



A New Frontier

2018 Annual Report

This is a printer-friendly version. Please access the full report at:
www.tballiance.org/annualreport2018

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.](#)

Message from the CEO and Chairman of the Board

Dear Stakeholders, Partners and Patients,

Throughout 2018, TB Alliance has turned to face a new frontier: we have made significant strides towards our goal of developing new tuberculosis (TB) cures that will contribute to ending TB worldwide.

With 10 million new cases per year and an estimated 1.6 million deaths, new tools to prevent, diagnose and treat all forms of this disease are urgently needed. As a nonprofit product development partnership, TB Alliance remains dedicated to developing and delivering affordable, fast-acting, safe and effective drugs that can lead to a world free from TB.

On December 14, 2018, TB Alliance proudly submitted its first ever New Drug Application (NDA) to the U.S. Food and Drug Administration (FDA) for the review and approval of the drug pretomanid, in combination with bedaquiline and linezolid (collectively known as the BPaL regimen), for the treatment of extensively drug-resistant TB and multidrug-resistant TB that is treatment-intolerant or non-responsive. This application, which has now been accepted by the FDA for Priority Review, is a major milestone for the organization.

Such advances are made possible by strong evidence generated from extensive research conducted at all stages of the pipeline. TB Alliance conducted three concurrent pivotal Phase 3 trials in 2018, evaluating new drug regimens for safety and efficacy against all forms of the disease.

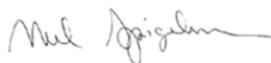
Drug discovery and early clinical development are critical to sustaining the pipeline of drug candidates. Here too, we continue to see important advances, with multiple new compounds now approaching clinical development.

At the policy level, the United Nations (UN) High-Level Meeting on TB resulted in a welcome Political Declaration by heads of state, in which they have committed to close the annual \$1.3 billion funding gap for TB research as well as ramping up treatment programs to find and treat all patients with TB. While significant resources and political will are still needed to ensure such ambitious promises are kept, this high-level recognition of the urgency of our mission is an encouraging step.

We have also seen welcome progress in improved TB therapy for children. Developed by TB Alliance and partners and first introduced in 2016, more than 800,000 courses of child-appropriate, fruit-flavored, dispersible medicines have been procured by 86 countries and counting.

None of our work or accomplishments would be possible without the strong support and commitment of our employees, partners, donors and especially our clinical trial participants. We cannot thank you all enough for your contribution to ending TB and improving countless lives around the world.

With another exciting year ahead, we look forward to continuing to work together toward the next frontier, building on this progress, and providing innovative treatments to all who need them.



Mel Spigelman
President and CEO, TB Alliance



Bruce Carter
Chairman of the Board, TB Alliance

Developing New Treatments

Pretomanid Begins Evaluation for FDA Approval

A new TB treatment is under regulatory review. On December 14, 2018, TB Alliance submitted its first New Drug Application (NDA) to the U.S. Food and Drug Administration (FDA). [The FDA has now accepted TB Alliance's application](#) for pretomanid and granted it Priority Review, with a decision expected to be rendered in third quarter 2019.



The application is for the use of pretomanid as part of an investigational drug regimen, in combination with bedaquiline and linezolid, for the treatment of extensively drug-resistant (XDR) TB, treatment-intolerant multidrug-resistant (MDR) TB, and treatment non-responsive MDR-TB. The regulatory submission of the pretomanid NDA is the result of significant commitments from donors, partners and community members.

Three Late Stage Clinical Trials Advancing Tomorrow's Cures

TB Alliance is working to introduce promising new TB treatments for all forms of the disease. In 2018, we concurrently led three late stage Phase 3 trials—each is expected to offer scientific insights that could impact the global epidemic.

Nix-TB:

Last year, the 109th and final participant in the Nix-TB clinical trial reached the primary endpoint. Nix-TB participants with XDR-TB and treatment-intolerant or non-responsive MDR-TB were treated with the [BPaL](#) (bedaquiline + pretomanid + linezolid) regimen for six months, or extended to nine months in some cases, with the intent to cure. Nix-TB is an open-label, single arm trial. In interim results on the first 75 participants presented at the [2018 Union World Conference on Lung Health](#), 89 percent of the trial participants had a favorable outcome with their clinical infection resolved and sputum cultures negative for TB after six months of treatment and six months of post-treatment follow-up.

ZeNix:

Launched in late 2017, ZeNix progressed substantially throughout 2018, attaining over 40 percent of its planned enrollment. ZeNix is a successor to Nix-TB and is evaluating lower doses and shorter durations of the drug linezolid in a modified BPaL regimen. If successful, this could enable BPaL to be used more broadly in people with TB, including those with less severe drug-resistance profiles. We expect to complete enrollment in 2019.

SimpliciTB:

[Launched in August 2018](#), SimpliciTB is a pivotal trial evaluating the potential of the [BPamZ](#) (bedaquiline + pretomanid + moxifloxacin + pyrazinamide) regimen to shorten treatment for both drug-sensitive and drug-resistant TB. SimpliciTB is evaluating whether BPamZ can treat drug-sensitive TB in four months – compared to the six-month standard treatment – and DR-TB in six months – compared to the current 9–20+ month treatment options. By the end of 2018, more than 50 patients were enrolled across nine sites. The trial is ultimately slated to span 26 sites in 10 countries.

Partner Profile: Pioneering Clinical Research in South Africa

Dr. Francesca Conradie is the principal investigator of Nix-TB, TB Alliance's first Phase 3 trial evaluating the BPamZ regimen. Throughout her career, Dr. Conradie has been a part of the research agenda that brought effective antiretroviral therapy to millions of South Africans living with HIV. Now, she is focused on TB research, especially new treatment strategies for drug-resistant TB. She has also been instrumental in the adoption of bedaquiline in the South African market. Conradie presented interim Nix-TB results at the 2018 Union Conference.

[View Dr. Conradie's presentation of interim Nix-TB data at the 2018 Union Conference](#)

Discovery

Advancing the Next Generation of TB Drugs

While new regimens are in the late stages of development, it is critical to pursue even shorter and simpler treatments that further improve therapy and protect against the development of drug resistance. Throughout 2018, TB Alliance saw significant progress in the advancement of next-generation TB drugs. Drug candidates known as [TBI-223](#) and [TBAJ-587](#) both completed preclinical development. TBI-223 began Phase 1 First-in-Human development in January 2019 and TBAJ-587 also stands ready to enter clinical development. A third candidate, TBAJ-876, was selected for further research ahead of potential clinical development.

TB Alliance engaged in new research collaborations with partners including the [Global Health Drug Discovery Institute \(GHDDI\)](#), [Fujifilm Corporation](#) and [Schrodinger](#). Additionally, as part of the TB Drug Accelerator, we continue our leadership in the development of new drug candidates in the discovery pipeline with the potential to be combined into impactful drug regimens.

TB Drug Candidates Approaching Clinical Development

[TBI-223](#)

Discovered in partnership with Institute Materia Medica, TBI-223 is an oxazolidinone with demonstrated efficacy against animal models of TB.

[TBAJ-587](#)

Discovered in partnership with Auckland Chemical Society Research Center and developed with assistance from Merck, TBAJ-587 belongs to the diarylquinoline class—the same drug class as bedaquiline.

[TBAJ-876](#)

Discovered in partnership with Auckland Chemical Society Research Center and developed with assistance from Eli Lilly, TBAJ-876 is also a diarylquinoline.

Partner Profile: Combining Drugs for Effective Cures

How do we decide which TB drug combinations – also known as regimens – to develop? Since 2007, TB Alliance has collaborated with the laboratory of Professor Eric Nuermberger at the Center for Tuberculosis Research at Johns Hopkins University to refine our preclinical regimen selection program. Together, we have evaluated numerous novel drug combinations and compounds to determine the most effective drug regimens and prioritize their development. This program also helps identify new combinations of drug targets that lead to faster killing of bacteria when simultaneously inhibited by new compounds. The program has contributed significantly to the development, refinement and qualification of new and existing mouse models to address key questions in TB drug and regimen development.

Access

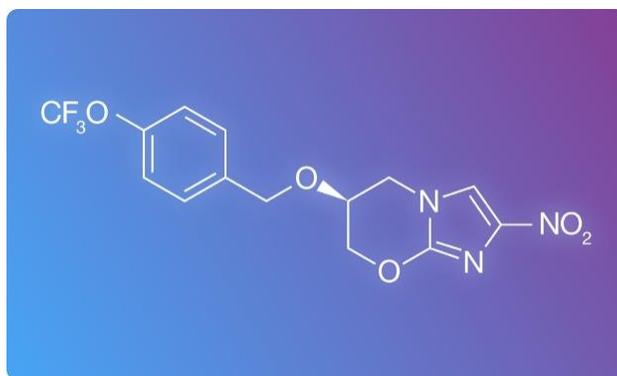
Children in 86 Countries Are Accessing Improved TB Medicines

After years of neglect, children around the world are beginning to have access to child-friendly TB medicines in the correct doses. Developed by TB Alliance and partners and first introduced in 2016, more than 800,000 courses of the child-appropriate, fruit-flavored and dispersible medicines have now been procured by 86 countries, including many with the highest TB burdens. In 2018, these treatments were featured in World Health Organization's [Best Practices in Child and Adolescent Tuberculosis Care](#). The new medicines are currently available to order through the Stop TB Partnership's Global Drug Facility and directly through manufacturers.

Video: TB Alliance and partners received the Global Health Technology Coalition's 2018 [Innovating for Impact Award](#) for the development and introduction of child-friendly TB medicines.

Preparing for Pretomanid

TB Alliance's "[AAA mandate](#)," has committed the organization to ensuring that all new treatments will be adopted, available and affordable to those with TB. With regulatory submissions planned or underway, TB Alliance has been working to enable quick and widespread access to [pretomanid](#) and the [BPaL](#) regimen at affordable prices pending regulatory approvals. Major achievements to date include building a foundation for commercialization partnerships for pretomanid as part of the BPaL and [BPaMZ](#) regimens, as well as engaging with additional generic manufacturers to foster competition and ensure sustainability and affordability of new treatments.



Partner Profile: New TB Cures for Children

Each year, one million children get sick with TB and about 210,000 needlessly die. That's nearly 600 preventable child deaths each day.

TB Alliance and partners have worked to help end the neglect of children with TB. Upon developing TB medicines in correct doses and appropriate forms and tastes for children, we sought partnerships with manufacturers who could help drive widespread uptake of these improved therapies. Macleods Pharmaceuticals was a key partner in our efforts, spearheading critical formulation and development work that helped these new medicines [reach children in need](#) as quickly as possible. With the assistance of a diverse network of partners, more than 800,000 courses of improved TB treatment for children have been ordered, benefitting children and families around the world.

Partnerships

United Nations High-Level Meeting Underscores Role of Partnerships in Fight Against TB

In 2018, the United Nations (UN) held a High-Level Meeting (HLM) on Tuberculosis – only the fifth time the UN devoted an HLM to a health issue. Heads of state convened and issued a [Political Declaration](#) that united them in an urgent global response to end the epidemic. A key pillar is to financially support the development of new TB drug regimens along with diagnostics and vaccines. Specifically, world governments committed to closing the \$1.3 billion annual gap in TB research and development funding as documented in [Stop TB's End TB Strategy](#). Though new financial commitments have been slow to materialize, the political declaration is expected to serve as a tool to hold governments accountable.

Find out more about this [landmark event](#).

View: [Twitter Moment](#)

New Partners in Action

Throughout 2018, TB Alliance announced collaborations with organizations focused on drug discovery, research and development. These new partnerships are a first step toward improved treatment options and better patient care for all those impacted by TB around the world.

- **Innovative Medicines Initiative (IMI) and the European Union**
[TB Alliance has joined the IMI's](#) Antimicrobial Resistance Accelerator Program to advance the pipeline of medicines to treat and prevent drug-resistant bacterial infections. The program will establish a Tuberculosis Drug Development Network to address the innovation gap in the discovery and development of a novel drug regimen for all forms of TB.
- **The Liverpool School of Tropical Medicine (LSTM) and UK MRC**
[LSTM and TB Alliance are collaborating](#) to investigate novel combination drug therapies that could help the fight against drug-resistant TB, following new funding from the UK Medical Research Council.
- **Schrödinger**
[Schrödinger and TB Alliance](#) agreed to a three year research collaboration in TB drug discovery. The partnership merges TB Alliance's expertise in TB biology with Schrödinger's advanced modeling capabilities to accelerate the development of next-generation treatments.

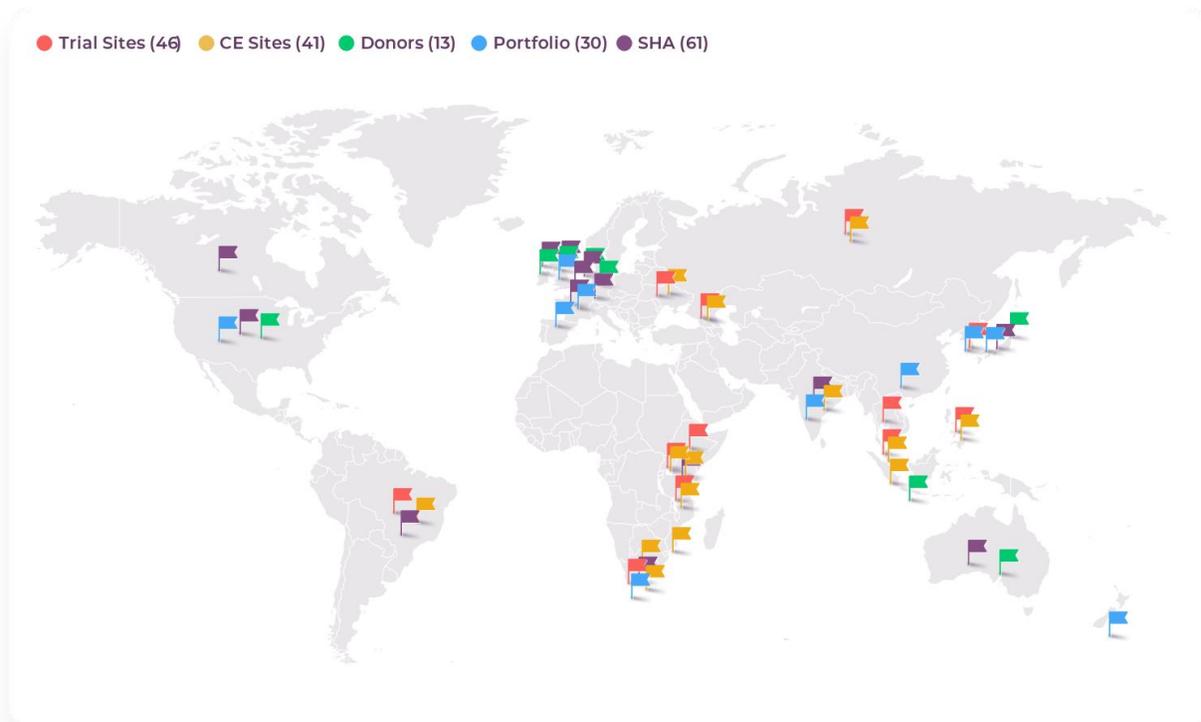
Communities: Essential Partners

Without patients and the support of their communities, research is not possible. TB Alliance maintains close relationships with the communities in which our research takes place. TB Alliance's Community Engagement program helps more than 40 sites educate and empower local communities to understand and influence research and TB-related issues locally and globally.

In 2018, Community Engagement sites participated in a variety of educational and advocacy activities, including events for World TB Day, World AIDS Day, and – through the [Louder than TB initiative](#) – participation in South Africa's "Walk the Talk" March, as well as advocacy campaigns around the HLM.

United Against TB: Our Global Network of Partners

Global problems like TB require global solutions. TB Alliance partners with researchers, funders, technical partners, communities and stakeholders of all kinds around the world to strengthen our scientific, operational and political capabilities to develop new TB treatments and fight TB rapidly and effectively.



Welcoming New Stakeholders

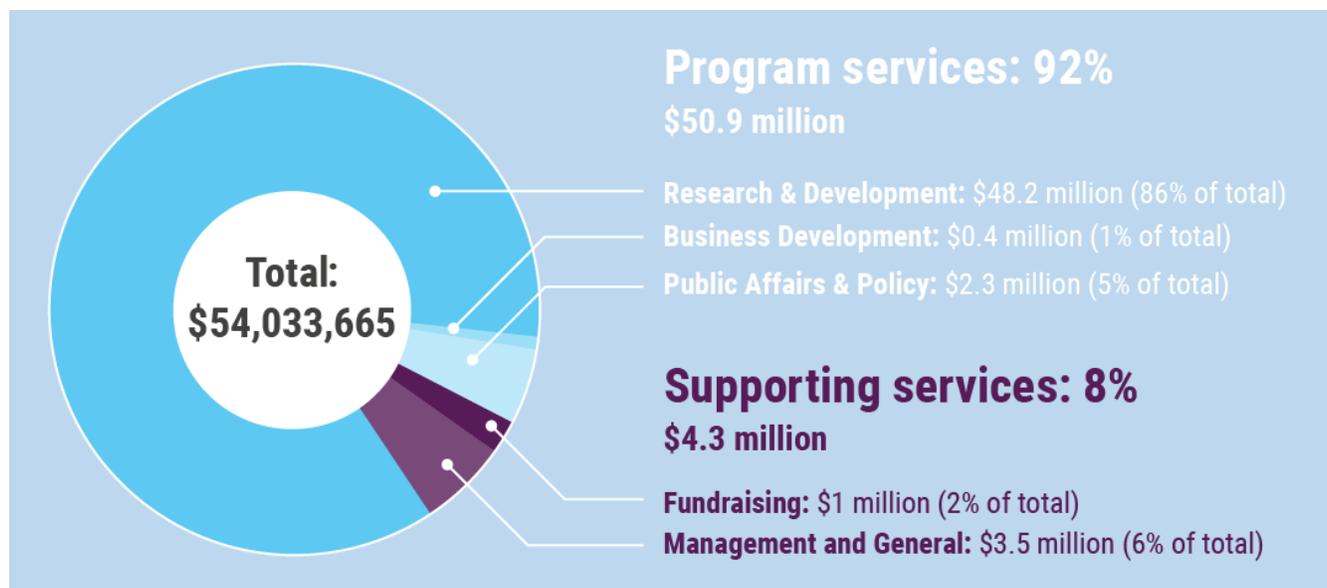
The TB Alliance [Stakeholders Association](#) (SHA) is an advisory committee of global organizations with diverse expertise that provides advice and support to TB Alliance's mission. In 2018, six new Stakeholder Organizations across five continents were added, representing clinical trial, technical, academic and advocacy partners, as well as a fellow "[PDP](#)."

- [Foundation for Neglected Disease Research](#) (FNDR)
- [Open Source Pharma](#)
- [Setshaba Research Centre](#)
- [TuBerculosis Vaccine Initiative](#) (TBVI)
- [The University of Dundee Drug Discovery Unit](#)
- [we are TB](#)

Read a summary of [2018 SHA Meeting in The Hague](#).

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.



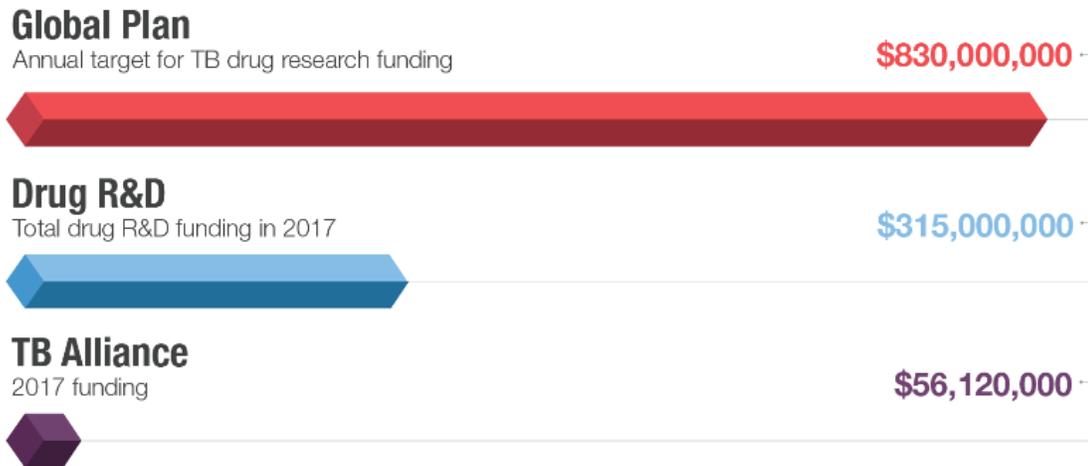
[Download our audited financial statements](#)

Stepping Up: World Leaders Express Commitment to Fund TB Research; Accountability Will Be Key

This past year saw new expressions of commitment to invest in TB research and development. Unfortunately, current funding levels remain far short of the \$2 billion annual funding target set in the [Stop TB Partnership's Global Plan to End TB, 2016-2020](#), which includes approximately \$830 million annually for TB drug research and development.

[Treatment Action Group's 2018 report](#) on TB research funding trends indicated that funding reached \$772 million in 2017, with \$315 million going to new cures. These figures stand at less than half the overall funding target, both for drugs specifically and research in general. At the United Nations High-Level Meeting on Tuberculosis in 2018, heads of state committed to fill this gap in the meeting's [Political Declaration](#), though plans to finance this commitment remain outstanding.

Despite a challenging funding environment, TB Alliance has made significant advances, including [introducing improved pediatric therapies](#) and submitting its first novel drug for FDA review and approval. It will take a global effort to hold world leaders accountable, but the case is clear: fully funding TB programs would expand and accelerate the development of life-saving treatments for all who suffer from TB.



TB Alliance is indebted to its partners, especially all participants in our clinical trials, for the progress seen in 2018.