28AB-ISMS36 **Hit to Lead Optimization of a New Class of Compound to Treat Human African Trypanosomiasis**

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We have recently reported the results of a DNDi-sponsored high-throughput screen (HTS) of the ~80,000-strong Walter and Eliza Hall Institute (WEHI) Stage 1 compound library for hits with growth-inhibitory activity against *T. b. brucei*,. Eleven hits with novel, drug-like structures and physicochemical properties were identified. We have already published the hit-to-lead optimisation of five of these hits. Herein we report our work on a new class of compounds based on the 2-phenylthiazole chemotype. These hits offer a very attractive starting point for an SAR analysis since they exhibit good physicochemical properties including a low molecular weight, a low polar surface area which necessary for CNS penetration in order to treat the second stage of HAT.