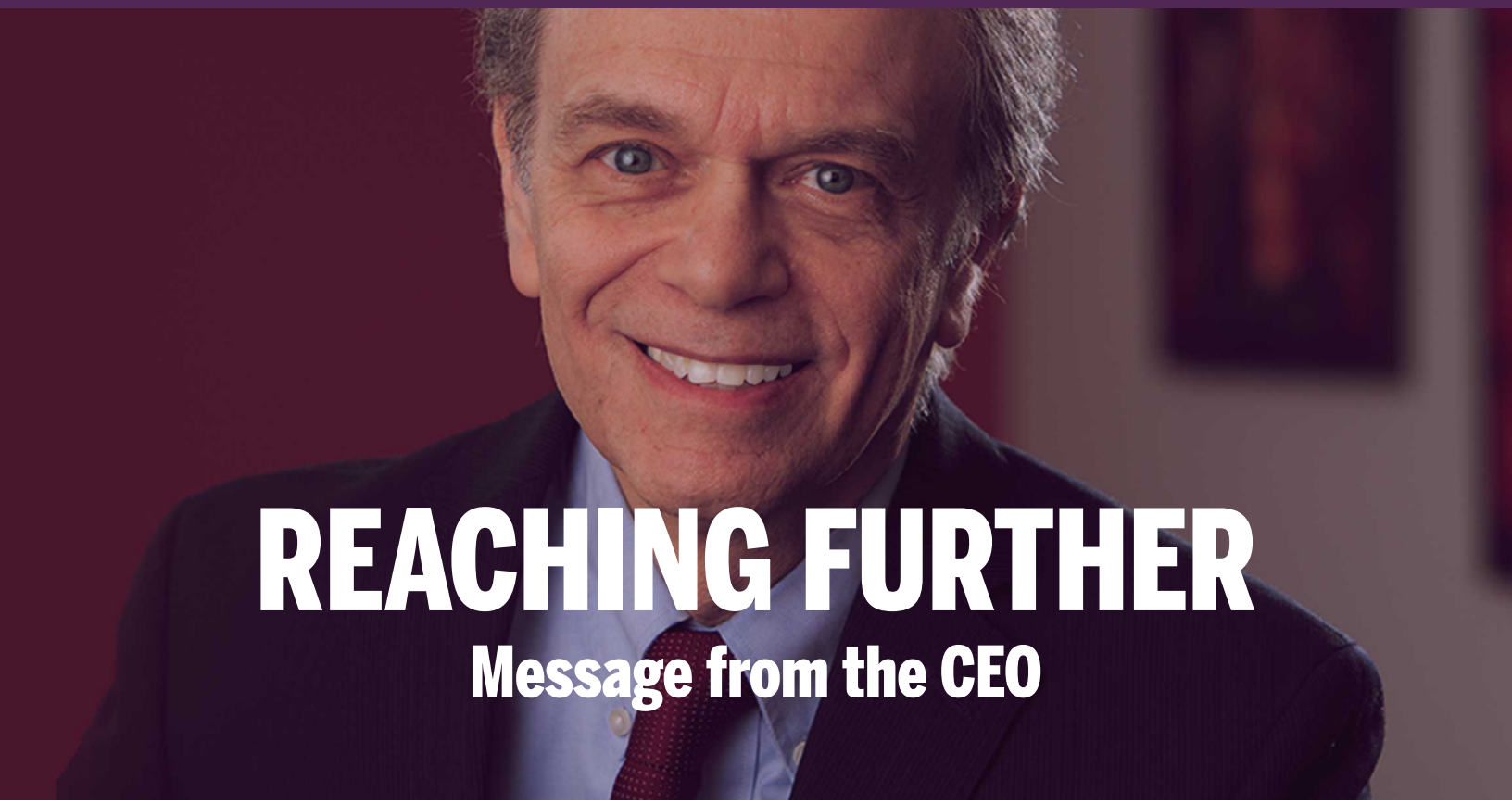


REACHING FURTHER

Message from the CEO

“We now have the audacity to envision a world where all TB patients can be treated for a few months with the same regimen, with excellent results.”

Dear Stakeholders, Partners and Patients,

For TB Alliance, 2015 was a milestone year marked by tremendous accomplishments, including reaching some of the most vulnerable and neglected patients with TB.

A major achievement was our first introduction of TB Alliance sponsored products. Working alongside key partners, including the World Health Organization and UNITAID, we were able to bring to market the first appropriately dosed and formulated child-friendly TB medicines. Historically, children with TB have been neglected, without access to appropriate medicines. Today, because of these new medicines, there is an incredible opportunity to improve treatment for the 1 million children around the world with TB and save countless lives.

Without an effective treatment, XDR-TB is a veritable death sentence for most patients. Over the past year, TB Alliance began the so-called Nix-TB clinical trial to test a new paradigm for developing novel, impactful regimens while simultaneously providing hope for patients with highly-resistant TB. The trial is progressing well, with the number of patients enrolled in 2015 tripling our expectations. The first set of study participants have completed the 6 month all-oral regimen and have been able to return home to their families. They will now be monitored for an additional two years to see if they have been cured of XDR-TB.

Over the past year, we've also completed the phase 2b trial of the BPaZ (bedaquiline, pretomanid and pyrazinamide) regimen, which is predicted to be the fastest-acting TB cure currently in clinical development. The regimen shows potential to treat virtually all patients with drug-sensitive TB as well as approximately half of all MDR-TB cases. The results of that trial are expected in 2016. If those results are positive, BPaZ could progress to Phase 3 registration trial.

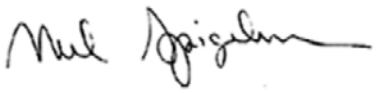
In the area of early research and discovery, TB Alliance progressed more compounds than ever before, adding projects and partners in a variety of new geographies. We also became a formal member of the Bill & Melinda Gates Foundation sponsored TB Drug Accelerator Program. These efforts should expand the strength of the global TB portfolio and help ensure a critical mass of new compounds advancing into the clinic over the next few years.

Despite this tremendous progress in 2015, we also faced some setbacks. The STAND trial remains on partial clinical hold and the program for TBA-354, a Phase 1 candidate, was discontinued. This highlights to us that the work we're doing is still fraught with risk, emphasizing the reality that even though we have the largest single TB drug pipeline ever assembled, we need more investment to build a sufficiently robust pipeline.

However, we also need to focus on the potential that lies ahead with the current development programs. We now have, for the first time ever, a totally novel regimen for which we've already seen patients benefit. As an organization and as a community, that should give us the audacity to reach into the future and envision a world where all TB patients can be treated for a few months with the same regimen, with excellent results.

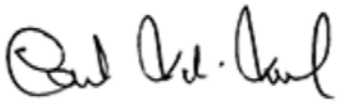
I would like to thank all of our partners — the donors, collaborators, and most especially the TB patients who have participated in our clinical trials. It is only through their commitment that progress has been made towards saving the lives of millions of TB patients around the world.

Sincerely,



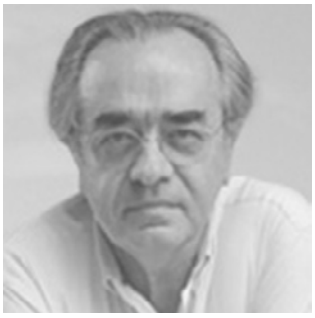
Dr. Mel Spigelman

President and CEO,
TB Alliance



Dr. Carlos Morel

Chariman of the Board,
TB Alliance



Children now have A CURE OF THEIR OWN

Fruit-flavored medicines in the correct doses for children are now available.

World's first availability of child-friendly TB medicines in correct doses.

In 2015, TB Alliance and partners announced the launch of child-friendly tuberculosis medicines in the correct doses. The improved treatments are the first to meet the current dosage guidelines set by the World Health Organization (WHO) and have the potential to simplify and improve treatment for the one million children who get sick with TB each year. Children with TB are especially neglected. Previously, there were no appropriate medicines for children with TB, which meant that caregivers and providers needed to split or crush tablets for children. The availability of these products is a result of a project largely funded by UNITAID.

This product introduction is especially important as it marks the first medicines that TB Alliance has brought to market. In keeping with TB Alliance's "AAA Mandate," the improved medicines for children are available, accessible, and affordable. The products are globally available for purchase through the Stop TB Partnership's Global Drug Facility and directly through the manufacturer, Macleods Pharmaceuticals.

Thanks to our partners

Together with our partners, including WHO, UNITAID, and USAID, we are working to ensure that no child dies of TB. Click here to read more about the important collaborations that are accelerating access to new childhood treatments.

“A Cure for me.”

Bangkok, Thailand: After years of inappropriate treatment, children will finally have TB medicines that are designed specifically for their needs.

Delft, South Africa: TB is the leading killer in South Africa. Adoption of improved TB medicines for children will help improve survival among the most vulnerable.

Delhi, India: The new child-friendly medicines will help India scale up treatment of children with TB. The medicines come in the correct doses, are dissolvable in water, and are berry-flavored.

Cape Town, South Africa: The new TB medicines will be easy for parents to administer and for children to take.

Manila, Philippines: No child should die of TB. Healthcare workers are preparing to mobilize to support country introduction of the improved TB medicines for children.

Introducing new medicines for children.

Cutting or crushing bitter tablets each day makes the job of treating children with TB even more difficult. However, the new berry-flavored TB medicines are easy for providers to administer and for children of all ages to take.

The medicines come in the correct, WHO-recommended dose, can be dissolved in a small amount of water, and offer the potential to improve adherence and child survival from TB.

Over the past year, research has continued to foster a better understanding of the market, find where children are most at risk, and create a more supportive environment for TB product introduction. Importantly, this has included research that helped lead to a substantial revision of the WHO's childhood TB estimates, doubling previous estimates. A study focused on the problem of underreporting of childhood TB in Indonesia, Nigeria, and Pakistan, was published in Plos One. Further, a suite of journal articles, including an assessment of the market for pediatric TB, analysis from stakeholder interviews on the challenges facing the market, and an assessment of country readiness for product introduction was published in a supplement to the *International Journal of Tuberculosis and Lung Disease*. The full supplement can be read here.

Click here to watch this video about a mother recounting her child's struggle with TB and learn what needs to be done to improve children's treatment and survival from this disease.

Accelerating adoption of new cures for children.

It's not enough to make new medicines for children available. We can't achieve our mission until every child in need can access these improved TB treatments. Over the past year, TB Alliance has established a number of partnerships to accelerate and maximize the use of these new cures around the world. Watch these videos and learn more.

"There is a lot of work that needs to be done, but it's a journey that we in Kenya are willing to take on."

Dr. Enos Masini, the National Treatment Program Manager of Kenya, discusses progress and plans in rolling out the improved childhood TB products.

"A simpler treatment has created a great enthusiasm to engage much more deeply in childhood TB."

Dr. Stephen Graham, Professor of International Child Health with the University of Melbourne, Australia, discusses the broad impact the TB Alliance's involvement in childhood TB has had on the broader sector.

Reaching Further: No Child Should Die of TB.

There is much to celebrate about the progress in childhood TB. Not only are new treatments available, some countries have already begun to procure the new medicines. Over the course of 2016, together with partners, we expect that the WHO prequalification of the medicines, market authorizations, and an additional commercial manufacturer of the products will continue to expand access of these products to those who need them.

TB Alliance is continuing to work with partners to round out the toolkit needed to treat children with drug-sensitive TB. This will include correctly dosed and child-friendly formulations of single drugs including ethambutol, often recommended in countries with a high prevalence of TB/HIV, and isoniazid, recommended for preventive therapy.

At the same time, when it comes to the neglect of children, the world will repeat the same mistakes again if there is not an increase in political commitment, funding, and other action in this area.

There are still no child-friendly treatments for drug-resistant TB, and the treatment regimens available for children, as with adults, take too long to cure. Traditionally, the development of TB drugs for children has a years-long lag behind that of adults, which itself has moved too slowly. For the children with TB around the world, time is literally a matter of life and death. As a community, we must continue to accelerate the development of pediatric versions of new TB drugs within product development programs and strategies — a paradigm described in an article TB Alliance wrote in collaboration with authors from the European Medicines Agency and Treatment Action Group. We must also continue to push for the adoption of new products such that the drugs are in the hands of the provider or caretaker when a child gets TB.

Educate yourself.

Visit our childhood TB resources page for more information and downloadable tools related to pediatric TB and new cures.

Sign the petition.

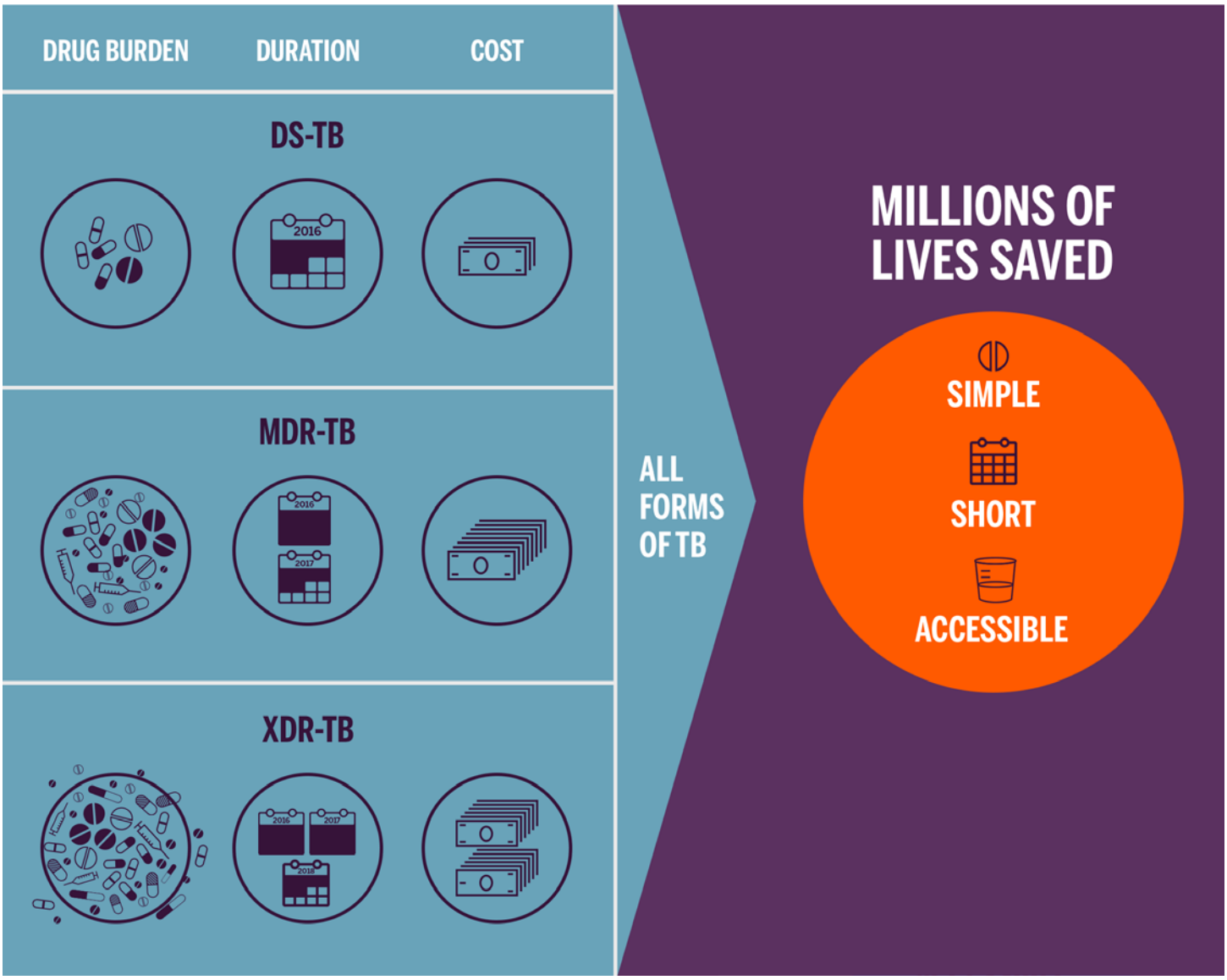
Tell world leaders to sign the petition.

UNPRECEDENTED EFFORTS in drug research

TB Alliance is advancing treatments that reach all in need through our pursuit of a universal regimen

To end the global TB pandemic, we need improved treatments for all people with TB. Of tremendous excitement in 2015 was the progress TB Alliance and its partners made in our research and development pipeline. This includes research that hold the promise to shorten and improve the treatment of drug-sensitive and MDR-TB, and also a new trial testing a potential treatment for XDR-TB, giving those patients a markedly enhanced hope for cure.

These trials are part of our product development strategy and help advance our vision of a "universal regimen" — a single ultra-short, simple, and accessible TB treatment that works in virtually all people with tuberculosis. To do this, we develop regimens that have reduced pill burden and duration of treatment, don't require injectable drugs, and will be accessible, affordable and available to the patients who need them. Over the past year, TB Alliance made significant progress in the pursuit of a universal regimen, as described through the milestones outlined below.


TB treatment today
Our vision
DRUG BURDEN
DURATION
COST
DS-TB
2016
MDR-TB
2016
2017
XDR-TB
2016
2017
2018
ALL FORMS OF TB
MILLIONS OF LIVES SAVED
SIMPLE
SHORT
ACCESSIBLE

Reaching tomorrow's cures

NC-005, a Phase 2b trial testing a novel regimen, completes enrollment

In 2015, TB Alliance completed enrollment of the NC-005 trial. This Phase 2b trial, conducted at 10 sites across Uganda, South Africa, and Tanzania, tested the efficacy and safety of BPaZ — bedaquiline (B), pretomanid (Pa), and pyrazinamide (Z) — over the course of two months of treatment. The trial also investigated a simpler dosing scheme for bedaquiline that could lead to fewer pills and an overall less complicated treatment for patients. Approximately 240 patients participated in the trial.

BPaZ is projected to be the shortest regimen of those currently in clinical development. Earlier studies and pre-clinical research shows that it has promise to reduce TB treatment to as little as three months — cutting treatment time by half for people with drug-sensitive TB, and to just an eighth of the current two-year treatment time for people with MDR-TB.

As bedaquiline and pretomanid are two novel agents, BPaZ has the potential to be useful in virtually all drug-sensitive TB patients, as well as approximately half of MDR-TB patients. If successful, the results of NC-005 could give way to a global Phase 3 trial that could lead to the worldwide registration of the BPaZ treatment. Results will be available in 2016.

Thanks to the sites that participated in the NC-005 trial

Thusong Clinic
Johannesburg, South Africa

University of Cape Town Lung Institute (Pty) Ltd
Cape Town, South Africa

Task Applied Science
Cape Town, South Africa

NIMR- Mbeya Medical Research Programme
Mbeya, Tanzania

Ifakara Health Institute
Bagamoyo, Tanzania

The Aurum institute: Tembisa Hospital
Tembisa, South Africa

Uganda Case Western Reserve University Research Collaboration
Kampala, Uganda

CHRU Themba Lethu Clinic
Johannesburg, South Africa

THINK: Tuberculosis & HIV Investigative Network of KwaZulu-Natal
Durban, South Africa

Klerksdorp Tshepong Hospital
Klerksdorp, South Africa

In 2015, TB Alliance and partners launched Nix-TB, which tests a new all-oral regimen for XDR-TB. The progress has been rapid, with the trial's enrollment tripling expectations.

Nix-TB is a critical step in the development of a universal treatment for all types of TB, as it is the first study to test a treatment comprised of all drugs with minimal or no pre-existing resistance. As such, if found to be safe and effective, the treatment could potentially be expanded for use in other types of patient populations. To read more about progress in the trial and its significance on the pathway toward a universal regimen, click here.

LEARN MORE

View our interactive portfolio

TB Alliance and partners are advancing the largest portfolio of TB treatments in history.

VIEW INTERACTIVE PORTFOLIO

Advancement in the discovery pipeline

In the area of early research and discovery, 2015 was an exciting year as TB Alliance progressed more compounds than ever before in our history.

We formally joined the Bill and Melinda Gates Foundation TB Drug Accelerator (TBDA) as a full partner. This allows us to markedly expand our collaborations with public and private partners working in the area of TB drug discovery and pre-clinical development. Through the TBDA, we can meaningfully contribute, adding knowledge and experience, and advance what we hope will be an expanded number of drug discovery portfolio candidates in the coming years.

In terms of projects, of particular importance was the advancement into preclinical development of a program which focuses on the enzyme DprE1, which is involved in cell wall biosynthesis. The treatment represents a new class of drugs and has a novel mechanism of action. This is important in fighting both drug-sensitive and drug-resistant strains of the disease.

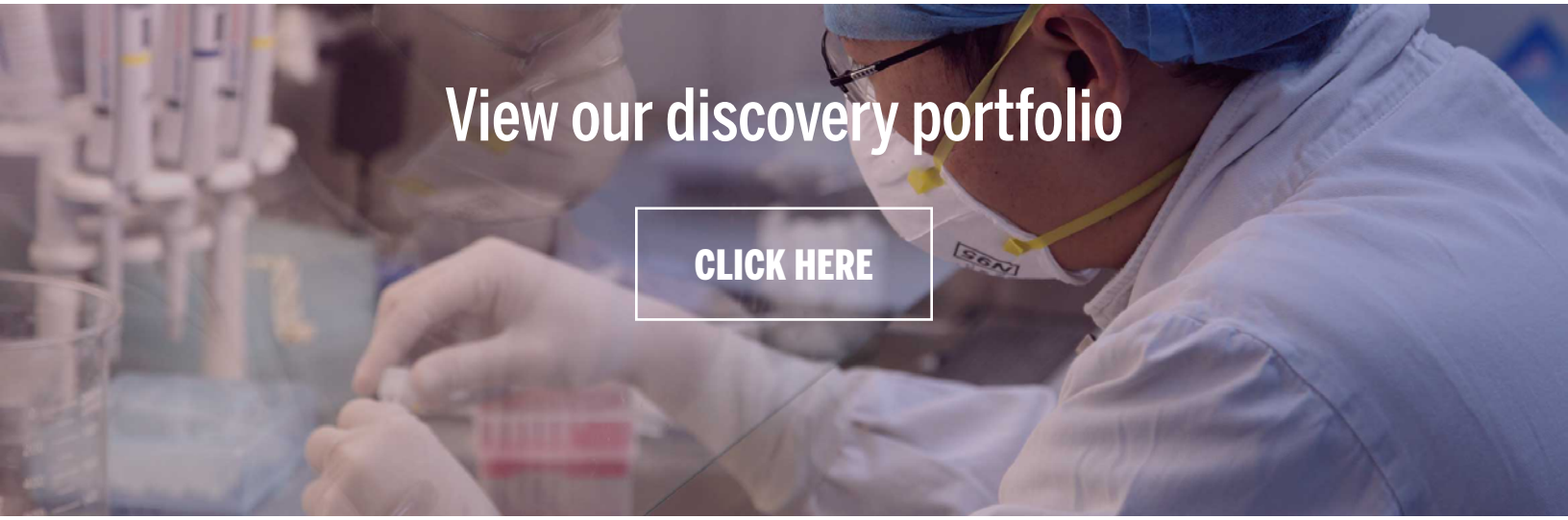
Other progress was seen in our portfolio of work with Japanese companies, funded through Global Health Innovative Technology Fund (GHIT). The partnerships with Daiichi Sankyo and Shionogi resulted in the advancement of compounds from screening programs to the hit-to-lead stage. The number of programs also expanded, with new partnerships formed with Chugai, Daiichi Sankyo Novare, HyphaGenesis, Mitsubishi-Tanabe, OP-Bio, and Sumitomo-Dainippon.

In the area of early research and discovery, 2015 was an exciting year as TB Alliance progressed more compounds than ever before in our history.

Over the course of the last year, TB Alliance expanded its focus on natural products — that is, compounds that are found from microorganisms and plants. Many of our partnerships with GHIT, as well a new partnership with Universitas Gadjah Mada in Indonesia, funded by the Indonesia Health Fund, are focused on this area. Because of the evolutionary process over millennia, many natural products are thought to have antibacterial activity and indeed, many of the current antibacterials today such as rifampicin have their roots in natural products. Conducting this type of antibiotic discovery using modern-day technology holds promise for uncovering novel TB drugs.

Other partners gained during 2015 include Roche, which is now collaborating with TB Alliance to test their PEPCK program compounds for anti-TB activities, and Schrödinger, which is enhancing our discovery capabilities by introducing cutting-edge computational chemistry and structure-guided drug design to several programs. Meanwhile, our current partners, including GlaxoSmithKline and Sanofi, are advancing several programs toward candidate nomination.

This year, we have also seen the advancement of many of our discovery programs from early to advanced status within the lead identification and lead optimization phases of development. For example, seven programs in the lead optimization phase are in an advanced stage of this process, with potential to enter preclinical development in the next two years pending successful outcomes of current studies. All of these programs focus on compounds that work against drug-sensitive and drug resistant strains, and therefore could help advance progress toward our vision of a universal regimen. This work lays the groundwork for what should be a tremendously successful 2016 and delivery of novel clinical compounds at a sustainable rate, in 2017 and beyond.



Other updates in clinical trials

The research and development of new TB treatments is not without risk; setbacks and attrition are to be expected.

Currently, the Phase 3 STAND trial, testing the PaMZ regimen, is on partial clinical hold. While participants in the study are continuing in the trial, new enrollment has been paused. This pause was recommended in 2015 by the trial's Data Safety Monitoring Committee (DSMC), so they could further analyze data related to potential toxicity and for TB Alliance to institute other changes in the trial to enhance patient safety. Since then, the DSMC has reviewed additional unblinded data and recommended that the trial resume enrollment. TB Alliance is now reaching out to multiple constituencies, such as the relevant regulatory agencies, before making a definitive decision on how to re-start the trial. Updates on the trial's status can be found here.

In January 2016, TB Alliance announced that it voluntarily halted further dosing of its Phase 1 compound, TBA-354, due to unexpected signs detected in clinical trial participants who were administered the compound. The organization has now made a decision to end this clinical trial program.

GREATER IMPACT
through policy and partnership

It is the commitment of our partners that allows us to reach further, faster, in delivering new, improved TB treatments.

TB Alliance is a not-for-profit product development partnership and is uniquely positioned to leverage a global network of public and private collaborators to most efficiently drive the development and market availability of new TB treatments.

Indeed, it is because and with our partners, that we have been able to achieve success in 2015.

Partnerships are especially critical given the scarce resources currently allotted to the development of new tools and technologies for TB. Funding of TB research, according to the updated Global Plan to Stop TB, has stagnated to about a third of what is necessary.

This is out of alignment with the ambitious plans that world leaders have issued over the past year to tackle TB. The United Nations' new Sustainable Development Goals, (which have transitioned from the Millennium Development Goals) explicitly call for the end of the TB pandemic by 2030. Similarly, the World Health Organization issued its new End TB Strategy, also setting elimination targets. Meanwhile, a plan to combat drug-resistant TB was recently issued by the U.S. White House. All of these plans acknowledge the central role of new treatments to elimination efforts.

Still, these actions have yet to translate into the necessary increases in funding to achieve the ambitious goals laid out by world leaders. If nothing further is done to stop the pandemic, it will cost the world a cumulative $16.7 trillion in the next 35 years, finds a report on antimicrobial resistance.

Despite the challenges, in 2015, TB Alliance made critical inroads in reaching some of the previously most unreachable populations of those suffering from TB. To do this, we brokered a number of new partnerships and strengthened existing ones. It is the commitment to our mission, vision, and work that our partners — be it donors, drug development partners, advisors, and others — that we can reach further, faster, in bringing improved new TB treatments to the people who need them.

Reaching Further: for Children

In 2015, TB Alliance and partners announced the launch of new, child-friendly TB treatments in the appropriate doses.

The development and availability of child-friendly TB treatments was largely funded by UNITAID, with supportive funding from USAID, Australia's DFAT, United Kingdom's DFID, and Irish Aid. This support means that, for the first time, there is now appropriate treatment for children with drug-sensitive TB, helping a population that has been utterly neglected.

However, it's not enough to develop needed treatments — we need to ensure they reach children in need. We would like to thank our project partner, WHO, for their work to support the policy, regulatory and uptake work needed to accelerate the availability of the products and Macleods, the first manufacturer of the fixed dose combinations, which came to market ahead of schedule.

Additionally, collaboration with Baylor University, The Global Fund to Fight AIDS, TB, and Malaria, KNCV, Management Sciences for Health, Medicins sans Frontieres, Stop TB Partnership, and UNICEF, and many others, will help accelerate adoption and use in high TB burden countries, helping us to achieve our collective goal of improved treatment of and child survival from TB.

Reaching the neglected children

There is still much that is needed to improve the treatment of children. Through 2016/2017, we will continue to work in partnership to prepare for the introduction of additional medicines to improve the toolkit for pediatric TB, including correctly dosed and child-friendly formulations of ethambutol, often recomended in countries with a high prevalence of TB/HIV, and isoniazid, recommended for preventive therapy.

Community Engagement

TB Alliance worked with its Community Engagement (CE) partners to create a school-base curriculum and a suite of educational materials to improve knowledge about TB among children. In addition to lessons in the classroom, children had a chance to create a mural in their local community to raise awareness of the disease. Other CE effoerts this year included a toolkit that captures and measures the impact of community and stakeholder engagement activities on clinical trial activity.

Reaching further: communities and patients

Without community, research is not optimal. TB Alliance partners with sites to invest in community engagement (CE) programs, with the goal of empowering communities and patients with improved knowledge of TB so they can have a voice in the research process. Over the past year, we increased our investment to ensure sites that conducted late-stage research had companion CE programs. This meant that, over the past year, we engaged with 25 research sites to support and develop CE programs as part of our small grants program.

TB Alliance is committed to work with other sponsors to share best practices in CE. In 2015, we partnered with AVAC and IAVI to create a Global Health Community Engagement Forum, the first forum of its kind, which took place September 27-29 in Johannesburg, South Africa. The Forum included more than 80 CE implementers across diseases, research sites, and networks to build a stronger, more strategic, and better understood community of participatory and stakeholder engagement practice.

Above all else, we thank the patients who participate in our clinical trials. Without their participation, we could not advance the development of new treatments and create a TB-free future.

Reaching for expanded support

Over the past year, TB Alliance achieved a number of partnerships with donors that allow it to accelerate new treatments for those in need.

This included a new five-year grant from the Bill & Melinda Gates Foundation; additional support from DFID; and a five-year grant from the Dutch Ministry of Foreign Affairs (DGIS), which is once again supporting TB Alliance.

The US FDA reinitiated support for TB Alliance's biobank with a two-year agreement to fund specimen collection; support from GHIT was expanded for discovery work; and TB Alliance received its first grant from the Indonesian Health Fund, comprised of individual donations from business leaders in Indonesia. This grant allows us to progress work that builds the country's capacity to fight the TB epidemic and is especially important in light of new evidence that the prevalence of TB is much higher than previously estimated.

Reaching deeper: growing the pipeline

It is through collaboration and partnership that TB Alliance has significantly expanded its efforts to discover new compounds that hold the promise to become tomorrow's TB cures.

Through our partnership with the TB Drug Accelerator (TBDA) consortium, we are experiencing heightened engagement with research organizations involved in TB drug discovery and pre-clinical development. The TBDA is presently a collaboration of eight pharmaceutical companies, eight academic universities, and TB Alliance which are working together to expand the number of candidates coming into the pipeline in the coming years by pooling capabilities, platforms, and expertise of member organizations. In particular, TB Alliance would like to recognize the contribution of Eli Lilly, which is dedicating in-kind support in conducting a GLP toxicology program. AbbVie has also contributed in-kind support for advancement of pre-clinical compounds.

We have also successfully grown our partnerships in Japan, with help and funding from GHIT, including new partnerships formed with Chugai, Daiichi Sankyo Novare, HyphaGenesis, Mitsubishi-Tanabe, OP-Bio, and Sumitomo-Dainippon. In Indonesia, TB Alliance has established a new partnership with Universitas Gadjah Mada, funded by the Indonesia Health Fund.

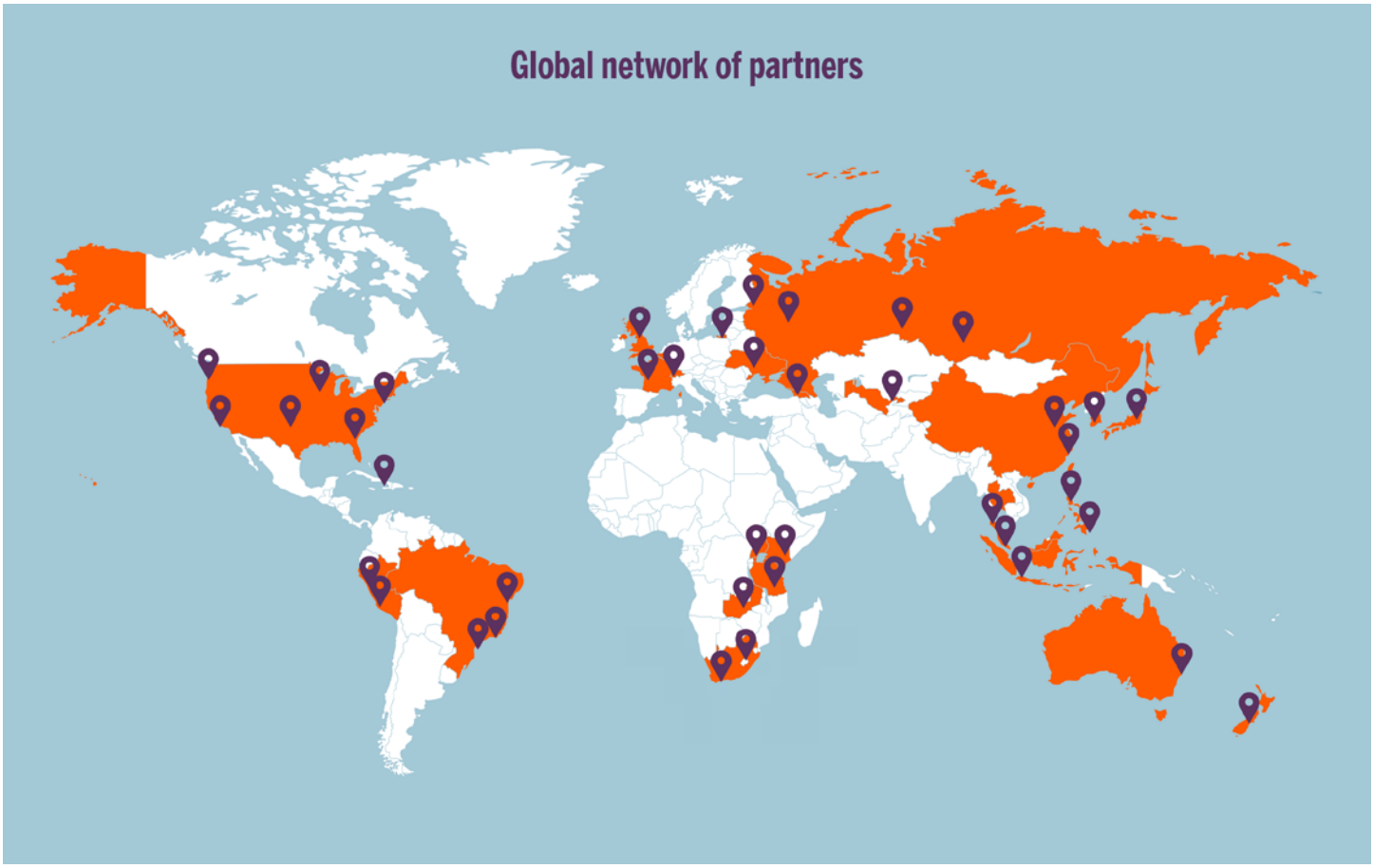
These partnerships complement our other collaborations with large pharmaceutical and smaller companies, and academic institutions. In 2015, Roche and Schrödinger joined TB Alliance's roster of partners. To find out more about this work, click here.

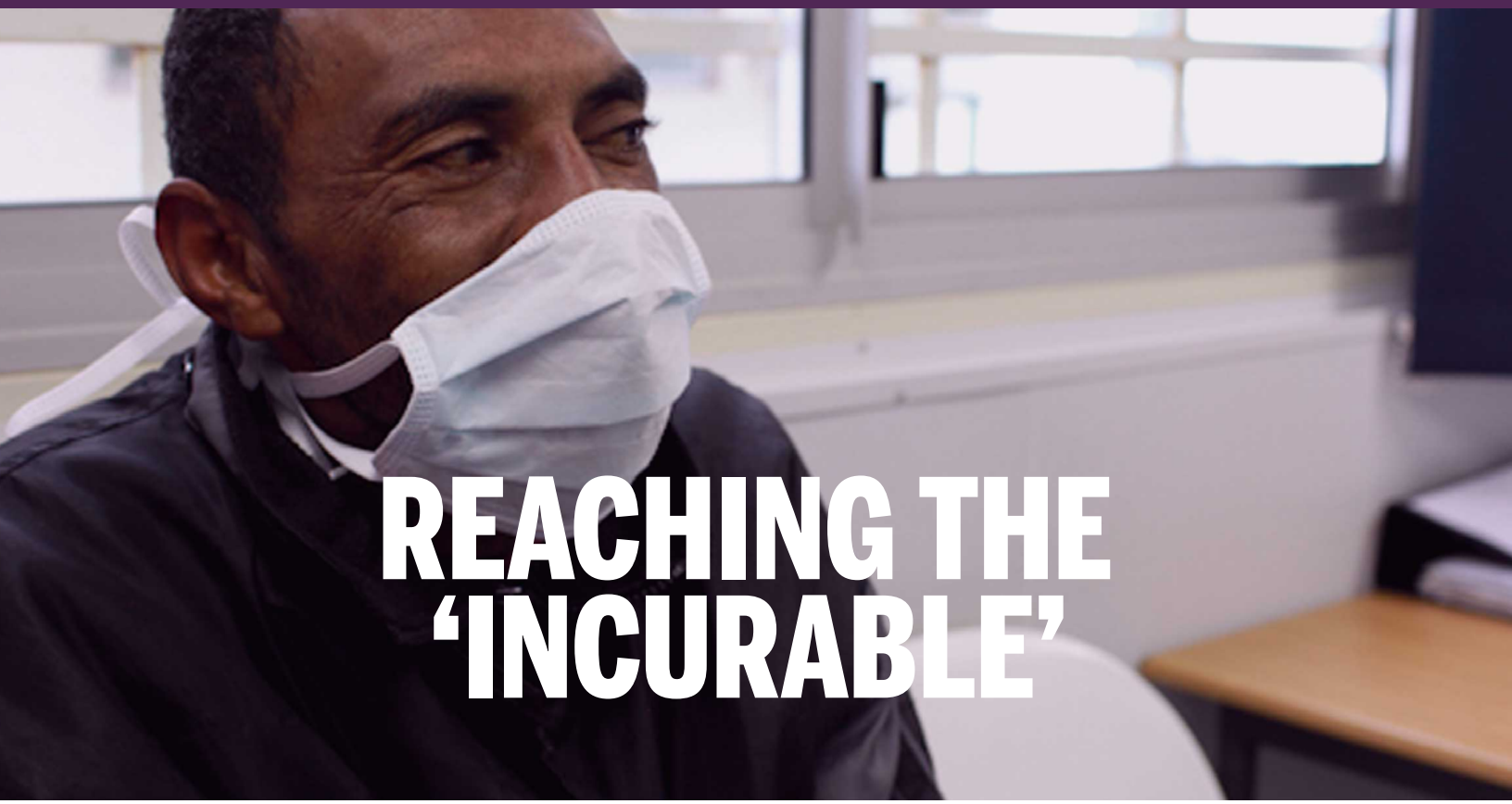
Reaching further: through research partners

Without our global network of research sites, we could not run the clinical trials needed to achieve improved TB treatments. Sites that participate in TB Alliance studies are located around the world, on the front lines of care of clinical trial participants. We are indebted to their work. In 2015, we would especially like to recognize the sites in Uganda, Tanzania, and South Africa which participated in the NC-005 trial, which completed enrollment for the Phase 2b trial.

The past year also marked the 5th Anniversary of the Critical Path to TB Drug Regimens (CPTR) Initiative. Co-lead by TB Alliance alongside the Critical Path Institute and the Bill & Melinda Gates Foundation, the Critical Path to TB Drug Regimens has helped advance a wide variety of tools, models, and approaches to support the acceleration of TB drug development, spur and coordinate the development of complementary technologies, and to better evaluate clinical data to help inform trial design and prediction.

In 2015, CPTR and the WHO's Special Programme for Research and Training in Tropical Diseases (TDR) have partnered to help maximize the knowledge and understanding gained from completed Phase 3 TB drug clinical trials. The partnership brings together an expert steering committee to analyze three contemporary Phase 3 trials (REMox TB, Rifaquin, and OFLOTUB), to improve understanding of fluoroquinolone-containing shortened regimens for drug-susceptible TB. Through this collaboration, we expect the development of new tools to optimize the design of future TB trial design. Most notably, CPTR's work led to the endorsement of the in vitro hollow fiber system of tuberculosis (HFS-TB) — a preclinical model to evaluate TB drugs individually or in combination — by leading regulatory authorities, including the European Medicines Agency (EMA) and the United States Food and Drug Administration (FDA).


Global network of partners



REACHING THE 'INCURABLE'

XDR-TB is a global health threat. We're accelerating a treatment that provides hope to the hopeless.

TB, like many other bacterial diseases treated with antibiotics, is growing increasingly resistant to the available drugs that have been in use for decades. Extensively drug-resistant TB, or XDR-TB, is caused by strains of *M. tuberculosis* that are resistant to at least four commonly used anti-TB drugs. XDR-TB is often considered a death sentence. The proof is in the shocking statistics: Those with XDR-TB, who are diagnosed and receive care, only have about a 15% chance of survival. That's far worse than say, Ebola, where patients have at least a 50% chance of survival.

The narrative used to be that drug-resistant patients defaulted or didn't take their medication properly, and therefore ended up with an extreme form of the disease. That's not necessarily true today. With an estimated 40,000 people infected with XDR-TB today, spread across 105 countries, many patients contract XDR-TB in the same way as other forms of the disease — through the air.

Introducing the Nix-TB trial.

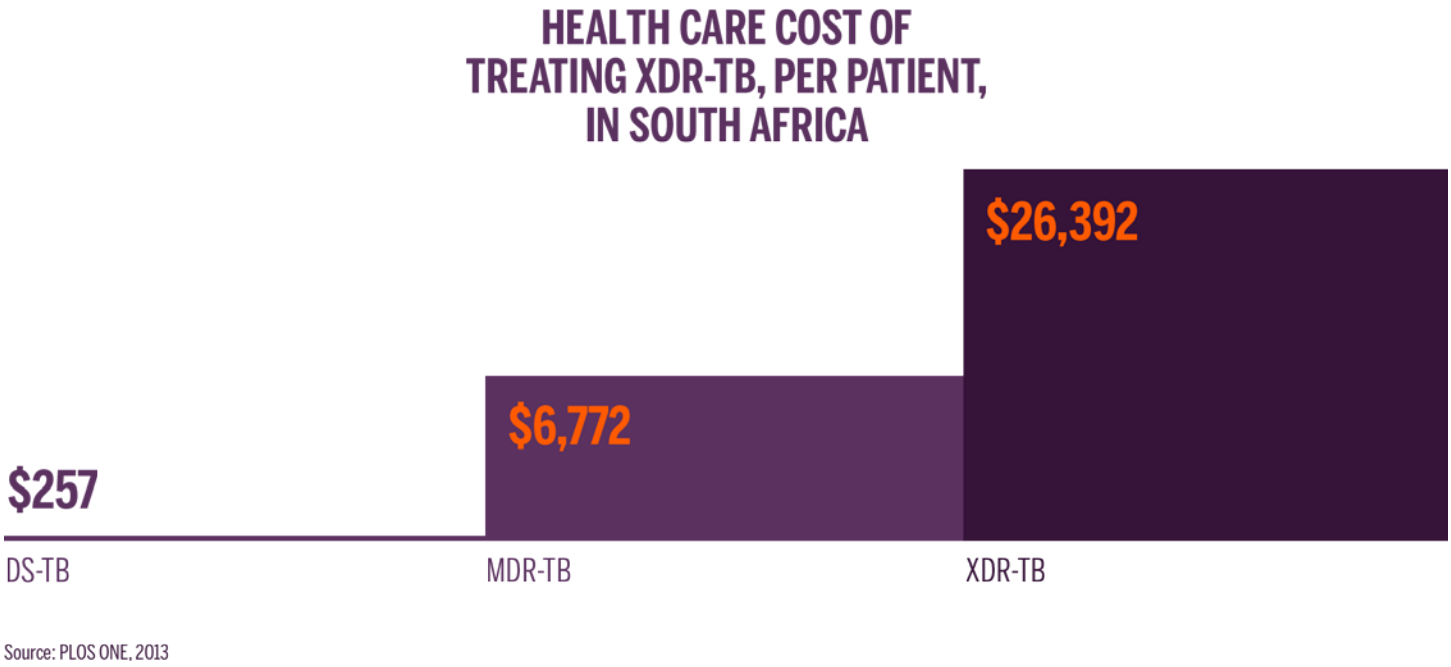
In May 2015, TB Alliance and partners announced the launch of the world's first clinical trial to study an XDR-TB drug regimen with minimal pre-existing resistance. This regimen is known as BPaL. If successful, the injection-free regimen being tested in the so-called Nix-TB clinical trial could transform XDR-TB treatment by significantly improving cure rates with a relatively short, simple, and effective regimen. By reducing the complexity and dramatically reducing the cost, the regimen being tested in the trial offers the promise to facilitate the global implementation of XDR-TB treatment in resource-poor nations.

Nix-TB tests a three-drug regimen consisting of bedaquiline, which received conditional regulatory approval in several high-TB disease burden countries; the novel antibacterial drug compound pretomanid, which is being tested in multiple clinical trials for TB; and linezolid, an oxazolidinone that has been used off-label to treat TB. This regimen is known as BPaL. The trial brings hope to those who have no other treatment options. The trial includes patients as young as 14.

Nix-TB is an open-label study that aims to cure people with XDR-TB (or those who cannot tolerate the current MDR-TB treatment) in six to nine months. After completing treatment, participants are monitored for two years to ensure they do not relapse. The trial has an adaptive design; if improved drugs or more effective schedules of drug administration become available during the course of the study, they can be incorporated into the trial. For example, the study has evolved to take into account findings from a dose-ranging study of linezolid.

Nix-TB is a partnership between TB Alliance, the sponsor of the trial; Janssen Pharmaceuticals, the discoverer of bedaquiline; and the initial sites in South Africa where the study is being conducted (Sizwe Hospital and TASK at Brooklyn Chest Hospital). The study will expand to include other partners and sites.

Currently, there are nearly 40 patients enrolled in the trial; 13 patients have completed the regimen and have been able to go home. These patients will now be monitored for potential relapse for two years as part of the trial. Over the course of 2016, we expect to receive results for those patients who have completed their treatment with six month follow up. The data will allow TB Alliance to determine next steps, if warranted, to advance testing of the regimen.



Source: PLOS ONE, 2013

Salvage treatment and its cost.

A recent report noted that drug-resistant TB is a significant driver of the trillions that antimicrobial resistance is expected to cost the world over the coming decades. That takes the form of global productivity as well as lives lost.

The good news is that, with the further rollout and availability of the GeneXpert diagnostic test, more patients today are being diagnosed with drug-resistant TB. However, there is still no effective medicines for them.

XDR-TB "treatment" today is necessarily one of last resort. There is no standard regimen — healthcare providers often use a mixture of whatever drugs patients are susceptible to. This could look similar to MDR-TB treatment, however, the regimens are typically more toxic and less efficatious.

The length of therapy and resources involved render care as exorbitantly expensive. In the United States and Australia, treating a single case of XDR-TB has cost as much as $1 million dollars. In other countries, including high TB burden countries, the actual cost may be less, but is still 100 times as expensive as treatment of drug-sensitive TB. So while XDR-TB may form only a small proportion of the overall TB burden, the cost and lack of efficacy in treating XDR-TB patients contributes disproportionately to the public health threat of TB.

Testing new cures for drug-resistant TB

Inadequate Treatment for Drug-Resistant TB:

Today, treatment for drug-resistant TB is long, complicated, toxic and expensive.

INJECTIONS

1/day
for at least 6 months.

PILLS

12–24/day
at least 24 months.

IV INFUSIONS

2/day
for 6-24 months.

NEW TB REGIMENS IN DEVELOPMENT:

TB Alliance is testing shorter, simpler, and safer cures for drug-resistant TB

PILLS

3-4/day

Toward a universal regimen.

Our vision is to treat the vast majority of patients with active TB with a single ultra-short, simple, and affordable TB regimen that works in virtually all people with tuberculosis. A multi-drug regimen with such broad utility would have a major impact on the global epidemic, saving millions of lives.

The Nix-TB study is a crucial step toward establishing a truly "universal" treatment, a regimen to which there is no pre-existing resistance and could therefore treat any type of TB.

As additional data is generated on the BPaL regimen, TB Alliance will determine whether it is appropriate to pursue the expansion of the BPaL regimen into those with MDR-TB or drug-sensitive TB.

In addition to helping pave the path to a universal regimen for virtually all TB patients, Nix-TB also provides an opportunity to accelerate potential life-saving treatments to patients with limited other options. The hope is it could more immediately help a fairly destitute population stricken with a virtually incurable disease.

LEARN ABOUT RESEARCH & DEVELOPMENT