to commercialize pretomanid for use in two regimens ([BPaL](#) and [BPaMZ](#)) to treat pulmonary TB. In October 2019, TB Alliance and [Macleods](#) announced a nonexclusive agreement to manufacture and sell pretomanid as part of the BPaL regimen in low- and middle-income countries. In December, [Hongqi Pharmaceutical](#) became the commercial partner for pretomanid as part of BPaL in the People’s Republic of China.

In October, the Stop TB Partnership’s [Global Drug Facility \(GDF\)](#) added pretomanid to its catalog of TB medicines. The “global access price” of US\$364 for a six-month treatment course will be available to 150 countries representing the vast majority of the global TB burden.

<sup>4</sup> Conradie F, et al. Bedaquiline, pretomanid and linezolid for treatment of extensively drug resistant, intolerant or non-responsive multidrug resistant pulmonary tuberculosis. *N Eng J Med* 2020;382:893-902.

## Reaching a Global Audience

“Pretomanid is not owned by a drug company but by the TB Alliance, a nonprofit based in New York that is seeking new treatments.” – *The New York Times*

[Scientists Discover New Cure for the Deadliest Strain of Tuberculosis](#) | August 14, 2019

“This success story points to the potential for future public-private partnerships to meet the urgent need for new therapies for infectious disease.” – *The Wall Street Journal*

[A New Dose of Hope in the Battle with Tuberculosis](#) | August 16, 2019

“The anti-tuberculosis drug pretomanid recently approved by the U.S. Food and Drug Administration will be a game changer for treating people with extensively drug-resistant TB.” – *The Hindu*

[Taking on TB: On New Anti-Tuberculosis Drug](#) | August 19, 2019

“The U.S. Food and Drug Administration’s approval of a new tuberculosis antibiotic this month could be a significant win not only for TB patients, but for a burgeoning nonprofit model for developing prescription drugs.” – PBS Newshour

[Nonprofit Drug Maker Produces TB Antibiotic after Private Companies Wouldn’t](#) | August 22, 2019

## Research & Development

### New Therapy Shows Promise of Regimen Development

TB Alliance has long advocated for and advanced the paradigm of [developing complete TB drug regimens](#), as opposed to individual drugs, as the most effective way to reshape TB therapy. Achieving approval from the U.S. Food and Drug Administration (FDA) for a [novel regimen](#) for highly drug-resistant forms of TB is the result of this model in action.

In 2019, TB Alliance continued to advance this strategy with additional regimens in development. An increased focus on [translational research](#) is designed to secure the portfolio of next-generation clinical-stage drug candidates from which we can form tomorrow's treatments.

Progress in additional novel regimen trials included the completion of drug-sensitive (DS) arms of the ongoing [SimpliciTB](#) trial. Additionally, the [ZeNix](#) trial, evaluating the use of alternative linezolid dosing in the BPaL regimen, completed enrollment at the end of 2019. The study of further new regimens in preclinical models continues to yield promise that universal, short, safe and simple TB therapies are possible.

### From Compounds to Regimens

Achieving a sustainable pipeline of fully novel, short, safe and effective universal regimens requires the discovery and development of new generations of clinical stage drug candidates. TB Alliance has made significant gains in strengthening its portfolio in 2019, with several key achievements, including:

#### [TBI-223](#)

Started Phase 1 trial

#### [TBAJ-876](#)

Completed IND enabling studies, expected to start Phase 1 trial in 2020

#### [TBAJ-587](#)

Advanced TBAJ-587 in partnership with [Innovative Medicines Initiative](#) (IMI)

Sustaining the pipeline:

- In collaboration with GlaxoSmithKline, the [KasA inhibitor](#) program yielded a compound that has advanced to pre-candidate status.
- Supported by a Center of Excellence in Translational Research (CETR) Grant from the National Institute of Allergy and Infectious Diseases (NIAID), TB Alliance and partners at the [University of Illinois at Chicago](#), [Harvard University](#), [Johns Hopkins University](#) and [Research Triangle Institute](#) formed a [multidisciplinary center to advance translational TB drug research](#).
- TB Alliance's [portfolio](#) of new TB research programs grew by four projects in the past year.

## Improving Our Understanding of TB Treatment

TB Alliance makes the findings of its research available by publishing findings on our website, [clinicaltrials.gov](https://clinicaltrials.gov), at conferences and in peer-reviewed journals on an open-access basis. In 2019, findings from nine TB Alliance studies were published, including the results of trials of new regimens and learnings regarding the pharmacodynamics, toxicity and dosing of new TB treatments and those under development. A library of our research papers can be found [here](#).

## Spotlight: Advancing New Treatments in Tbilisi, Georgia

The National Center for TB and Lung Diseases (NCTLD) in Tbilisi, Georgia, is a key partner in TB Alliance's clinical development of new, shorter regimens for TB. Dr. Lali Mikiashvili is the site's lead investigator for the ZeNix clinical trial, which is evaluating a new regimen for highly drug-resistant TB. She has more than 25 years' experience in treating people with TB.

"We are proud to be engaged in this research," says Dr. Mikiashvili. "In partnership with TB Alliance, we are evaluating the potential of new treatments for people suffering from one of the most dangerous diseases in the world."

Georgia has comparatively high rates of drug-resistant TB. In 2018, the WHO reported that approximately 18 percent of all TB cases were resistant to at least one first-line drug, compared to a global average of about 5 percent. By advancing research into new TB drug regimens, the NCTLD is helping to shape the future of TB treatment.

## Access

### More than One Million Child-Friendly TB Treatment Courses Ordered by 90+ Countries

In June 2019, TB Alliance announced that [1 million treatment courses](#) of child-friendly tuberculosis (TB) medicines had been ordered by more than 90 countries in the three years since introduction of the products.

The new medicines, which were first introduced nationally in Kenya in September 2016, are easier for caregivers to administer and for children to take. Previously, caregivers had to cut or crush multiple, bitter-tasting adult pills or combine incorrectly dosed formulations to achieve the appropriate doses for children. This made the six-month treatment journey difficult for children and their families, contributing to challenges with adherence, treatment failure and death from the disease. The [treatments](#) are the first to meet the World Health Organization's (WHO) guidelines for childhood TB treatment. They are improved formulations of first-line TB treatment that come in the correct doses for children, require fewer pills, are fruit-flavored and dissolve in water.

### Spotlight: Chelsea

In 2016, when Chelsea was three, she was diagnosed with tuberculosis. This is her story of [#TBCourage](#):

In 2016, Chelsea's grandmother, Norah, noticed that Chelsea was coughing, losing weight and was having trouble breathing regularly. Sometimes her cough was so bad that she would fall off her bed at night. Norah brought her granddaughter to a hospital in Nairobi where [Chelsea was diagnosed with TB](#). Chelsea was among the first to receive a child-friendly TB treatment before the national rollout of the medicines in Kenya. Two days after she started her medication, Chelsea slept soundly for the first time after so many difficult nights. She has now completed her treatment and is cured. She is an active and healthy girl.

*Thanks to Centre for Health Solutions – Kenya (CHS) for contributing this story.*

### Ensuring Availability and Affordability of New TB Treatments In-Country

Along with the child-friendly formulations that are now available, TB Alliance is committed to ensuring that every treatment it develops becomes adopted, available and affordable to those who need it. In August 2019, TB Alliance received [regulatory approval](#) for a new treatment to treat highly drug-resistant forms of TB, and has announced three global collaborations to manufacture and commercialize the new treatment option to make certain that it is globally accessible.

TB Alliance is working with partners around the world to support progress on in-country access plans. In September 2019, Stop TB Partnership's TB REACH program announced funding for multiple countries to implement the treatment. Stop TB's Global Drug Facility announced the price for countries serviced by them in October 2019.

## Our Latest Studies

To optimize the development and introduction of new TB products, it is important to thoroughly understand the market. TB Alliance has investigated key characteristics of health systems to ensure products in development are in line with local needs and realities to help ensure new regimens have their maximum impact on the pandemic.

### **Acceptability of the new regimen**

TB Alliance and partners collected feedback on whether a new TB drug regimen will be acceptable in the indicated patient population. This study engaged caregivers, and programmatic and laboratory stakeholders in comparing the new regimen versus the standard of care in three countries: Indonesia, Kyrgyzstan and Nigeria.

[View results](#)

### **Cost-effectiveness**

TB Alliance and partners evaluated the cost-effectiveness of a new TB drug regimen compared to the local standard of care through three diverse geographic and epidemiologic settings (the Philippines, Georgia and South Africa), with varying degrees of a drug-resistant TB burden and HIV/TB co-infection.

[View results](#)

## Partners

### Global Partnerships

As a product development partnership, none of TB Alliance's work would be possible without the sustained commitment of its diverse network of partners. We engage with researchers, funders, technical partners, communities and stakeholders of all kinds in service of our mission of radically improving TB treatment for every patient. We rely on the generosity of our donors – including foundations, national governments, and private individuals – for supporting the science that is foundational to breakthroughs.

● Trial Sites (32) ● Community Engagement Sites (32) ● Donors (14) ● Portfolio (30) ● Stakeholders Association (63)



### Spotlight: Mylan

In April 2019, TB Alliance and Mylan announced a global commercialization partnership to manufacture and sell a new compound as part of two novel regimens to treat TB. This partnership is central to TB Alliance's market access strategy. One of the treatments for highly drug-resistant forms of TB has been added to the Stop TB Partnership's Global Drug Facility product catalog only two months after receiving approval by the US Food and Drug Administration. Mylan also prioritized submitting the product for registration in several key, high-burden countries, including South Africa and India, and will continue to do so throughout 2020. Through Mylan's global reach and wealth of experience in delivering quality, affordable medicines, new treatments are on the path to reaching those who need them most.

### Communities Ending TB

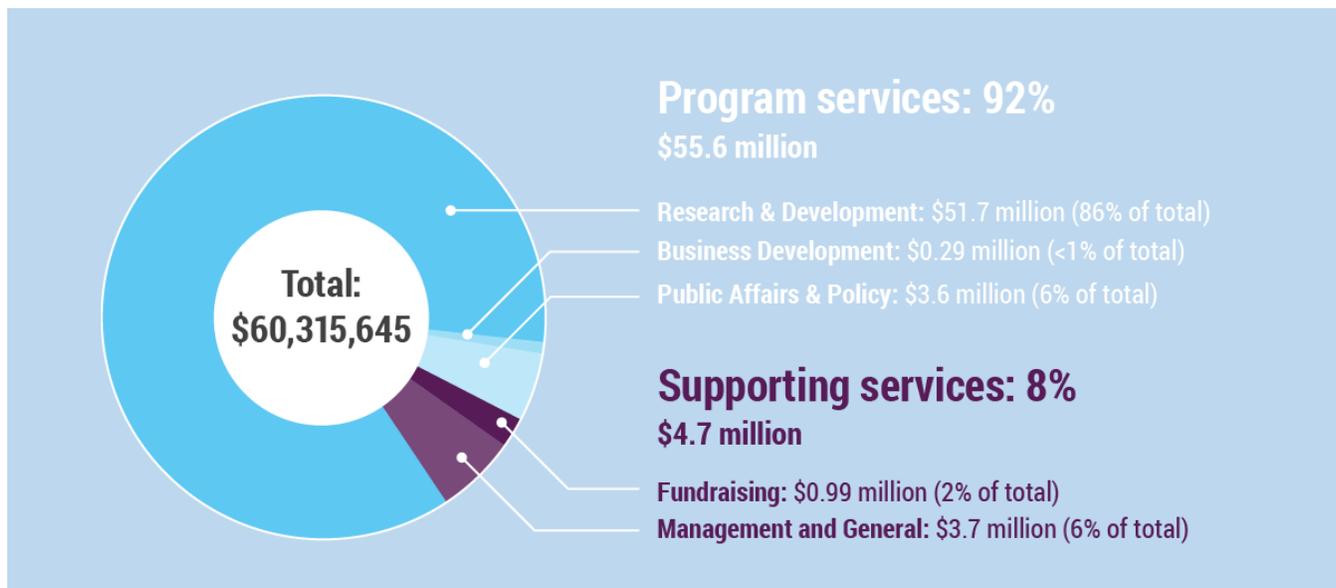
Established in 2008, TB Alliance's community engagement (CE) program is a platform for communities to engage with clinical research programs as they collaborate to evaluate new TB treatments that can shorten and simplify treatment for all. TB Alliance works with community partners to implement Good Participatory Practice principles for all of its research programs. Pillars of this program include providing opportunities for research sites to learn from one another, increasing knowledge about TB and TB research, supporting CE strategies at trial sites with technical assistance, and supporting peer-to-peer mentoring and evaluation. In 2019, 32 CE programs held events in nine countries in support of TB awareness, screening and treatment.

## Stakeholders and Civil Society

The Stakeholders Association (SHA), an institution established at the founding of TB Alliance in 2000, elected Mitchell Warren as its new president in June 2019. Warren, who also serves as Executive Director of AVAC, succeeds Karl Hofmann, who led the SHA since 2013. Recent advances have generated widespread interest in the treatment of highly drug-resistant forms of TB, and sustained dialogue with civil society groups emerged as a key element of TB Alliance's stakeholder and access strategy. TB Alliance is committed to engaging in transparent, open dialogue with civil society as it develops and introduces new products intended to treat people with TB.

## Leveraging Resources

TB Alliance makes every effort to ensure that donor money is put to effective use and contributes directly to the development of impactful new TB drug regimens that are adopted, available and affordable.



[Download our audited 2018 financial statements](#)

## Bridging the Funding Gap

The science of TB drug development is challenging, but the rate-limiting factors governing the pace and scope of progress in the development of new and improved TB treatment regimens, diagnostics, and vaccines continue to be the resources devoted to these causes. The recently released [Global Plan to End TB \(2018–2022\)](#) calls for \$10.8 billion to be invested in TB product research over the five-year period. Though investment in TB has increased in recent years, the annual investment remains far from what is needed to achieve the ambitious targets set in the [United Nations Sustainable Development Goals](#) and the [United Nations High-Level Meeting on TB](#).

To achieve success and advance research in a precarious funding environment, TB Alliance is working to bridge the TB funding gap by efficiently developing new treatments, engaging in unconventional partnerships that can leverage scarce resources, and drawing global attention to areas in greatest need of support.

## Global Plan

Annual target for TB drug research funding

\$830,000,000



## Drug R&D

Total drug R&D funding in 2017

\$315,000,000



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*TB Alliance is indebted to its partners, especially all participants in our clinical trials, for the progress seen in 2019.*