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Molecules to Medicines

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Dr. Monalisa Chatterji is presently a team leader, Astra Zeneca India Pvt. Ltd., Bangalore. She possess varied discovery research experience in academia and industry, leading research groups, driving new opportunities, mentoring, drug development understanding, managing in house and collaborative projects, managing alliances. She has number of publications and a patent for "Anti-CD6 antibodies in T-cell mediated auto-immune disorders" to his credits. She is the recipient of AZ star award, Young Scientist Award, Anna Fuller Fund fellowship, James Hudson Brown-Alexander Brown Coxe fellowship and Sreenivasaya Medal.

Increase in drug resistant tuberculosis (TB) necessitates immediate development of new drugs/regimens. The global TB pipeline has been slowly expanding; with the focus of simplifying and improving TB treatment. AZD5847, an oxazolidinone, currently at ph2, is being developed by AstraZeneca as oral therapy for treatment of drug sensitive and resistant TB including HIV co-infections. AZD5847 is active on extracellular drug sensitive and resistant isolates of *Mycobacterium tuberculosis* in (Mtu) vitro, is active against intracellular bacterium and is efficacious in high-and low dose aerosol infection models in BALB/c mice in vivo. It exerts superior bactericidal activity compared to linezolid in intracellular and mouse chronic infection model and has better safety margins with respect to mitochondrial protein synthesis inhibition. Finally, AZD5847 administered for 14 days in healthy volunteers as part of Ph1 trial, was well tolerated at doses predicted to be clinically relevant for the treatment. Pre-clinical toxicity assessment in rats and dogs is currently ongoing to support Ph2b clinical study. A novel chemical class, 1-4 azaindoles, in early discovery portfolio is being optimized for oral TB therapy. The series emerged form scaffold morphing and is a non-covalent inhibitor of DprE1 protein. 1,4 azaindoles are bactericidal *in vitro* and efficacious in macrophase and, Mouse TB infection model. Thus, the anti-mycobacterial compounds described here have the potential to be part of new TB regimen for treatment of drug sensitive and drug resistant TB.

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