CHANGE STARTS HERE

TB ALLIANCE
GLOBAL ALLIANCE FOR TB DRUG DEVELOPMENT

2013 ANNUAL REPORT

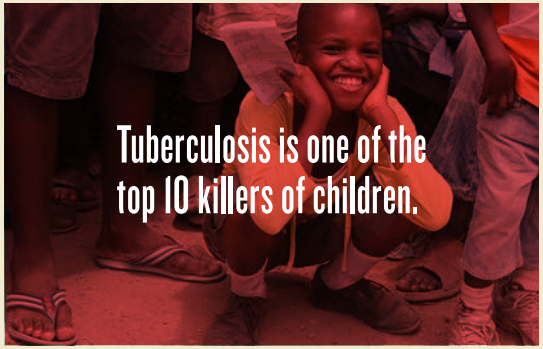
WITH THE CHILDREN

CHILDREN WITH TB ARE THE NEGLECTED OF THE NEGLECTED.

TB is one of the leading killers of children. Despite the extent of the problem, there are no child-friendly treatments in the correct formulations available today.

Now there will be.


We are tackling key issues that impede the supply of optimal TB medicines for children.


Tuberculosis is one of the top 10 killers of children.


Appropriate treatments for children with TB simply do not exist.

IN THE PAST YEAR, GREAT PROGRESS HAS BEEN MADE IN PURSUIT OF NEW TOOLS TO IMPROVE TB TREATMENT AND REDUCE CHILD MORTALITY.

Tuberculosis is one of the top 10 killers of children. Despite the extent of the problem, appropriate treatments for children simply do not exist. A new partnership, formed in late 2012 and signed in 2013, could catalyze the change needed to stop this neglect. TB Alliance, with UNITAID, USAID, the World Health Organization, and others, has embarked on an effort to increase availability and access to appropriate and affordable pediatric TB treatments, while working to speed the time in which new and better drugs will be available for this vulnerable population.

TB Alliance's work in pediatric TB tackles key issues that currently impede the development and supply of optimal medicines for children. This effort seeks to create an active, competitive and sustainable market for existing and future child-appropriate TB drugs, helping to end the terrible neglect of children with this disease.

TB Alliance and its partners are working toward an initial set of goals, which include development of first-line treatments for children, including newborns, in the correct WHO-recommended doses and in formulations that are easier to administer to children. Today, healthcare providers often give children drugs made for adults that must be cut or crushed, leading to poor outcomes and the development of drug-resistant TB. The availability of drugs in the correct dosages and formulations for children will improve treatment today, while paving the way for more rapid introductions of new child-friendly formulations for tomorrow. Critically, much work needs to be done to quantify the TB market and understand the dynamics around regimen uptake to catalyze manufacturers to produce the needed pediatric treatments.

Over the past year, substantial progress was made. Some notable achievements include convening leading pediatric TB experts to help generate concrete steps to better quantify the pediatric TB market; conducting several research studies to ascertain the current state of the market; and entering into a collaboration (the first of what's expected to be several) with Svizera Europe to facilitate the commercialization of a correctly-dosed child-friendly regimen.

"There's a real anticipation in the field that this (work) will lead to the more rapid development and avaiability of fixed dose combinations."

– Dr. Anneke Hesseling
PEDIATRIC TB RESEARCH PROGRAM, DESMOND TUTU TB CENTRE

WATCH AND LEARN MORE ONLINE AT: WWW.TBALLIANCE.ORG/CHILDREN

CHANGE STARTS WITH CONFRONTING THE TB PANDEMIC

TUBERCULOSIS CONTINUES TO INFECT AND KILL, ROBBING MILLIONS OF HEALTH, HOPE, AND PROSPERITY. WE NEED CHANGE TO SAVE LIVES. PLEASE SUPPORT OUR FIGHT FOR BETTER, FASTER, AFFORDABLE TB TREATMENTS.

TUBERCULOSIS IS ONE OF THE WORLD'S MOST DEVASTATING GLOBAL HEALTH CRISES.

The pandemic infects 8.6 million and kills 1.3 million each year, while robbing millions more of health, hope, and prosperity. Women, children, and those living in poverty are the worst hit. TB is the second leading infectious disease killer behind HIV, and the leading killer of people with HIV.

The current TB therapy is highly inadequate and is growing increasingly resistant to available therapies. Today, drug-resistant TB, such as MDR-TB and XDR-TB, is an unchecked public health threat. Part of the problem comes from the inadequacy of the current TB treatments. Today's drug regimen must be taken for 6 months or longer. MDR-TB or XDR-TB treatment can require up to 30 months of treatment, including thousands of pills and months of daily injections.

Long treatment times and side effects result in poor adherence, burdening patients and health systems with a disease that becomes more difficult and expensive to treat each time a patient doesn't complete their course of drugs. Few of the roughly 450,000 new MDR-TB patients each year receive proper care, and of those, more than 1 in 3 will still not be cured.

For children, treatment options are even worse, as there currently are no products on the market designed to treat pediatric TB with appropriate formulations. Therefore, they must be treated by manipulating adult regimens, which complicates treatment, promotes poor outcomes, and risks the development of drug resistance.

Without new treatments, we cannot stop the pandemic.

NEARLY 9 MILLION NEW CASES OF TB EMERGE EACH YEAR

1.3 MILLION PEOPLE WITH TB NEEDLESSLY DIE EACH YEAR

TB IS THE LEADING CAUSE OF DEATH AMONG THOSE WITH HIV

UP TO 40% OF CASES IN HIGH-TB BURDEN COUNTRIES OCCUR IN CHILDREN

TB KILLS 500,000 WOMEN EACH YEAR

CHANGE STARTS IN CLINICAL TRIALS

IN 2013, THREE GAME-CHANGING CLINICAL TRIALS WERE COMPLETED. THERE IS NOW NEW HOPE FOR BETTER, FASTER-ACTING TB TREATMENTS.

REGIMEN:
PaMZ

STAGE:
PLANNING FOR PHASE 3

POSITION:

In NC-002, the novel drug combination PaMZ met its primary endpoint. TB Alliance is now planning for a global Phase 3 registration trial of the PaMZ regimen, consisting of PA-824 (Pa), moxifloxacin (M), and pyrazinamide (Z). Data from NC-002 is still under evaluation. The full results of the study will be available in 2014.

The PaMZ regimen has the potential to shorten and simplify treatment for TB and to be compatible with commonly used antiretrovirals. Importantly, the NC-002 study was the first to treat patients with both drug-sensitive and some forms of MDR-TB. NC-002 further supports TB Alliance's unified development pathway — a development plan designed to accelerate the delivery of impactful novel treatments.

NC-002 was an eight-week Phase 2b clinical trial that enrolled more than 200 patients at eight sites in South Africa and Tanzania.The trial followed TB Alliance's two-week New Combination 1 (NC-001) trial, completed in 2011, which was the first study to test novel TB drugs in combination.

REGIMEN:

JPaZ

STAGE:

PROCEEDING TO PHASE 2B

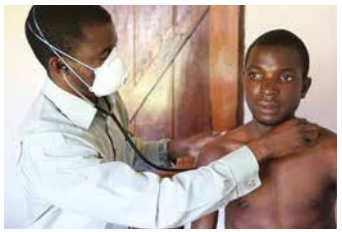
POSITION:

NC-003 was a Phase 2a trial designed to identify combination therapies with the potential to further shorten treatment of TB and MDR-TB. The regimens tested in the two-week trial included various combinations of PA-824 (Pa), bedaquiline (J), pyrazinamide (Z), and clofazamine. NC-003 was successful in meeting its milestones, and identified JPaZ as a promising combination regimen. JPaZ will now be advanced to a Phase 2b two-month trial.

The regimen includes two important new drugs (PA-824 and bedaquiline), bringing the world closer to a totally novel universal regimen.

NC-003 also tested pyrazinamide and clofazimine individually to answer important questions raised by the field regarding the early bactericidal activity (EBA) of those treatments. Full results of the NC-003 trial will be made available in 2014.

NC-003 was performed at two sites in South Africa and enrolled 105 patients with pulmonary TB.



REGIMEN:

REMox

STAGE:

PHASE 3 TRIAL COMPLETED

POSITION:

In 2013, TB Alliance and partners completed the Phase 3 REMox TB clinical trial, which tested the potential of a moxifloxacin-containing regimen to cut TB treatment by a third — from 6 to 4 months. REMox TB was conducted at 50 sites in 9 countries. Results are expected in 2014, but already, the trial has achieved impact.

Prior to REMox TB, there was little infrastructure to support late-stage clinical research. Efforts to map and build local capacity were part of the early stages of REMox TB and today, several sites have emerged as global leaders in TB R&D. REMox TB has also served as a springboard for the deepest and most complete engagement of communities in TB research to date, and cemented that as a best practice for the field.

REMox TB helped catalyze the tools to conduct research as well as the planning to deliver any new beneficial products. These efforts will help to actualize the potential delivery of REMox, as well as other future new TB treatments.

"Any (advance) that reduces the time span a patient is on medication is definitely welcome."

– Dr Joseph Sitieni
MINISTRY OF HEALTH, KENYA

WATCH ONLINE AT: WWW.TBALLIANCE.ORG/ANNUALREPORT2013/CLINICAL.HTM

CHANGE STARTS WITH DISCOVERY

DISCOVERY EFFORTS TODAY, NEW TREATMENTS TOMORROW

TB Alliance currently manages more than 20 projects in its pipeline, spanning the spectrum from early drug discovery through late-stage testing.

WE CANNOT WIN THE WAR AGAINST TB WITHOUT NEW, FASTER-ACTING, AND AFFORDABLE TOOLS. NOVEL REGIMENS ARE THE KEY.

—

These tools could tackle multiple, if not all, types of TB, dramatically reducing the time it takes to cure the disease and transform treatment.

There are not enough novel candidates in the pipeline today—new and promising TB drug candidates must be discovered for tomorrow. TB Alliance works with partners around the world, including the TB Drug Accelerator Program, to augment discovery efforts and find the most promising targets and programs, wherever they may be. This past year saw significant progress in the pursuit of future TB treatments.

In 2013, much of the growth of TB Alliance's discovery efforts was fostered by new collaborations made possible through the Global Health Innovative Technology Fund (GHIT Fund), a new public-private partnership to leverage Japanese companies and their expertise and resources in the fight against infectious disease. New partnerships included those with Daiichi Sankyo, Shionogi, and Takeda. TB Alliance will screen the libraries of these organizations for compounds with promising activity against *M.tb.*, the bacterium that causes tuberculosis. Such collaboration represents not only new opportunities for TB drug discovery, but a new commitment from Japan to contribute to global TB research and development.

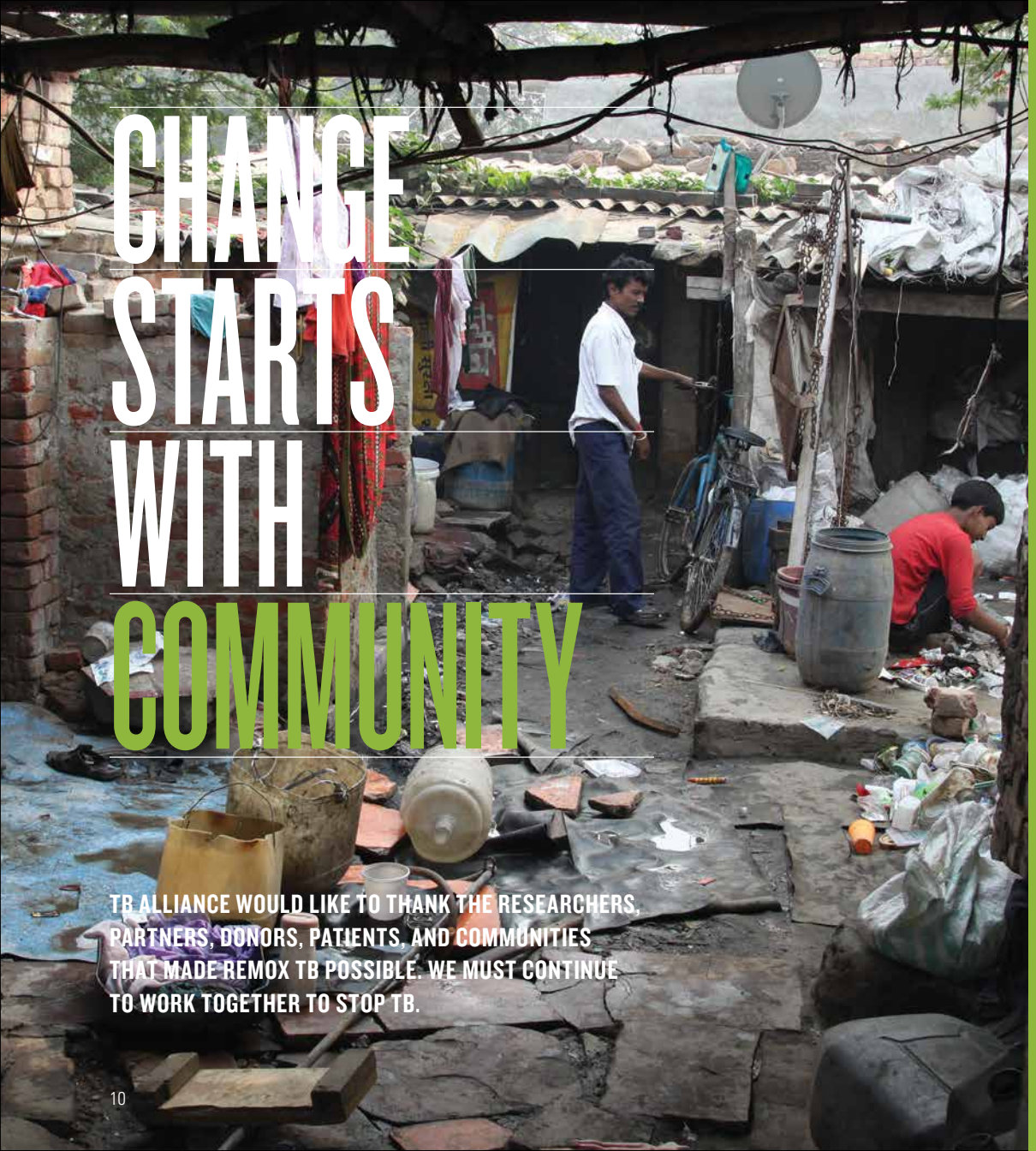
We cannot win the war against TB without new, faster-acting, and affordable tools.

GHIT represents a new commitment from Japan to contribute to global research.

Discovery programs that were already underway also saw progress including TBA-354, which completed preclinical development in 2013. TBA-354 is a nitroimidazole that demonstrates more potent anti-bactericidal and sterilizing efficacy compared to PA-824, and more favorable pharmacokinetic properties when administered orally than delamanid, which are both in the same class. It is a potential backbone of future novel TB regimens.

Building tomorrow's pipeline will require increased investment, as well as collaboration. In 2013, TB Alliance convened a Discovery Partners Workshop at GSK's Diseases of the Developing World Centre in Tres Cantos, Spain, which was attended by scientists from key organizations working in TB drug discovery, including many of the world's leading pharmaceutical companies *(pictured left)*. This inaugural meeting fostered an important exchange of information in the field which should help TB research groups both coordinate and improve drug discovery efforts moving forward.

VIEW OUR PIPELINE ONLINE AT: WWW.TBALLIANCE.ORG/PORTFOLIO



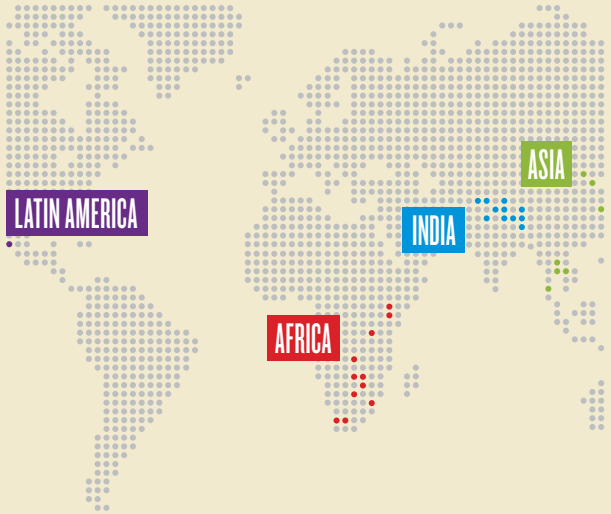
CHANGE STARTS WITH COMMUNITY

TB ALLIANCE WOULD LIKE TO THANK THE RESEARCHERS, PARTNERS, DONORS, PATIENTS, AND COMMUNITIES THAT MADE REMOX TB POSSIBLE. WE MUST CONTINUE TO WORK TOGETHER TO STOP TB.

WITHOUT COMMUNITY, RESEARCH IS NOT POSSIBLE.

A global community of patients, providers, and supporters have made the REMox trial possible. Their work, as part of a broader community engagement effort, not only enhanced the skills and knowledge of people living with and affected by TB but inspired others to support TB R&D and uptake of new regimens.

REXox CLINICAL TRIAL SITES



REMox TB was a global clinical trial that, even before its results are known, has made an impact. In particular, the REMox TB trial enabled TB Alliance to establish and widely roll out its Community Engagement (CE) efforts, educating communities about TB research and collaborating with them to foster improved knowledge, input, and involvement in the clinical trials taking place where they live. REMox TB had the first CE program of its kind for TB drug trials. It has increased the visibility of the need for CE in TB research and helped to drive the field toward inclusion of CE as a best practice and gold standard in TB drug research.

We are proud of our local community partners and all they have been able to achieve. Each clinical trial site with a CE program has deployed specific initiatives developed and driven by the local community in which they are implemented. Their effect, in aggregate, has enhanced the skills and knowledge of people living with and affected by TB — not only surrounding research, but in inspiring others around the world to support and participate in TB R&D, and uptake of new regimens. Importantly, the true impact of CE must be measured on a community, and individual, level. However, there has been much work to develop monitoring and evaluation tools to measure CE's impact on clinical trials across disease and research areas. This tool, and others – such as a research literacy toolkit and training-of-trainers program – are just some of the outcomes of CE efforts to date.

TB Alliance CE efforts have already been expanded to complement Phase 2 trials, as was the case with the NC-002 trial of the PaMZ regimen. TB Alliance is now working to further enhance the scope of this work and develop a strategy for incorporating community engagement into pediatric studies.

Although REMox TB has been completed, the community and groups involved will continue to play a critical role. Importantly, their role in disseminating the trial results to Community Adivsory Boards and other community stakeholders cannot be underestimated. Additionally, as new regimens come to market, the community support for new regimens in development will be an important aspect in the global advocacy for the rapid and robust adoption and implementation of new and improved TB cures.

COMMUNITY ENGAGEMENT

Supports trial enrollment and retention through Community Engagement activities

Increases knowledge and understanding of TB drug trials

"A good research result isn't very useful if you haven't engaged the community along the way."

– Mitchell Warren
EXECUTIVE DIRECTOR, AVAC

WATCH ONLINE AT: WWW.TBALLIANCE.ORG/ANNUALREPORT2013/COMMUNITY.HTM

DEAR DONORS, STAKEHOLDERS, PARTNERS, AND PATIENTS,

DR. MEL SPIGELMAN
PRESIDENT AND CEO
TB ALLIANCE

DR. CARLOS MOREL
CHAIRMAN OF THE BOARD
TB ALLIANCE

This past year was a seminal one for the TB Alliance, and for all those involved in the fight against TB. In 2013, we have shown that regimen development is not only feasible, but holds the promise for rapid transformation of TB therapy. We completed 3 potentially landmark clinical trials this past year.

WATCH A VIDEO MESSAGE ONLINE AT: WWW.TBALLIANCE.ORG/ANNUALREPORT2013/LETTER.HTM

"We are hopeful that 2014 will be another year of tremendous progress and change. We urge each of you to continue to pledge your partnership and support to the vision of a TB-free world."

The PaMZ regimen met its primary endpoint in an eight-week, Phase 2B trial, showing the potential to not only shorten therapy of drug-sensitive TB (something that has not been done for more than 40 years), but also to dramatically shorten and simplify therapy for many with drug-resistant TB. As we further evaluate the wealth of data from this trial, we continue planning for the Phase 3 clinical trial as the final step on the path to global registration.

We have also shown that a second novel regimen, known as JPaZ, was extremely effective in its initial combination trial and will now progress to an eight-week Phase 2B study. This regimen includes two completely novel drugs, to each of which there is no pre-existing resistance, and has the potential to treat an even greater proportion of all TB patients, including some with highly drug-resistant TB, in as little as a few months.

The global Phase 3 REMox TB trial was completed this past year as well. This was a pioneering trial conducted at 50 site in nine countries, and truly laid the groundwork for future TB research. Results will be known in 2014.

TB Alliance has also made tremendous progress in a massively underserved area within TB — the therapy of childhood TB. In 2013, we began a comprehensive, multilateral collaboration to develop appropriately formulated first line TB treatments for children, while simultaneously preparing the market to ensure sustainable access to those treatments by all children in need.

We are extremely indebted to and thankful for our collaborators and donors as well as our dedicated staff, who have been vital in furthering the realization of our commonly shared bold vision. We are, however, especially indebted to the thousands of patients who, over the years, have participated in our clinical trials. Without you, our work is not possible.

We are hopeful that 2014 will be another year of tremendous progress and change. We urge each of you to continue to pledge your partnership and support to the vision of a TB-free world.

DR. MEL SPIGELMAN
PRESIDENT AND CEO
TB ALLIANCE

DR. CARLOS MOREL
CHAIRMAN OF THE BOARD
TB ALLIANCE

"We are extremely indebted to and thankful for our collaborators and donors as well as our dedicated staff, who have been vital in furthering the realization of our commonly shared bold vision."

CHANGE STARTS WITH YOU

TO READ MORE VISIT: TBALLIANCE.ORG/ANNUAL REPORT

TB ALLIANCE
GLOBAL ALLIANCE FOR TB DRUG DEVELOPMENT

Now is the time to realize a transformative change for global health. Simpler, faster, and more affordable TB cures will change lives. More support is needed to ensure we are able to complete the development of the life-saving treatments that are so close to reaching those in need. The time to act is now. Help support our quest for new TB cures by contributing at: donatenow.networkforgood.org/531267.

DONORS:

Australian Aid

Bill & Melinda Gates Foundation

European Commission

Global Health Innovative Technology Fund

Irish Aid

Institute of Allergy and Infectious Disease

UK Aid

UNITAID

United States Agency for International Development

United States Food and Drug Administration

@TBALLIANCE

Photography Credits: Inside cover, pages 2 (top right, middle row, bottom middle), 4, 5, 6, 7, 8, 10, 11 (bottom), **John Michael Maas**; page 11 (top), **Erica Sanga**; page 12 (left), **Anneke Schoneveld**; page 12 (right), **Analucia Limp;** page 9, **José Luis Pindado González**
CONCEPT AND DESIGN BY: IDEAS ON PURPOSE / IDEASONPURPOSE.COM