TB remains a leading cause of morbidity and mortality, claiming an estimated 1.4 million lives each year. TB is caused by bacteria (Mycobacterium tuberculosis) that most often affect the lungs and is spread from person to person through the air. When people with lung TB cough, sneeze or spit, they propel the TB germs into the air. A person needs to inhaled only a few of these germs to become infected.

About one-third of the world's population has latent TB, which means people have been infected by TB bacteria but are not (yet) ill with disease and cannot transmit the disease. People infected with TB bacteria have a lifetime risk of falling ill with TB of 10%. However persons with compromised immune systems, such as people living with HIV, malnutrition or diabetes, or people who use tobacco, have a much higher risk of falling ill.

When a person develops active TB (disease), the symptoms (cough, fever, night sweats, weight loss, etc.) may be mild for many months. This can lead to delays in seeking care, and results in transmission of the bacteria to others. People ill with TB can infect up to 10-15 other people through close contact over the course of a year. Without proper treatment, up to two thirds of people ill with TB will die.

The current multidrug therapy for this disease is prolonged, requiring six months of treatment. Moreover, the alarming rise in incidence of multi- and extensively resistant TB, caused by the evolution and spread of strains of Mycobacterium tuberculosis that are resistant to first- and second-line drugs, underscores the urgency of the need for new, treatment-shortening therapies for drug-susceptible, as well as MDR- and XDR-TB.

Following four decades of neglect, there has been a major resurgence of interest in TB drug discovery and development, which has yielded a promising global TB drug pipeline that currently includes more than 10 drugs in clinical development.

In this talk, I will focus specifically on the very early stage of the drug discovery process, by summarizing some of the lessons that have been learned from research programs that have sought to identify novel anti-mycobacterial compounds by target-led and phenotypic approaches.

The second part of the talk will highlight new experimental approaches that are aimed at addressing persisting challenges in this field.