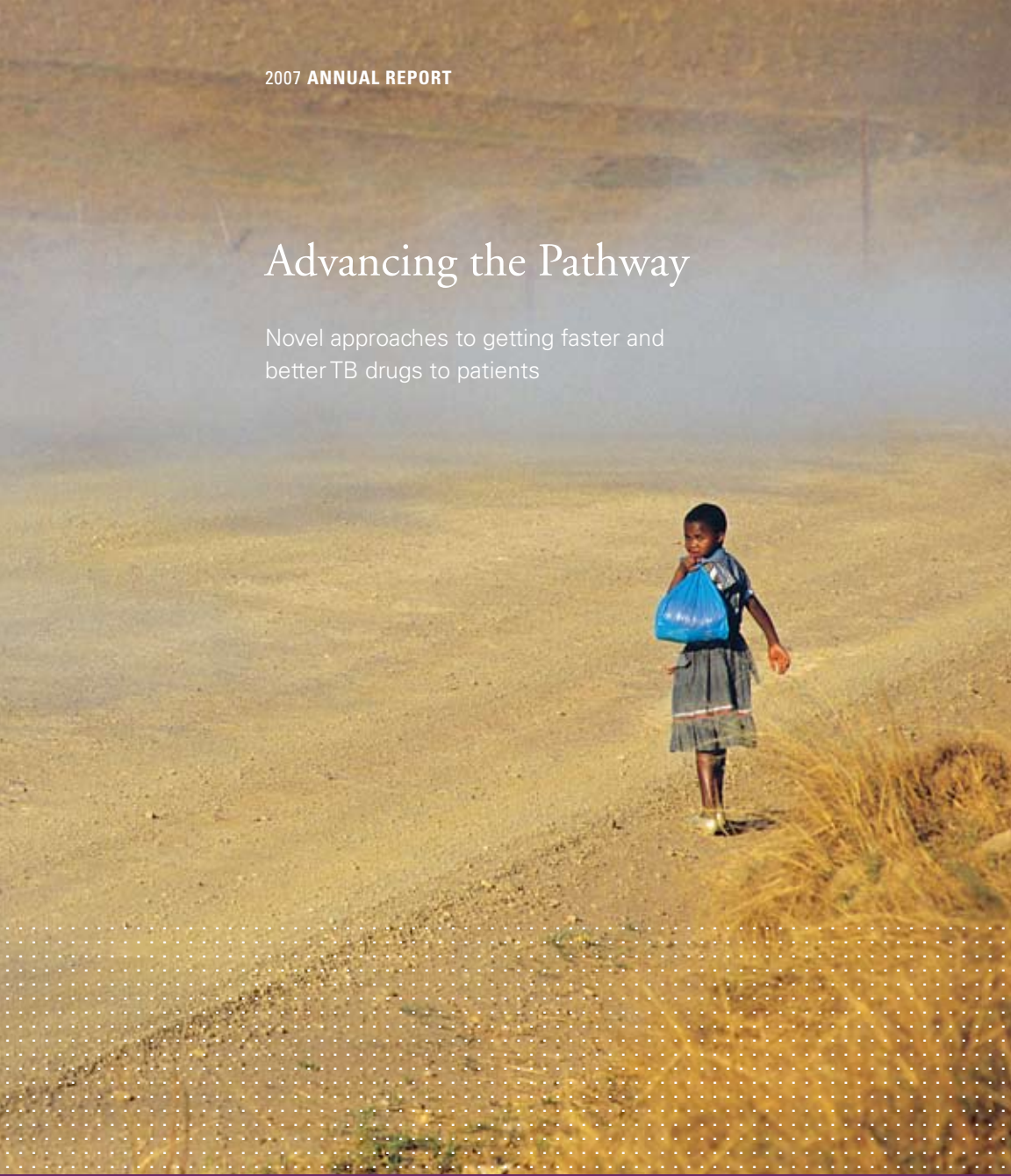
2007 **ANNUAL REPORT**

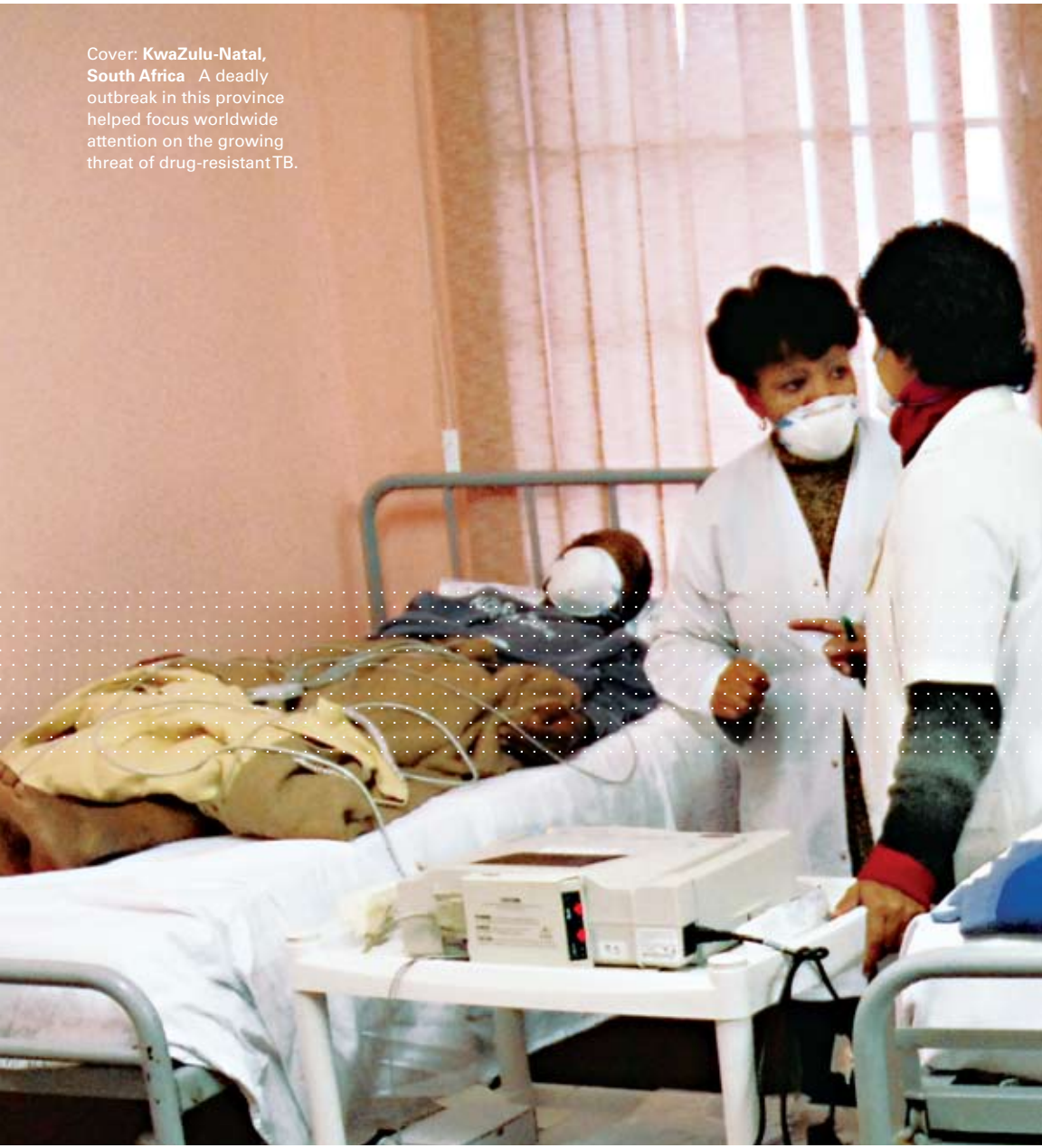
Advancing the Pathway

Novel approaches to getting faster and better TB drugs to patients



TB ALLIANCE

GLOBAL ALLIANCE FOR TB DRUG DEVELOPMENT

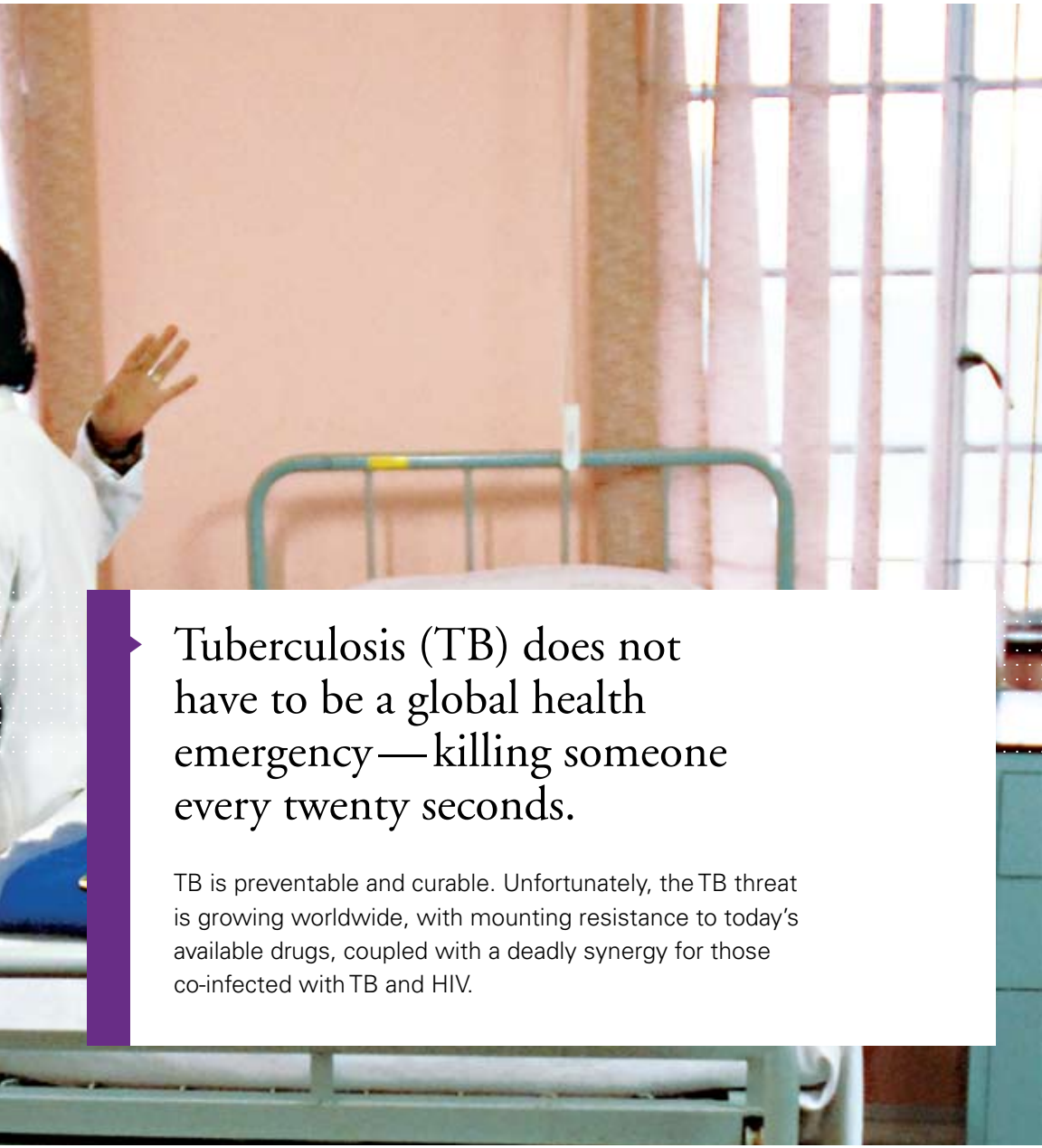


Cover: **KwaZulu-Natal, South Africa** A deadly outbreak in this province helped focus worldwide attention on the growing threat of drug-resistant TB.

Over 2 billion people carry the bacterium that causes TB

One in 10 of those infected will develop active TB

Active TB kills about 4,400 people a day —1.6 million every year



Tuberculosis (TB) does not have to be a global health emergency—killing someone every twenty seconds.

TB is preventable and curable. Unfortunately, the TB threat is growing worldwide, with mounting resistance to today's available drugs, coupled with a deadly synergy for those co-infected with TB and HIV.

If not treated, each person with TB will infect on average 10 to 15 people every year

Today's lengthy treatment is difficult to complete and not always available

Without faster, simpler drugs, countless lives remain in peril

Millions of lives hang on the development of a better, faster treatment.

Today's TB drug regimens take too long to administer and require too many pills. The current four-drug combination for drug-susceptible disease includes antibiotics over a half-century old that must be taken for at least six months. Erratic or inconsistent treatment breeds drug resistance. New, faster and better drugs are desperately needed to save millions of lives needlessly lost each year to drug-susceptible and drug-resistant disease.

A mounting threat

TB strains that are resistant to many or all of today's available drugs are a growing, ominous global health threat.

The spread of drug-resistant TB is a man-made tragedy, caused by inadequate or incomplete treatment with a cumbersome, decades-old drug regimen that takes at least six months to cure TB. Drug-resistant strains emerge when bacteria are sporadically exposed to antibiotics, or when patients are unable to complete the lengthy and burdensome treatment.

Multidrug-resistant TB (MDR-TB) is defined by resistance to at least isoniazid and rifampicin, two of today's four standard first-line drugs. The World Health Organization (WHO) estimates that there are nearly a half-million new cases of MDR-TB each year. These cases are difficult to manage and have much lower cure rates. For MDR-TB patients, treatment can take up to two years, with second-line drugs that are more expensive, do not always work, and have significant side effects.

Extensively drug-resistant TB (XDR-TB) can develop when the limited second-line drugs are also inadequately delivered and become ineffective, leaving very few treatment options.

The WHO has branded XDR-TB "a threat to the security and stability of global health." XDR-TB has been identified in all regions of the world. The growing threat of drug-resistant TB has triggered major global news coverage this year, raising questions about the safety of air travel and prompting debates over the need to quarantine patients.

The specter of untreatable TB heightens the need to accelerate the development of new drug regimens that work more quickly and make it easier for patients to be cured. Novel drugs and drugs that attack novel targets are needed to fight resistant strains. A shorter regimen, reliably administered, that is easier for patients to complete would also minimize the development of further resistance.

MDR-TB

MULTIDRUG-RESISTANT TB

Resistance to at least *isoniazid* and *rifampicin*, two of today's four standard first-line TB drugs. There are an estimated 450,000 new MDR-TB cases every year.

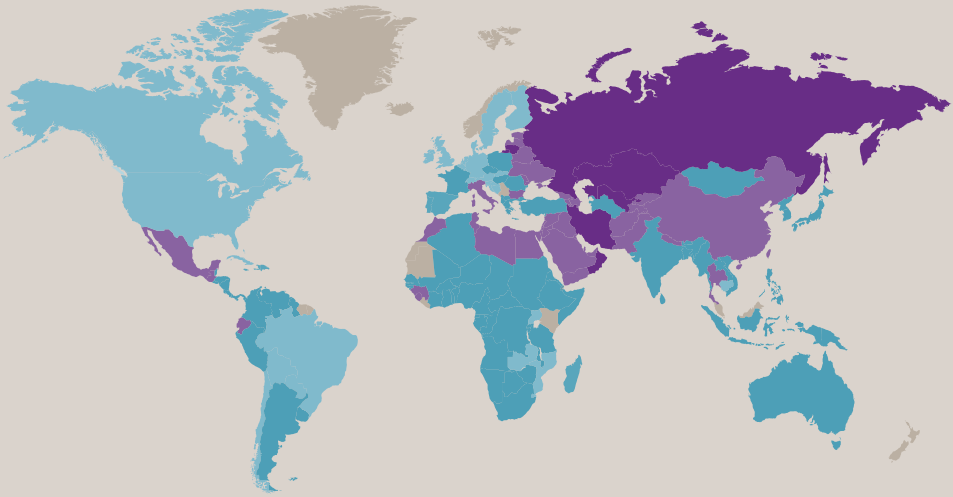
XDR-TB

EXTENSIVELY DRUG-RESISTANT TB

MDR-TB plus resistance to: (i) any fluoroquinolone, and (ii) at least one of the three injectable second-line drugs *capreomycin, kanamycin* and *amikacin*.

DISTRIBUTION OF MDR-TB RATES AMONG PREVIOUSLY TREATED CASES

No Estimate · < 6% · 6%–20% · 20%–40% · > 40%



World Health Organization, 2006/2007

THE EMERGENCE OF XDR-TB

Although the WHO believes that XDR-TB remains rare, it has been identified in all regions of the world. The only global study done on this emerging threat found that nearly 20% of MDR-TB cases in the hardest-hit regions were XDR-TB. Health authorities believe the global average is far lower, although exact rates are not yet known.

We do not have time to wait.

The Global Alliance for TB Drug Development (TB Alliance) is leading the development of the most comprehensive portfolio of TB drugs ever assembled by accelerating discovery, preclinical and clinical testing of known and novel classes of antibiotics to shorten and simplify TB treatment. We are committed to ensuring that all drugs developed through our research partnerships will be affordable, widely adopted, and available to all who need them.

The standard drug development model, when applied to TB, can take more than two decades from discovery through testing of the novel drug regimens patients urgently need.

The TB Alliance is mapping a new, faster route that will take us from the early stages of discovery in the laboratory to helping new drug regimens reach patients in countries around the world.

We are not just developing drugs. We are streamlining the way TB drugs are developed.

A comprehensive drug portfolio is just the beginning. The TB Alliance is accelerating TB drug development by priming the pipeline with an innovative approach to research, drug development, and preparation for registration and adoption.

- We are testing new and existing drugs with an aggressive, fast-track combination approach.
- We are working with global drug regulatory authorities to explore new, faster ways of ethically testing drugs in clinical trials.
- We are helping to ensure that there are clinical trial sites ready for the work that lies ahead.
- By engaging people in the field throughout the world, we are learning where the challenges may lie in getting new regimens widely adopted and available.

We are reinvigorating and reinventing the path to new, better TB treatments by identifying and bridging the gaps.



ADVANCING THE SCIENCE
WITH NEW RESEARCH TOOLS

Evaluation of New Drug Combinations

Fast-tracking the testing of new regimens

Identification of Biomarkers

Identifying new determinants of successful treatment

Mouse Model of Tuberculosis

Optimizing a preclinical research model

DISCOVERY → **DEVELOPMENT** → **AVAILABILITY**

Clinical Trial Site Assessments

Identifying clinical research facilities and targeting improvements

Trial Site Community Engagement

Engaging key constituencies

Regulatory Mapping

Understanding regulatory pathways in high-burden countries

Market Analysis

Identifying market dynamics that affect availability

Product Profile Analysis

Defining the value proposition of new regimens

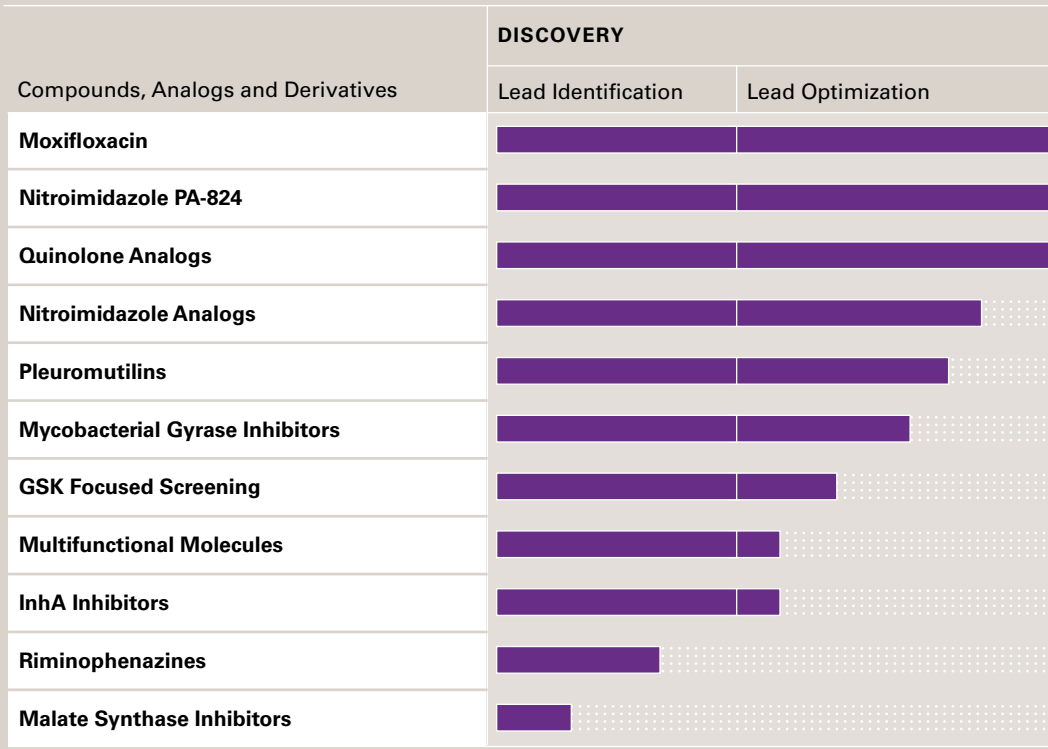
Regulatory Preparation Forums

Learning what is needed for registration

LAYING THE GROUNDWORK FOR
REGISTRATION AND ADOPTION

TB Alliance Portfolio

TB ALLIANCE PROGRAMS



TB DRUG DEVELOPMENT PROCESS

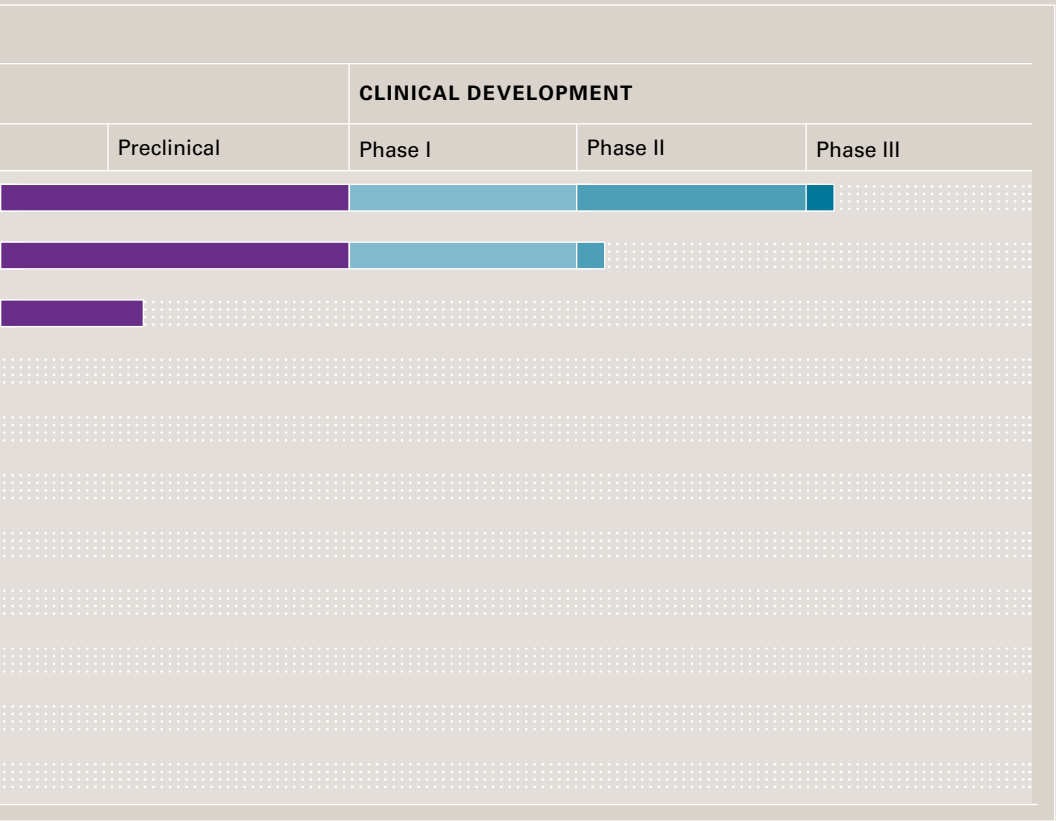
DISCOVERY

Identify lead structural series; **optimize** activity *in vitro*, efficacy in animals, and other pharmacological properties. Perform **preclinical** safety studies allowing filing of a new drug application. Use combination testing to identify the best potential new regimens for clinical development.

PHASE I

Test drug candidates and regimens in small numbers of healthy volunteers for safety, tolerability, and pharmacokinetic properties.

The TB Alliance, working with its public and private partners worldwide, is leading the development of the most comprehensive portfolio of TB drug candidates in history.



PHASE IIa-IIb

Evaluate single drug candidates (Phase IIa) and multi-drug regimens (Phase IIb) in TB patients for potential efficacy and further assessment of safety.

PHASE III

Test multidrug regimens in large numbers of TB patients for efficacy and safety in well controlled clinical trials.

REGULATORY

Regulatory authorities license the drug/regimen after reviewing all preclinical and clinical results.

ADOPTION/ AVAILABILITY

National TB control programs adopt the new drug/regimen, ensuring that it is available to those who need it.

A new strategy for TB research

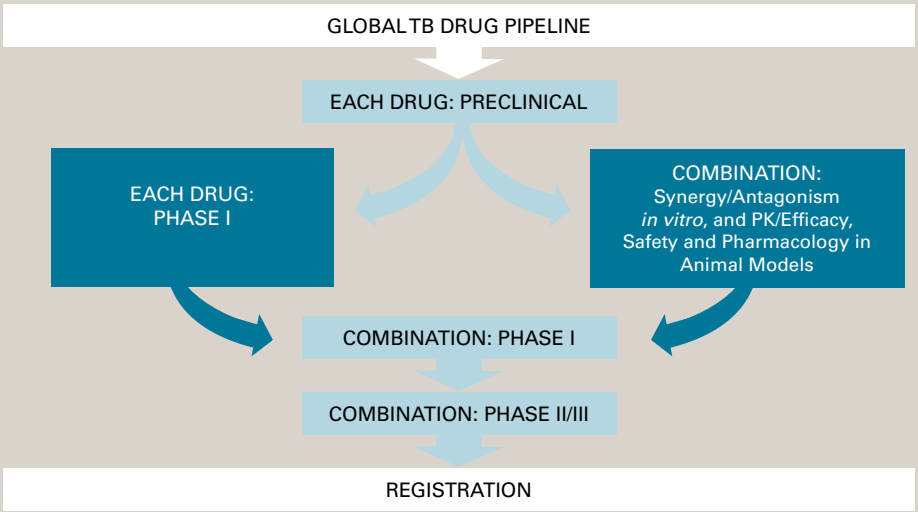
Today, the TB Alliance is managing numerous new drug projects across various stages of development, from the laboratory to patients in the clinic.

We know that we will need a robust, replenishing pipeline of compounds because no new drug, by itself, can cure active TB. The need for new, novel regimens has us mapping innovative ways to fast-track development of drugs in combination. We are committed to developing drugs that will shorten treatment, be effective against susceptible and resistant strains, be compatible with antiretroviral therapies used for those co-infected with TB and HIV, and improve treatment of latent infection.

In conventional TB drug development, new drug candidates are evaluated sequentially by adding each into the existing regimen or by substituting the candidate for one of the current drugs. Each new potential combination is put through multiple stages of clinical trials, requiring at least six years to complete. Under conventional testing, a new regimen of four new drugs would require more than 24 years of development—too long to wait.

To shorten and improve a process that can take decades, we launched a groundbreaking combination testing initiative designed to jumpstart the development of drug regimens. The TB Alliance is testing known TB drugs and potential new compounds in rational combinations early in the development pathway to determine their possible synergistic and antagonistic effects. The tests begin with *in vitro* studies measuring activity against *Mycobacterium tuberculosis* (*M.tb*), the bacillus that causes TB. Successful combinations will then advance to *in vivo* animal testing.

FASTER DEVELOPMENT OF NEW DRUG COMBINATIONS



Our new preclinical combination testing program will provide clear markers pointing to the potential best choices for combinations in clinical trials based on scientific information that will greatly improve the chances of success. Together with a new, fast-track regulatory strategy, this initiative could dramatically reduce the time it takes to move new drug regimens from the laboratory through clinical testing.

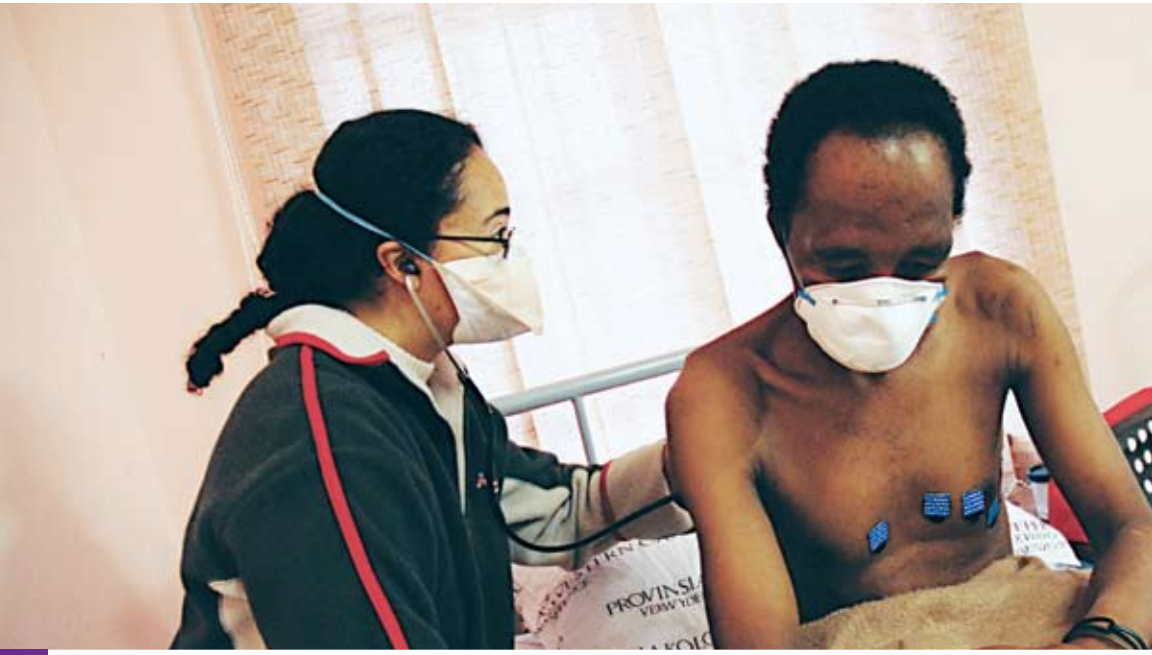
One of the tools being used to help guide preclinical combination research is a comprehensive database of TB drugs and their properties. Compiled by TB Alliance scientists, this database will help researchers compare all published information on drug side effects, pharmacology and metabolism.

New research tools are also needed to speed evaluation of drug candidates in clinical trials. Identifying biomarkers that can provide early confirmation that a new treatment is working would be of great benefit to the clinical development of new TB therapies —much the way that CD4 counts and viral load are early indicators that drugs are working for patients with HIV/AIDS.

Unfortunately, TB treatment has no such early gauge of success. Researchers rely on measuring a reduction of *M.tb* in sputum to show drug candidates are working. This test does not prove that a regimen will cure disease. Real proof requires that TB drug combinations be tested in large-scale Phase III clinical trials with a lengthy enrollment period, six months of treatment, and at least twelve months of follow-up to confirm there is no relapse.

The TB Alliance and its partners launched a research effort to identify potential biomarkers that might serve as an early indicator of response to treatment or of ultimate cure. If reliable biomarkers for TB can be identified, researchers would have molecular signals of cure that could significantly shorten the time needed for clinical development.

These efforts are optimizing laboratory and clinical work so life-saving new drugs are developed efficiently. The combination drug testing program will help fast-track the choice of regimens to be tested, while biomarkers will confirm more quickly that those new regimens are working.



Advancing research in the clinic

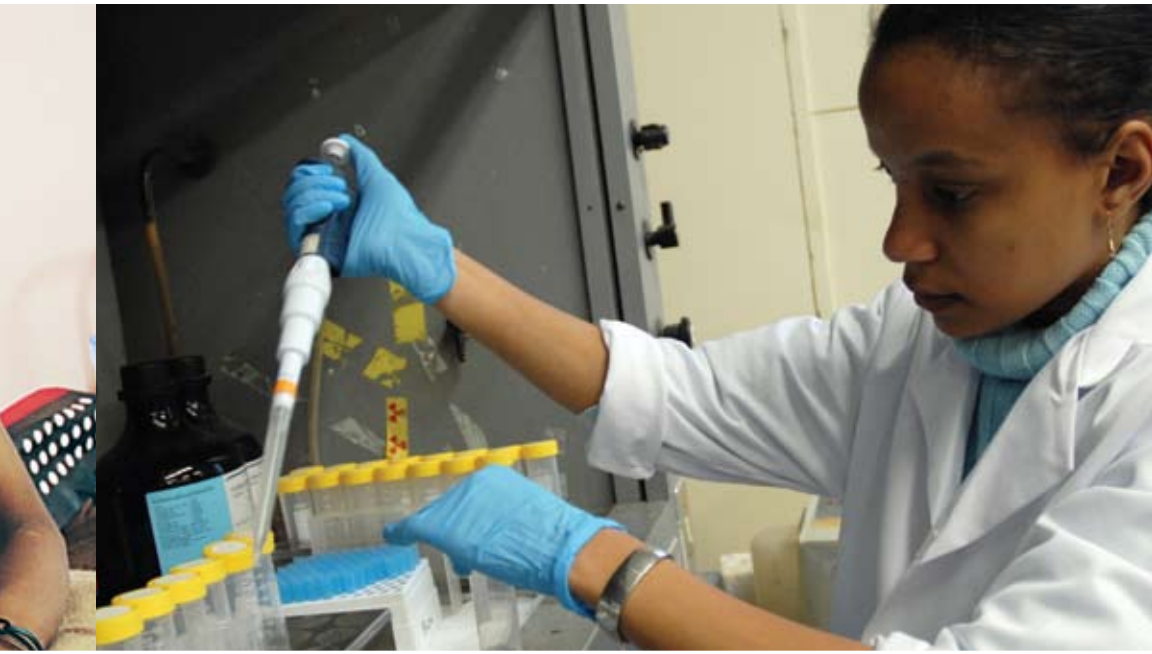
As promising drug candidates advance through the development pipeline, the need intensifies for a robust clinical trial network capable of supporting multiple large-scale TB drug trials. To ensure the quality of our clinical research, we are conducting an ongoing global assessment of potential TB clinical trial sites and laboratories.

The first phase of this assessment spanned the globe, with researchers evaluating sites in Africa, Asia, Eastern Europe, and North and South America. Sites and associated laboratories were assessed for their ability to carry out Phase II and III TB drug trials that will meet international registration or drug approval standards.

We were pleased to find that a number of potential sites are ready to conduct clinical trials with minimal ramp-up needs. Some of the sites evaluated are now part of the TB Alliance clinical studies program.

At two South African sites, we are conducting a Phase II study of PA-824, a novel nitroimidazole that is the first new TB drug candidate developed by a not-for-profit organization to reach clinical trials. PA-824 offers promise for potential treatment-shortening and for activity against drug-resistant disease.

Clinical centers in Kenya, South Africa, Tanzania and Zambia are conducting the first Phase III testing of the antibiotic moxifloxacin as a substitution for one of two current TB drugs. Researchers are testing whether a new regimen containing moxifloxacin can help shorten the standard TB drug regimen from six to four months.



CLINICAL TRIAL SITES AND LABORATORIES ASSESSED TO DATE



Defining the regulatory strategy

No new class of TB drugs has been approved in over 40 years. During this hiatus, the regulatory landscape has changed dramatically. Drug approvals now require clinical trials involving more patients, more rigorous documentation, and more thorough analyses. The decades-long gap has resulted in a lack of specific guidelines for regulatory evaluation and approval of TB therapies. Modern TB-specific regulatory guidelines simply do not exist.

The TB Alliance routinely meets with key regulators on the planning and execution of our projects and the design of clinical trials to test new, faster-acting combinations.

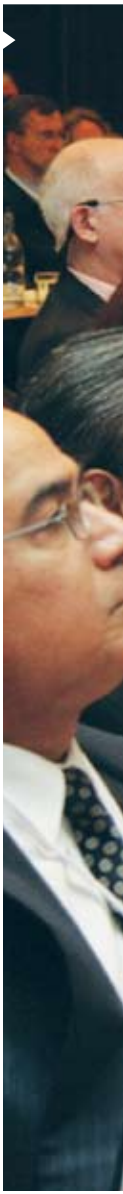
Our new strategy is based on the reality that regimens, rather than compounds, are the appropriate units of treatment that can ultimately be assessed for their activity in treating TB. Now, regimens would be tested as a single entity—based on the promise that the regimen and each drug showed in earlier clinical and preclinical research. Instead of substituting single drugs into existing combinations, this novel approach would allow markedly more effective TB regimens to move more quickly towards approval.

New treatments must be available in all countries where TB is prevalent. To achieve this, our new drugs must meet each country's regulatory standards. The TB Alliance is creating a global regulatory filing roadmap that will define what is needed in different countries for approval.

Our ongoing "Regulatory Open Forum" meetings are designed to identify and address crucial issues involved in advancing new TB treatments to registration, and ultimately to patients. These meetings bring together regulators, TB drug developers and other interested stakeholders, such as TB care providers, public health policy-makers, and community advocates, from major industrialized and high-burden countries.

Attendees at the most recent Open Forum, held in London in December 2006, addressed key issues in the critical path to TB drug registration: the need for biomarkers for TB drug development; how to develop regimens containing multiple novel agents; and how best to design pivotal trials, including conducting registration trials in high-burden countries.

Through ongoing consultation with those who influence approval and availability of new TB drugs—globally and at the country level — the TB Alliance is helping to pave the way to getting new TB drugs to patients around the world.



Understanding the pathway to patients

Developing new treatments does not ensure they will be available to the patients who need them.

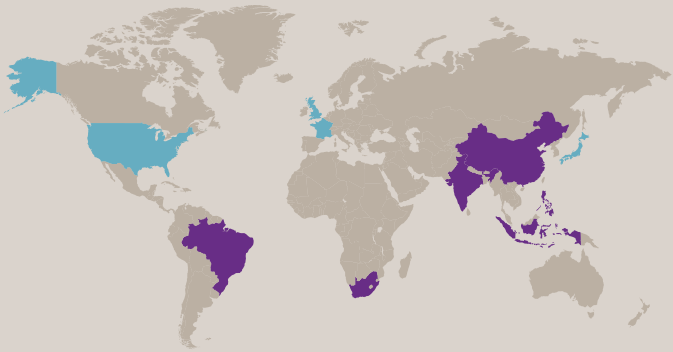
At the TB Alliance, we know that understanding how drugs actually reach patients is critical. That is why we are analyzing how patients access today's TB drugs and identifying the people and organizations that affect availability. We want to share our understanding with key stakeholders to help make certain that healthcare systems can put new medicines in reach, the world over.

In our new study, *Pathway to Patients: Charting the Dynamics of the Global TB Drug Market* (*Pathway to Patients*), we provide a detailed description of how today's TB medicines reach patients in 10 strategically-selected countries, and an estimate of the value of the global market for first-line TB drugs.

The study, published this year, points to the variability of the market dynamics among the countries studied, the array of complexities faced at all levels of the supply chain, and the highly fragmented nature of the global market. The findings also allowed us to project an estimate for the global market of first-line TB drugs (the four drugs commonly used in combination to treat drug-susceptible disease) of approximately US$315 million per year.

Pathway to Patients, the first comprehensive study of the dynamics of the global TB drug market, reveals:

- The variability and complexities faced at all levels of the TB drug supply chain
- The highly fragmented nature of the global marketplace in terms of purchase, supply and delivery
- The important role of local and regional, as well as national governments in procurement and distribution
- A preference by most national TB control programs studied to procure drugs from domestic manufacturers
- The limited commercial market potential for new TB drugs



COUNTRIES STUDIED:

- **High Burden**
  Brazil, China, India, Indonesia, the Philippines, South Africa
- **High Income**
  France, Japan, UK, US

Full study findings and methodology are available at www.tballiance.org.

Defining the value propositions of new regimens is another important strategic initiative underway. This new study is aimed at better understanding what those on the front lines of TB control would ideally require from a new TB regimen, and the type of information they will need to evaluate whether a novel treatment is appropriate for their TB program.

Researchers interviewed patients, local healthcare providers, TB and HIV disease control program heads, and representatives of WHO and global technical agencies in five representative countries—Brazil, China, India, Kenya and South Africa. This information will help influence the planning for new regimens that respond to the needs of patients and TB control programs.

Our research suggests the need to closely monitor a number of evolving factors that may alter the flow of TB drugs in the years ahead. For example, the introduction of new tools to diagnose and prevent TB, along with policy and funding influences, could change the treatment landscape.

Understanding the structure of the global TB drug market today and learning more about it as we move forward will prove essential to planning for the introduction of new TB drug regimens.

Our commitment to ensuring that all new drugs we develop are *affordable*, *adopted* and *available* (AAA) means we are already planning for the successful launch of new drugs. In doing so, we are working with key stakeholders to understand the possible hurdles facing implementation of our AAA mandate. It will take cooperation at the global and national levels, and the work of many, to map the most effective route to equitable availability.


Laboratory
HOW WE TEST FOR TB:
SPUTUM TEST
Cough
Spit
LABORATORY

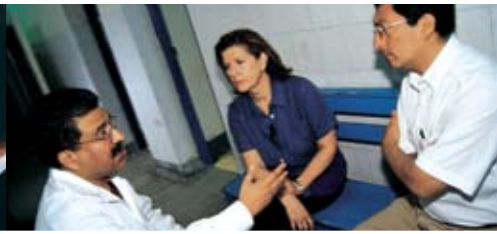
Paving the pathway

The TB Alliance has no laboratories and no clinics of its own. We operate as a virtual research and development organization, maximizing the expertise and existing resources of our global network of partners to minimize costs. Our collaborators span the globe—representing almost every continent—to support our development of faster and better TB regimens.

Drug development is expensive, even for a budget-minded, not-for-profit organization.

The TB Alliance has raised over US$200 million to date, with generous funding from The Bill & Melinda Gates Foundation, the Rockefeller Foundation, and the governments of Ireland, The Netherlands, the United Kingdom and the United States. The U.S. National Institute of Allergy and Infectious Diseases and GlaxoSmithKline provide significant in-kind contributions.

However, we know we are going to need a far greater commitment to complete our mission.



Attrition will take a toll on the number of compounds currently in our pipeline. We are going to need increased funding, as well as innovation in science, to help us replenish our pipeline and increase the number of promising new compounds to fight TB.

Additional support from governments and other funders is needed to help us continue to accelerate the pace of our research at each phase of the pipeline and realize our goals. While we are working to map a new regulatory strategy to enhance rapid development of markedly improved treatment regimens, we do not yet have the funding to complete all of that development work. Only continued support will carry our advancements forward and make new, better regimens a reality.

We are working at the national and global level to highlight the critical need for new TB drugs and to secure commitments to join the effort. Our advocacy work in the public sector, especially with key decision-makers, is aimed at increasing the funding for TB drug development and helping influence the policy decisions that will lead to widespread availability of new treatments.

The TB Alliance and its partners are working to create and follow a revolutionary new pathway to produce life-saving, new, faster and better TB drug regimens. We thank those who are supporting us and encourage others to join as we work to help rid the world of this ancient disease.

Pipeline Update

Mycobacterium tuberculosis (*M.tb*), the bacillus that causes TB, is a complicated foe. TB treatment must eradicate at least two populations of *M.tb*: the rapidly growing bacteria that can often be killed quickly; and a more slowly growing, or persistent population of bacteria that may linger. The TB Alliance is committed to conquering this challenge by developing novel, faster-acting drugs to simplify and shorten TB treatment regimens.

Clinical testing of drug candidates

All drug candidates, including any proposed TB drug, must go through a well-established series of clinical trials in people to ensure safety and efficacy.

Initial Phase I studies are small, limited tests of the safety, and metabolic and pharmacologic profiles of drugs. These studies, which are standard for all drug development, are usually conducted in healthy volunteers.

Because of the peculiar nature of the disease, the next round of TB clinical trials is conducted differently than most new drug trials.

Phase II trials are usually the first opportunity to test new TB drugs in patients. Phase IIa trials study the short-term potency of a single drug, given by itself, to TB patients. Although the drug alone is not expected to be a cure (and the trial participants are given standard combination therapy immediately after the trial), these Early Bactericidal Activity (EBA) studies give a preliminary indication of potential efficacy. They measure the killing of *M.tb* in patients' lungs as represented by how many live bacteria remain in their sputum.

If EBA results are positive, the Phase IIb studies test the drug as part of a full combination therapy for TB, with a two-month assay or test as an initial indicator of the drug's effectiveness.

As with other indications, the final proof of safety and efficacy before registration or regulatory approval comes from longer Phase III trials in larger numbers of patients. For TB, a single new drug candidate is tested by substituting it for a drug in the standard first-line regimen. These replacement trials for drug-susceptible disease continue to test for disease relapse for a year or more after the completion of a full course of combination treatment.

TACKLING DRUG-RESISTANT TB

The development of multidrug-resistant TB (MDR-TB) removes from the arsenal two of the most potent drugs in the standard first-line regimen. Although second-line drugs exist, they are generally less effective, more expensive, and more toxic.

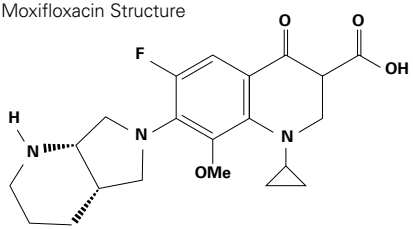
Novel drugs that attack new targets in *M.tb*, or that attack old targets in new ways, are the best defense against MDR-TB. When used in new, shorter regimens, these drugs have an even greater chance of preventing the development of resistance. Shorter regimens should be easier for patients to complete, leading to less adherence failure and less resistance.

The greatest challenge is extensively drug-resistant TB (XDR-TB). With XDR-TB so severely limiting the existing treatment options, the need for novel drugs is even more acute. Completely novel drugs in the TB Alliance pipeline offer potential for treating XDR-TB, and any shortening of the treatment regimen should reduce the future emergence of drug-resistant strains.

Moxifloxacin

Partnership with Bayer HealthCare AG (Bayer)

Moxifloxacin Structure



Moxifloxacin is a widely-used antibiotic with demonstrated efficacy for the treatment of acute respiratory and skin infections in humans. Developed and marketed by Bayer HealthCare AG (Bayer) for these indications, moxifloxacin has an excellent safety record, having been used more than 76 million times, in 141 countries.

Preclinical studies in mice suggest that moxifloxacin has the potential to be part of a more effective treatment regimen for TB, reducing the treatment period from at least six months to four months or less. Phase II studies have also suggested that it may be effective for treatment shortening. Moxifloxacin is the first drug in the TB Alliance portfolio to enter a pivotal Phase III trial for TB.

Moxifloxacin's mechanism of action differs from those of today's current first-line drugs. It acts by inhibiting an enzyme called DNA gyrase, which is essential for bacterial survival. Unlike some existing TB drugs, moxifloxacin does not interact with enzymes that are involved in the body's handling of antiretroviral (ARV) therapies used to treat HIV patients, avoiding problems for people who need to be treated for both TB and HIV.

The latest advance in this program is REMoxTB—a historic Phase III TB trial with moxifloxacin, which was launched in late 2007. REMoxTB will initially enroll patients at trial sites in Kenya, South Africa, Tanzania, and Zambia. The trial will assess whether each of two, four-month regimens substituting moxifloxacin for one of the current standard drugs (ethambutol or isoniazid) is equally effective as the standard six-month therapy in terms of failure and relapse. This builds on the results from three Phase II studies, which used a similar substitution strategy with moxifloxacin.

REMoxTB is part of the global clinical development program that the TB Alliance, in partnership with Bayer and others, is conducting to determine moxifloxacin's potential for use as a TB treatment. Among those helping to lead the moxifloxacin studies are some of the world's premier clinical trial experts: the TB Clinical Trials Consortium of the U.S. Centers for Disease Control and Prevention; The Johns Hopkins School of Medicine; and University College, London, working with the British Medical Research Council.

BAYER–TB ALLIANCE PARTNERSHIP

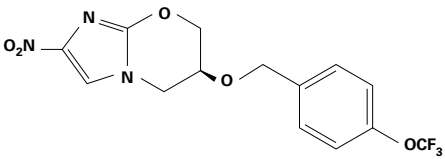
In a groundbreaking agreement, Bayer and the TB Alliance announced a research partnership in late 2005 to test moxifloxacin — a profitable, proven antibiotic — for an indication that primarily affects the poor. The Bayer–TB Alliance partnership is committed to making moxifloxacin affordable and available for TB patients in developing countries, where it is needed most.

Bayer is donating moxifloxacin for each clinical trial site and is covering the costs of regulatory filings. Both partners are working toward a common goal of registering moxifloxacin for TB. An approved moxifloxacin-based regimen could reduce the current, burdensome TB treatment time by at least two months.


BD Plastipak

PA-824

PA-824 Structure



PA-824 is the first TB drug developed by a not-for-profit product development partnership to reach clinical trials. It comes from an established class of antibacterial agents—the nitroimidazoles—but one that is only now being developed clinically as a new approach to the treatment of TB.

In a landmark 2002 agreement with Chiron, now part of Novartis, the TB Alliance received worldwide exclusive rights to PA-824 and its analogs for the treatment of TB. Chiron pledged to make this technology royalty-free in endemic countries.

PA-824 potentially offers a number of attractive characteristics as a TB drug, including its novel mechanism of action, its *in vitro* killing of all tested drug-resistant clinical isolates, and its potent activity in mice. In fulfilling this preclinical promise, PA-824 combines two vitally important activities in a single compound: the rapid killing of actively dividing bacteria; and potential treatment shortening resulting from the killing of persistent bacteria. Because it is a novel drug, PA-824 has the potential to treat drug-resistant disease.

Phase I studies with PA-824 revealed that the drug was well tolerated with no definitive dose-limiting adverse events. A moderate elevation in serum creatinine levels in individuals receiving PA-824 was seen in the initial Phase I studies. An increase in creatinine can be a sign of impaired kidney function, but further tests revealed that the change was fully reversible and kidney function was not compromised.

Based on the positive results from Phase I tests in healthy volunteers, PA-824 has entered a Phase II extended Early Bactericidal Activity (EBA) study in TB patients in Cape Town, South Africa. This study is examining the short-term potency of PA-824 given as a single drug. If EBA results are positive, the drug will be moved into Phase IIb studies in which PA-824 will be given in combination with other effective drugs to further test its safety, tolerability and efficacy.

The PA-824 project got a boost this year when it was granted orphan drug status by the US Food and Drug Administration. This status confers a number of positive effects, including the waiver of the nearly US$1 million fee usually paid on submission of a New Drug Application.

Beijing, China Representatives of the TB Alliance and Institute of Materia Medica at the formal signing of a partnership to study riminophenazines.

Turning molecules into drug candidates

Healthy drug development pipelines need continuous innovation. The TB Alliance is constantly searching for and evaluating new drug targets, new leads, and new drug candidates.

One of the key ingredients in this search is diversity. Diverse targets mean more ways to kill TB bacteria, and diverse chemical structures mean more chances of finding the most potent compounds in a particular drug class. The best targets are both novel and important in persistence; this raises the chances of shortening therapy in both drug-susceptible and drug-resistant disease.

The process begins with large libraries of chemical compounds or chemical variants of promising leads. Carefully selected chemicals are tested directly against the molecular drug targets or for their ability to kill both drug-susceptible and drug-resistant strains of *M.tb*. Some of these *in vitro* tests mimic conditions in the *M.tb*-infected human lung, so that this early stage has the best chance at uncovering drugs relevant for treating disease.

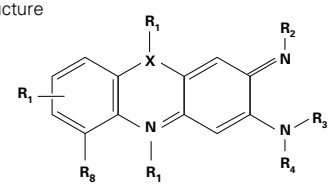
Once compounds have been shown to kill *M.tb in vitro*, they are tested for activity against TB disease in animals. These *in vivo* tests, usually in mice, help to narrow down a larger group of compounds to a select few. The tests assess a drug candidate's safety, its ability to kill actively dividing TB bacteria in the animal, and its ability to eliminate all TB bacteria, including those that are dividing slowly. This last test is a closer mimic of the human disease.

After a few (usually one to three) drug candidates have been selected, *in vivo* studies in animals define the best possible dosages, drug combinations, and frequency of treatment, and help to ensure that the compounds are safe before they reach the clinic.

Riminophenazines

Partnership with Institute of Materia Medica (IMM)

Riminophenazines
Structure



Riminophenazines have been effective in treating mycobacterial infections like leprosy, though existing compounds have poor solubility and can cause cosmetic side effects such as pronounced skin discoloration in patients.

In 2007, the TB Alliance entered into partnership with the Institute of Materia Medica (IMM) in Beijing to design and synthesize new, safe, more soluble and more efficacious compounds in this promising class.

Riminophenazines are thought to inhibit energy metabolism, which is needed even in slow-growing *M.tb* persisters. Riminophenazines therefore show promise for treatment shortening. They show no cross-resistance with any other class of TB drugs; their lack of intrinsic P450 interactions means that they should be safe to co-administer with antiretrovirals (ARVs) in patients who are co-infected with TB and HIV. Several series of compounds are now being synthesized under this partnership to explore the potential of this class to treat both drug-susceptible and drug-resistant disease.

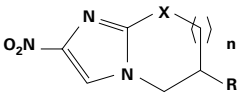
IMM & BTTTRI – TB ALLIANCE PARTNERSHIP

The Institute of Materia Medica (IMM), a member of the Chinese Academy of Medical Sciences, is one of the primary institutions for drug research and development in China. It has expertise and integrated capabilities in chemistry, pharmacology and drug manufacturing. The Beijing Tuberculosis and Thoracic Tumor Research Institute (BTTTRI) is a leading research institute focused on TB research. BTTTRI will work closely with IMM to perform *in vitro* and *in vivo* assays on new riminophenazines synthesized at IMM. The data generated at BTTTRI will inform the iterative efforts of IMM chemists as they design better compounds with high activity against *M.tb*.

Nitroimidazole Analogs

Partnership with University of Auckland, New Zealand

Nitroimidazole Analogs Structure



Nitroimidazoles have a long history as antibacterial agents. Metronidazole, derived from a modified bacterial natural product, was discovered in the 1950s; it is widely used to treat protozoan and bacterial infections.

The progress of the nitroimidazole PA-824 into Phase II clinical trials, plus the nitroimidazoles' novel mechanism of action and PA-824's excellent efficacy in mice, have raised further interest in this class. The nitroimidazole analog program is intended to provide additional compounds. Successful compounds may act as second generation drug candidates that exceed PA-824 as a TB drug in efficacy, safety, or tolerability.

Over 600 new nitroimidazoles have been synthesized and over 40 have been evaluated for efficacy in the acute mouse model. Several compounds show excellent efficacy in this system. Based on this exciting result, exploration of chemical variants to further optimize pharmacokinetics and drug metabolism is continuing. As part of a novel class, nitroimidazoles have the potential to treat drug-resistant TB.

Multifunctional Molecules

Partnership with Cumbre Pharmaceuticals

Up to four drugs, taken simultaneously, are needed to outwit and kill *M.tb*.

However, multiple TB drugs, when taken together, may not work together optimally. Once swallowed, they can travel to different parts of the body, and even drugs that reach the same location may peak in concentration at different times. Therefore, any single location in the body may end up with sufficient amounts of only one or two of the drugs at the same time.

The partnership between the TB Alliance and Cumbre Pharmaceuticals is aimed at addressing this problem. By chemically linking different drugs, initially in pairs, multiple drugs are forced to function as one. The project is exploring three new classes of these bi-functional TB drugs: the rifamycin-nitroimidazoles, the quinolone-nitroimidazoles, and the oxazolidinone-nitroimidazoles. In each case, a single new drug is created by fusing together two existing drugs.

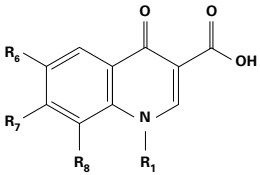
Because they are linked, the two drugs are guaranteed to reach the same sites in the body in the same amounts and at the same time. The bacterium cannot escape, and it is almost impossible for it to become resistant to two drugs at once.

Developing large, linked compounds is challenging. In each class, however, promising bi-functional compounds have shown potent antibacterial activity. Optimization of at least one of these classes is expected to continue during 2008.

Quinolone Analogs

Partnership with Korean Research Institute of Chemical Technology (KRICT) and Yonsei University

Quinolone Analogs Structure



Quinolones are a proven and potent class of antibacterials. One member of the quinolone class, moxifloxacin, has just advanced into Phase III clinical trials for TB.

Quinolones work against *M.tb* by inhibiting DNA gyrase, a key target for potential breakthrough drugs for TB. But the quinolones have never been optimized for a TB indication, until now.

Quinolones possess many desirable attributes for a first-line therapeutic agent against TB. These include potent bactericidal activity against both replicating and non-replicating *M.tb*, potential to treat patients co-infected with TB and HIV, no cross-resistance with current first-line drugs, favorable long-term safety indicators, oral bioavailability, and an ability to penetrate the human cells where *M.tb* can hide.

With the scientific guidance and financial support of the TB Alliance, researchers at the Korean Research Institute of Chemical Technology (KRICT) and Yonsei University in South Korea have synthesized over 600 quinolones and narrowed them down to just four compounds for preclinical evaluation. These compounds have very potent *in vitro* activity against *M.tb*, and initial efficacy tests in mice are extremely promising.

If results continue to be positive, the one or two best compounds will continue through Investigational New Drug (IND)–enabling studies to prepare for clinical development.

InhA Inhibitors

Partnership with GlaxoSmithKline

Isoniazid is a first-line TB drug that hits *M.tb* quickly, rapidly killing off the majority of the faster-growing bacteria. It is thought to do so by blocking an enzyme called InhA. Unfortunately, resistance to isoniazid is widespread.

The InhA project with GlaxoSmithKline (GSK) seeks to hit the same ultimate target as isoniazid, but in a way that gets around isoniazid resistance.

Most isoniazid resistance arises because KatG, an enzyme needed to activate isoniazid, is mutated to become nonfunctional. The new inhibitors are designed so they do not need to be activated by KatG. They should therefore work against the majority of isoniazid-resistant strains.

An initial screen for InhA inhibitors produced leads that inhibited the isolated InhA enzyme but were less effective in killing whole *M.tb* bacteria and in treating a mouse model of TB. More recently, a second screen of 600,000 compounds has yielded a number of promising compounds that have potent activity against isolated InhA and whole *M.tb* bacteria. Refinement of analogs of these compounds is continuing.

GSK–TB ALLIANCE PARTNERSHIP

The TB Alliance and GlaxoSmithKline (GSK) have a unique partnership designed to yield new compounds that attack different targets of *M.tb* with novel mechanisms of action.

GSK maintains a research and development site in Tres Cantos, Spain, concentrated on diseases of the developing world (including TB and malaria). The Tres Cantos group is fully integrated with and benefits from the expertise of the rest of GSK's scientific infrastructure. GSK and the TB Alliance have dedicated significant resources to this effort, and strategic decisions are made by a joint steering committee that brings together senior management and technical expertise from both organizations.

Mycobacterial Gyrase Inhibitors

Partnership with GlaxoSmithKline

DNA gyrase is essential for *M.tb* survival. GSK and the TB Alliance are developing novel inhibitors of DNA gyrase. This builds on the potential of fluoroquinolones such as moxifloxacin, which is in Phase III clinical trials sponsored by the TB Alliance and Bayer, and which also targets DNA gyrase. The new compounds in the GSK project, however, may be active against fluoroquinolone-resistant *M.tb* (and thus against XDR-TB) because they bind to a different site on DNA gyrase.

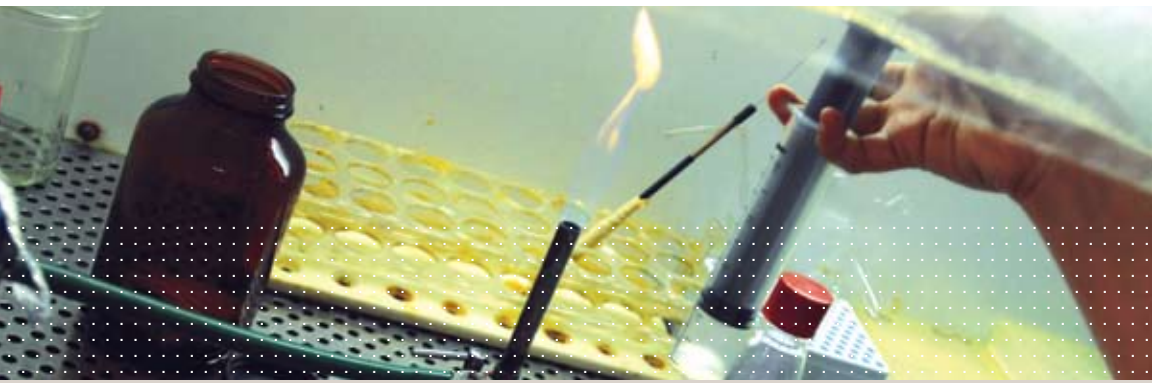
Under the GSK partnership, over one thousand compounds that inhibit DNA gyrase have been tested against *M.tb*. Several of the most promising candidates have shown *in vivo* efficacy in mice. Studies on chemical variants and their pharmacokinetic properties are continuing.

Pleuromutilins

Partnership with GlaxoSmithKline

Oral pleuromutilins are a new class of antibiotics being studied at GSK for its potential to treat human disease. Pleuromutilins interest scientists because of their ability to selectively inhibit multiple steps in bacterial protein synthesis. GSK is currently exploring this class for treatment of respiratory tract infections. Pleuromutilins bind at a unique site on the bacterial ribosome, making cross-resistance with other ribosome-directed drugs unlikely.

GSK's detailed knowledge about this drug class is contributing to the collaboration with the TB Alliance. More than one thousand pleuromutilin derivatives in the GSK collection have been screened against *M.tb*, and representatives of one lead series are being tested for *in vivo* efficacy in mice.



Malate Synthase Inhibitors

Partnership with GlaxoSmithKline

TB treatments take a long time to complete because it is difficult to target the slow-growing *M.tb* organisms. Although not yet experimentally validated as a drug target, malate synthase may be a key enzyme that *M.tb* uses to switch its food source to suit its slow-growing, persistent state. Inhibiting malate synthase should starve the persisters and shorten the time needed for treatment.

The TB Alliance is working with GSK and Texas A&M University to synthesize and test novel compounds to inhibit malate synthase. Researchers at Texas A&M are leading the biochemistry and structural biology effort. High throughput screening with more than one million compounds has been conducted at GSK's Tres Cantos site, and inhibitors have been identified for further optimization.

Focused Screening

Partnership with GlaxoSmithKline

GSK's extensive antimicrobial library is being used to screen for novel compounds with the ability to kill *M.tb*. This project ensures that that the full potential of GSK's libraries is explored, and it acts as a source for new projects in the GSK mini-portfolio.

For example, one current project is targeted at electron transport, which is essential for maintaining the bacterium's energy status and is needed even in dormant bacteria.

Dear Friends, Donors and Stakeholders:

This year, TB has been in the global spotlight, as lethal and increasingly untreatable strains that know no borders have captured headlines and interest around the world.

Drug-resistant TB — a man-made threat caused by inadequate or inappropriate treatment — is a wake-up call for all of us. Without novel, faster and easier-to-use treatments, TB's global threat will intensify, driven by its deadly synergy with HIV/AIDS, complicated by drug-resistant strains, and amplified by the consequences of poverty. But there is good reason for hope.

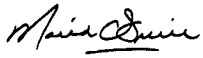
After years of scientific neglect, TB drug development is in high gear. We are very pleased that the TB Alliance is leading this resurgence with the largest, most diverse pipeline of potential new life-saving drugs to date. By adopting a bold roadmap for TB drug development, the TB Alliance is blazing a trail in TB drug discovery, preclinical and clinical testing, and is helping to ensure that new regimens are available to patients.

The TB Alliance is accelerating TB drug development by strengthening the pipeline, starting in the laboratory, with an innovative method of identifying promising drug combinations. Our new preclinical combination program will test groups of compounds quickly and efficiently to potentially identify the most clinically relevant drug combinations.

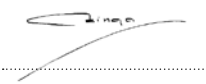
Concurrently, we are developing new ways to shorten the time it takes to clinically test drug candidates. We are working closely with global regulatory agencies to explore new clinical strategies, using new drug combinations that have the potential to treat sensitive and resistant TB. We are helping to reinvigorate TB clinical trial site capacity by identifying and assessing potential sites worldwide and strategically investing in clinical programs. We are working to map and understand the pathway to patients, learning where the challenges may lie in getting new regimens adopted and widely available to all who need them.

The TB Alliance reaffirms its unwavering commitment to affordable new TB drugs and regimens that shorten treatment, are effective against susceptible and resistant strains, will be compatible with antiretroviral therapies for those HIV-TB patients currently on such therapies, and can be made available and be adopted in the field.

Shorter TB regimens will save lives, reduce the risk of creating drug-resistant strains, and lighten the enormous burden that TB places on patients and overstretched health systems. By combining the best science, focused strategy and dedication, we envision a better way to fight TB in partnership with our collaborators, donors, and stakeholders.



Dr. Maria C. Freire
Chief Executive Officer and President



Dr. Gijs Elzinga
Chairman of the Board

Dr. Gijs Elzinga
Chairman of the Board

Dr. Maria C. Freire
CEO and President

MESSAGE FROM MARIA FREIRE

Dear Friends,

I have had the privilege of leading the TB Alliance for six extraordinary years. During this time, the Alliance has grown from a nascent organization to one that now has the largest pipeline of potential new TB drugs in history, a diverse team of top professionals, and funding of over US$200 million from foundations and governments around the world. These achievements make me confident that the TB Alliance will succeed in delivering a new, effective and faster cure for TB.

With this conviction, a great sense of accomplishment, and having achieved what I set out to do, I prepare to hand over the leadership of this strong organization to a new executive who will be fortunate to work with all of you in the fight against TB.

Today, as ever, I recognize the importance of this cause and I continue to be inspired by the indefatigable efforts of those who will not accept the current condition. I have benefited from your generous, supportive guidance and your friendship. I trust that both will endure.

With deep appreciation,

Maria C. Freire, Ph.D.

Financials and Acknowledgements

Independent Auditor's Report

Board of Directors of The Global Alliance for TB Drug Development, Inc.

We have audited the accompanying statement of financial position of The Global Alliance for TB Drug Development, Inc. ("TB Alliance") as of December 31, 2006, and the related statements of activities, functional expenses and cash flows for the year then ended. These financial statements are the responsibility of TB Alliance's management. Our responsibility is to express an opinion on these financial statements based on our audit.

We conducted our audit in accordance with auditing standards generally accepted in the United States of America. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. An audit includes consideration of internal control over financial reporting as a basis for designing audit procedures that are appropriate in the circumstances, but not for the purpose of expressing an opinion on the effectiveness of TB Alliance's internal control over financial reporting. Accordingly, we express no such opinion. An audit also includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements, assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation. We believe that our audit provides a reasonable basis for our opinion.

In our opinion, the financial statements referred to above present fairly, in all material respects, the financial position of The Global Alliance for TB Drug Development, Inc. as of December 31, 2006, and the changes in its net assets and its cash flows for the year then ended, in conformity with accounting principles generally accepted in the United States of America.

Information for the year ended December 31, 2005 is presented for comparative purposes only and was extracted from the financial statements of The Global Alliance for TB Drug Development, Inc. for that year, on which we expressed an unqualified opinion, dated April 25, 2006.

BDO Seidman, LLP

June 5, 2007

Statement of Financial Position

(with comparative totals for 2005)

YEAR ENDED DECEMBER 31,	**2006**	2005
ASSETS		
Cash and cash equivalents (Notes 2 and 3)	**$ 22,547,261**	$ 15,227,673
Cash – restricted (Notes 2 and 5)	**–**	142,150
Investments at fair value (Note 3)	**14,271,671**	6,775,000
Accounts receivable	**867,145**	704,968
Other assets	**215,512**	197,181
Property and equipment, net (Notes 2 and 5)	**228,310**	262,245
	$ 38,129,899	$ 23,309,217
LIABILITIES AND NET ASSETS		
Liabilities:		
Accounts payable and other liabilities	**$ 1,962,768**	$ 1,028,194
Accrued payroll and payroll related liabilities	**141,354**	126,345
Capital lease obligation	**–**	12,130
Deferred revenue (Note 6)	**11,059,140**	2,278,165
Deferred rent	**163,513**	152,634
Total liabilities	**13,326,775**	3,597,468
Commitments (Note 7)		
Net assets:		
Unrestricted net assets (Note 2)	**24,803,124**	19,711,749
	$ 38,129,899	$ 23,309,217

See accompanying Notes to Financial Statements.

Statement of Activities

(with comparative totals for 2005)

YEAR ENDED DECEMBER 31,	**2006**	2005
PUBLIC SUPPORT AND OTHER REVENUE:		(Unrestricted)
Contributions	**$ 18,519,930**	$ 9,095,672
Grants	**5,230,535**	3,354,555
Contributed services (Note 4)	**25,088**	441,688
Interest and dividend income	**983,865**	501,527
Net realized and unrealized gains or investments	**222,092**	–
Miscellaneous income	**5,209**	12,903
Total public support and other revenue	**24,986,719**	13,406,345
EXPENSES:		
Program services:		
Research and development	**14,808,362**	7,874,983
Business development	**322,652**	224,656
Public affairs and policy	**2,858,293**	1,195,266
Total program services	**17,989,307**	9,294,905
Supporting services:		
Management and general	**1,872,104**	1,188,344
Fundraising	**227,572**	287,936
Total supporting services	**2,099,676**	1,476,280
Total expenses	**20,088,983**	10,771,185
Change in net assets before foreign translation gain (loss)	**4,897,736**	2,635,160
Foreign translation gain (loss) (Note 2)	**193,639**	(275,554)
Change in net assets	**5,091,375**	2,359,606
Net assets, beginning of year	**19,711,749**	17,352,143
Net assets, end of year	**$ 24,803,124**	$ 19,711,749

See accompanying Notes to Financial Statements.

Statement of Cash Flows

(with comparative totals for 2005)

YEAR ENDED DECEMBER 31,	2006	2005
CASH FLOWS FROM OPERATING ACTIVITIES:		
Change in net assets	**$ 5,091,375**	$ 2,359,606
Adjustments to reconcile change in net assets to net cash provided by operating activities:		
Depreciation and amortization	**101,838**	104,711
Realized gain on sales of investments at fair value, net	**(50,478)**	–
Unrealized gains on investments at fair value	**(171,614)**	–
(Increase) decrease in assets:		
Restricted cash	**142,150**	(5,925)
Accounts receivable	**(162,177)**	(635,227)
Other assets	**(18,331)**	(20,953)
Increase (decrease) in liabilities:		
Accounts payable and other liabilities	**934,574**	545,664
Accrued payroll and related liabilities	**15,009**	31,369
Deferred revenue	**8,780,975**	(212,467)
Deferred rent	**10,879**	43,478
Net cash provided by (used in) operating activities	**14,674,200**	2,210,256
CASH FLOWS FROM INVESTING ACTIVITIES:		
Purchase of investments	**(10,449,579)**	–
Proceeds from sale of investments	**3,175,000**	1,000,000
Additions to property and equipment	**(67,903)**	(46,422)
Net cash provided by (used in) investing activities	**(7,342,482)**	953,578
CASH FLOWS FROM FINANCING ACTIVITIES:		
Repayments of capital lease obligation	**(12,130)**	(27,529)
Net increase in cash and cash equivalents	**7,319,588**	3,136,305
Cash and cash equivalents, beginning of year	**15,227,673**	12,091,368
Cash and cash equivalents, end of year	**$ 22,547,261**	$ 15,227,673
SUPPLEMENTAL DISCLOSURE OF CASH FLOW INFORMATION:		
Cash paid for interest	**$ 242**	$ 2,166

See accompanying Notes to Financial Statements.

Notes to Financial Statements

1. ORGANIZATION

The Global Alliance for TB Drug Development, Inc. ("TB Alliance") is a non-profit organization incorporated on July 24, 2000 under the General Corporation Law of Delaware and authorized to conduct business in New York under the Not-for-Profit Corporation Law of New York. It operates as a not-for-profit, with offices in Brussels, Belgium; Pretoria, South Africa; and New York, New York.

The TB Alliance was formed to accelerate the development of effective new medicines to treat tuberculosis and ensure their affordability and availability in high-endemic countries.

Advocating for a worldwide mobilization against the TB epidemic through innovative research into new therapeutics, the TB Alliance develops innovative partnerships and involves scientists and researchers globally. It builds a portfolio of promising drug candidates and outsources research and development projects to public and private laboratories to develop affordable new drugs that will shorten the treatment of tuberculosis, be effective against multi-drug resistant strains and improve treatment of latent infection.

2. SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES

(a) Basis of Presentation

The financial statements have been prepared on the accrual basis and the presentation follows the requirements of the Financial Accounting Standards Board in its Statements of Financial Accounting Standards ("SFAS") No. 117, "Financial Statements of Not-for-Profit Organizations". Under SFAS No. 117, the TB Alliance is required to report information regarding its financial position and activities according to three classes of net assets: unrestricted net assets, temporarily restricted net assets and permanently restricted net assets.

(b) Financial Statement Presentation

The classification of a not-for-profit organization's net assets and its support, revenue and expenses is based on the existence or absence of donor-imposed restrictions. It requires that the amounts for each of three classes of net assets, permanently restricted, temporarily restricted, and unrestricted, be displayed in a Statement of Financial Position and that the amounts of change in each of those classes of net assets be displayed in a Statement of Activities.

Income from investment gains and losses, including unrealized gains and losses, dividends, interest and other investments should be reported as increases (or decreases) in unrestricted net assets unless the use of the income received is limited by donor-imposed restrictions.

These classes are defined as follows:

(i) Permanently Restricted — Net assets resulting from contributions and other inflows of assets whose use by the TB Alliance is limited by donor-imposed stipulations that neither expire by passage of time nor can be fulfilled or otherwise removed by actions of the TB Alliance.

(ii) Temporarily Restricted — Net assets resulting from contributions and other inflows of assets whose use by the TB Alliance is limited by donor-imposed stipulations that either expire by passage of time or can be fulfilled and removed by actions of the TB Alliance pursuant to those stipulations. When such stipulations end or are fulfilled, such temporarily restricted net assets are reclassified to unrestricted net assets and reported in the Statement of Activities.

(iii) Unrestricted — The part of net assets that is neither permanently nor temporarily restricted by donor-imposed stipulations.

(c) Cash and Cash Equivalents
The TB Alliance considers short-term investments with original maturities of three months or less to be cash equivalents.

(d) Restricted Cash
Restricted cash consists of cash held by banks providing collateral for the TB Alliance's leased equipment.

(e) Investments
Investments are valued at fair value in the statement of financial position. Unrealized gains and losses are included in the Statement of Activities.

(f) Depreciation and Amortization
The cost of property and equipment is depreciated over the estimated useful lives of the assets using the straight-line method. Leasehold improvements are amortized over the lesser of the life of the lease or asset. The estimated useful lives of the assets are as follows:

Computer equipment	3–5 years
Furniture and equipment	3–5 years
Leasehold improvements	5–10 years

(g) Income Taxes
TB Alliance is exempt from Federal and state income taxes under Section 501(c)(3) of the Internal Revenue Code (the "Code") and therefore has made no provision for income taxes in the accompanying financial statements. In addition, the TB Alliance has been determined by the Internal Revenue Service not to be a "private foundation" within the meaning of Section 509(a) of the Code. There was no unrelated business income for 2006.

(h) Contributions and Grants
Contributions received are recorded as unrestricted, temporarily restricted or permanently restricted support, depending on the existence and/or nature of any donor restrictions. Contributions with purpose or time restrictions (defined by management as unrestricted amounts due in more than one year) are reported as increases in temporarily restricted net assets and reported in the Statement of Activities in the unrestricted class of net assets. When a donor restriction expires, that is, when a time restriction ends or purpose restriction is fulfilled, temporarily restricted net assets are reclassified to unrestricted net assets and reported in the Statement of Activities as net assets released from restrictions. Restricted gifts and grants, received and utilized in the current year, are reflected in the Statement of Activities in the unrestricted class of net assets.

Public grants from the government agencies are recorded based on the terms of the grantor allotment, which generally provides that revenue is earned when the allowable costs of specific grant provisions have been incurred or provided.

(i) Promises to give
Unconditional promises to give are recognized as contribution revenue in the period received and as assets, decreases of liabilities, or expenses depending on the form of the benefits received, and are classified as either unrestricted, temporarily restricted, or permanently restricted support. Promises to give are recorded at net realizable value if expected to be collected within one year. Unconditional promises to give that are expected to be collected in the future years are recorded at the present value of these estimated future cash flows.

Conditional promises to give are not recognized until they become unconditional, that is, when the conditions on which they depend are substantially met. Contributions of assets other than cash are recorded at the estimated fair value.

(j) Contributed Goods and Services
Contributed goods and services are recognized as revenue and expenses if such goods and services meet the criteria for recognition as stated in Statement of Financial Accounting Standards ("SFAS") No. 116, "Accounting for Contributions Received or Contributions Made."

(k) Program Services
(i) Research and Development — the TB Alliance creates and manages a portfolio of new anti-TB drug candidates by identifying, evaluating and acquiring promising molecules from scientific laboratories worldwide and outsourcing their development to appropriate public and private partners. Further, the TB Alliance invests in infrastructure research projects that accelerate anti-TB drug development and analyzes existing scientific gaps to address these as part of the overall development strategy.

(ii) Business Development —the TB Alliance negotiates, implements and manages agreements with public and private organizations worldwide and does so by adhering to sound business practices while ensuring the public good. Specifically, the TB Alliance negotiates terms that support the development and access of new affordable anti-TB drugs equitably to those areas most in need, while encouraging the private sector to help develop new medicines for TB indications.

(iii) Public Affairs and Policy — the TB Alliance manages critical alliances with public and private organizations to raise awareness about TB and advocate for public and private involvement in research for new anti-TB medicines. It develops landmark studies to support policy developments seeking to accelerate anti-TB drug research and mobilizes networks of researchers and investigators worldwide to focus on the development of these medicines.

(l) Use of Estimates
In preparing financial statements in conformity with generally accepted accounting principles, management is required to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosures of contingent assets and liabilities at the date of the financial statements and revenues and expenses during the reported period. Actual results could differ from those estimates.

(m) Concentration of Credit Risk Financial instruments which potentially subject the TB Alliance to concentration of credit risk consist primarily of temporary cash investments. At various times during the year, the TB Alliance had cash deposits at financial institutions which exceeded the FDIC insurance limit.

(n) Comparative Financial Information
The financial statements include certain prior-year-summarized-comparative information. Accordingly, such information should be read in conjunction with the prior year financial statements from which the summarized information was derived. With respect to the statement of functional expenses, the prior year expenses are presented by expense classification in total rather than by functional category. Such information does not include sufficient detail to constitute a presentation in conformity with accounting principles generally accepted in the United States of America.

(o) Reclassifications
Certain prior-year-balances have been reclassified to be consistent with the current year financial statement presentation. The reclassifications had no impact on changes in net assets.

(p) Foreign Currency Translation
All elements of the financial statements reflecting the TB Alliance's operations in Brussels are translated into U.S. dollars using applicable exchange rates. For assets and liabilities, this is the rate in effect at the statement of financial position date, with the exception of property and equipment which is measured at the historical rate. For revenue and expense items, translation is performed monthly using the average rate for the month. The exchange rate as of December 31, 2006 was 1.32030 EUR/USD.

Foreign currency is translated in accordance with the provisions of SFAS No. 52, "Foreign Currency Translation". Under the provisions of SFAS No. 52, the local currency used in the TB Alliance's foreign operations is considered to be the functional currency of these operations. Translation of the financial statements of these operations resulted in a translation gain as follows:

DECEMBER 31, 2006	
Cumulative translation gain adjustment, beginning of year	$188,317
Translation adjustment	193,639
Cumulative translation gain adjustment, end of year	$381,956

The cumulative translation gain is included in unrestricted net assets.

3. INVESTMENTS AT FAIR VALUE

The TB Alliance's cost and fair value of investments are summarized as follows:

DECEMBER 31, 2006	FAIR VALUE	COST
Marketable debt securities	$14,271,671	$14,100,057

In addition to the above investments, the portfolio included $12,759 of accrued and unpaid interest and $4,494,263 of cash and cash equivalents at December 31, 2006.

4. CONTRIBUTED SERVICES

Included in the TB Alliance's statement of activities is approximately $25,088 and $441,688 for the years ended December 31, 2006 and 2005, respectively, of in-kind contributions which were related to project management costs.

5. PROPERTY AND EQUIPMENT, NET

Property and equipment, net, stated at cost, consists of the following:

DECEMBER 31, 2006	
Computer equipment	$295,147
Furniture and equipment	212,464
Leasehold improvements	133,450
Total property and equipment	641,061
Less: Accumulated depreciation and amortization	(412,751)
Property and equipment, net	$228,310

6. DEFERRED REVENUE

In November of 2006, the Department of Development of the Netherlands Ministry of Foreign Affairs ("DDC") approved an 8,000,00 EUR three-year grant for the period from 2006 to 2009 for research and development of medicines, vaccines and diagnostic aides in the domain of AIDS, tuberculosis and malaria.

The contract stipulates that any unused funds be returned to the DDC at the expiration of the grant term. As of December 31, 2006, the TB Alliance received $3,689,000 related to this grant. The remaining unspent funds of $3,397,963 are recorded as deferred revenue as of December 31, 2006.

In May 2006, the TB Alliance received a conditional promise to give award from the Bill & Melinda Gates Foundation in the amount of $104,403,823 for the period of May 1, 2006 to May 1, 2011. To date, the TB Alliance has received $15,072,558 of the award. As of December 31, 2006, TB Alliance recognized $7,411,381 income on the grant for project milestones achieved and has included $7,661,177 in deferred revenue. The remaining amount of $96,992,442 has not been recognized in the financial statements.

7. COMMITMENTS

The TB Alliance has operating lease agreements for office space in New York, New York; Brussels, Belgium and Pretoria, South Africa. The TB Alliance New York office lease expires in July 2014, the Brussels lease agreement expires in November 2009 and the Pretoria lease expires in October 2009.

The following is a schedule of future minimum rental payments under the Brussels, Pretoria and New York operating leases as of December 31, 2006:

YEAR ENDED DECEMBER 31,	
2007	$ 246,818
2008	243,160
2009	258,292
2010	254,413
2011	259,501
Thereafter	740,875
	2,003,059

The TB Alliance has research and development agreements with several research institutions to fund various research and development contracts useful for treatment of TB. The agreements' expiration dates are undeterminable as of December 31, 2006.

The following is a schedule of future minimum research and development payments under the above agreements as of December 31, 2006:

YEAR ENDING DECEMBER 31,	
2007	$5,396,693
2008	1,436,529
2009	500,000
2010	500,000
2011	500,000
Thereafter (per year)	500,000

8. PENSION PLAN

The TB Alliance has a 401(k) plan that covers all employees who are age 21 and older. Employees may contribute up to 15% of their pay each pay period. Catchup deferral of up to $5,000 in 2006 is available for eligible employees 50 years old or older during the plan year. The TB Alliance matches 50% of the first 3% of the pay contributed through the employee's salary deferral. Discretionary contributions are also made to the plan. Pension expense was $128,946 for the year ended December 31, 2006. In January 2006, the TB Alliance converted into a 401(k) Safe Harbor Plan.

Stakeholders

The following institutions formally pledged to accelerate the development of TB drugs. They advise, guide and support the efforts of the TB Alliance:

American Lung Association

American Thoracic Society

Association of the British Pharmaceutical Industry

Bangladesh Rural Advancement Committee

Bill & Melinda Gates Foundation

European Commission

Global Business Coalition on HIV/AIDS

Global Forum for Health Research

Global Fund to Fight AIDS, TB and Malaria

International Union Against Tuberculosis and Lung Disease

JATA Research Institute of Tuberculosis, Japan Anti-Tuberculosis Association

KNCV Tuberculosis Foundation

Lupin Laboratories

Médecins Sans Frontières-Doctors Without Borders

Medical Research Council of South Africa

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

National Institute of Pharmaceutical Education and Research, India

New Jersey Medical School Global Tuberculosis Institute

Novartis India, Ltd.

Partners in Health

Philippines Coalition Against Tuberculosis

RTI International

RESULTS

Rockefeller Foundation

Sequella, Inc.

Stop TB Partnership

TB Alert

Treatment Action Group

Tropical Disease Foundation

U.K. Department for International Development

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

U.S. Agency for International Development

U.S. Centers for Disease Control and Prevention

Wellcome Trust

World Bank

World Health Organization

Recognition of Support

The TB Alliance gratefully acknowledges the generosity of the following institutions that provide key funding or in-kind support and expertise:

Bill & Melinda Gates Foundation

Bayer HealthCare AG

Irish Aid

GlaxoSmithKline

The Netherlands Ministry of Foreign Affairs

RTI International

Rockefeller Foundation

Stop TB Partnership

United Kingdom Department for International Development

United States Centers for Disease Control and Prevention

United States Agency for International Development

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

Scientific Advisory Committee

Members of the Scientific Advisory Committee provide the TB Alliance with invaluable scientific expertise.

Board of Directors

Dr. Gijs Elzinga
Chairman of the Board
Deputy Director-General,
Netherlands' National
Institute of Public Health
and the Environment

Dr. Olusoji Adeyi
Coordinator, Global Partnerships
of Communicable Diseases,
Human Development Network
The World Bank

Dr. Bruce Carter
President and Chief Executive Officer,
ZymoGenetics

Dr. Maria C. Freire
Chief Executive Officer and President,
Global Alliance for TB Drug
Development

Mr. Mark Kessel
Managing Director,
Symphony Capital LLC

Dr. Anthony MBewu
President,
Medical Research
Council of South Africa

Dr. Carlos Morel
Scientific Coordinator,
Oswaldo Cruz Foundation

Dr. Lee Reichman
Executive Director,
New Jersey Medical School
Global Tuberculosis Institute

Mr. Parag Saxena
Chief Executive Officer
and Managing Member,
Vedanta Capital

Dr. George A. Scangos
President and Chief Executive Officer,
Exelixis, Inc.

Dr. Peter Small
Senior Program Officer, HIV, TB &
Reproductive Health, Global Health Program,
Bill & Melinda Gates Foundation

Prof. Petro Terblanche
President,
TB Alliance Stakeholders Association
Executive Director, Technology & Innovation,
Medical Research Council of South Africa

Dr. Thelma Tupasi-Ramos
President,
Tropical Disease Foundation

Staff and Consultants

Maria C. Freire, Ph.D.
Chief Executive Officer and President

Mel Spigelman, M.D.
Director, Research and Development

Bradley Jensen
Director, Finance and Administration

Nina Schwalbe, M.P.H.
Director, Policy

Al Hinman
Director, Communications

Karen Ackermann
Assistant, Research and Development

Derek Ambrosino
Assistant, Communications

Asmita Barve, M.A., M.B.A.
Grants Analyst

Ketty Belizaire
Clinical Operations Manager

Cynthia Brewster
Assistant Controller

E. Priya Eddy, Ph.D.
Project Leader, Research

Serdar Elmali
Information Technology and Networking

Permi Gill, M.F.A.
Executive Assistant to the CEO and President

Ann Ginsberg, M.D., Ph.D.
Head of Clinical Development

Ciara Goldstein, M.A.
Policy Associate

Heather Ignatius, M.A.
Policy Officer

Yvette Jones
Assistant, Research and Development

Lon Kaiser
Information Technology, Help Desk

Martino Laurenzi, M.D., Ph.D.
Clinical Research Scientist

Zhenkun Ma, Ph.D.
Head of Research

Cuyler Mayer
Communications Officer

Khisimuzi Mdluli, Ph.D.
Project Leader, Research

Raisa Y. Medina
Junior Accountant

Marie Messina
Assistant, Research and Development

Ingrid Payne
Finance and Administration Specialist

Doris Rouse, Ph.D.
Portfolio Project Manager

Stephanie S. Seidel
Assistant, Policy

Gerald J. Siuta, Ph.D.
Consultant, Business Development

Almarie Uys, Ph.D.
Senior Clinical Research Associate

Christo van Niekerk, M.D.
Clinical Research Scientist

William Wells, M.I.A., Ph.D.
Senior Communications Officer

Karen M. Wright
Senior Advisor

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 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
Global Alliance for TB Drug Development, 80 Broad Street, 31st Floor, New York, NY 10004

Concept and Design: Ideas On Purpose, New York, NY
www.ideasonpurpose.com

Photography: Cover, **Per-Anders Pettersson**; inside front cover, pages 1, 4, 8, 9 (top left), 12, 14, 15, 18, 19, 20 (middle), 21, 22 (top left, bottom), 29, 30, **Eric Miller**; pages 2, 3, **Al Hinman**; pages 6, 7, 20 (top left), 27 (bottom), 35, **Seokyong Lee**; pages 9 (top right), 24, 25, 26, 27 (top), 36 (bottom), 39 (bottom), **Atul Loke**; pages 16, 17, **Alpesh Patel**; page 20 (top right), **Douglas Engle**; pages 22 (top right), 37, 38 (bottom), back cover, **John-Michael Maas**; pages 23 (top left), 41 (top left), **Daniel Besson**; page 23 (top right), inside back cover, **Vera Lentz/Black Star**; page 41 (top center, right), **Martin Santander**; page 41 (middle right), **David Berkwitz**; page 32, **Qiyong Lou**; page 33, **Juliana Thomas**

The TB Alliance accelerates the discovery and development of faster-acting, affordable drugs to fight tuberculosis. Through innovative science and with partners around the globe, we aim to ensure the widespread availability of a faster, better cure for tuberculosis that will advance global health and prosperity.

www.tballiance.org

TB ALLIANCE

GLOBAL ALLIANCE FOR TB DRUG DEVELOPMENT