

# Herantis Marks A Successful 2021; An Ambitious and Promising 2022 Ahead to Advance Robust CNS Pipeline

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*Dr Craig Cook, CEO, commented "2021 was indeed a defining year for Herantis as we move into the next chapter for the company and our programs. The year saw us focus all our research and resources on the key value drivers of the company – our CNS assets - allowing the true fundamentals of the company to take center stage. The cutting-edge science and the multimodal mechanism-of-action gives our assets the opportunity to be truly disease modifying therapies - in other words, they have the ability to slow, stop or even reverse the Parkinson's disease process. This strongly differentiates Herantis from several other scientific approaches in the field of neurodegenerative diseases and will, if successful, have a significant therapeutic impact on the lives of patients. During 2022 our focus will be squarely on getting our CNS program/s to the clinic within the next 12 – 18 months."*

Herantis Pharma Plc ("Herantis"), focusing on disease modifying therapies for debilitating neurodegenerative diseases, gives a 2021 year end summary of the progress of the company and the plans for 2022.

Herantis has two programs under development:

- 1) rhCDNF (recombinant human Cerebral Dopamine Neurotrophic Factor), a biotechnological protein that has been used safely in a Phase I study (intracranial administration via surgery) in patients with Parkinson's disease and is now being developed for intranasal brain administration via simple nasal spray
- 2) HER-096, an advanced small synthetic chemical peptidomimetic version of the active parent rhCDNF protein. It combines the compelling MoA of rhCDNF protein and the ability to be delivered to the brain after simple skin injection

For 2021 the highlights were:

- *evidencing the true disease-modifying potential of rhCDNF and HER-096 for Parkinson's disease*
- *confirmation of the long-term safety of intraputaminal rhCDNF*
- *confirming the impact of rhCDNF and HER-096 on biomarkers of Parkinson's disease*
- *identification of novel biomarker candidates to accelerate future clinical development in Parkinson's*
- *affirming that HER-096 can impressively cross the blood brain barrier and enter the brain*
- *demonstrating that HER-096 induces unequivocal protection and restoration of neurons in preclinical models of Parkinson's disease*
- *establishing a respected and internationally renowned Scientific Advisory Board*

For 2022 the main objectives will be:

- *successful completion of HER-096 non-clinical program to support the first-in-human study*
- *filing for regulatory approval to start a first-in-human study with HER-096*
- *defining the patient population for further clinical development*
- *confirmation of feasibility of rhCDNF brain distribution following intranasal spray administration*

For more detailed information please refer to the more comprehensive information below.

## **2021**

2021 was all about focusing our research on our core CNS assets, where significant progress has been made on several fronts the most important of which include:

- **Disease modifying therapeutics:**
  - *evidencing the true disease modifying potential of our CDNF programs was a key objective of 2021.* We now know that HER-096 and rhCDNF act powerfully on the key pathology in Parkinson's disease - proteostasis and the unfolded protein response (UPR) – by restoring proteostasis and the UPR via multiple mechanism. It is now generally believed that a such a comprehensive multi-level mechanism of action is necessary for a true disease-modifying therapy. *Human and animal data generated during 2021 increasingly evidenced the modulating effect on proteostasis, neuroinflammation, and thus the disease-modifying potential of rhCDNF and HER-096.*
- **Confirmation of the long-term safety of intraputamenal rhCDNF**
  - In August 2021 we completed the 13-months safety follow-up for the remaining 15 patients in the first-in-human rhCDNF study. Prior to this follow-up study, patients had received up to 12 monthly intracranial infusion with rhCDNF. In the follow-up study we demonstrated the long-term safety and tolerability after chronic treatment with rhCDNF.
- **Impacting biomarkers of Parkinson's disease:**
  - *evaluating and confirming the impact of rhCDNF and HER-096 on biomarkers of Parkinson's was another key objective of 2021.* Diseases take a long time to develop, and biomarkers – ie markers of disease data can compress drug development timelines, increase patient response rates and reduce development costs. This year, Herantis launched its novel biomarker-based program demonstrating that human biomarkers in Cerebrospinal Fluid (CSF) change in response to rhCDNF treatment, and that these biomarker changes correlated with improvements in motor function and dopamine brain signals in the patients. These key observations will be used to define the patient population for our clinical program and shape our development activities to fit our assets.
- **Crossing the blood-brain barrier (BBB):**
  - *the further key objective for 2021 was to confirm that HER-096 can get into the brain in pharmaceutically active concentrations, to exert its therapeutic action.* The BBB is a natural barrier protecting the brain from foreign substances. Herantis' HER-096 was specifically designed to be able to cross the blood-brain barrier, and key studies during 2021 confirmed that we have been impressively and uniquely successful in the engineering of HER-096 and its ability to cross the BBB. The concentration of HER-096 in the brain reaches more than 20% of the plasma concentration when administered under the skin, 20-50 fold more than with therapies such as monoclonal antibodies (mAb's). This means that pharmacologically active levels can be easily reached in the brain by a single injection.
- **Protecting neurons from Parkinson's disease:**
  - In 2020, we demonstrated pre-clinically that HER-096 strongly protects neurons in a prophylactic setting ie when it is administered at the same time as disease onset. In 2021, we went a major step further by demonstrating that HER-096 convincingly protects neurons in a therapeutic setting ie when it is administered after the onset of disease once the Parkinson's pathology has already taken hold. This is a difficult threshold and a major achievement, which we have now demonstrated for both rhCDNF as well as HER-096. In fact, the data convincingly showed there is significant increase in dopamine neuron survival, and very strong reduction in the damaging neuro-inflammation processes and toxic alpha-synuclein levels.

To maximize our effort, we were also very pleased to have assembled an impeccable Scientific Advisory Board with renowned world authorities in Parkinson's disease who, sharing our excitement for and belief in the

potential of our assets, have agreed to join the board and will play an intricate role together with the Herantis team in shaping our chances of success.

In summary 2021 has been a challenging but ultimately very rewarding year for Herantis, leveraging our key strengths and opportunities.

## **2022**

The year 2022 will be fully focused on getting our asset/s into the clinic within the next 12 – 18 months.

- **Filing for regulatory approval to start a first in human study with HER-096**
  - o *the main focus for 2022 is to get HER-096 ready for the clinic for study in humans.* This will require completion of the pre-clinical and safety toxicology programs for HER-096, planned for H2 2022, which will then allow the necessary dossier to be submitted to regulators for approval for the first-in-human study in healthy volunteers and patients, and formal clinical trial start thereafter. The main endpoints of this Phase Ia study will be i. safety, ii. evidence of HER-096 crossing into the brain at pharmaceutically active concentrations in humans, and iii. exploratory biomarkers.
- **Further defining optimal patient population for HER-096 and rhCDNF**
  - o *a key objective for 2022 will be to further understand the target patient population with most potential to respond to HER-096 or rhCDNF,* underpinned by our strong biomarker data and biomarker-driven precision medicine program. During 2022 we will advance that work to further define the right patient population, the right biomarkers, and the right outcome measures tailored to the strengths of HER-096 and rhCDNF. This target patient population will then be the focus of our formal clinical studies in patients, to commence following the Phase Ia study above.
- **Confirmation of feasibility of rhCDNF brain distribution following intranasal spray administration**
  - o For rhCDNF the focus will be to confirm feasibility of brain distribution via the intranasal route following nasal spray administration. Liquid and powder formulations as well as nasal spray device compatibility will be completed during H1 2022, following which the key experiments to confirm brain distribution will be conducted during H2 2022.

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**About Herantis Pharma Plc**

Herantis focuses on disease modifying therapies for debilitating neurodegenerative diseases by restoring the neuronal protective mechanism of proteostasis, a key system in neurodegenerative disease. Proteostasis regulates proteins within the body and influences the fate of every protein from synthesis to degradation. Its failure results in a vicious cycle of pathological accumulation of protein aggregates, neuroinflammation and various forms of cellular stress that is widely implicated with the development of many neurodegenerative diseases including Parkinson's Disease, Alzheimer's and other diseases. rhCDNF (a biological protein) is Herantis' lead program and a clinical stage asset; and HER-096 (a synthetic peptide version of rhCDNF) is Herantis' follow-on program. CDNF is a natural protein that occurs naturally in the body whose natural role is to protect neurons by balancing and supporting proteostasis, thereby preventing and counteracting disease generating mechanisms. Herantis is taking this natural ability and harnessing it as a treatment for neurodegenerative disease. Both rhCDNF and HER-096, via their multimodal mechanism of action, have the potential to improve neuronal survival and stop the progression of Parkinson's and other neurodegenerative diseases with a significant therapeutic impact on the quality of patients' lives.

The shares of Herantis are listed on the Nasdaq First North Growth Market Finland and Nasdaq First North Growth Market Sweden.

For more information, please visit <https://www.herantis.com>

### **Forward-looking statements**

This company release includes forward-looking statements which are not historical facts but statements regarding future expectations instead. These forward-looking statements include without limitation, those regarding Herantis' future financial position and results of operations, the company's strategy, objectives, future developments in the markets in which the company participates or is seeking to participate or anticipated regulatory changes in the markets in which the company operates or intends to operate. In some cases, forward-looking statements can be identified by terminology such as "aim," "anticipate," "believe," "continue," "could," "estimate," "expect," "forecast," "guidance," "intend," "may," "plan," "potential," "predict," "projected," "should" or "will" or the negative of such terms or other comparable terminology.

By their nature, forward-looking statements involve known and unknown risks, uncertainties and other factors because they relate to events and depend on circumstances that may or may not occur in the future. Forward-looking statements are not guarantees of future performance and are based on numerous assumptions. The company's actual results of operations, including the company's financial condition and liquidity and the development of the industry in which the company operates, may differ materially from (and be more negative than) those made in, or suggested by, the forward-looking statements contained in this company release. Factors, including risks and uncertainties that could cause these differences include, but are not limited to risks associated with implementation of Herantis' strategy, risks and uncertainties associated with the development and/or approval of Herantis' drug candidates, ongoing and future clinical trials and expected trial results, the ability to commercialize drug candidates, technology changes and new products in Herantis' potential market and industry, Herantis' freedom to operate in respect of the products it develops (which freedom may be limited, e.g., by competitors' patents), the ability to develop new products and enhance existing products, the impact of competition, changes in general economy and industry conditions, and legislative, regulatory and political factors.

In addition, even if Herantis' historical results of operations, including the company's financial condition and liquidity and the development of the industry in which the company operates, are consistent with the forward-looking statements contained in this company release, those results or developments may not be indicative of results or developments in subsequent periods.