BENTLEY UNIVERSITY
Center for Integration of Science and Industry

What non-profit development of pretomanid can teach about paths to innovation and global access to treatments for diseases of poverty

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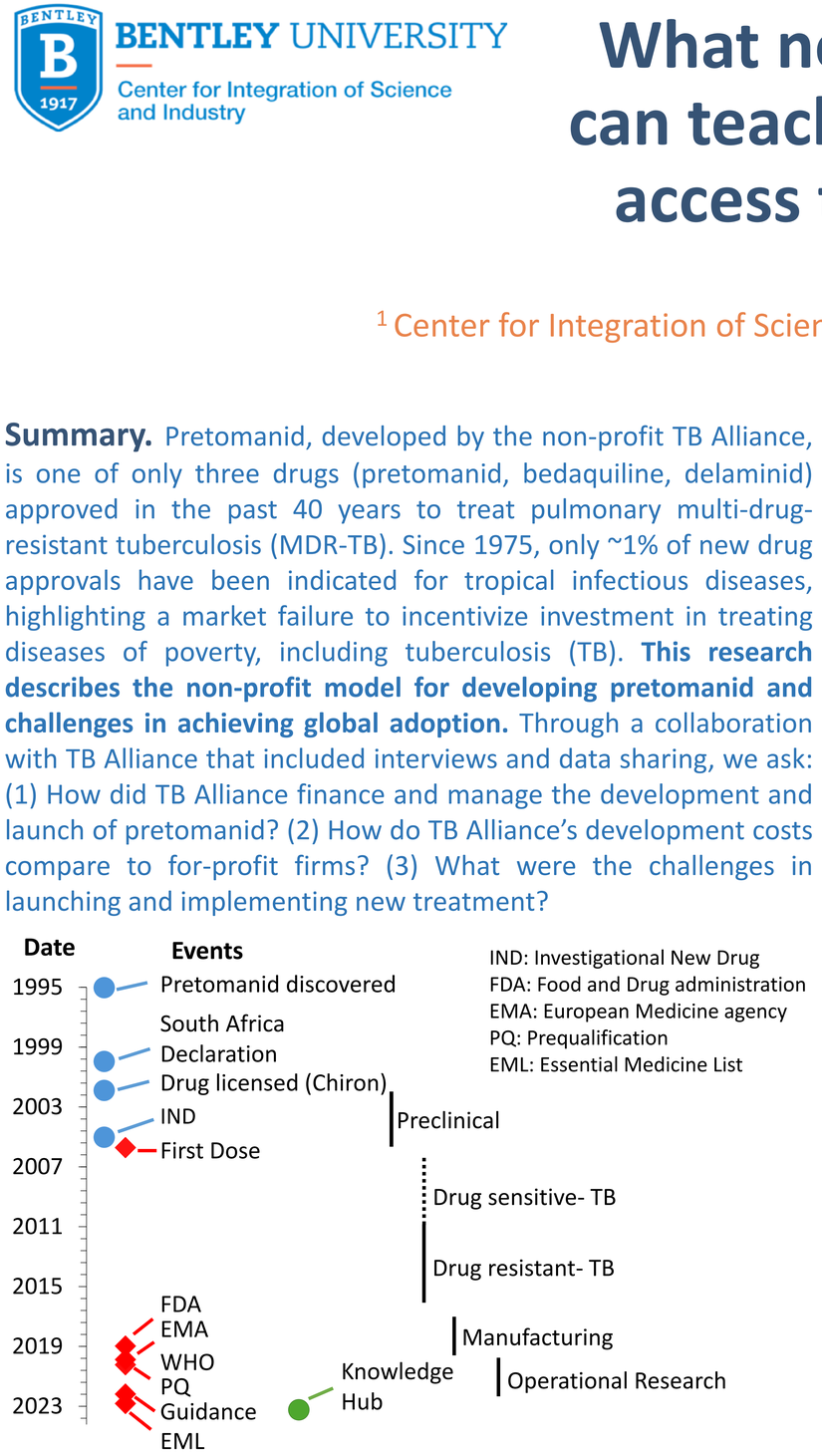
Summary. Pretomanid, developed by the non-profit TB Alliance, is one of only three drugs (pretomanid, bedaquiline, delaminid) approved in the past 40 years to treat pulmonary multi-drug-resistant tuberculosis (MDR-TB). Since 1975, only ~1% of new drug approvals have been indicated for tropical infectious diseases, highlighting a market failure to incentivize investment in treating diseases of poverty, including tuberculosis (TB). **This research describes the non-profit model for developing pretomanid and challenges in achieving global adoption.** Through a collaboration with TB Alliance that included interviews and data sharing, we ask: (1) How did TB Alliance finance and manage the development and launch of pretomanid? (2) How do TB Alliance's development costs compare to for-profit firms? (3) What were the challenges in launching and implementing new treatment?

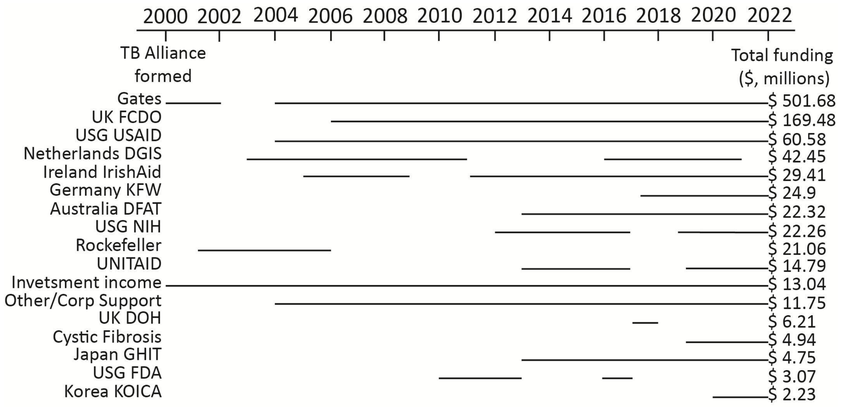


History and timeline.

Pretomanid (PA-824) originated at Pathogenesis, a for-profit firm later acquired by Chiron. TB Alliance licensed PA-824 and managed development through FDA approval (2019), EMA approval (2020), implementation studies (real-world evidence), multifaceted WHO review, national reviews, and implementation. **TB Alliance operates with a small team of experienced professionals from the biotech/pharma industry, outsourcing clinical development to CROs and manufacturing distribution nonexclusively to generic manufacturers.**

Revenue and costs.

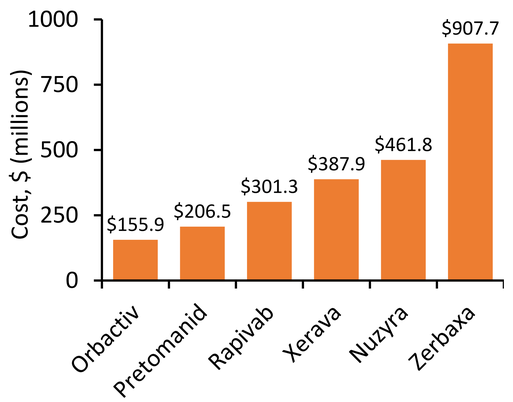
Philanthropy and governments provide 95% of TB Alliance's funding, with Gates Foundation providing >$500 million since 2000. TB Alliance is not a "public-private partnership" in that they independently managed development and adoption of PA-824, but their operational model involves contracting with leading for-profit firms for development and manufacturing processes. **TB Alliance received $105M from sale of a priority review voucher but receives no revenue from PA-824 sales outside of high-income countries (except China, Russia).**



Pretomanid's development cost is estimated to be $206M, comparable to the reported costs of other anti-infective development by for-profit firms. This is consistent with the strategy of outsourcing clinical trials to leading (for-profit) Clinical Research Organizations (CROs). **These costs do not include the cost-of-capital required by for-profit firms.**

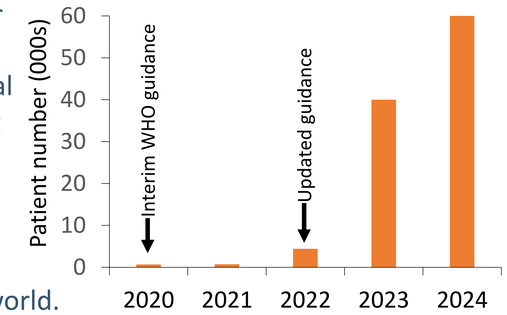
Development Stage	Cost ($, millions)
Prior to 2012	$ 36.58
After 2012	$ 17.46
Phase 1	$ 0.25
Phase 2	$ 80.8
Phase 3	$ 57.32
Formulation	$ 0.78
Regulatory	$ 13.2
Total Cost	$ 206.6

Costs adjusted for inflation to 2018

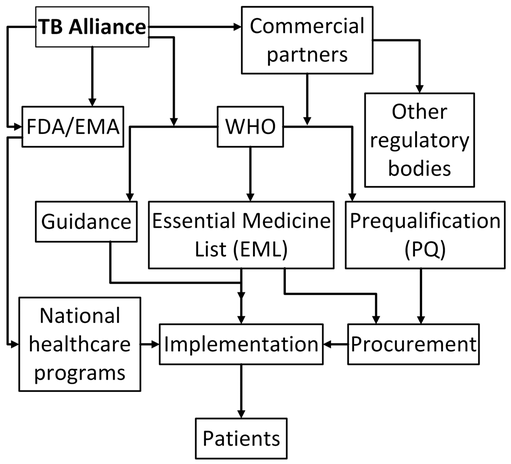


Implementation and impact.

Pretomanid has a 90% cure rate for MDR-TB (pulmonary + non pulmonary), a disease with a worldwide incidence of ~400K/year and ~50% mortality. At the end of 2024, **100,000 patients were treated with pretomanid.** Initial WHO guidance recommended limited settings usage in 2020, broad implementation for drug resistant TB in 2022, and listed it as an essential medicine in 2023 (making lower cost drug available to 150 countries). TB Alliance continues to support implementation and training around the world.



By 2023, 21 countries outside the US and EU had approved pretomanid (BPaL combination) for drug resistant TB.



Conclusion.

Pretomanid's development is a model for the role of non-profits in redressing the market's failure to incentivize treatments for diseases of poverty. TB Alliance's operational model adheres closely to for-profit best practices, eliminating value extraction by shareholders and foregoing revenue from sales in high-income countries. TB Alliance relies on philanthropy and grants to sustain operations and new drug development. The complex adoption process allows non-profits like TB Alliance to form trusted partnerships in advancing public health.

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