

DNDI MODEL: FROM SCREENING THROUGH LEAD OPTIMISATION PROGRAMMES TO PRECLINICAL CANDIDATES

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The Drugs for Neglected Diseases *initiative* (DNDi) was founded in 2004 with the goal to develop new treatments for neglected tropical diseases. Part of this strategy is development of modern antibiotics for the kinetoplastid diseases African trypanosomiasis, Chagas' disease and leishmaniasis. To achieve this goal from lead identification to preclinical development, we have adopted a model that works as a virtual biotechnology company. Slightly different strategies have been adopted for the three stages of drug discovery - compound screening, lead optimization and preclinical development. DNDi has funded several groups in academia and industry to develop medium-to-high throughput screens against all three parasites. This has allowed us to license access to compound libraries from several pharmaceutical and biotechnology companies and to screen them in a timely manner. Selected drug leads are then prioritized for lead optimization. The process of lead optimization is conducted by separate consortia of scientists spanning the disciplines of medicinal chemistry, DMPK and pharmacodynamics. These research consortia constitute what is the minimal critical mass for drug discovery and have guaranteed support from DNDi for several years. Because the teams are not built around a single chemical series or drug target, series in development can be rapidly killed if it is decided that optimization is not feasible and new series can be accessed from the prioritized list of leads, which were identified in the screening campaigns. Finally, preclinical development, which constitutes process development, manufacture to Good Manufacturing Practice (GMP) standards and conduct of IND enabling safety studies to Good Laboratory Practice (GLP), is outsourced to contract research organizations (CROs). Over the past three years, these consortia have produced a preclinical drug candidate for human African trypanosomiasis and several promising leads for leishmaniasis and Chagas' disease.