

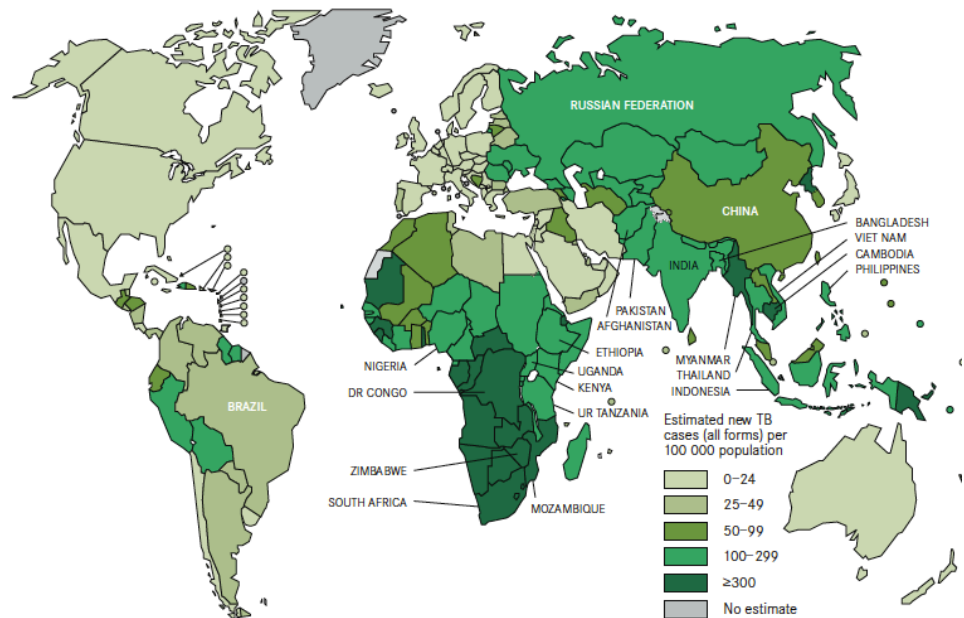
Sutezolid for the Treatment of Tuberculosis

Clinical Development Status: Phase 2

Since 2000, Sequella has applied its scientific expertise to develop drug candidates for the treatment of tuberculosis (TB) and other infectious diseases important to global health. In 2013, Sequella licensed the worldwide rights to develop sutezolid from Pfizer, who had selected it from among all the oxazolidinones as best in class for the treatment of TB. Sutezolid was safe and well-tolerated in Phase 1 clinical trials, and a Phase 2 clinical study demonstrated potential efficacy in the treatment of TB.

TB is a public health crisis and unmet medical need.

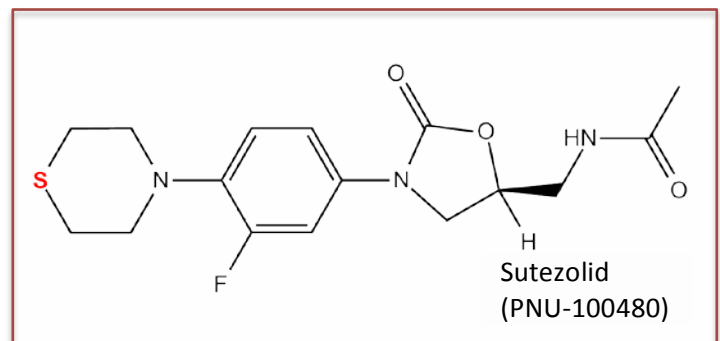
TB is the cause of the largest number of human deaths attributable to a single etiologic agent, killing nearly 2 million people each year. The poor efficacy of existing TB drugs requires that they be administered in a multidrug regimen for at least six months. This results in poor patient compliance and leads to development of multidrug-resistant TB (MDR-TB) and extremely drug-resistant TB (XDR-TB). MDR-TB and XDR-TB are even more difficult to treat



(5-8 drugs for up to 24 months) and have significantly higher mortality. Decades of misuse of existing antibiotics and poor compliance have created an epidemic of drug resistance that threatens TB control programs worldwide. New drugs and treatment regimens with activity against drug-susceptible and drug-resistant TB are desperately needed to manage this public health crisis.

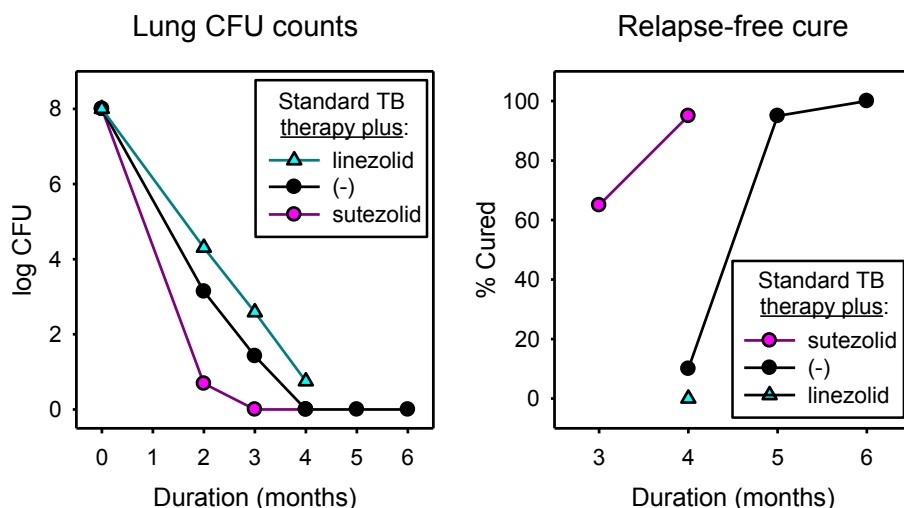
Sutezolid has promising activity against drug-susceptible and drug-resistant TB.

Sutezolid (previously known as PNU-100480) is an oxazolidinone that was identified contemporaneously with linezolid, which is FDA-approved for severe infections caused by Gram-positive bacteria that are resistant to other antibiotics. However, sutezolid has better antimycobacterial activity than linezolid both in vitro and in a mouse model of TB.¹⁻³ Sutezolid has an improved safety profile compared to linezolid⁴ and shows better time-dependent killing in an ex vivo whole blood culture test.⁵ In addition, it has activity against both drug-susceptible and drug-resistant TB.⁶



Sutezolid has promising activity in combination with other new TB drugs. Sutezolid and SQ109, another TB drug candidate in Sequella's pipeline, have additive effects in vitro and SQ109 improved synergistically the time to kill intracellular Mtb in an infected macrophage assay.⁷ SQ109 and bedaquiline, the first new TB drug candidate to be approved by the FDA, are apparently the two best drugs to pair with sutezolid in a new TB regimen for all forms of drug susceptible and drug resistant TB.⁸

The addition of sutezolid to the standard TB treatment regimen leads to significantly improved efficacy. *In vivo* studies in the chronic mouse model of TB demonstrated that the addition of sutezolid to the standard TB regimen has the potential to significantly shorten treatment. It not only reduced the numbers of bacteria in the lungs more quickly, but also led to a relapse-free cure with a shorter duration of treatment.



Clinical Development. Sutezolid received Orphan Drug designation in both U.S. and E.U. and is currently in clinical development for the treatment of adult pulmonary TB caused by drug sensitive or drug resistant strains of *M. tuberculosis* (IND #104806). Sutezolid was safe and well-tolerated at doses up to 1200 mg daily for up to 14 days, or 600 mg twice daily for up to 28 days.⁴ A Phase 2 trial demonstrated that sutezolid has significant early bactericidal activity and may have clinical efficacy in humans in a larger Phase 2 trial.

Market for New TB Drugs. The combined U.S. and EU market only for treatment of MDR-TB, drug sensitive TB, and latent TB is estimated to be \$400M. In the U.S., an estimated 15-30M people are latently infected with Mtb, approximately 450,000 of whom are treated or prophylaxed for TB annually. Worldwide, 2 billion people are latently infected with *M. tuberculosis* and there are nearly nine million active cases of TB.

Intellectual Property. Sequella licensed the worldwide rights to the development of sutezolid for all indications. There are more than 20 issued patents and additional patent filings, including U.S., E.U., Japan and China patents for compositions of matter and uses of sutezolid. These patents provide broad coverage for composition, methods, and use claims for treatment of tuberculosis and other infectious pathogens.

References. Copies of all referenced papers are available upon request: please contact katherinesacksteder@sequella.com.

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