TB ALLIANCE

GLOBAL ALLIANCE FOR TB DRUG DEVELOPMENT

2009 Annual Report

ACCELERATING THE PACE

98% of TB deaths occur in developing countries

2.2 BILLION PEOPLE

are infected with TB

Over the next decade, TB will rob

$1–3 TRILLION FROM THE WORLD'S POOREST COUNTRIES

The average TB patient's household suffers a 30% drop in yearly earnings

TB IS THE LEADING INFECTIOUS KILLER

of people with HIV/AIDS and is the second leading infectious cause of death for adults globally

40 YEARS AND COUNTING

without a new TB drug

TB kills more women than all other maternal mortality causes combined

7% of the GDP of some countries is lost to TB

MORE THAN HALF A MILLION CASES

of drug-resistant TB emerge each year

EVERY 20 SECONDS,

a person dies from TB

Extensively drug-resistant TB—which is oftentimes incurable—has been reported in

MORE THAN 50 COUNTRIES AND IS SPREADING THROUGHOUT THE WORLD

6–24 MONTHS OF TREATMENT

are needed to cure a TB patient

→ **The TB Alliance is a humanitarian organization working to find faster and better cures for tuberculosis**

NEW DRUGS ARE NEEDED TO OUTPACE

Tuberculosis devastates. It is one of the world's oldest and deadliest diseases, killing nearly two million people each year. It imprisons families, communities, and countries in poverty and most commonly strikes individuals during what should be their most productive years.

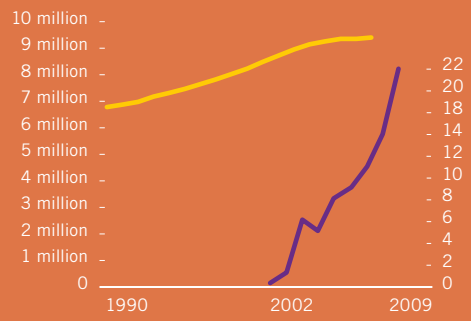
Since 1990, the annual number of new TB cases has increased by more than 40 percent, and today TB incidence is at an all-time high, with more than 9.2 million new cases each year. In some regions, more than 20 percent of recorded TB cases are drug-resistant, and if left unchecked, this situation is likely to grow worse.

→ **HEADING OFF A GLOBAL EPIDEMIC:**

To outpace the spread of the TB epidemic, new, faster, and better cures are needed.

Estimated TB incidence (new cases per year)

TB Alliance Programs



TB

With new drugs we can outpace the spread of TB. Since our inception in 2000, the TB Alliance has been making rapid progress toward our vision of new, faster-acting TB treatments that will be effective against susceptible and resistant strains, be compatible with antiretroviral therapies for those TB/HIV patients currently on such therapies, and be widely available and affordable to all.

We have assembled the largest pipeline of potential new TB drugs in history and are catalyzing research and development, health systems, and people all over the globe to realize our vision. Through this work and by developing novel and more effective TB drugs, we can outpace the spread, and reverse the impact, of this deadly disease.

THE TB ALLIANCE IS MAKING RAPID PROGRESS IN THE FIGHT AGAINST TB

There are enormous scientific, regulatory, and social hurdles to overcome to make up for the decades-long drought of TB research. But with a long-term commitment to fighting the disease, extensive expertise in the field, and strategic approaches to partnering, the TB Alliance is making rapid progress on the long path toward finding faster, better cures for tuberculosis. The organization's advances are evident in the pipeline, but also in the new partners, projects, and people it has catalyzed to join the quest for better TB cures.

→ ACCOMPLISHMENTS

Largest TB drug portfolio in history

The TB Alliance has built the largest pipeline of TB drugs in history. After significant expansion in 2009, the organization now stewards the development of more than 20 projects in its portfolio, including three compounds in clinical testing.

Page 6

Assembling tomorrow's TB regimen

The world needs novel drug regimens, fast. The TB Alliance is spearheading a new development paradigm that will more quickly identify the best possible regimens, using both existing drugs and new drug candidates.

Page 14

Bridging research to patients

Our new Market Access department is mapping the TB drug landscape and conducting first-of-its-kind research to ensure novel drug regimens reach the patients who need them.

Page 20

Exponential project growth

We have doubled our pipeline in two years. In 2009 alone, we added eight new projects representing a wide range of innovative approaches to fighting TB.

Page 8

New leadership and capabilities

Growth and progress must be carefully orchestrated to deliver on the promise of new TB drug regimens. With an expanded leadership team, the TB Alliance gained new organizational capabilities to guide its future, starting today.

Page 16

REMoxTB: Blazing a trail

Beyond testing the efficacy of a four-month regimen containing moxifloxacin, the REMoxTB trial is building the global capacity to overcome the many challenges associated with TB drug development.

Page 22

New partnership to develop TMC207

We teamed up with Johnson & Johnson's Tibotec to jointly develop the Phase II compound TMC207. This promising compound will be the first-ever TB drug candidate to undergo active parallel development tracks for both drug-susceptible and drug-resistant disease.

Page 10

Cultivating new allies: Building solutions from within

The Chinese government, which has begun funding TB R&D, is investing to meet the needs of its people. The TB Alliance is partnering at many levels within the country to help realize progress.

Page 18

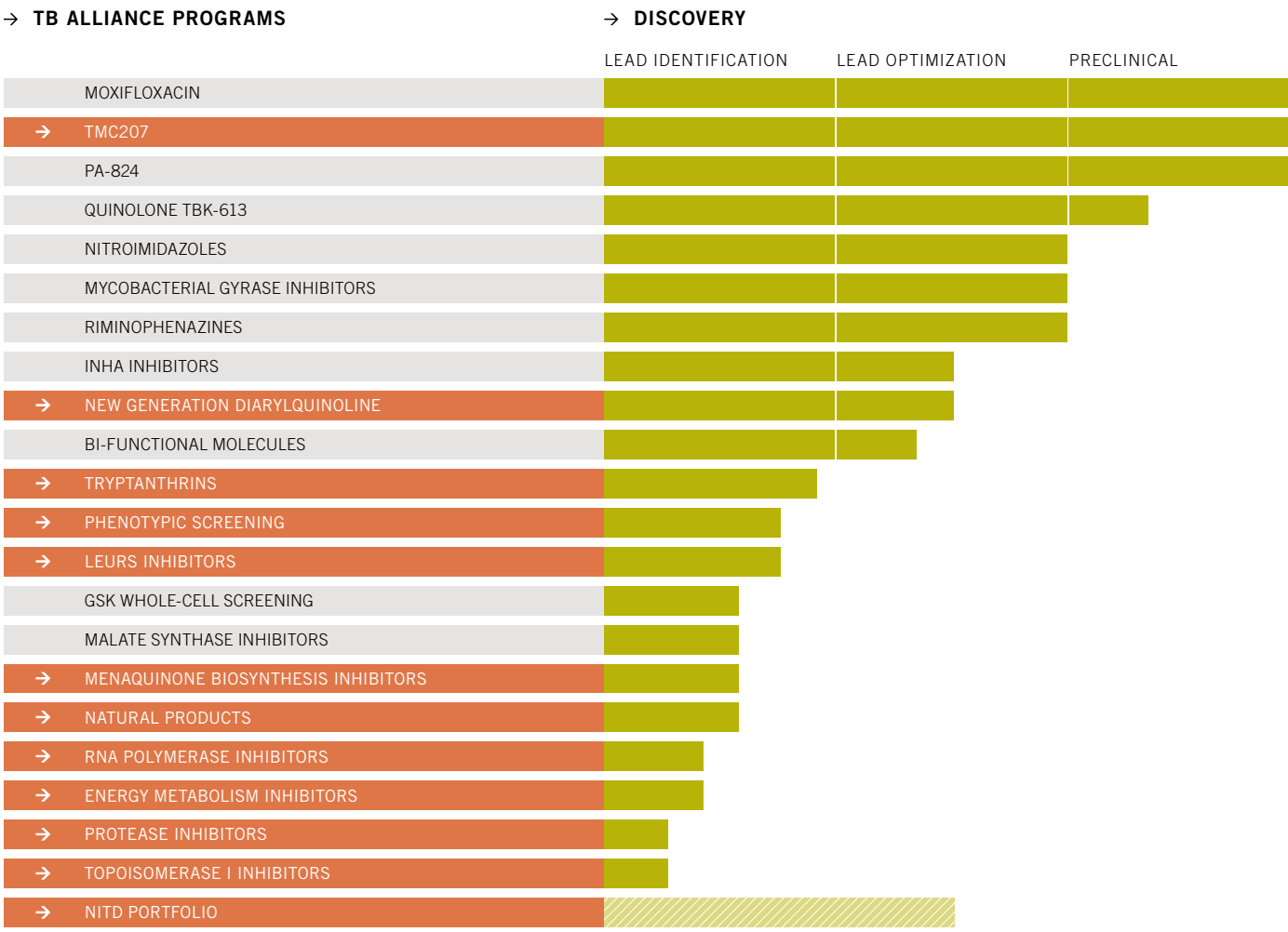
Hitting home

We are on the brink of curbing TB's deleterious effects on humanity and the global economy. A patient's story reminds us why it's important to redouble our efforts.

Page 24

RAPID PROGRESS

DOUBLING THE PIPELINE IN TWO YEARS

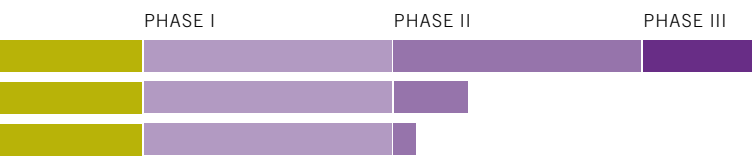


AS OF OCTOBER 2009

The TB Alliance is growing what was already the largest TB drug pipeline in history.

→ NEW PROJECTS ADDED IN 2008-09

→ CLINICAL DEVELOPMENT



Over the past two years, the TB Alliance has doubled what was already the largest pipeline of TB drug candidates in history.

These promising compounds, many of which have novel mechanisms of action and offer completely new ways to fight the disease, are intended to treat drug-sensitive and drug-resistant TB, show promise for shortening treatment times, and be compatible with treatment for HIV/AIDS. The advances in the pipeline offer hope that, even with natural attrition rates, there will soon be new, effective drugs with which to form novel TB regimens.

The TB Alliance adheres to rigorous selection criteria that allow only high-priority projects that balance impact, feasibility, and time to registration to be added to our portfolio. All clinical decisions are overseen by an accomplished Scientific Advisory Board and Portfolio Committee to ensure that precious resources are dedicated only to projects that hold promise for patients.

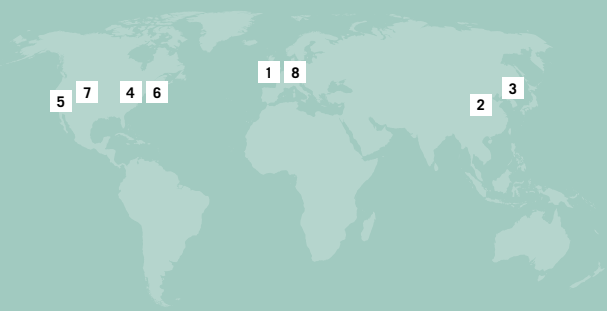
OUR R&D PARTNERS

- Anacor Pharmaceuticals
- Bayer Healthcare AG
- GlaxoSmithKline
- Korea Research Institute of Chemical Technology
- Novartis
- Johnson & Johnson/ Tibotec
- Beijing Tuberculosis and Thoracic Tumor Research Institute
- British Medical Research Council
- Colorado State University
- Infectious Disease Research Institute
- Institute of Materia Medica
- Institute of Microbiology
- The Johns Hopkins University
- New York Medical College
- Rutgers: The State University of New Jersey
- Stellenbosch University
- Texas A&M University
- University of Auckland
- University of Cape Town
- University College London
- University of Illinois at Chicago
- University of Pennsylvania School of Medicine
- Yonsei University

NEW PROJECTS

Expanding the portfolio through partnership

As a product development partnership (PDP), the TB Alliance works with a global network of partners from industry, academia, and other research organizations to pursue its mission of developing new TB treatments. Such partnerships enable the organization to bring the best science, technologies, and expertise to the field of TB drug discovery and development while keeping overhead costs low through our lean, virtual R&D structure. In 2009 alone, the TB Alliance added eight new projects to our portfolio.



8 NEW PROJECTS IN 2009

1. TMC207, BELGIUM
2. NATURAL PRODUCTS, CHINA
3. TRYPTANTHRINS, KOREA
4. RNA POLYMERASE INHIBITORS, NEW JERSEY
5. LEURS INHIBITORS, SAN FRANCISCO
6. TOPOISOMERASE I INHIBITORS, NEW YORK
7. MENAQUINONE BIOSYNTHESIS INHIBITORS, COLORADO
8. NEW GENERATION DIARYLQUINOLINE, BELGIUM

→ **BRAZIL**

As a virtual R&D organization, the TB Alliance works closely with local researchers. Dr. Ann Ginsberg (center), Chief Medical Officer, examines study samples.

TMC207

A new paradigm promises to speed development of this novel compound

PARTNER

JOHNSON & JOHNSON/TIBOTEC

This past year, the TB Alliance partnered with Tibotec (a Johnson & Johnson company) to grow our late-stage TB drug portfolio with the addition of TMC207. This Phase II drug is a diarylquinoline that offers a novel mechanism of action by specifically inhibiting mycobacterial ATP-synthase, which is responsible for the cell's energy production.

Because of its unique mechanism of action, TMC207 shows promise to treat both drug-sensitive and drug-resistant disease. Leveraging the resources of both development partners, the compound is the first-ever TB drug candidate to undergo active parallel development tracks for both forms of the disease. This approach makes the most efficient use of resources and speeds progress toward maximally benefiting patients and combating the global tuberculosis burden.

TMC207 has already shown promise in MDR-TB patients. Interim data from an ongoing Phase II study of TMC207 were published earlier this year in the *New England Journal of Medicine*. In the placebo-controlled study, 48 percent of patients receiving TMC207 in combination with standard treatment converted their sputum culture to negative after eight weeks compared with just 9 percent who received placebo and standard treatment.

We are working to outpace TB, particularly MDR-TB, which is exponentially more difficult and expensive to treat, and without new tools, could become a global epidemic. To that end, the TB Alliance and Tibotec plan to harness the full potential of this novel class of drugs by speeding development of TMC207 and conducting a robust backup program with the aim of discovering and developing a new generation of diarylquinolines for the treatment of both drug-susceptible and drug-resistant TB.

1 CHENNAI, INDIA
A TB patient receives the standard four-drug TB regimen, which he must take regularly for at least six months under the observation of medical staff.

2 MDR-TB
Drug-resistant TB, shown here under a microscope, is expensive and extremely difficult to treat. There are estimated to be 500,000 new cases of MDR-TB worldwide each year. Fewer than 5% of MDR-TB patients receive appropriate treatment.

3 CAPE TOWN, SOUTH AFRICA
TB researchers at the Tiervlei Trial Center sort patient sputum samples. In South Africa, HIV is fueling a growing TB epidemic.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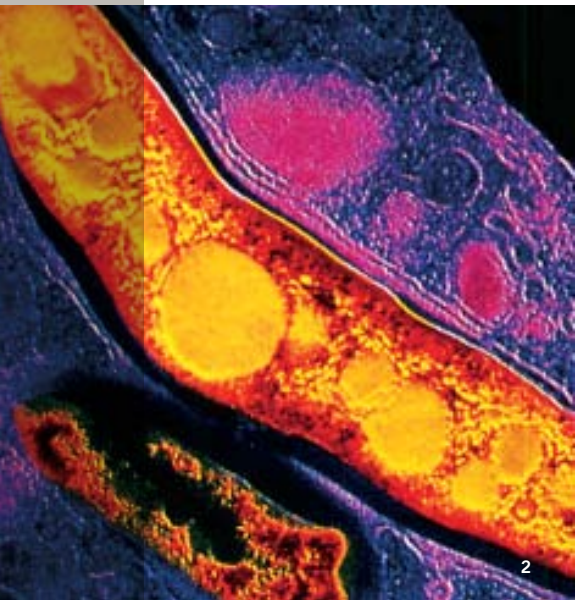

2


3

1 BEIJING, CHINA
The TB Alliance and the Institute of Microbiology of the Chinese Academy of Sciences are working together to develop new TB drugs from natural sources.

2 LUSAKA, ZAMBIA
A patient is examined at a local TB clinic. Patients often have to take long, burdensome trips to receive proper care.

3 CAPE TOWN, SOUTH AFRICA
Through our programs, the TB Alliance helps to build and strengthen the infrastructure needed to carry out TB research.

1


2


3

Natural Products

PARTNER

INSTITUTE OF MICROBIOLOGY OF THE CHINESE ACADEMY OF SCIENCES (IMCAS)

Scientists in China have made significant contributions in developing new drugs, such as artemisinin, from natural sources. Following this tradition, one of China's top research institutions, IMCAS, investigated and identified many natural product extracts with promising anti-tubercular activity. Building on this work, the TB Alliance is collaborating with IMCAS to screen additional extracts from traditional Chinese medicines and purified natural products and to isolate and identify active compounds for further optimization and development.

LeuRS Inhibitors

PARTNER

ANACOR PHARMACEUTICALS

A novel class of compounds, oxaboroles, was identified by the California-based company Anacor Pharmaceuticals as potent leucyl tRNA synthetase inhibitors, an essential target in many pathogenic microorganisms. Preliminary studies indicate that the oxaborole series is highly potent *in vitro* against *M.tb*. To explore the potential of this novel drug target and compound class, the TB Alliance partnered with Anacor Pharmaceuticals to rapidly move this promising series into *in vivo* proof of concept studies for a TB indication.

RNA Polymerase (RNAP) Inhibitors

PARTNER

RUTGERS, THE STATE UNIVERSITY OF NEW JERSEY

RNAP is one of the best-validated drug targets for treatment of TB. Rifamycins, a class of compounds that inhibit RNAP, currently play a major role in shortening first-line TB therapy. Recent studies indicate that rifamycins at high doses have the potential to even more drastically reduce treatment time. However, the use of these drugs in high doses is limited by their potential to cause toxicities and side effects.

A key goal of this program, undertaken in partnership with Rutgers, is to identify novel inhibitors of RNAP that can maximally inhibit the enzyme at clinically attainable doses and, therefore, shorten therapy. New drugs that function outside the rifamycin binding site on RNAP will be prioritized, as these will likely be effective against rifamycin-resistant tuberculosis bacteria and beneficial in treating current MDR-TB as well as drug-sensitive disease.

THE IDEAL TB DRUG

The TB Alliance aims to identify novel drugs and regimens that will have maximum impact on TB treatment and control. To provide the best chance of achieving these goals, discovery and development programs are geared to produce drugs that meet most, if not all, of these criteria:

- shorten the duration of treatment compared to existing therapies
- be effective against drug-sensitive and drug-resistant disease
- elicit no clinically significant drug-drug interactions, including with ARVs
- possess an improved safety profile compared to existing agents
- be affordable.

ASSEMBLING TOMORROW'S REGIMENS

The future is within reach

With three compounds in the clinic, the TB Alliance is bringing about change for TB drug development. But the standard pace of change is just not fast enough.

→ **INDIA**
With nearly two million new cases every year, India has the highest TB burden of any country in the world.

SPEEDING NEW REGIMENS TO PATIENTS

With three compounds in clinical development, we can begin to envision a world of truly novel TB treatment regimens. Tomorrow's ideal therapy will likely contain several new drugs, including at least two or three completely new compounds. But what will the ideal combination of novel drugs be? The number of possibilities will continue to increase as current candidates progress through (while other compounds continue to enter) the development pipeline.

Still, with two million people dying from TB each year, a novel regimen will take too long to reach patients. Part of the problem stems from the current approach to drug development. All TB treatment consists of multi-drug regimens to ensure the disease is cured and that resistance to the drugs won't develop. However, the current drug development paradigm typically replaces or adds one drug at a time into the existing treatment regimen. The clinical evaluation of each substitution takes 6–10 years. That means creating a completely novel four-drug regimen under the current model would take a minimum of 24 years. Too many patients will die if we continue working at this pace.

With funding from The Netherlands Ministry of Foreign Affairs and the Bill & Melinda Gates Foundation, and working with The Johns Hopkins University, the University of Illinois at Chicago, and several pharmaceutical companies, the TB Alliance is embarking on a new paradigm of TB drug development that has the potential to drastically shorten development timelines by identifying promising novel drug combinations in preclinical models and carefully accelerating their advancement into clinical testing. This initiative is trailblazing a more collaborative approach to TB treatment and may prove to serve as a model for other therapeutic areas where combination drug therapy is necessary.

24 → 6 YEARS

A Visionary Approach to Assembling Regimens

The TB Alliance combination testing program could revolutionize the way tuberculosis drugs are developed and the formation of new and shorter regimens. What's required is new orchestration and ways of working between partners. The TB Alliance is uniquely positioned to help execute this promising initiative.

3 COMPOUNDS IN THE CLINIC

With several drugs in late-stage testing, the promise of a new treatment regimen is on the horizon. Tomorrow's TB drug regimen may contain one or more compounds currently being tested by the TB Alliance.

Moxifloxacin Phase III

PARTNER

BAYER HEALTHCARE AG

Currently undergoing a global Phase III trial to investigate treatment-shortening potential when substituted for either of two drugs in the existing first-line treatment regimen.

PA-824 Phase II

PARTNER

IN-LICENSED FROM CHIRON (NOW NOVARTIS)

A nitroimidazo-oxazine that is currently in the clinic for evaluation of dose range, safety, and efficacy, moving toward testing in combination with other TB drugs for both drug-sensitive and M(X)DR-TB.

TMC207 Phase II

PARTNER

JOHNSON & JOHNSON/TIBOTEC

A novel drug undergoing parallel Phase II trials investigating the safety and efficacy of TMC207 for the treatment of both drug-sensitive and drug-resistant TB.

NEW LEADERSHIP & CAPABILITIES

Orchestrating the future of TB drug development

At the TB Alliance, the momentum is undeniable. After many years of steadily building the tuberculosis drug pipeline, in 2009 we've accelerated the pace and now boast more than 20 projects in our portfolio, including three drugs in clinical testing. We are on the brink of a revolution.

However, to deliver on the promise of potential new TB treatments, such rapid growth must be carefully orchestrated. We have taken steps to ensure that the right infrastructure is in place to support late-stage clinical trials, continued development of the discovery pipeline, efficient use of resources, and our organizational commitment to ensure that new TB drugs, once proven effective, are available to the people who need them.

→ **TOP**
Dr. Mel Spigelman (center), President and CEO, brings groups together in pursuit of new TB cures.

→ **BOTTOM**
Dr. Zhenkun Ma (center), Chief Scientific Officer, and Dr. Ann Ginsberg (right), Chief Medical Officer, discuss R&D strategy with partners.

At the TB Alliance, our projects, people, and proficiencies are cornerstones of success. While growth and progress of the pipeline leads the way, we continually strive to improve our ability to support that pipeline. Some of the highlights of our organization's growth in 2009 include:

PEOPLE

In 2009, the TB Alliance expanded our leadership team with the roster of talent required to support the new pipeline. In January, the veteran Director of R&D, Dr. Mel Spigelman, was named President and CEO. The additions of Colleen Pero, Chief Administrative Officer, Stephen Jasko, Chief Financial Officer, and Marshall Burke, Senior Vice President of External Affairs, offer organizational support and allow us to aggressively pursue resource mobilization initiatives. The entire TB Alliance team can be viewed at http://www.tballiance.org.

PROJECTS

We have doubled our portfolio's depth over the past two years to create a truly robust TB drug pipeline. While the TB Alliance will continue to pursue promising new projects, the number of compounds in development will likely remain more constant as ongoing projects are reevaluated against preset milestones and the standards for inclusion into our portfolio increase as standard treatment improves.

The TB Alliance adheres to rigorous selection criteria when considering new projects, and subjects all programs to regular, thorough internal and external performance audits to ensure that the compounds selected are not only promising in their own right, but complement a global portfolio and fit within the broader equation of regimen change. Only the compounds with the most potential advance, and those that do must be affordable and ultimately made available to the people who need them.

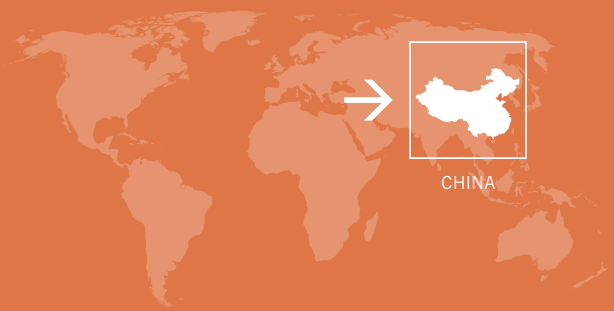
PROFICIENCIES

As the TB pipeline progresses, it's important to make sure all drug projects are appropriate for end users and adopted by global stakeholders. The TB Alliance extended its commitment to such work by formally establishing the Market Access department at the end of 2008. This group will continue its work to map the landscape and understand the markets into which new TB drugs will go, and make sure that the drugs the Alliance develops are available to the people who need them.

CULTIVATING NEW ALLIES

Building solutions from within

Solutions to stopping TB must be developed, in part, by the people who need them. Therefore, high-burden countries have an important role to play in bringing forth the needed funding, science, and commitment to stopping the spread of tuberculosis around the world and the death of their people.



→ **CHINA**

TB Alliance partners include the Institute of Materia Medica of the Chinese Academy of Medical Sciences and the Institute of Microbiology of the Chinese Academy of Sciences, both renowned Chinese national institutes.

One country taking the initiative in the fight against TB is China. China plays an important role in TB drug research as both an emerging economy and the country with the second-highest TB burden in the world. Recognizing this, the TB Alliance has developed strong partnerships in China, working hand-in-hand with multiple world-class research institutions and accomplished contract research organizations. Through these collaborations, the TB Alliance is helping to foster in-country tuberculosis research capabilities and develop self-sustaining TB research initiated within high-burden countries.

In March 2009 in Beijing, immediately preceding a high-level WHO Ministerial Meeting on MDR-TB, the TB Alliance announced a partnership with the Institute of Microbiology, a member of the Chinese Academy of Sciences (IMCAS). The partnership further explores IMCAS's unique collection of natural products, including microbial metabolites and traditional Chinese medicines. Preliminary work indicates that many of these natural products have demonstrated anti-tubercular activity. Jointly funded through a grant from the Chinese government, the program is an example of how the TB Alliance can forge cost-effective, innovative collaborations and leverage a wide variety of resources.

The IMCAS collaboration is the second partnership the TB Alliance has formed with a top-tier Chinese research institute. In 2007, the Alliance partnered with the Institute of Materia Medica (IMM) of the Chinese Academy of Medical Sciences, along with the Beijing Thoracic Tumor and Tuberculosis Research Institute (BTTTRI), to investigate a class of drugs called riminophenazines. A member of the riminophenazine class has been effective in treating mycobacterial infections like leprosy, though existing compounds have been known to cause side effects such as pronounced skin pigmentation. Thus, riminophenazines long remained a potentially effective, but relatively unexplored, class of drugs. Since 2007, the TB Alliance and IMM joint project has successfully progressed and novel lead compounds are now being selected for preclinical development. In 2008, this project was awarded direct funding from the Chinese government as part of China's largest-ever grant for drug R&D. In making this historic commitment, we anticipate that China will be an important force in the fight against TB in the future and an example of the major impact emerging countries can make against this deadly disease.

TB FACTS: CHINA

2nd
highest TB burden in the world

Greater than
1 in 5
MDR-TB cases occur in China

Approximately
550
people die from TB every day in China

BRIDGING RESEARCH TO PATIENTS

New drugs can only stop TB if they reach those in need

At the TB Alliance, we're committed to ensuring that new TB regimens will be affordable, adopted, and available—a philosophy we call our "AAA" mandate.

→ **MOLDOVA**
A patient co-infected with tuberculosis and HIV takes medicine at the TB hospital in Bender.

Our commitment to access through the AAA mandate sounds simple enough, but actually requires a thorough understanding of how drugs reach countries and are delivered to patients. In the case of TB drugs, we are helping to build that understanding, as market data are scarce and integration of new TB drugs is rarely considered from a health systems' perspective. For this reason, the TB Alliance is working with partners such as Management Sciences for Health, the Clinton Foundation, IMS Health, and National TB Programs to conduct research and analyze markets, not only to inform new drug introduction but also to improve efficiencies and economies surrounding delivery of existing TB drugs. Our AAA considerations, such as the cost of goods, method of delivery, acceptability of trade-offs, and needs of specific patient populations, must be integrated early in the research process and be reevaluated as potential new drugs move from one phase of research to the next.

As moxifloxacin, TMC207, and PA-824 progress through clinical trials, it is important to scale up this work even further. To this end, in 2008, the TB Alliance formalized its Market Access department, which is working to navigate the complex landscape by reconciling logistical, patient-specific, and resource-related dynamics to shape a comprehensive access plan.

To date, the TB Alliance's market access work has focused on the drug market, especially its size and drug delivery mechanisms, and on stakeholder opinion and decision making. "What Countries Want," which was published in August 2009, evaluated key stakeholders' perceptions of the value proposition of any potential new regimen change. From this study, we learned that treatment shortening is a priority for countries. Stakeholders said they would be willing to pay more for new TB drugs that achieve that goal. We also completed the Country Introduction Study, a survey of the 22 high-burden countries, that highlighted how costs, risks, and benefits have been balanced during past TB regimen changes and will likely influence any future discussions. Publications and additional research on other topics will be forthcoming.

It is through this AAA work that we link clinical research to the realities experienced by patients, providers, and programs, thereby ensuring that our efforts, above all else, benefit patients around the world suffering from tuberculosis.

MARKET ACCESS OVERVIEW

A comprehensive market access strategy is integral to the affordability, adoption, and availability of newly developed TB treatments. Successful implementation requires incorporating a variety of perspectives and engaging a diverse group of stakeholders.

REMoxTB

Blazing a trail for future TB cures

In 2009, the TB Alliance continued to enroll patients and engage additional sites to support the Phase III REMoxTB clinical trial. This trial is designed to test the efficacy of two different four-month moxifloxacin-containing regimens against the current six-to-nine-month standard treatment. There have been few TB drug registration trials over the past 40 years and, as a result, little infrastructure exists for moxifloxacin—or any other TB drug—to be thoroughly evaluated.

REMoxTB is unique in that the Phase III trial is simultaneously testing a drug and building global clinical trial capacity and infrastructure for tuberculosis research. In facing this challenge, the TB Alliance first assessed the capacity of more than 90 sites in over 40 countries to conduct TB drug trials. This study indicated that substantial work was needed to build a global clinical trial network capable of supporting the growing pipeline. To this end, the Alliance is working to strengthen clinical research capacity in several of these countries.

Building infrastructure also means training those in the field, engaging regulatory agencies, and forging links with the community so that TB researchers and patients can learn from one another in the context of the communities in which they live and work.

→ **1. WORLD TB DAY IN ZAMBIA**

A local Community Advisory Board organized events to promote TB awareness. The day's activities included traditional music and dancing.

→ **2. WORLD TB DAY IN TANZANIA**

Members of a Community Advisory Board marched through Mbeya, Tanzania with a banner proclaiming, "I Am Fighting TB, Join Me Now, Tuberculosis Research REMoxTB!" Such programs link the REMoxTB trial to the community and help build awareness of TB issues and research.

1

2

In parallel with the expansion of the REMoxTB trial, the TB Alliance also grew its Community Engagement Small Grants Program. This program assists REMoxTB sites in forming site-level community engagement strategies and develops open lines of communication between trial researchers and local patient populations. Many sites have developed Community Advisory Boards (CABs), which work to educate their local constituencies about TB disease, treatment, and research for new TB drugs, while also informing researchers of community issues and concerns related to the trial.

Through the TB Alliance Community Engagement Program, CABs at REMoxTB sites in Tanzania, South Africa, and Zambia organized local and regional activities to commemorate World TB Day 2009, which raised awareness about TB disease, its treatment, and efforts to develop improved TB drugs. As the REMoxTB trial continues to expand, the TB Alliance is working with representatives of communities surrounding additional sites in Asia, South America, and Africa to establish community engagement strategies.

Other infrastructure work includes a pilot project to gather data on the prevalence of fluoroquinolone resistance in various regions, a biomarker project that could markedly speed future TB drug development programs, and important research to map the landscape and define roll-out strategies to ensure any new TB drugs reach patients in need. This work is necessary to lay the foundation not only for clinical trials, but also for regulatory engagement and ultimate success in achieving market access.

Efforts to build capacity and infrastructure will ensure that systems are in place that will enable moxifloxacin and other improved TB treatments to efficiently reach patients in need.

KEY CHALLENGES: CONDUCTING GLOBAL TB TRIALS

Study design

Trials require a large number of patients and geographically diverse sites, and bring with them practical challenges associated with working in the developing world.

Clinical capacity

Few existing sites are capable of conducting trials to modern regulatory standards, yet TB trials must be conducted where TB patients are.

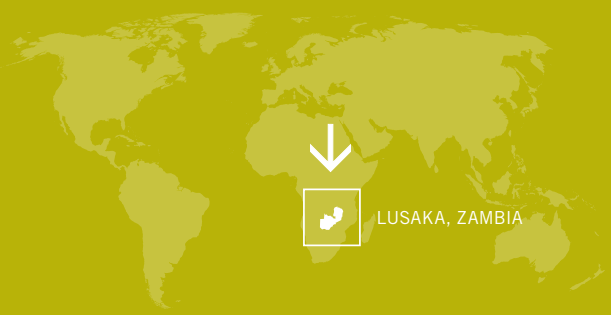
Regulatory issues

Limited TB drug development activity has led to a lack of specific, unified regulatory guidelines. Major regulators are making advances in needed guidances to speed drug development.

HITTING HOME

One family's story

TB anywhere is TB everywhere. Indeed, tuberculosis affects every country in the world, with more than 9 million new cases emerging each year. Still, the world's poorest populations, and those co-infected with HIV, are the ones who bear the brunt of TB's deadly impact. Two million people die each year from TB, leaving behind fractured families and often insurmountable economic hardship.



→ **KANYAMA TOWNSHIP, LUSAKA, ZAMBIA**
TB devastates lives, families, and even entire communities. TB patients and their families are often forced to restructure their lives to ensure treatment is completed successfully.

A FAMILY'S STORY

Grey Chuma, a husband and father of three living in Kanyama Township in Lusaka, Zambia, has watched TB devastate his life even though he doesn't have the disease. As primary caregiver to his 60-year-old mother who was diagnosed with TB earlier this year, Grey has watched her become sick and weak. He must now devote his days to ensuring she makes the daily journey to the clinic to get her treatment.

Grey and his mother live far from the TB clinic, and the cost of the two bus rides required to get there is more than they can afford. Instead, Grey transports his mother by propping her on his brother's bicycle, and pushing her along bumpy, dirt roads several kilometers each way. This arduous trip to and from the clinic to get her medicine takes up to four hours, and forced Grey to leave his steady job in order to devote his time to his mother's TB treatment. Today, making ends meet is difficult.

Grey's story demonstrates how TB perpetuates poverty. With only sporadic income from reselling cabbage and other vegetables, Grey can no longer afford to send his children to school, and has had to invite his sister and her daughter to move in with his family to help alleviate some of the burden. With a total of eight family members now sharing his one-room dwelling, the likelihood of other family members developing TB is drastically increased.

Grey's fight against TB is echoed wherever TB is most prevalent. The reality is that current TB treatment places an undue burden on patients.

A new, faster-acting, simpler TB regimen would serve to make compliance much easier for Grey's mother and the millions of others also fighting TB. Treatment default results in the development of drug-resistant strains that are much more difficult and up to tens of thousands of dollars more expensive to treat. By working to produce new, improved TB treatments, the TB Alliance is helping to improve the lives of patients, fight the cycle of TB and poverty, and address drug-resistant TB right at its origins.

A PATIENT'S JOURNEY FOR TB TREATMENT (4-HOUR TRIP)

1st hour

Grey Chuma transports his mother about five kilometers, by bike, to the TB clinic.

2nd hour

Grey's mother arrives at the clinic, and waits in line to receive her TB drugs.

3rd hour

After receiving the treatment, Grey and his mother start the return trip back to their township.

4th hour

Grey's mother finally returns to her home, which she shares with 7 family members, some of whom moved in to help care for her.

→ Grey dedicates his days to ensuring his mother receives TB treatment. Each morning, he props her onto a bicycle, and pushes her along the bumpy, dirt roads to the TB clinic so that she can receive her medication.

A REVOLUTION IS WITHIN OUR GRASP

WITH YOUR

TB still kills 5,000 people every day… and the problem is getting worse.

For more than 40 years, there have been no new tuberculosis drugs and little hope to improve the complex and burdensome current course of treatment that so many patients are unable to complete. This flawed regimen has fueled the development of deadly and difficult-to-treat multi-drug resistant and extensively drug-resistant TB, which when combined with the growing numbers of TB/HIV co-infected patients, jeopardizes healthcare systems, economies, and communities throughout the world.

Today, the TB Alliance is on the brink of delivering a monumental achievement by developing new, faster-acting TB cures. In less than a decade, we have assembled the largest portfolio of potential new TB drugs in history, which could save millions of lives.

SUPPORT

WE CAN TRANSFORM LIVES

With three drugs in late-stage testing, we are on the cusp of bringing forth profound advances to alleviate human suffering. However, achieving new cures requires our most promising compounds to complete the necessary development processes, including the most expensive undertakings of all—the final stages of drug testing.

TB perpetuates the poverty cycle and is one of the world's worst killers, yet it is among the most neglected and underfunded diseases in the world. With the global recession pushing even more people into poverty, the time to act is now. The potential of the future starts today. Please support us in finding new and faster cures for TB. For more information about the TB Alliance and how to support our cause, please visit our website at **www.tballiance.org**.

DEAR

FRIENDS, DONORS, AND STAKEHOLDERS:

The precious hope of new drugs stands in stark contrast to the grim reality of the TB epidemic.

TB incidence is at an all-time high. Unfortunately, the rate of TB/HIV co-infection has also risen considerably—approximately 25% of all patients who die of TB are HIV-positive. Perhaps most unsettling, the rate of drug-resistant TB disease is growing, with many regions around the world reporting high rates of multi-drug and extensively drug-resistant TB.

Now more than ever, we need to make progress to combat this disease. And in fact, in 2009, the TB Alliance has accelerated the pace in the fight against TB by further expanding and developing our armamentarium of promising compounds. In the past year, we've added eight new projects to what was already the largest pipeline of TB drugs in history. Now, with more than 20 projects in our portfolio—three of which are in clinical development—the promise of delivering new, markedly improved TB regimens is rapidly approaching reality.

Dr. Mel Spigelman
PRESIDENT AND CEO

Dr. Bruce Carter
CHAIRMAN OF THE BOARD

However, with these scientific advances come new challenges and great responsibility. The cost of later-stage clinical drug development far outstrips that of earlier-phase research. This means that success brings with it the need for additional funding as well as better understanding of the markets into which new TB drugs will enter.

To support this progress, we've grown as an organization, further strengthening our leadership team and adding the management, research, and support capabilities that are necessary to deliver on the promise of new TB drugs. Part of this includes formalizing our market access efforts to ensure we meet the goals of Affordability, Adoption, and Availability—our "AAA" mandate—and that our products reach all those who so urgently need them.

Initiatives like our revolutionary combination testing program, parallel development tracks for drug-sensitive and drug-resistant disease, and our work to map the TB drug landscape and maximize uptake show that we are accelerating the pace of progress and delivering advances that will help enable the world to eclipse the global TB pandemic. It is with this philosophy in mind that we embark toward another year of exciting initiatives and potentially ground-breaking work.

We are extremely grateful for the interest, support, and commitment from all of our partners and stakeholders, especially in light of the current global economic turmoil. Today, more than at any time in recent memory, we can appreciate the economic stability and independence that so many individuals and nations saddled with the burden of TB are unable to achieve. Underlying all investments in tuberculosis treatment and control is a commitment to removing barriers preventing the empowerment of individuals and communities. Thank you once again for sharing that vision and commitment.

Together, we can turn our rapid progress into real change for all those affected by tuberculosis everywhere.

Sincerely,

Dr. Mel Spigelman
President and CEO

Dr. Bruce Carter
Chairman of the Board

← **INDIA**
Advances achieved by the TB Alliance will strengthen health systems throughout the world while simultaneously saving costs associated with administering TB treatment.

FINANCIALS AND ACKNOWLEDGEMENTS

STATEMENT OF FINANCIAL POSITION

YEAR ENDED DECEMBER 31, 2008

ASSETS	
Cash and cash equivalents	$ 16,449,713
Assets limited to use	899,958
Investments at fair value	34,004,450
Accounts receivable	2,154,037
Pledges receivable	2,806,521
Other assets	194,699
Fixed assets, net	3,016,339
	$ 59,525,717

LIABILITIES AND NET ASSETS	
Liabilities:	
Accounts payable and other liabilities	$ 2,379,052
Accrued payroll and payroll-related liabilities	1,115,106
Deferred revenue	24,555,552
Deferred rent	1,102,300
Total liabilities	**29,152,010**
Commitments	
Net assets:	
Unrestricted net assets	30,373,707
	$ 59,525,717

STATEMENT OF ACTIVITIES

YEAR ENDED DECEMBER 31, 2008

PUBLIC SUPPORT AND OTHER REVENUE	Unrestricted
Contributions	$ 28,250,136
Grants	6,482,967
Interest and dividend income	1,015,819
Net realized and unrealized (losses) gains on investments	(38,545)
Miscellaneous income	—
Total public support and other revenue	**35,710,377**
EXPENSES:	
Program services:	
Research and development	26,885,734
Business development	344,645
Public affairs and policy	2,586,737
Total program services	**29,817,116**
Supporting services:	
Management and general	3,751,009
Fundraising	168,293
Total supporting services	**3,919,302**
Total expenses	**33,736,418**
Change in net assets before foreign translation gain	**1,973,959**
Foreign translation (loss) gain	**(91,062)**
Change in net assets	**1,882,897**
Net assets, beginning of year	**28,490,810**
Net assets, end of year	**$30,373,707**

Comprehensive 2008 TB Alliance financial statements are available at:
www.tballiance.org/newscenter/publications.php

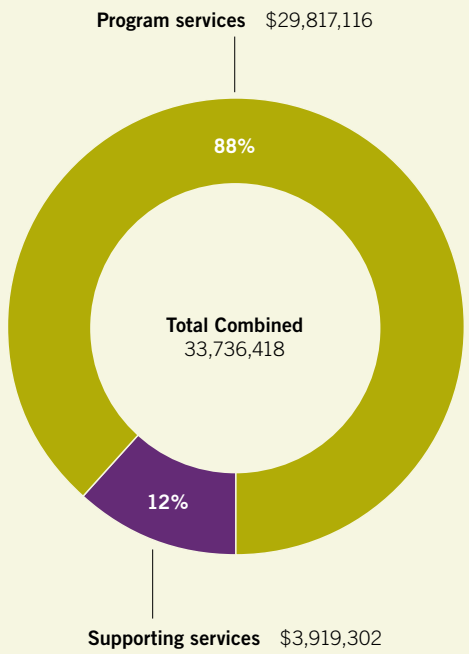
STATEMENT OF CASH FLOWS

YEAR ENDED DECEMBER 31, 2008

CASH FLOWS FROM OPERATING ACTIVITIES:	
Change in net assets	$ 1,882,897
Adjustments to reconcile change in net assets to net cash provided by operating activities:	
Depreciation and amortization	264,175
Loss on disposal of fixed assets	104,683
Realized gain on sales of investments at fair value, net	(199,495)
Unrealized losses (gains) on investments at fair value	238,040
(Increase) decrease in assets:	
Assets limited to use	(26,480)
Accounts receivable	(1,569,371)
Pledges receivable	(2,806,521)
Other assets	98,380
Increase (decrease) in liabilities:	
Accounts payable and other liabilities	(1,828,586)
Accrued payroll and related liabilities	936,085
Deferred revenue	3,866,161
Deferred rent	717,792
Net cash provided by operating activities	**1,677,760**
CASH FLOWS FROM INVESTING ACTIVITIES:	
Purchase of investments	(53,126,085)
Proceeds from sale of investments	40,541,660
Purchase of fixed assets	(2,911,033)
Net cash used in investing activities	**(15,495,458)**
Net (decrease) increase in cash and cash equivalents	**(13,817,698)**
Cash and cash equivalents, beginning of year	**30,267,411**
Cash and cash equivalents, end of year	**$16,449,713**

PROGRAM SERVICES VS. SUPPORTING SERVICES

YEAR ENDED DECEMBER 31, 2008



STAKEHOLDERS

American Lung Association

American Thoracic Society

Association of the British Pharmaceutical Industry

Bangladesh Rural Advancement Committee

Bill & Melinda Gates Foundation

Eli Lilly and Company

European Commission

Global Business Coalition on HIV/AIDS, TB and Malaria

Global Forum for Health Research

Global Fund to Fight AIDS, TB and Malaria

Infectious Diseases Society of America

International Union Against Tuberculosis and Lung Disease

JATA Research Institute of Tuberculosis

KNCV Tuberculosis Foundation

Lupin Laboratories

Médecins Sans Frontières – Doctors Without Borders

National Institute of Allergy and Infectious Diseases, National Institutes of Health, United States

National Institute of Pharmaceutical Education and Research, India

New Jersey Medical School Global Tuberculosis Institute

Novartis India, Ltd.

Oswaldo Cruz Foundation

Partners in Health

Philippines Coalition Against Tuberculosis

RESULTS

Rockefeller Foundation

RTI International

Sequella, Inc.

Patient Representative, Pervaiz Tufail

South African Medical Research Council

Stop TB Partnership

TB Alert

Treatment Action Group

Tropical Disease Foundation

U.K. Department for International Development

U.S. Agency for International Development

U.S. Centers for Disease Control and Prevention

UNDP – World Bank – WHO Special Programme for Research and Training in Tropical Diseases

Wellcome Trust

World Bank

World Health Organization

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President, TB Alliance Stakeholders Association; Director, Tuberculosis Center of Competence, Cape Biotech Trust

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Skyelar Yaffie

→ **INDIA**

We are all connected by the air we breathe. Crowded living conditions are conducive to the spread of tuberculosis and drug-resistant tuberculosis.

ABOUT THE TB ALLIANCE

The Global Alliance for TB Drug Development is a not-for-profit, tax-exempt organization recognized under section 501(c)3 of the United States Internal Revenue Code; contributions are tax-deductible in the United States. Its Belgium branch office was also registered in the Annex of the Belgian State Gazette for non-profit organizations on February 28, 2002.

For inquiries, please contact:
info@tballiance.org
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New York, NY 10005

CONCEPT AND DESIGN

Ideas On Purpose New York, NY
ideasonpurpose.com

PHOTOGRAPHY

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FANCY
WEDDING
CARDS

The 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.

tballiance.org