



Taking a STAND Against TB

PaMZ Aims to Revolutionize TB Treatment

The advancement of PaMZ through clinical testing is a major step in the development of highly impactful novel TB treatments.

PaMZ is the first drug regimen designed to treat both drug-sensitive (DS-TB) and some forms of multidrug-resistant TB (MDR-TB) and be compatible with anti-retroviral treatments. Developed by the TB Alliance with partners from around the world, PaMZ is one of the most significant potential innovations in the fight against TB/HIV in decades.

About NC-002 (Phase 2b)

The PaMZ regimen has successfully completed an eight-week Phase 2b study in which it was compared to the standard treatment regimen. The results show PaMZ killed more TB bacteria in patients than standard therapy* and did so at a faster rate, indicating its potential to shorten therapy to four months for drug-sensitive and some forms of MDR-TB.

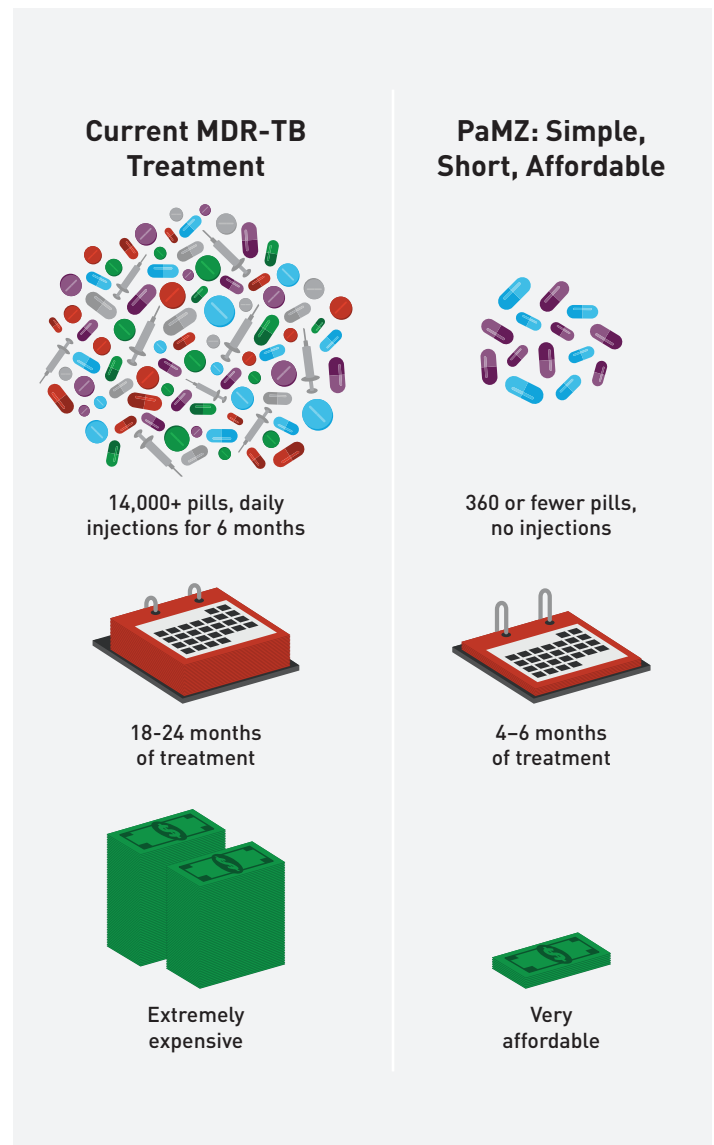
The NC-002 trial was the first to test the same drug regimen for treating both DS and DR-TB. It enrolled more than 200 patients in seven sites across South Africa and Tanzania. Twenty percent were co-infected with HIV. The previous NC-001 trial had been the first to test novel TB drugs in combination.

The study data for PaMZ suggest bactericidal activity that outstrips the activity of standard TB therapy and predicts dramatic shortening of MDR-TB treatment. This provides sufficient evidence to advance PaMZ to a Phase 3 trial.

**The standard therapy in NC-002 consisted of a regimen of isoniazid, rifampicin, and ethambutol.*

About STAND (Phase 3)

The STAND (Shortening Treatments by Advancing Novel Drugs) trial is the first Phase 3 registration trial testing a drug regimen for use against both TB and MDR-TB. STAND will be a global endeavor, slated to enroll more than 1500 patients in more than



50 sites in 10 countries. If PaMZ performs successfully in the STAND trial, it will proceed to global registration and made available to the people who need it.

About PaMZ

The PaMZ regimen consists of two new drug candidates, PA-824 and moxifloxacin, and pyrazinamide, which is part of the current first-line treatment.

The PaMZ regimen shows promise to:

- Treat both TB and some forms of MDR-TB, enabling scale-up of treatment
- Shorten the treatment time of both TB and especially MDR-TB
- Simplify treatment, eliminating 97% of the pills and all injections needed to complete MDR-TB therapy
- Avoid interactions with antiretroviral drugs, improving treatment for the millions of HIV-TB co-infected patients
- Reduce the cost of MDR-TB treatment by 90% or more in most regions.

New TB Treatments Are Needed

Tuberculosis is a global pandemic, killing 1.4 million each year. It is second only to HIV as the leading infectious killer of adults worldwide, a leading killer of women and children, and the leading infectious cause of death among people with HIV/AIDS. The World Health Organization (WHO) estimates that two billion people are infected with the bacillus that causes the disease.

Today's TB drug regimen takes too long to cure, is too complicated to administer, and can be toxic. As a result, many patients do not or cannot complete their treatment, which leads to the development of deadlier drug-resistant strains, which can then be spread

directly. Despite the flaws with and growing resistance to current TB treatments, no new TB drugs have been developed in nearly 50 years, and despite some recent advances in MDR-TB therapy, its treatment remains complex, lengthy and prohibitively expensive for most patients and high-burden countries. Even when treated along WHO guidelines, more than one in three MDR-TB patients don't achieve cure.

Shorter, simpler and novel TB treatments are needed to successfully combat both TB and MDR-TB.

Speeding the Pace of Innovation

STAND doesn't only represent the hope of new TB cures, but also the promise of an innovative scientific approach to developing new products. Since the 1950s, researchers have known that TB must be treated with a combination of multiple drugs to prevent the development of drug resistance. Traditionally, when developing a new drug, researchers would just add on or replace a single drug within the existing standard treatment. Each of these trials could last six years or longer, which means that a novel TB regimen could take decades to develop using this model.

In 2010, TB Alliance began developing PaMZ using a new model that would allow multiple new drugs to be developed at once – making a combination of drugs, and not a single drug, the basis for innovation. This pathway could reduce the time needed to develop a completely novel TB treatment regimen by as much as 75 percent. If the STAND trial is successful, it will mark the first time a new TB drug regimen is developed and registered using this innovative design.

