



BILL & MELINDA GATES MEDICAL RESEARCH INSTITUTE

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Calibr and Bill & Melinda Gates Medical Research Institute announce licensing agreement for novel candidate tuberculosis treatment compound

Calibr transitions investigational compound CLB073 to Gates MRI to advance development

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LA JOLLA, CA and CAMBRIDGE, MA — Calibr, a division of Scripps Research dedicated to the “bench to bedside” development of transformative medicines, and the Bill & Melinda Gates Medical Research Institute (Gates MRI), today announced a strategic licensing agreement to advance development of a novel investigational compound for tuberculosis treatment. Under the agreement, Calibr is granting Gates MRI an exclusive license to continue the development of the investigational compound CLB073 for tuberculosis treatment. Calibr will transition CLB073 to Gates MRI for further development.

“Eradicating tuberculosis will require enhancing the world’s current therapeutic options—meaning shortening treatment duration and overcoming drug resistance,” says Case McNamara, PhD, senior director of Infectious Disease at Calibr. “At Calibr, we have been working with collaborators, through the support of the Bill & Melinda Gates Foundation, to discover and develop novel medicines for diseases that require improved treatment regimens, such as tuberculosis. We hope our collaboration with Gates MRI to advance CLB073 will ultimately be able to help the millions of people who contract this deadly disease.”

Tuberculosis is a severe disease caused by the bacterium *Mycobacterium tuberculosis* (*Mtb*). *Mtb* is known to sequester in lung macrophages following infection. Macrophages are a type of immune defense cell that typically kill infecting microorganisms. *Mtb* has

the ability to establish a prolonged infection in these cells and, under certain conditions, relies on the macrophage's cholesterol supply as a key carbon source for growth.

To develop a drug capable of targeting *Mtb* in a new way, scientists at Calibr collaborated with researchers at the Cornell University College of Veterinary Medicine, including David Russell, PhD, the William Kaplan Professor of Infection Biology, and Brian VanderVen, PhD, an associate professor of Microbiology & Immunology. Together, they discovered and pre-clinically studied CLB073, which uses a novel mechanism to weaken *Mtb*'s intramacrophage survival. CLB073 works by modulating cholesterol catabolism and eliminating the bacteria's carbon source. CLB073 activates adenylyl cyclase (Rv1625c), which ultimately blocks the ability of *Mtb* to metabolize cholesterol. With this novel mechanism, CLB073 holds the potential to complement and potentiate the current tuberculosis standard of care, with the intent of improving efficacy and shortening the duration of treatment time. This is especially critical for multidrug-resistant *Mtb*, which has compromised many frontline drugs. This work was executed through the TB Drug Accelerator, a partnership for tuberculosis (TB) drug discovery and development funded by the Bill & Melinda Gates Foundation.

In preclinical mouse studies, CLB073 significantly enhanced efficacy of the Nix-TB drug regimen¹—the tuberculosis standard of care for drug-resistant tuberculosis.

“Tuberculosis is one of the world's most significant infectious causes of human disease and death,” said Emilio Emini, PhD, chief executive officer of the Bill & Melinda Gates Medical Research Institute. “CLB073, discovered by Calibr scientists and now licensed to the Gates MRI for further development, may represent a potentially important constituent of future TB therapeutic regimens.”

About Tuberculosis

Tuberculosis (TB) is a major global cause of illness and disability, and it is one of the leading causes of death from an infectious disease worldwide, responsible for an estimated 1.5 million deaths per year.

The most commonly used drug regimen for the treatment of drug-sensitive TB requires patients to take multiple drugs usually for a minimum of six months with routine clinical monitoring. Patients with drug-resistant forms of the infection can face longer and more complex treatment journeys, often with significant side effects that require increased monitoring. The need for drug-resistance testing prior to treatment initiation is an added challenge. A substantially shorter drug regimen for the treatment of both drug-susceptible and drug-resistant forms of TB could provide a significant benefit to both patients and health systems and may overcome the need for accompanying drug-resistance testing.

¹ WHO consolidated guidelines on tuberculosis. Module 4: treatment - drug-resistant tuberculosis treatment, 2022 update. Geneva: World Health Organization; 2022.

About Calibr

Calibr was founded on the principle that the creation of new medicines can be accelerated by pairing world-class biomedical research with state-of-the-art drug discovery and development capabilities. Leveraging the unique scientific framework of Scripps Research, Calibr has created a portfolio of drug candidates based on Scripps technologies and is shaping a new paradigm for advancing nonprofit biomedical research to impact patients.

About the Bill & Melinda Gates Medical Research Institute (Gates MRI)

The Bill & Melinda Gates Medical Research Institute is a non-profit medical research organization dedicated to the development and effective use of novel biomedical interventions addressing substantial global health concerns, for which investment incentives are limited, including malaria, tuberculosis, enteric and diarrheal diseases, and diseases that impact maternal, newborn, and child health. For further information please visit www.gatesmri.org.