



2012 ANNUAL REPORT

REALIZING THE PROMISE

Innovation has put transformative TB drugs within reach.
With our partners, TB Alliance is realizing the promise of the
pipeline with faster, better, and affordable TB drugs for all.



TB ALLIANCE

GLOBAL ALLIANCE FOR TB DRUG DEVELOPMENT

ABOUT THE WEB EXCLUSIVE CONTENT
THIS SYMBOL DENOTES ADDITIONAL CONTENT
FEATURED ON OUR ONLINE ANNUAL REPORT
AT TBALLIANCE.ORG/ANNUALREPORT

Nearly

9 million

new cases of TB emerge each year

Today's MDR-TB therapy
includes more than
12,000 pills
plus injections

RACING AGAINST A KILLER PANDEMIC

Only with better, faster, affordable
drugs can we defeat TB

Tuberculosis (TB) is a global pandemic, killing someone approximately every 25 seconds—nearly 1.4 million in 2011 alone. Although TB is an ancient disease, the proliferation of drug-resistant TB, including multidrug-resistant TB (MDR-TB) and extensively drug-resistant TB (XDR-TB), has heightened the already urgent need for improved treatments to stop the pandemic. Only with dramatically shorter treatments—to replace today's cumbersome six–24 month treatment—can we eventually conquer and control this disease.

Today, the global pipeline of promising new TB drugs is larger than ever and the potential to transform treatment has never been closer. With our global network of partners, TB Alliance is realizing the promise of the pipeline by testing drugs together to find the most beneficial TB regimens, regardless of sponsor. Through this work, we are telescoping the time needed to bring life-saving treatments—and the health and prosperity that accompanies improved outcomes—to the people who need them.

Russia will spend
\$1.2 billion
fighting TB in 2012

**TB is the
leading cause
of death**
among those with HIV

Fewer than
**3% of China's
MDR-TB patients
receive proper
therapy**

**Up to 40% of cases
in high-TB burden
countries occur in
children**

TB kills
**500,000
women
each year**



VOICES OF TB: THE PEOPLE BEHIND THE PROMISE

"We all must cut through the boundary of perceived loss of value that inhibits entirely open collaboration in a field that is just too tough to be tackled alone. I sincerely hope that the TB Alliance and partners will lead the way."

Dr. Nick Cammack,
*Head of Diseases of the
Developing World R&D,
GlaxoSmithKline*

"By participating in the REMox TB trial, clinicians were trained to become investigators responsible for medical decisions and data collection crucial to the trial's success. Nurses became study coordinators and now have new potential career paths."

Dr. Almarie Uys,
*Manager, Clinical Trials,
TB Alliance*

"The TB Alliance is an established leader in TB drug development, rich in experience and expertise."

Dr. Jan Gheuens,
*Interim Program Director,
Tuberculosis, Global Health,
Bill & Melinda Gates
Foundation*

"You'll be amazed to know how the community understands their participation. It actually makes them very proud being part of the trials."

John Mdluli,
*Community Engagement
Coordinator, Aurum Institute
for Health Research*

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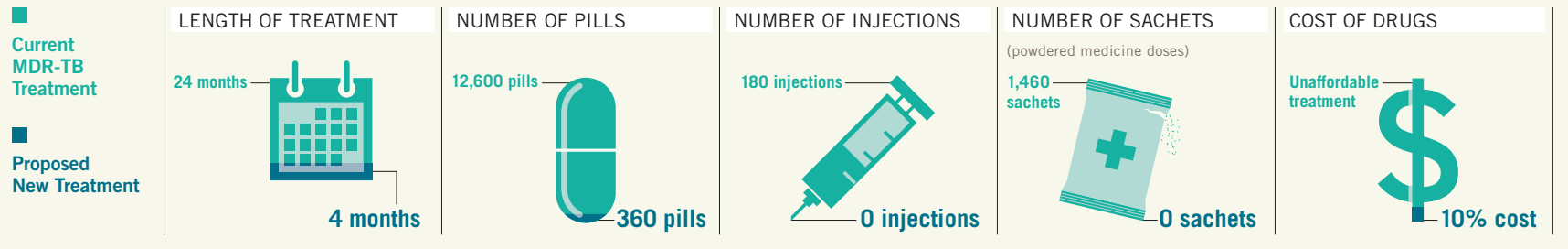
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THE PROMISE OF NEW TB DRUG REGIMENS

New drug combinations could shorten and improve treatment for TB, including drug-resistant TB. For example, the PaMZ regimen (PA-824 + moxifloxacin + pyrazinimide) could dramatically reduce the burden of treatment for some MDR-TB patients.



TRANSFORMING TREATMENT

A new wave of clinical trials brings innovative regimens closer than ever

DEVELOPING TOMORROW'S TREATMENTS TODAY

Tuberculosis must be treated with a combination of drugs. Therefore, in order to truly revolutionize TB therapy, regimens with multiple new agents are needed. TB Alliance and partners have established a game-changing R&D paradigm, allowing new TB drug combinations to be tested and brought to market more quickly than ever before. This new approach to regimen development powers our most recently launched and completed clinical trials of

novel drug combinations. To scientists, these flagship studies represent the cutting edge of TB drug development. To public health professionals, they represent an opportunity to develop the cheaper, simpler, and more effective tools needed to control and reverse the TB pandemic. To those affected by TB, they represent new promise for health and prosperity, everywhere.

2012: TB ALLIANCE CLINICAL MILESTONES

This year, TB Alliance and its partners have advanced the promise of urgently needed beneficial TB treatments. Milestones include the publication of full results of the first-ever trial of a novel TB regimen (PaMZ), the launch of two additional regimen trials, the completion of a Phase III trial of a four-month regimen, and the discovery of further shortened treatment regimens. Along with our partners and the Critical Path to TB Drug Regimens (CPTR) initiative, we are working to realize the promise of new tools needed to revolutionize TB treatment around the world.

“There really is reason for optimism with TB because of the state of the TB research.”

Dr. Anthony Fauci,
US NIAID Director, at the launch of NC-002, World TB Day 2012



NC-001: FIRST REGIMEN TRIAL YIELDS POSITIVE RESULTS

In 2012, the results of the first novel TB drug combination trial NC-001 (New Combination 1) were published in *The Lancet*. These findings revealed that the experimental regimen PaMZ (PA-824 + moxifloxacin + pyrazinamide) killed more bacteria than today's TB treatment through the first two weeks of treatment. This promising regimen may treat TB and many MDR-TB patients with the same totally oral treatment, thereby eliminating the need for injectable drugs. In doing so, it could reduce the length of some MDR-TB treatment by 80% and its cost by as much as 90%.

NC-002: FIRST COMBINED TB & MDR-TB TRIAL LAUNCHES

On World TB Day 2012, TB Alliance launched the NC-002 (New Combination 2) trial to test PaMZ for two months in TB and MDR-TB patients—the first trial to test a single regimen's ability to treat both drug-sensitive TB and MDR-TB. This trial is currently enrolling patients in multiple sites, helping to enhance clinical trial capacity for future regimen-development efforts. Positive results from this study would set the stage for pivotal Phase III registration trials of the PaMZ regimen.

NC-003: SECOND-GENERATION REGIMENS ENTER THE CLINIC

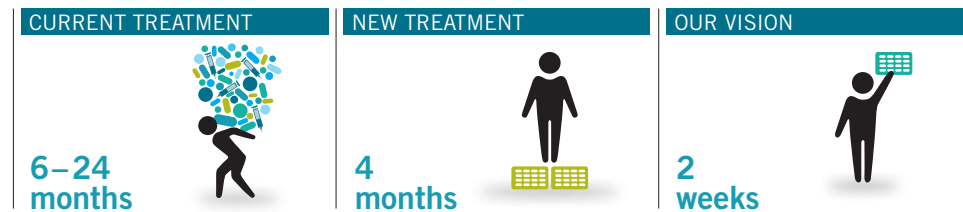
TB Alliance uses a robust preclinical regimen-identification program to explore promising next-generation drug combinations. In 2012, TB Alliance also launched NC-003 (New Combination 3), the first clinical trial of second-generation novel regimens identified through this program. Four different second-generation regimens with the potential to further shorten treatment of TB, including MDR-TB, are being studied in this two-week trial.



TO VIEW OUR
UPDATED
PIPELINE, GO TO
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ACHIEVING OUR VISION

TB Alliance envisions a two-week or shorter regimen—just like most other antibiotic therapy—to replace today's six–24 month treatment. This goal can only be achieved in multiple waves of innovation, requiring new approaches and the consistent generation of new, promising TB drug candidates.



SEE MORE AT
WWW.TBALLIANCE.ORG/ANNUALREPORT

PROGRESS THROUGH PARTNERSHIP

TB Alliance is a not-for-profit product development partnership (PDP) that builds partnerships between the public, private, academic, and philanthropic sectors to drive the development of new TB cures. We combine the research and development expertise of our staff with the skills and resources of our partners to efficiently leverage and advance the most promising science from around the world. It is through these partnerships that TB R&D has progressed and, today, the pipeline for TB drugs is larger than ever before. In 2012, TB Alliance added sanofi-aventis and Scripps Research Institute to our already extensive list of partners, which includes many of the world's leading drug developers.



STRENGTHENING THE PIPELINE

New partnerships and collaborations will realize the promise of improved cures

REGIMEN DEVELOPMENT BEGINS IN THE LABS

The path to new TB drug regimens begins early on in drug discovery. To speed improved cures to patients, it is critical to stock the clinical development pipeline with promising new compounds, identify exciting drug combinations, and test them early in the development process. Preclinical testing of the PaMZ regimen allowed TB Alliance to rapidly advance the regimen into clinical trials.

This year, working with Johns Hopkins University on our preclinical combination-

identification program, we discovered promising drug regimens. Using preclinical models, we have already identified regimens with the potential to reduce TB treatment to less than two months.

Additionally, we have advanced a next-generation nitroimidazole, TBA-354. This compound, discovered in partnership with University of Auckland and University of Illinois at Chicago, is slated to enter clinical development in 2013.

COMMUNITY ENGAGEMENT FORUM 2012

TB Alliance convened its third Community Engagement forum in 2012. This forum, the largest to date, included participants from all sites with Community Engagement (CE) programs, including those sites sponsored by the National Institutes of Health AIDS Clinical Trial Group, advocates, and other stakeholders, as well as members of the Global TB Community Advisory Board and CPTB Stakeholder and Community Engagement Workgroup. Topics of this year's forum focused on best practices and the challenges of implementing CE activities for TB drug trials, monitoring and evaluation of CE activities, good participatory practice, and advocacy. These forums bring together a unique set of voices in the TB research process, enabling an enriching exchange of perspectives and insight on how to advance TB control and research.



As the number of clinical trials expands, so does our Community Engagement program. Without informed and engaged communities, clinical research for new TB drugs is not possible.



VIEW A SLIDESHOW FROM THE 2012 COMMUNITY ENGAGEMENT FORUM AT WWW.TBALLIANCE.ORG/ANNUALREPORT



EMPOWERING COMMUNITIES

**Building local capacity
to support TB research**

Engaging site-level community stakeholders is integral to advancing the goals of clinical research and meeting the needs of those participating in such research. Over the past year, TB Alliance's Community Engagement (CE) program continued to empower local TB patients, healthcare workers, advocates, and community leaders to become independent voices in the TB drug research movement. CE programs accompanied REMox TB clinical trial sites and are underway at all active NC-002 clinical trial sites.

TB Alliance CE programs are dedicated to building local capacity to understand and advocate for TB drug development. Recently disseminated resources include informational materials for trial participants about the importance of completing treatment, awareness-raising activities executed by local Community Advisory Boards, research literacy toolkits, guidelines for CE in trials, and tools to capture the impact of CE in TB drug research.

TEST & TREAT LINKING NEW TOOLS TO IMPROVED HEALTHCARE

For new regimens to have maximal impact, TB drugs and diagnostics must evolve in concert. Healthcare systems need tools to properly and accurately diagnose patients with TB. Simplified, low-cost drug-susceptibility testing would allow patients to be treated only with drugs to which they are sensitive—a modern standard too rarely used in TB treatment.

In 2012, TB Alliance signed a Memorandum of Understanding with the Foundation for Innovative New Diagnostics (FIND). This agreement paves the way for closer collaboration, priority setting, and information sharing. Through this partnership, we are developing a target product profile to inform diagnostics developers as to what tools are needed to complement new drug regimens in development. Such coordination will maximize the global impact of both new TB drugs and diagnostics.



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REALIZING THE PROMISE: CHILD-FRIENDLY REGIMENS

Children are among the most neglected TB patients, and have been underserved by TB research efforts. This year, TB Alliance has begun to map the landscape and develop plans to ensure that new and optimized existing regimens reach the half-a-million children with TB as quickly as possible.



REACHING PATIENTS

Realizing adopted, available,
affordable therapy for all

Access initiatives move center stage as new product launches near. In 2012, the TB Alliance and its partners completed enrollment and treatment of patients in the REMox TB trial. This trial is testing a four-month moxifloxacin-containing regimen in drug-sensitive TB patients. If clinical trial results are positive, registration would be sought by 2014 in conjunction with our partner, Bayer HealthCare. This new regimen would offer a shorter TB treatment for millions suffering around the world.

In preparation for results from the REMox TB trial, TB Alliance is augmenting the project's focus—from science and clinical trials to access—to ensure that an approved and beneficial product will be available as soon as possible to those in need. We have redoubled efforts to engage with high-TB burden countries, donors, the World Health Organization, and technical assistance agencies on issues from country and global decision making to uptake planning and product presentation.

THE REAL COST OF LENGTHY TREATMENT

TB treatment is often provided free of charge, but patients still pay the price. A study conducted by the Liverpool School of Tropical Medicine, the National Institute of Medical Research in Tanzania, and BRAC in Bangladesh, in collaboration with TB Alliance, has documented the impact of TB treatment on patients. In the last two months of therapy, the economic toll of a patient's disease is equivalent to 90% of their usual earnings. Lost income and travel costs to reach the healthcenter are both high. A shorter regimen like those tested in the REMox TB trial would eliminate two months of these costs, thus greatly reducing a patient's burden—and helping to stop the cycle of TB and poverty.

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REALIZING THE PROMISE: TREATING XDR-TB

TB Alliance has proposed the Nix-TB (New Chemical Entities in XDR-TB) study to give access to entirely novel, experimental TB regimens to those with no other treatment options. This trial would help advance the pathway for a universal regimen—which holds the ultimate promise to treat all forms of TB.



The TB market is poised to change dramatically over the coming years with the potential introduction of a moxifloxacin-containing regimen for drug-sensitive TB, two new MDR-TB drugs, as well as continued introductions expected in the diagnostics field. TB Alliance brings critical technical resources that can help guide product introduction to maximize the public health impact of new products. To strengthen this role, we have formed an Access Advisory Committee to assist and

support strategies and approaches to achieve adoption, availability, and affordability of new treatment regimens. The group includes specialists with expertise in planning, launching, and delivering products in high-TB burden countries.

Together, we intend to improve the global TB treatment landscape for patients and care providers alike.

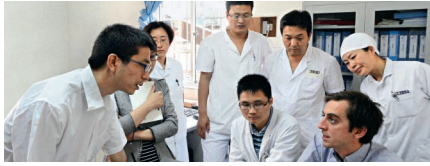
TB Alliance's "AAA Mandate" ensures that new and beneficial TB treatments will be



Adopted

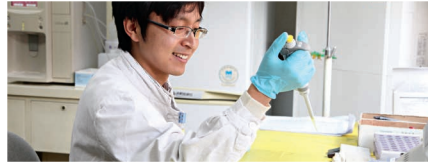
Available

Affordable



→ INNOVATION

Complex global problems require novel approaches. TB Alliance fuses technical experience and expertise with bold new thinking to forge innovative models of research, partnership, and support.



→ EFFICIENCY

Our commitment to innovation yields not only scientific and humanitarian breakthroughs, but forges quicker and more cost-effective paths to success. For each dollar invested, we leverage an additional 60 cents of in-kind contributions from our partners.



→ SUSTAINABILITY

TB Alliance is growing the global infrastructure and skill base needed to develop new and improved TB therapies. We are equipping scientists, communities, and countries with the tools to sustain the fight against TB.



→ PARTNERSHIP

In addition to traditional academic and pharmaceutical partners, we collaborate with several Product Development Partnerships (PDPs) to foster innovation and efficiencies through the sharing of information and resources.



MULTIPLYING OUR IMPACT

**With your partnership,
we can save more lives.**

TB Alliance is working to dramatically reduce the length of treatment and make improved drug regimens adoptable, available, and affordable to all. Our vision is to reduce the length of TB therapy to two weeks or less and finally provide the tools needed to make TB a disease of the past. Significant progress is on the horizon, but long-lasting financial and political support is still desperately needed.

Achieving our ultimate goal requires a more robust selection of new drug candidates. More choices mean more chances of finding the combinations that unlock the path to faster, better, and affordable therapy. Additional

resources are required to conduct the research to test and bring promising new treatments through approval, launch, and to patients.

Our regimen identification program has identified drug combinations that may be able to cure TB in less than two months. We are realizing the promise of the pipeline—but we can't achieve a TB-free world without your help.

Each person can help realize the promise of better, faster, and affordable TB regimens.

FOR MORE INFO AND TO VIEW COMPLETE FINANCIAL DATA, VISIT TBALLIANCE.ORG.

**Dear donors, stakeholders,
partners, and patients,**

This year has been another of significant change and achievement. Multiple waves of innovation are rippling through our once-stagnant TB drug development world. With our dedicated partners and new scientific approaches, we are accomplishing more than ever in a fraction of the time that would have been necessary a few years ago.

Positive results from the first regimen trial of PaMZ led to the initiation of NC-002—the first study that looks to realize the

promise of treating drug-sensitive TB and MDR-TB patients with the same regimen. With the completion of patient treatment in REMox TB, we are closer to the first new product to shorten the treatment of drug-sensitive TB in almost 50 years. Meanwhile, we continue to identify even shorter potential regimens, ones that could treat TB in as little as six weeks and be used without concerns of pre-existing resistance.

We have built new partnerships in the discovery space and ramped up work to prepare for the launch of a moxifloxacin-containing four-month TB regimen. We

are now collaborating more closely than ever with TB diagnostic scientists and developers to ensure new products will have their greatest impact and reach patients everywhere.

With the continued support of partners, donors, and stakeholders, we are poised to realize the promise of a revolution in TB care through the introduction of novel products. This revolution will be powered by innovation, leadership, and collaboration—all attributes to which we continually aspire.

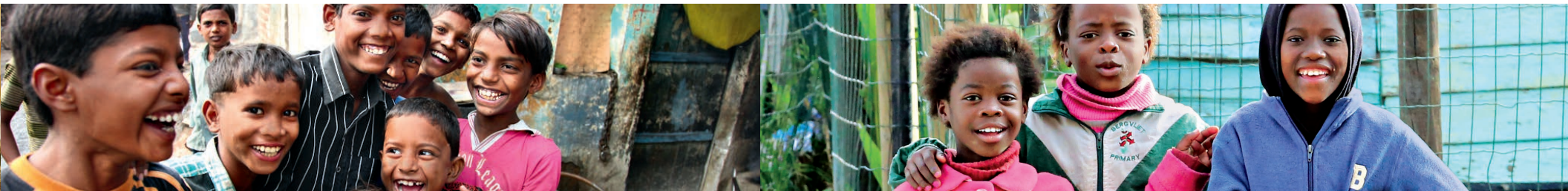
All the best,



Dr. Mel Spigelman
President and CEO,
TB Alliance



Dr. Bruce Carter
Chairman of the Board,
TB Alliance



**“We are accomplishing
more than ever in
a fraction of the
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been necessary a
few years ago.”**



DR. MEL SPIGELMAN
CEO AND PRESIDENT



DR. BRUCE CARTER
CHAIRMAN
OF THE BOARD



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ONLINE AT **TBALLIANCE.ORG**

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The TB Alliance operates with support from the following organizations:

Bill & Melinda
Gates Foundation

European Commission

Irish Aid

National Institute
of Allergy and
Infectious Disease

UK Aid

United States Agency for
International Development

United States Food and
Drug Administration

TB Alliance accelerates the discovery and development of faster-acting and affordable drugs to fight tuberculosis. Through innovative science and with partners around the globe, we aim to ensure equitable access to faster, better tuberculosis cures that will advance global health and prosperity.

Concept and Design Ideas On Purpose, ideasonpurpose.com

Photography Cover, inside cover, pages 1 (middle right, far right), 3 (top), 4, 5 (top right), 6 (middle row), 7 (left), 7 (top right), 8 (top middle, top left), 9 (middle row), back cover, **John-Michael Maas**; page 1 (center left), **Nicholas Cammack**; page 1 (second from left), **Debbie Yzbek**; pages 2, 3, **Eric Miller (Panos)**; page 5 (left), **Erica Sanga**; page 5 (right), **Jane Ong'ang'o**; page 6 (top right), **Richard Lord**; page 7 (middle right), **Seokyong Lee**; page 8 (middle left), **Vera Lentz/Black Star**; page 8 (top left), **Almari Conradie**; page 9 (bottom left), **Anneke Schoneveld**; page 9 (bottom right), **Yuen Lui**



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