

PreDiCT-TB

**Model-based preclinical development of
antituberculosis drug combinations**

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**2 billion latent
infections**

**8.8 million
new cases/yr**

**1.5 million
deaths /yr**

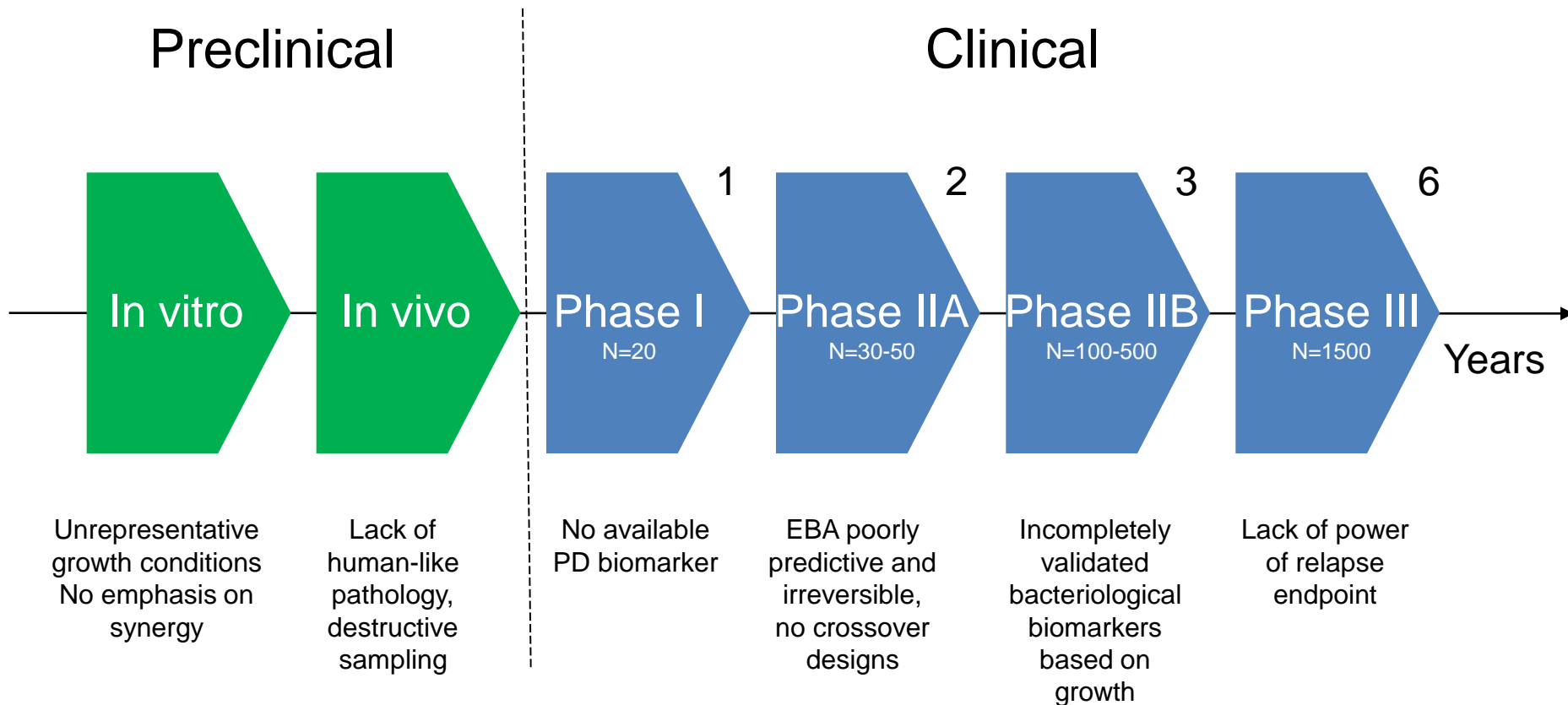
26% of avoidable
adult deaths in
developing world



Challenges in TB Drug Development

Preclinical

Clinical



PreDiCT-TB Priorities

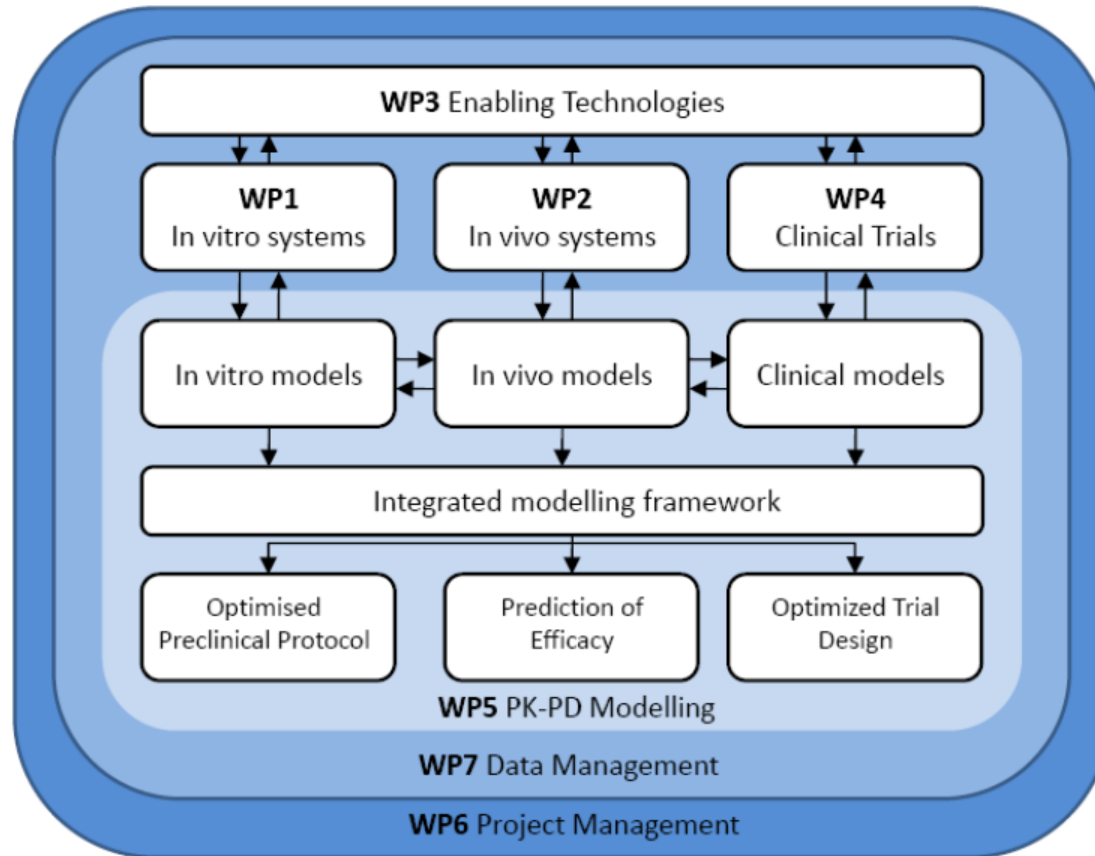
- Work with regimens as unit of development from the earliest possible stage
- Capitalise on interdisciplinarity (experimentalists, modellers and trialists)
- Enhanced understanding and monitoring of pharmacodynamics through novel technologies
- Integrated modelling approach and framework



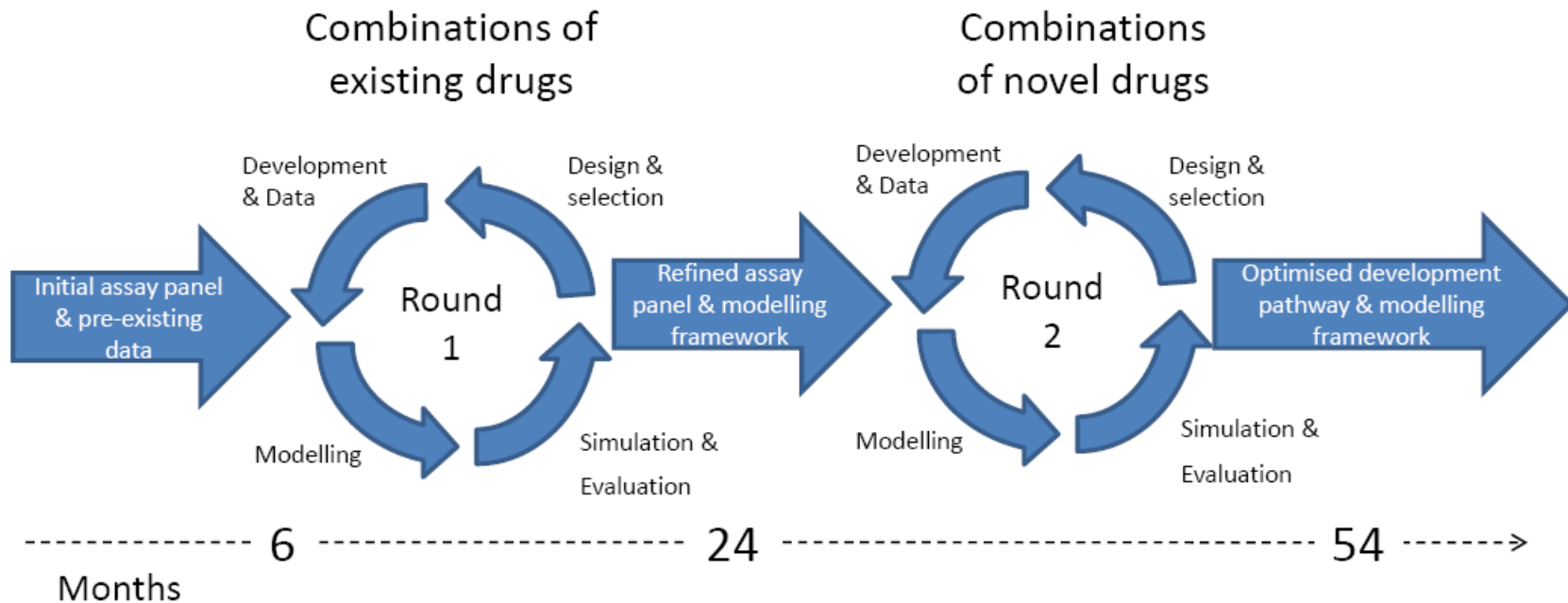
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PreDiCT-TB Workplan

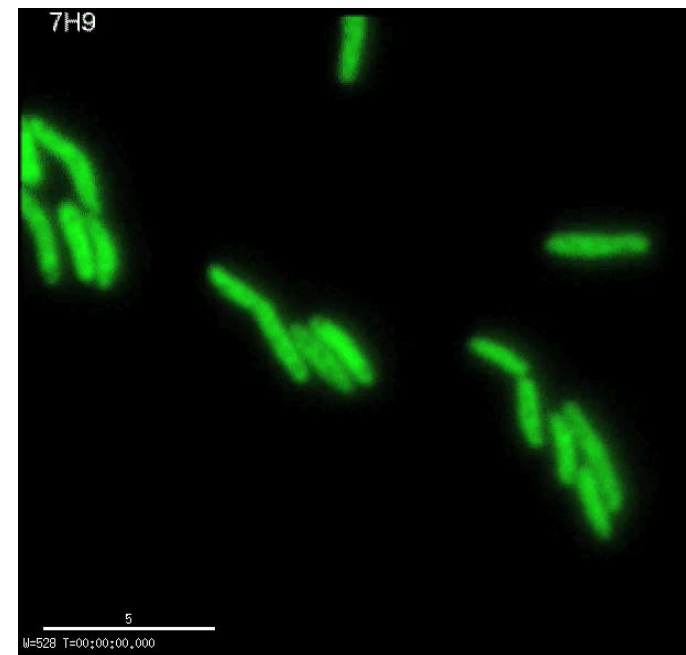


PreDiCT-TB Strategy



WP1-in vitro/ex vivo systems

- Elaborate current pharmacodynamic model
- Reflect diversity of target states
- Focus on lethality not growth



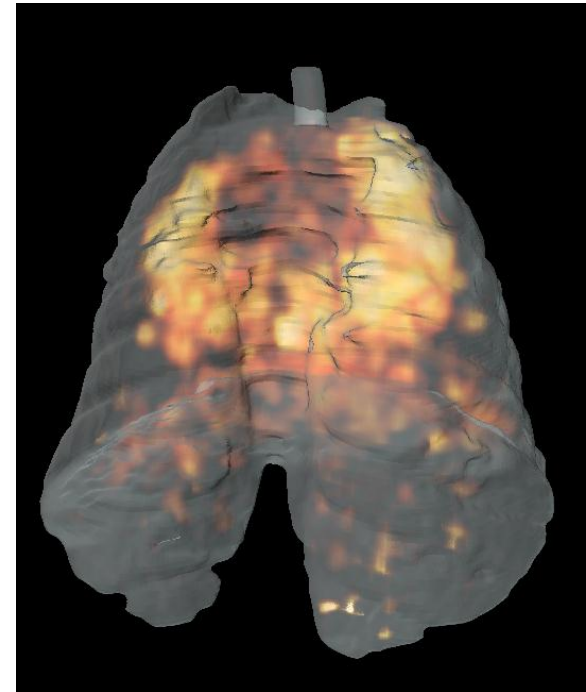
WP2- in vivo systems

- Reflect range of tractable species in hierarchical strategy
- Intensified PK and PD sampling using cannulated, non-invasive and improved bioanalytical approaches
- Primate and immunologically “humanised” mouse models



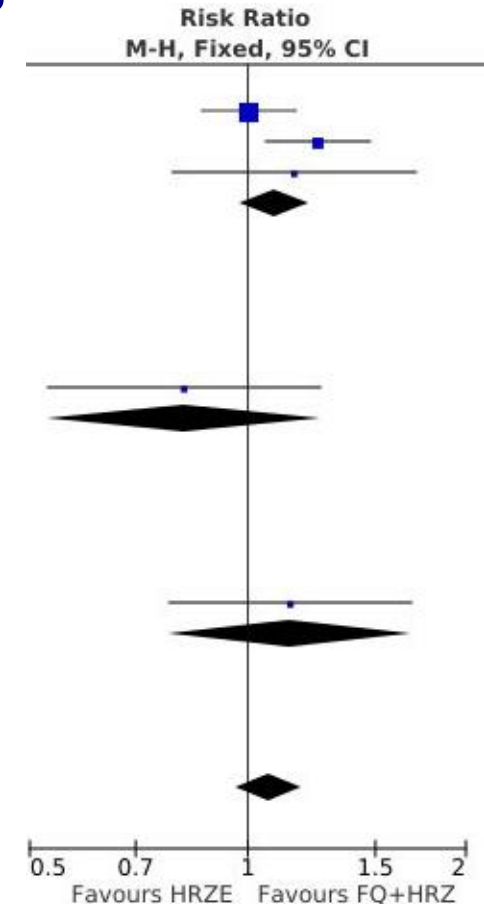
WP3- enabling technologies

- Support intensified non-invasive sampling
- Improve precision of pharmacodynamic monitoring
- Biomarkers that reflect heterogeneity in PD and cell death independently of culture



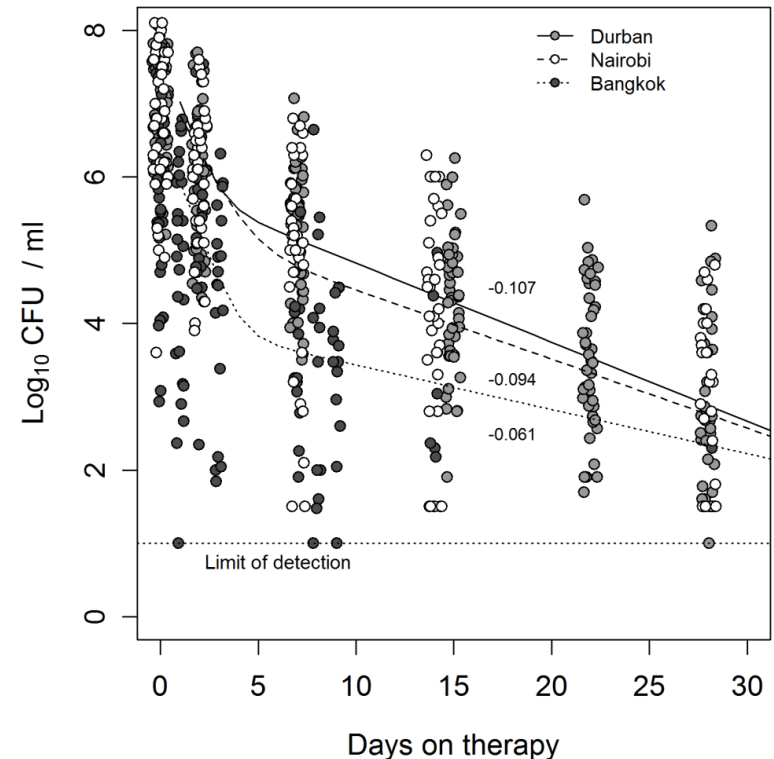
WP4- clinical trials

- Assemble database of existing IPD clinical trial data
- Provide context for evaluation of preclinical modelling predictions
- IP policy to facilitate public use of database



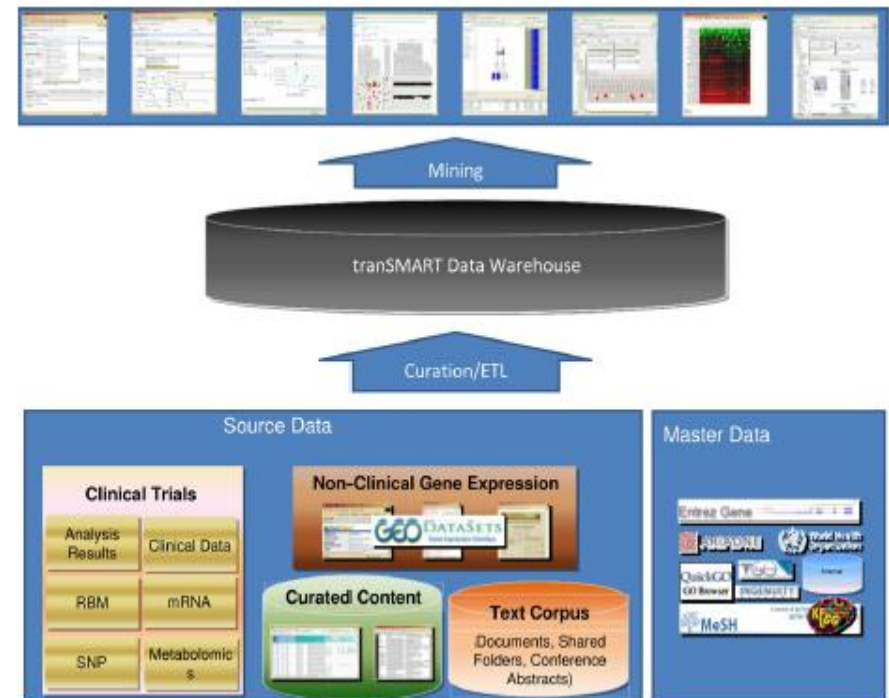
WP5-PKPD modelling

- Optimal design consulting with experimentalists
- Flexible approach incorporating mechanistic information where available
- Clinical trial simulation and innovative design



WP7-Data management

- TranSMART relational database system
- Assist in ensuring flow and governance of data between partners and WPs
- Cloud-based with open source interface for diverse datasources



Summary

- Model-based approach to preclinical development of combinations
- New technologies to enhance pharmacodynamic model
- Strong emphasis on interdisciplinarity
- Open model of collaboration with wider impact
- Multiple points of contact with allied external groups such as CPTR, TB Alliance and other EU consortia

