

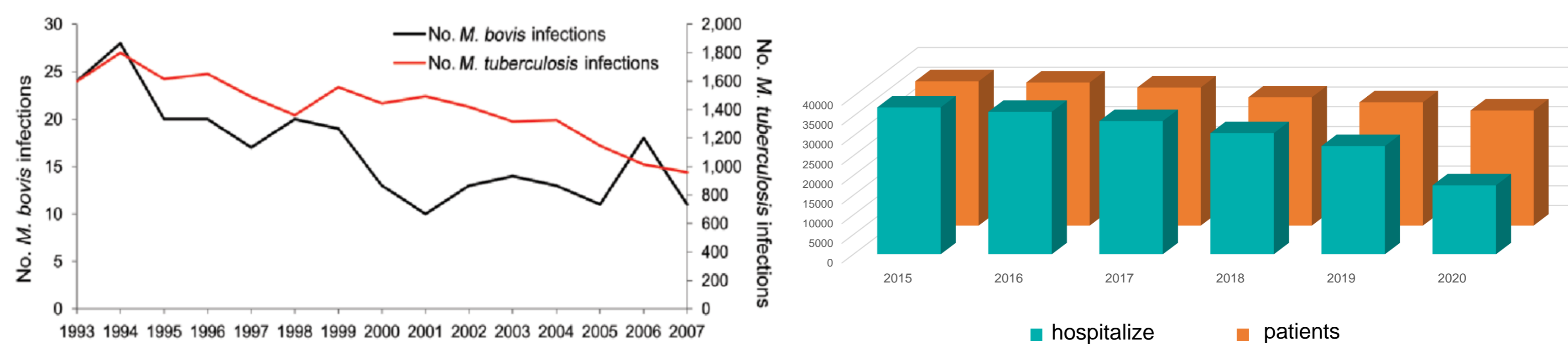
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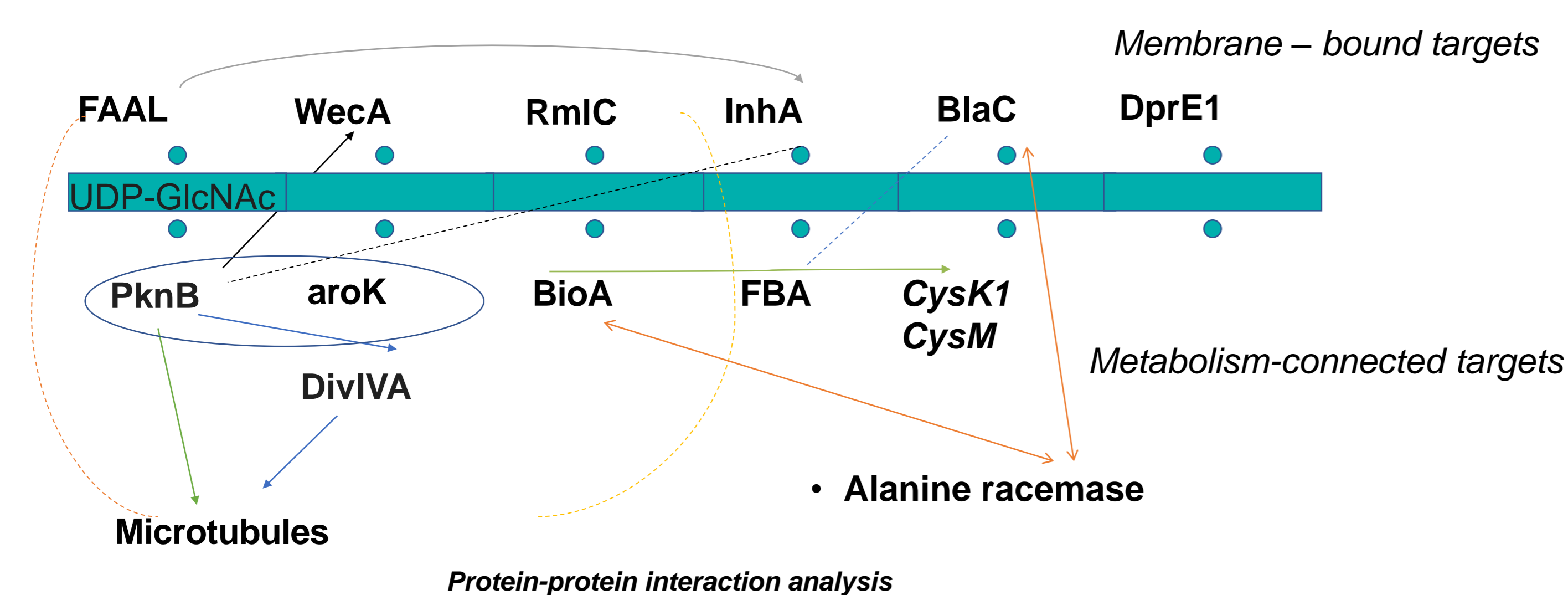
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The aim of this research has been the identification of novel inhibitors of *M. tuberculosis* that cause fatal conformational changes in tuberculosis-specific drug targets to address a pressing need for novel and effective anti-tuberculosis treatments.

Our joint cheminformatics team has performed a protein-protein interaction (PPI) analysis starting from the known protein targets, already employed in the reported tuberculosis treatments, followed by molecular docking studies.



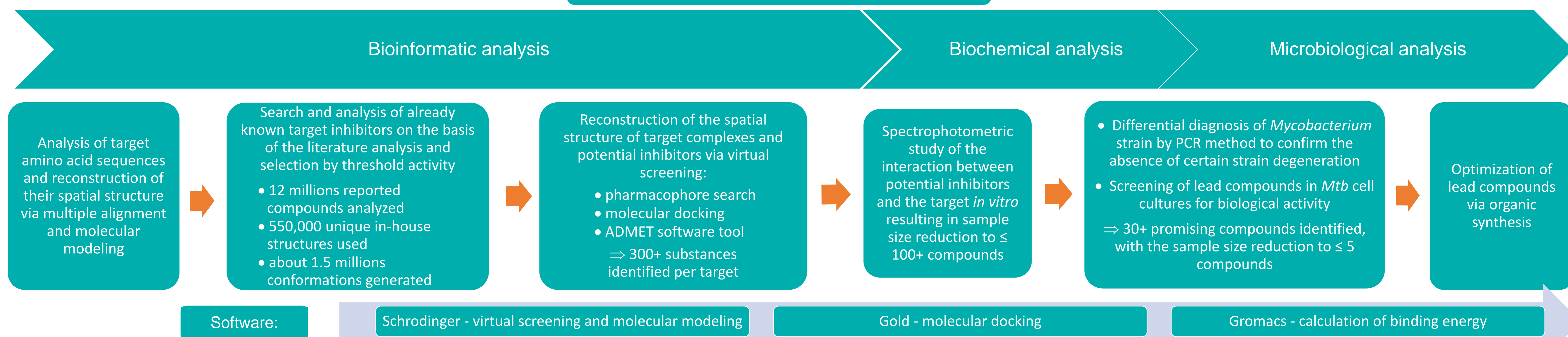
Incidence statistics in the world and Ukraine by years



Tuberculosis (TB) is the leading cause of death from an infectious disease worldwide. About a quarter of the world's population is infected with its latent form, while one in ten of those will become ill with active tuberculosis during their lifetimes, with 20 % of new tuberculosis patients being affected by multi-drug resistant tuberculosis.

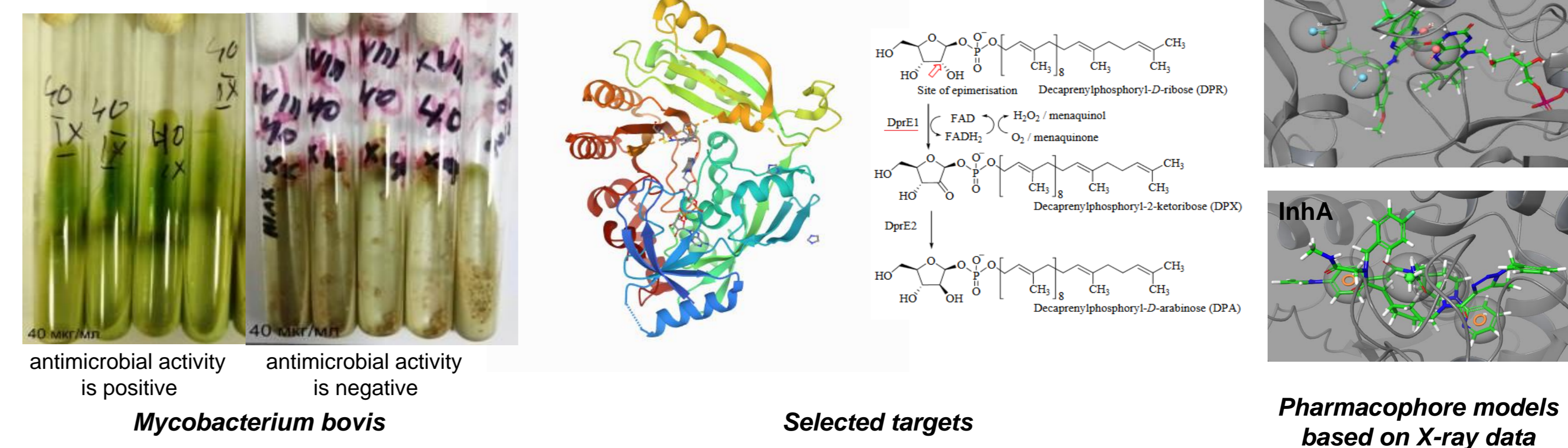
COVID-19 pandemic has significantly jeopardized the progress previously achieved in the fight against tuberculosis, causing disruptions in timely diagnostics and treatment, combined with impossibility or lower quality of care for many patients all over the world.

### General methodology of research



Based on the analysis of the active sites of the selected targets RmlC, DrpE1, and InhA, coupled with ligand-target interactions, we performed *in silico* screening against the Life Chemicals HTS Compound Collection. The *M. tuberculosis* crystal structures 2P8C, 7KXA, and 1PM7 were chosen for studying the ligand interactions.

The reference set of active ligands was used to test the docking procedure and to identify hydrophobic regions as well as relevant donor and acceptor bonds. In the process of virtual screening, the presence of cofactors was taken into account, as it is known that they take part in the binding of known inhibitors.



Thus, the compound design based on structural analysis of identified virtual hits against the RmlC, DrpE, and InhA targets has allowed us to discover active scaffolds and propose new chemical families of potential inhibitors of those promising anti-tuberculosis targets.

Finally, synthetic approaches to obtain promising analogues, including scaffold hopping and combinatorial chemistry are being developed.

