MESSAGE FROM THE CEO AND BOARD CHAIR

"TB Alliance and our partners are launching a wave of next-generation clinical trials that have the potential to transform the TB epidemic."

Dear Stakeholders, Partners, and Patients,

2015 will be even more exciting as we prepare to introduce an appropriate, child-friendly pediatric formulation of first-line therapy.

In 2014, we made tremendous progress, especially in the clinical development arena. TB Alliance and our partners are launching a wave of next-generation clinical trials that have the potential to transform the TB epidemic.

One of the most critical developments over the last year has been the launch of the Phase 3 STAND trial (Shortening Treatments by Advancing Novel Drugs), which tests a regimen with one novel drug, pretomanid (formerly PA-824), along with moxifloxacin and pyrazinamide (PaMZ). The regimen shows promise for its ability to shorten and improve treatment for drug-sensitive, active TB – and more dramatically, for many patients with multi-drug resistant TB. The STAND trial is the first Phase 3 trial to test a single regimen against both drug-sensitive TB and MDR-TB. It is a truly global endeavor and is planned to run at 50 sites across 15 countries.

TB Alliance also launched a trial this year which tests a treatment with two novel drugs, pretomanid and bedaquiline, in combination with pyrazinamide. That regimen, known as BPaZ, could be effective in an even greater number of patients and potentially further shorten the duration of TB therapy.

We are preparing to launch a study called NiX-TB, which will support a larger effort to test three drugs with virtually no existing resistance. This is a seminal step on the road to actualizing our vision of an ultra-short, affordable, and universal regimen to treat all patients with active TB. That trial will begin with patients with XDR-TB whose survival rate is dismal and who are truly bereft of treatment options.

Two thousand and fifteen will be an even more exciting year, as we prepare to introduce an appropriate, child-friendly pediatric treatment – the first that has ever been marketed that is compliant with current WHO guidelines. We will continue to advocate to bring pediatric TB out of the shadows, improve treatment, and reduce

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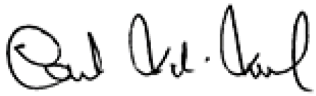
childhood deaths from TB.

Without our broad network of partners, we would not be able to do any of this work. Some of the most critical partnerships we have are with communities in which we run our trials. Those who have truly given of themselves are the patients who participate in the studies.

By expanding our work, into areas of MDR-TB, XDR-TB, and pediatric TB, we expand our potential impact to help bring this deadly pandemic under control.

None of this would have been remotely possible without the generosity of our donors. We can't begin to thank them enough for helping us, but more importantly, helping those affected by TB make the progress that's been made.

However, to cross the finish line, we will need more resources than we have had in the past. We invite others to join the fight. We need everyone's help – that's what it takes to tackle TB.



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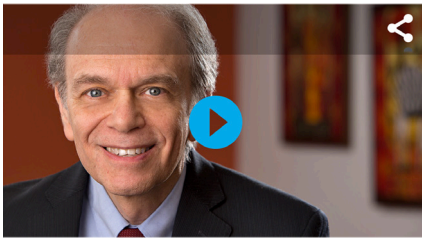
Our Vision: Short, Simple, Affordable Treatment for All

Message from the CEO



Tuberculosis remains one of the world's leading global health threats, killing more than 4,000 people each day. Today's treatments cannot most effectively combat the pandemic because they are too long and complex, and poorely effective against drug-resistant TB.

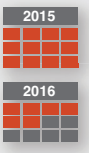
TB Alliance's ultimate vision is to have a transformative impact on the disease by introducing an ultra-short, simple, and affordable TB regimen that works in virtually all people with tuberculosis. A multi-drug regimen with such broad utility would would have a major impact on the global epidemic, saving millions of lives.

To achieve this impact, new regimens must be Adopted, Available, and Affordable.

Read more about our "AAA Mandate," click here.

Today's treatment for active TB must be taken for 6 months to 2 years, or more. Our vision is to treat a vast majority of patients with active TB with a single shorter, simpler, and more affordable regimen, and save millions of lives.

TB Treatment Today

	DRUG BURDEN	DURATION	COST	CURE RATE
DS-TB		 2015		
MDR-TB		 2015 2016		
XDR-TB		 2015 2016 2017		

Our Vision

ALL FORMS OF ACTIVE TB

SIMPLE

7 DAYS

AFFORDABLE

MILLIONS OF LIVES SAVED

Clinical Research Paves Way for New Products

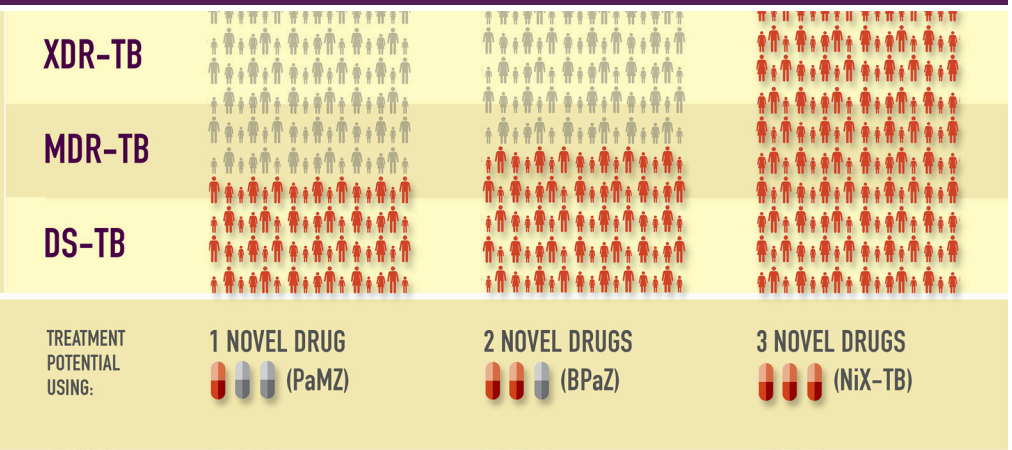
TB Alliance Overarching Clinical Strategy

TB Alliance's goal is to reduce the global burden of TB through the development and availability of dramatically improved treatments. TB must be treated with multiple drugs. Achieving maximum impact on the epidemic requires a short, simple, and affordable regimen comprised of all new drugs, circumventing the challenges posed by resistance to some of the antibiotics available today. Such a "universal" regimen could erase the distinctions of MDR-TB or XDR-TB by being effective in virtually all people with active TB. This would significantly improve TB control efforts globally.

Over the past year, TB Alliance launched a new wave of clinical trials, detailed below. These trials demonstrate the major progress made toward our goal of a fully novel regimen, by constituting treatments with one, then two, and then three novel drugs.

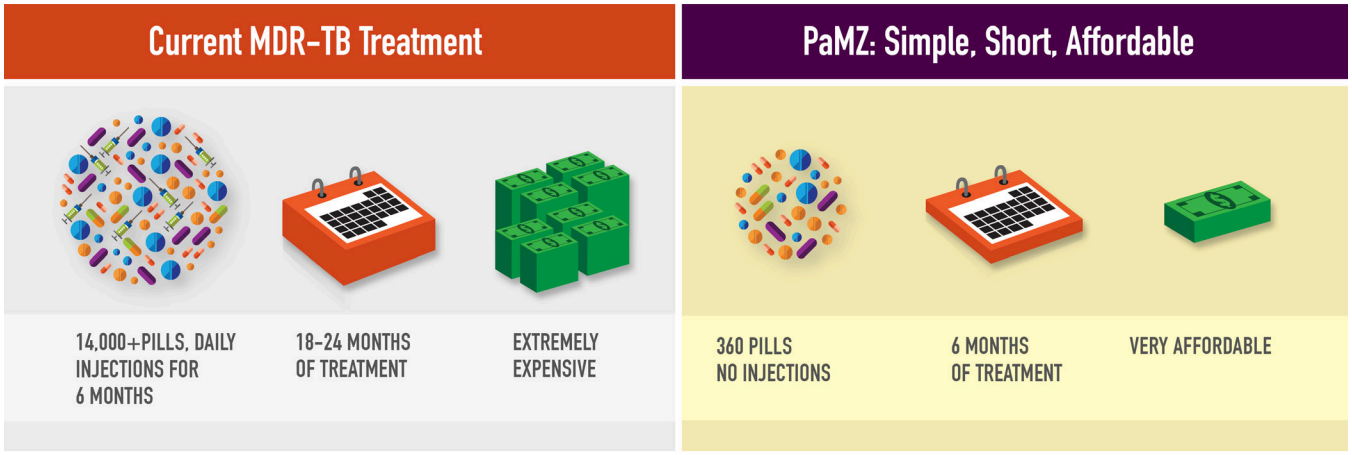
A universal regimen holds potential to treat all forms of TB

TB Alliance is taking major steps toward a fully novel TB cure with a series of new trials

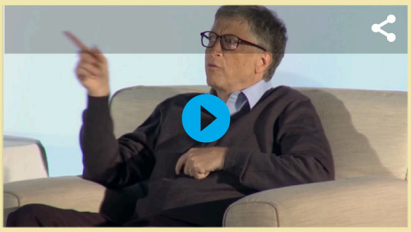


PaMZ Marches Forward: Global Phase 3 STAND Trial Launched

The PaMZ regimen, consisting of one novel drug candidate pretomanid, (formerly PA-824), moxifloxacin, and pyrazinamide, is the most advanced novel regimen currently in development. It shows promise to improve treatment for those with drug-sensitive TB and those with TB/HIV co-infection. It also shows the potential to markedly improve treatment of many patients with multi-drug resistant tuberculosis (MDR-TB) by being dramatically shorter, simpler, safer, and more affordable than current standard therapy.



Bill Gates on Promise of STAND



Bill Gates explains how PaMZ can revolutionize TB treatment for some MDR-TB patients.

FOSUN PHARMA TO HELP ADVANCE PaMZ REGIMEN IN CHINA.

Based on results of previous research, PaMZ has now advanced to its final stage of testing. The global Phase 3 clinical trial called STAND (Shortening Treatments by Advancing Novel Drugs) has begun, and is expected to enroll up to 1500 patients in 15 countries at approximately 50 sites around the world. It will be the first Phase 3 trial to test both drug-sensitive and MDR-TB patients with the same regimen. The trial will be conducted by TB Alliance, University of St. Andrews, University College London, among other partners.

Novel Regimen with Bedaquiline and Pretomanid Advances to Phase 2B Trial

VIEW OUR PORTFOLIO

The BPaZ regimen is comprised of two novel drugs, bedaquiline and pretomanid, in addition to pyrazinamide. The regimen shows potential to treat drug-sensitive tuberculosis and some forms of drug-resistant TB in as little as three months. Based on the published results of the Phase 2a two-week trial and earlier studies, BPaZ advanced to a two-month Phase 2b clinical trial, called NC-005, which began in 2014. The trial will enroll patients, whose TB organisms are sensitive to the drugs in the regimen, at 10 sites in South Africa, Tanzania, and Uganda.

NiX-TB to Test New XDR-TB Regimen; May Pave Way for Broad Impact

TB Alliance, over the course of 2014, initiated the foundational studies and other work needed to soon begin the NiX-TB (New Investigational Drugs for XDR-TB) trial. The study is expected to be among the first clinical trials to test a new treatment specifically for XDR-TB (extensively drug resistant tuberculosis) patients. XDR-TB is one of the deadliest forms of TB. Today, only a fraction (11%) of people with XDR-TB will be cured.

The regimen being tested in NiX-TB to treat XDR-TB is comprised of three drugs with little or no known resistance: bedaquiline, pretomanid, and linezolid. However, the true potential of such a regimen is even greater. Given the lack of pre-existing resistance to the drugs in this regimen, it shows potential to be a universal regimen – in other words, a single TB regimen that can treat virtually all patients with active TB – with a relatively simple and affordable regimen. The NiX-regimen must first be tested in XDR-TB patients because it may be more toxic than current MDR-TB therapy, but if the regimen proves successful and safe, that will pave the way for expanding the study, leading to potential use in MDR-TB patients and then potentially to drug-sensitive TB patients.

Study to Determine Proper Drug Doses for Babies for the First Time

Children with TB are neglected. Today, there are no appropriate child-friendly medicines to treat children with TB. We are currently working with partners to reformulate existing drugs for drug-sensitive TB into appropriate, child-friendly products, and have engaged manufacturers to ensure there will be a sustainable supply of these new products. Those products are expected to be available by 2016.

If children with TB are neglected, then babies with TB have been completely ignored. The dosing of TB medicines for newborns and infants weighing 5 kg or less had never been adequately studied. In 2014, Desmond Tutu TB Center, an academic research center of the University of Stellenbosch, South Africa, collaborated with TB Alliance to launch a trial to determine the appropriate doses and formulations of today's TB treatments for the youngest infants.

Additionally, the learnings from this project will inform the development of child-appropriate formulations of new TB treatments currently in the development pipeline, thereby reducing the delay between the availability of new TB treatments for adults and children.

Short, simple, and affordable cures can help save more lives

Reaching Children

New Cures for Children to Save Lives

Pediatric TB is a leading killer of children. Despite the extent of the problem, today, there are no appropriate child-friendly TB treatments. Working with the World Health Organization (WHO) and other partners, TB Alliance made significant progress in 2014 in advancing new treatments for children while continuing to fight to bring pediatric TB out of the shadows. This effort has catalyzed a multitude of stakeholders, and new child-friendly forms of today's treatments are expected to begin reaching children in 2016.

Click here to learn more about the need for pediatric TB treatment

When my daughter learned she had TB

A mother recounts her daughter's battle with TB and the stigma associated with it.

Preparing for Launch

Parents often have to crush multiple large and bitter pills made for adults in order to treat children. This leads to potentially inaccurate doses.

TB Alliance is working with pharmaceutical partners to develop child-friendly correctly dosed TB treatments that meet internationally recognized quality standards. These manufacturers are conducting the necessary studies needed by regulatory authorities to introduce improved products for children on a global basis. Over the past year, additional partnerships have been signed to ensure a sustainable and affordable supply of the new first-line treatments.

With product launch nearing, we have intensified our efforts to ensure the impact of the new products. In collaboration with WHO and national stakeholders, we have supported the development of action plans for the scale up of responses to childhood TB in more than half of the high TB burden countries. In addition, we have partnered with Management Sciences for Health and the Clinton Health Access Initiative to identify and navigate potential hurdles to product introduction in high burden priority countries.

This work will ensure the new child-friendly treatments reach children in need.

- Click here to view TB Thought Leader Series Webinar on preparation for new product introduction

Additionally, there has been much progress in understanding the burden of pediatric TB, which is critical to scaling the response to the issue. In 2014, we participated in a study published in *The Lancet* that took a new approach to quantifying the number of children with TB. This research will be used synergistically with other research efforts to improve the world's understanding of the global pediatric TB burden.

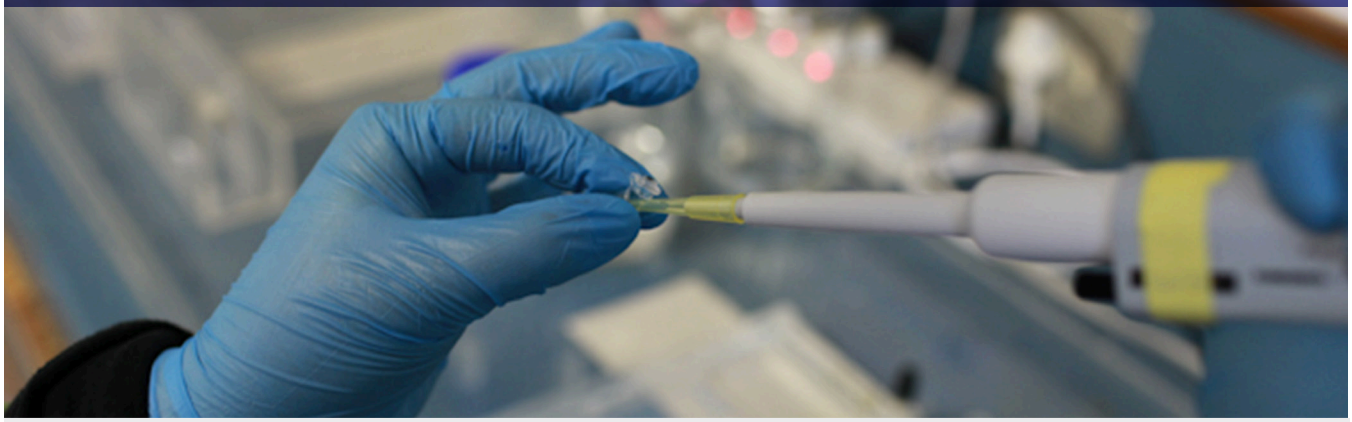
- Click here to listen to a podcast describing advances in understanding the childhood TB burden.

Working with Partners

TB Alliance's mission is centered around having impact on the global TB pandemic. No one organization could do that alone, especially in the neglected area of pediatric TB. We are fortunate to have a multitude of collaborations in this area, working to achieve our collective goal. This includes the World Health Organization, UNITAID, USAID, CHAI, Desmond Tutu TB Centre (University of Stellenbosch), MSH, Stop TB Partnership Global Drug Facility, and many others. In 2014, TB Alliance also established its Pediatric Advisory Group, which gathers thought leaders from around the world to lend their voice and expertise in paving the way for improved access to better treatments for childhood TB.

Click here to view TB Alliance's Pediatric Advisory Group

Breakthroughs in Drug Discovery



A Pipeline Poised to Deliver

TB Alliance's ultimate goal is to make available an ultra-short, simple, and affordable TB treatment that could treat the vast majority of TB patients. To develop such a multi-drug regimen requires a steady stream of new, promising TB drug candidates. For this reason, TB Alliance works in a wide variety of partnerships at all stages of the drug discovery and development process. This helps ensure promising new treatments are discovered and then brought through development in the most efficient way possible.

State of TB Alliance's Discovery Portfolio

Nader Fotouhi on the future of drug discovery at TB Alliance

Partnering for Tomorrow's Cures

Filling the pipeline is a global imperative to develop tomorrow's treatments. Over the past year, TB Alliance advanced TBA-354, a next-generation nitroimidazole, into Phase 1 testing. Globally, it is the first TB drug candidate to progress into clinical trials in six years. TBA-354 shows favorable properties when compared to pretomanid (formerly PA-824), a drug from the same class.

VIEW OUR PORTFOLIO

In 2014, the organization made particular progress advancing its large discovery-stage portfolio, focusing on those programs that are best positioned to soon deliver other drug candidates into the clinic. As a result of this work, we are now poised to advance a number of candidates into clinical development.

Our ability to leverage resources from collaborators allows us to cost-efficiently operate and more effectively advance discovery-stage programs. Many new projects and partners joined the pipeline in 2014, including multiple programs in-licensed from Novartis, a collaboration with OPBIO dedicated to developing TB drugs from natural products, and additional partnerships stemming from the Japanese Global Health Innovation and Technology (GHIT) Fund.

In 2014, TB Alliance became a member of the Bill & Melinda Gates Foundation's TB Drug Accelerator Program. This program brings TB drug developers together to share work and knowledge and accelerate the most worthy discovery programs. TB Alliance's participation in this group will help smooth new drugs' pathway from the lab to the clinic. Additionally, TB Alliance received an Innovation Grant from the Bill & Melinda Gates Foundation, which will fund the exploration of several promising, but untraditional drug discovery efforts over the next two years.

Building Better Regimens

TB ALLIANCE JOINS TB DRUG ACCELERATOR PROGRAM

We are assembling tomorrow's short, simple, and effective TB regimens. The close relationship between our discovery and development programs allows knowledge gained from trials to feed back into the discovery of new drug candidates. As our efforts evolve, our discovery team is pursuing new strategies to develop even more promising new regimens. Previously, we sought to compose a regimen of a variety of drugs that attack the TB bacteria in different ways. However, one new approach that is being explored is to overwhelm the TB bacteria with multiple drugs that all hit the same target or pathway.

To fully pursue such strategies at the clinical stage will require the development of many new drug candidates.

Strong Partners, Empowered Communities

Everyone has a Role to Play in Tackling TB

Everyone has a role to play in tackling TB. As a product development partnership, one of TB Alliance's core strengths is its ability to convene and facilitate collaboration among a global network of partners. These partnerships span the public and private sectors, and include collaborations with the pharmaceutical industry, manufacturers, academics, civil society, donors, healthcare providers, patients, and the broader global health sector, thereby enabling us to tackle the monumental goal of improved treatment for all. Here, we highlight our partnership with communities.

Scaling Partnerships with Affected Communities

Community Involvement

Click here to see a slide show of the 2nd Community Engagement Forum

Without informed and engaged communities, clinical research is not possible.

TB Alliance is an early pioneer in supporting and making Community Engagement (CE) a critical component of any TB research trial. Through our CE program, TB Alliance works with people affected by TB to empower them with knowledge and skills to promote open communication and participation in the TB drug research conducted in their communities.

In 2014, CE programs played a critical role in relaying the results of the Phase 3 REMox trial to communities that participated in that research. At the same time, CE coordinators were tasked with scaling up their work in preparation for the STAND trial. CE programs will be initiated at many new research sites participating in the STAND trial in Asia, Eastern Europe, and South America as well as Africa where the program has been ongoing for several years.

Measuring the Impact of Engagement

This year, TB Alliance helped introduce a toolkit for monitoring and evaluation of community engagement efforts. The tools were developed in partnership with AVAC and will serve as a way to quantify work undertaken by communities. This will help document the effect of CE for potential donors, partners, or other TB researchers that could implement similar programs. At the same time, such a tool allows the monitoring of progress and more concretely defining of successful strategies to obtain shared goals.

CE representatives were trained on the monitoring and evaluation toolkit at the 2nd Community Engagement Forum, which included 35 representatives from sites working with communities in Kenya, South Africa, and Tanzania. In addition to training, the CE Forum offered a chance for CE coordinators to share their experiences and learn from one another.

Patients Speak on Cost of TB Treatment

READ MORE ABOUT THE STUDY

VIEW THE FULL STUDY

The cost of TB treatment incurred by health systems is well known. However, what is less known is the financial burden of TB treatment that patients shoulder themselves.

In 2014, TB Alliance, working with five other organizations, published the first study to quantify the true cost of TB treatment to patients. The study analyzed nearly 100 patients in each Tanzania and Bangladesh, and looked at factors including lost economic productivity, cost of travel, food supplements, and other indirect financial impacts of the disease. Overall, the total cost per patient in the final two months of the continuation phase was catastrophic; in Tanzania, it constituted 77% of 2-month national income per capita and in Bangladesh, 89% of 2-month national income per capita. The findings lend further support to show how shorter TB treatments can result in economic improvement for patients.

Stakeholders Help Define an Acceptable Treatment

At the 2014 Union World Conference on Lung Health, TB Alliance brought together national treatment program managers, treatment providers, patients, and advocates to understand their preferences relating to new products in development. Feedback was received on issues relating to the pill size, number of pills, shape, and color. The feedback will be directly applied to the development of the PaMZ regimen, currently undergoing late stage development, as well as future treatments in the pipeline. This work helps ensure we meet the commitments of our "AAA Mandate," which will enable our products to be widely used and have significant impact on the TB pandemic.

2014 Union World Conference

TB patients and stakeholders from around the world assemble to offer advice on key characteristics of new products

PARTNERSHIPS ANNOUNCED IN 2014

- TB Alliance and partners complete REMox TB Phase 3 Trial, build infrastructure for future TB research
- Key Partnerships with UNITAID, USAID, and manufacturers push STEP-TB program forward
- Bill & Melinda Gates Foundation Announces Support for STAND trial
- TB Alliance and University of Stellenbosch Announce Launch of Study to Determine Proper TB Treatment for Babies with TB
- TB Alliance Grants Fosun Pharma Rights to Develop, Market Promising TB Cure in China
- Novartis Provides Drug Candidate Compounds to TB Alliance
- Developing New Tuberculosis Drugs from Marine Natural Products: Joint research program between OPBIO and TB Alliance announced
- TB Alliance Spins-out Non-TB Assets to TenNor Therapeutics