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TB Alliance Launches Five-Country Phase 2 Clinical Trial Evaluating Next-Generation TB Drug

Early results presented at the Union World Conference on Lung Health suggest promise of new compound to fight tuberculosis that will be tested as part of Phase 2 trial

The first participant has been dosed in this partially double-blind study to evaluate the safety and efficacy of what has the potential to be a "universal regimen" to treat TB

PARIS (16 November 2023)—TB Alliance launched a new Pan-Phase 2 clinical trial incorporating elements of Phase 2a, b and c, identified as NC-009, to evaluate the safety and efficacy of a combination of a new experimental compound, TBAJ-876, with pretomanid and linezolid, components of TB Alliance's BPaL regimen. This regimen has the potential to shorten and improve treatment for both drug-sensitive and drug-resistant tuberculosis (TB)—one of the world's deadliest infectious diseases. Results from preclinical and Phase 1 studies presented at the Union Conference showed that the new compound, when compared with bedaquiline (a TB medicine in the same drug class), eliminated TB bacteria faster and had a potentially safer profile.

"A 'universal' TB medicine needs to be highly effective while causing very few adverse effects; initial Phase 1 trial results show that TBAJ-876 could possibly move the needle in this direction," said Dr. Mel Spigelman, President and CEO of TB Alliance. "If we can develop a regimen that is composed of novel compounds with minimal pre-existing resistance that is both highly potent and safe, it could blur the distinction between drug-sensitive and drug-resistant TB allowing for treatment of virtually all patients with active TB with the same regimen."

The new trial, NC-009, will test different doses of TBAJ-876 in combination with pretomanid and linezolid against the current standard of care for drug-sensitive TB—isoniazid, rifampicin, pyrazinamide, and ethambutol (HRZE). Another arm of the trial will also test pretomanid and linezolid in combination with bedaquiline (BPaL), a regimen recommended by the World Health Organization to treat some forms of drug-resistant TB, against drug-sensitive TB. The study aims to enroll 300 participants with drug-sensitive TB at 21 clinical trial sites in five countries: Georgia, Philippines, South Africa, Tanzania, and Uganda.

"To truly get ahead of the tuberculosis pandemic in all of its forms, we need to continually innovate," said Dr. Francesca Conradie, Principal Investigator for the NC-009 clinical trial in South Africa. "Recent innovations in drug-resistant TB therapy have been enormously important, but we need to continue to develop shorter, simpler, and more people-friendly cures, including in drug-sensitive TB where there hasn't been a new drug approved in more than 50 years."

New Experimental Compound

TBAJ-876 is a diarylquinoline, a category of antibiotic that targets a key enzyme of the tuberculosis bacteria involved in energy production. Bedaquiline, a TB drug approved for the treatment of drug-resistant TB by the US FDA in 2012, is in the same diarylquinoline drug class. At the Union Conference in Paris, data were presented—showing that the new experimental compound has the potential to become an important component in TB regimens moving forward:

- In *in vitro* studies, TBAJ-876 demonstrated anti-mycobacterial activity approximately 10-fold greater than bedaquiline.
- In mouse models of TB, TBAJ-876, together with pretomanid and linezolid, cured infections with shorter treatment durations than HRZE and BPaL regimens.
- TBAJ-876 also demonstrates greater activity against TB strains resistant to bedaquiline (*Rv0678* mutants), suggesting it will also be more effective in treating these emerging strains.
- In preclinical studies, TBAJ-876 showed the potential to be safer than bedaquiline, including low potential for QT prolongation.
- In Phase 1 studies involving 165 healthy subjects, few, generally mild, adverse events were observed.

About TB

TB is a difficult infection to cure, requiring patients to take a combination of medicines for at least four to six months. Even after symptoms disappear, medicines still need to be taken so that all traces of the disease can be fully eradicated. The scope and intensity of TB globally is in large part fueled by antiquated and inadequate TB drugs. Novel drug regimens are urgently needed to bring the TB pandemic under control.

About BPaL

The BPaL regimen—which combines the antibiotics bedaquiline (B), pretomanid (Pa), and linezolid (L)—was first clinically studied by TB Alliance. Pretomanid, as part of the BPaL regimen, received its first regulatory approval in August 2019 for use against highly drug-resistant strains of TB. Previously, less than two-thirds of drug-resistant TB patients around the world had been successfully treated. Treatment options were limited, expensive, toxic, and lengthy – requiring patients to take more than 20 pills per day for 9-20 months.

About TB Alliance

TB Alliance is a not-for-profit organization dedicated to finding faster-acting and affordable drug regimens to fight TB. Through innovative science and with partners around the globe, we aim to ensure equitable access to faster, better TB cures that will advance global health and prosperity. TB Alliance operates with support from Australia's Department of Foreign Affairs and Trade, Bill & Melinda Gates Foundation, Foreign, Commonwealth and Development Office (United Kingdom), Cystic Fibrosis Foundation, Germany's Federal Ministry of Education and Research through KfW, Global Disease Eradication Fund (South Korea), Global Health Innovative Technology Fund, Irish Aid, Korea International Cooperation Agency, National Institute of Allergy and Infectious Diseases, South Korea's Ministry of Foreign Affairs, Unitaid, and the United States Agency for International Development. For more information, please visit: www.tballiance.org.