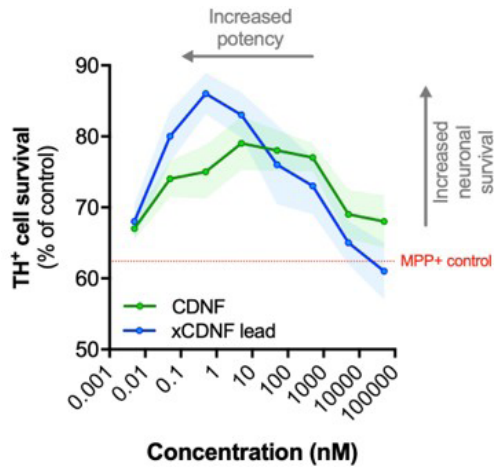
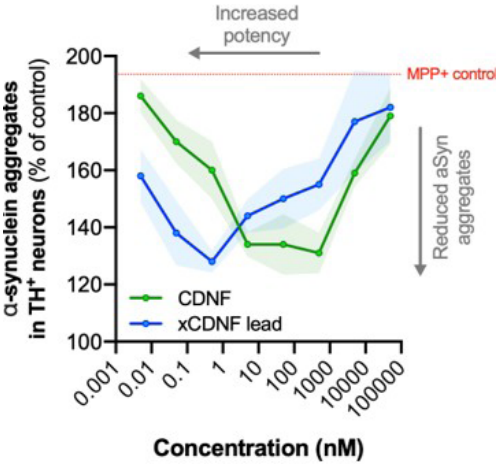
HERANTIS PHARMA

PIPELINE PROGRAMME SUMMARY:

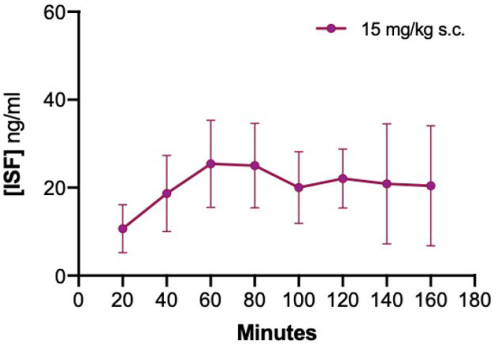
XCDNF (CEREBRAL DOPAMINE NEUROTROPHIC FACTOR – BASED PEPTIDOMIMETICS)



xCDNF peptidomimetic shows at least 10-fold higher potency than CDNF in rat neuron cultures



xCDNF peptidomimetic significantly reduced alpha-synuclein aggregates in rat neuron cultures



Extended residence time in brain interstitial fluid following single subcutaneous injection of xCDNF.

Herantis is pioneering research and development into CDNF-based therapeutics for Parkinson's disease (PD) and similar neurodegenerative diseases, such as Lewy Body Dementia (LBD). These diseases are characterised by increased levels of cellular stress and the breakdown of proteostasis, which is the normal mechanism that directs the synthesis and folding of proteins, and also the removal of misfolded proteins. CDNF acts upon three key elements of proteostasis; synthesis, folding, and degradation, and can thereby reduce cellular stress and prevent formation of protein aggregates (such as Lewy bodies). However, CDNF cannot readily penetrate an intact blood-brain-barrier (BBB).

The xCDNF pipeline programme is intended to deliver optimised, metabolically stable peptidomimetic APIs that retain the neuroprotective effects of CDNF, but are also able to readily penetrate the BBB. Herantis is currently performing lead optimisation studies on several candidates to maximise their plasma half-life, BBB penetrance and potency. The xCDNF optimisation programme has already generated a number of promising NBEs with associated new intellectual property.

In rodent models, our peptidomimetic compounds were shown to be trafficked to the basal ganglia in therapeutic concentrations, following simple subcutaneous injection. More importantly, our studies have shown that peptidomimetic APIs retain the biological activity of whole protein CDNF and can greatly exceed its potency. Herantis' discovery team is now in the final stages of lead identification and structure optimisation. This involves iterative study of structure-activity relationships, e.g. impact on cellular stress and BBB penetrance, synthetic route development, and target binding kinetics. Our selected lead candidate is expected to enter a formal preclinical program in H2 2021, followed by a first-in-human Phase I safety study in 2023-24. Herantis intends to pursue preclinical development programmes for both PD and LBD. Since the therapeutic hypothesis for these indications is the same, these programmes will likely be complementary and are likely to involve similar in vivo efficacy models. This is expected to simplify development and accelerate overall progress.

Comprehensively, the total available market for neurodegenerative diseases was estimated to be worth €29.2Bn in 2018 and is projected to reach €54Bn by 2026 (CAGR = 7.2%). Parkinson's disease represents a serviceable market of €3.8Bn, growing to €5.0Bn by 2024. PD is the second most common form of neurodegeneration, affecting 7 to 10 million people worldwide, with over 60,000 new diagnoses in the US each year. Lewy Body Dementia is expected to reach a market size of €1.25 – 1.7Bn in 2025. Based on the market shares of incumbent therapeutics for PD and LBD, the overall market opportunity for xCDNF is estimated to be approximately €4.2Bn.

xCDNF peptidomimetics have the potential to be disease-modifying therapeutics for PD and LBD. However, these compounds also have the great advantage of a simple delivery route (i.e. via subcutaneous injection). We anticipate xCDNF will be launched as a simple injectable formulation, with a straightforward regulatory route and numerous patient-friendly administration possibilities.