

# Herantis Pharma Provides R&D Update and Information About New Biomarker Program

Herantis Pharma Plc, Press Release, 26 October 2021 at 08:00 EEST

**Herantis Pharma Plc (“Herantis or the Company”)**, focusing on disease modifying therapies for debilitating neurodegenerative diseases, today hosts a live webinar providing an R&D update at 11:00 EEST/10:00 CEST with the company’s CSO, Dr. Henri Huttunen and COO, Antti Vuolanto.

## Highlights:

- Launch of Herantis’ novel biomarker-based program for our disease modifying assets
- Strong data on impact of rhCDNF on disease biomarkers including an update on clinical follow-up study
- Data on successful and impressive blood brain barrier (BBB) crossing of HER-096 in excess of 20%
- Essential role of CDNF in development and survival of dopamine neurons, without which neurons become dysfunctional and die
- Results from an animal model of Parkinson’s disease (HER-096) showing potent therapeutic effects with up to almost 70% improved neuronal survival compared to controls, strong reduction of alpha-synuclein levels, and normalization of brain inflammatory changes in Parkinson disease
- Update on non-invasive routes of administration for rhCDNF, specifically intranasal formulations
- Visibility of an \$8bn market opportunity, amidst the burden of what is now termed the Parkinsons pandemic

## Webinar Registration Information

Please register for the R&D Webinar via the following link: [Register Here](#)

“As a pure play CNS biotech company in 2021, we are very pleased with the progress we are making on identifying Parkinson’s Disease biomarkers, non-invasive administration routes, the data we have shown on blood brain barrier penetration, and the neuroprotective potential of our assets,” comments Craig Cook, CEO of Herantis. “Now, our focus is on shaping our development programs to further identify the biological and biomarker-based Parkinson’s Disease populations that will benefit the most from CDNF, as well as establish new and innovative research paths that fit our rhCDNF and HER-096 assets. Our newly assembled Scientific Advisory Board with world renowned Key Opinion leaders will play an intricate role, together with the Herantis team, to optimize and maximize our chances of success.”

## About CDNF

CDNF (Cerebral Dopamine Neurotrophic Factor) occurs naturally in the body to protect neurons by preventing and counteracting disease generating mechanisms. Herantis is taking this powerful natural ability and harnessing it into a treatment for neurodegenerative diseases. After nearly a decade of research, the company is beginning to see the fruits of those intensive and extensive research activities coming to actualization. This includes our biomarker data, blood brain barrier (BBB) penetration data, and our assets neuroprotection data. Herantis currently has two programs in development: the first program, rhCDNF (recombinant human CDNF), is a biotechnological protein that has been used safely in a successful Phase I study in patients with Parkinson’s Disease via direct intracranial administration and is now being developed and prepared for a follow-on Phase I study using intranasal and/or subcutaneous administration. The company’s second program, xCDNF (HER-096), is a small synthetic peptidomimetic version of the active area of CDNF protein. Herantis recently selected the lead compound, HER-096, to take into further development and IND enabling prior to entering the clinic.

## Summary of Today’s Webinar:

**BIOMARKERS** are becoming especially important in the development of CNS treatments due to the fact that biomarkers provide an early window into the onset of diseases, their progression, and the response to therapy, enabling a rapid and more efficient assessment of drug effect. This fact is now also being recognized by regulators giving equal consideration and importance to biomarkers as well as clinical observations (as evidenced by the recent approval of the first disease modifying drug for Alzheimer’s based on the biomarker beta amyloid, Biogen’s aducanumab), whereas previously only clinical observations were considered while biomarkers were marginal.

Biomarkers are a key component of Herantis' CNS clinical development programs for our CDFN (rhCDFN) and xCDFN (HER-096) assets. To maximize this effort, Herantis has formed a Scientific Advisory Board with leading experts in the field as announced yesterday. Recently, Dr. Kira Holmström, PhD., joined Herantis team as Head of Biomarker Development bringing over 15+ years of molecular and biomarker industry expertise in neurodegenerative diseases.

In the near-to-mid-term, we will focus on identifying and selecting key biomarkers for the continued development of rhCDFN and HER-096. This includes preclinical biomarker research, biomarker sample library analysis, and an observational biomarker study in human patients which will pave the road to formal clinical development studies in patients.

During 2021, a key focus of the company has been on the therapeutic effect of its assets on disease biomarkers. As a result, Herantis is well-positioned with unparalleled biomarker data for its assets, rhCDFN and HER-096, in Parkinson's Disease.

- **CDFN (rhCDFN):** The impact of rhCDFN on disease biomarkers has been established in patients from the Phase I study in Parkinson's Disease ([Press Release from 27 August 2020](#)), where it was observed that biomarkers in Cerebrospinal Fluid (CSF) change in response to rhCDFN treatment in some patients. Moreover, these changes also correlated with improvements in motor function and biological dopamine signals of these patients, an important observation. The biomarker signature from the Phase I study also notably suggests modulation of proteostasis in response to rhCDFN treatment, thus confirming its mechanism of action on this key system that fails in Parkinson's disease. In addition, independent research confirmed that there is a direct molecular interaction with alpha-synuclein, which is a key pathology of Parkinson's Disease and manifestation of failing proteostasis mechanisms.
- **xCDFN (HER-096):** Pre-clinical experiments with Herantis' lead candidate HER-096 continue to show strong effects on biomarkers of Parkinson's Disease, with an almost complete eradication of alpha-synuclein aggregates, a hallmark of Parkinson's Disease pathology. A similar effect was seen on neuroinflammation which is another key cause of damage in Parkinson's Disease. Additionally, HER-096 showed down regulation of key molecular markers of disease such as IRE1 (RNA-activated protein inositol requiring enzyme 1), ATF6 (Activating transcription factor 6) and PERK (Protein kinase RNA-like endoplasmic reticulum kinase). For most of these markers the impact was so profound as to almost normalize the levels of these markers of disease. This was observed in both preventative models of disease as well as therapeutic models of disease. Importantly, these effects correlated with a significant increase in dopamine neuronal survival, by up to a significant almost 70% versus controls in some experiments, reflecting significantly reduced cell death as a result of HER-096 treatment.

**BLOOD BRAIN BARRIER CROSSING:** Crossing the blood brain barrier (BBB) is notoriously difficult for drugs since it is designed to keep substances out of the brain and is the key reason for many failed drug development programs. In 2021, Herantis has made great progress in crossing the BBB with our assets, rhCDFN and HER-096:

- **xCDFN (HER-096):** In 2021, successful experiments showed that HER-096 can cross the BBB, 20% of HER-096 crossed the BBB following administration reaching therapeutic brain concentration via skin injection.
- **CDFN (rhCDFN):** In the later half of 2020, Herantis announced a strategic decision to pivot from invasive surgical administration (which was used in Phase I study) to a nasal spray route of administration (a more patient and physician friendly route of administration). We are focused on developing two intranasal formulations: a powder (together with a company Nanoform based in Finland); and a liquid (together with a company Medpharm based in UK). On 9 September 2021, Herantis announced positive results from the Proof of Concept (PoC) project in collaboration with Nanoform, which demonstrated that the nanoforming process was successfully applied to rhCDFN ([Press Release from 9 September 2021](#)). Both intranasal formulations are progressing on track. Next steps will include biodistribution studies to evaluate the ability to cross into the brain following nasal administration.

**NEUROPROTECTION AND MECHANISM OF ACTION:** The company has, via its own as well as independent research, continued to generate increasingly strong validation for the mechanism of action of CDNF (rhCDNF). Specifically, CDNF restores the key cellular systems Proteostasis and the Unfolded Protein Response pathway to reduce disease-driven stress that can trigger cell death and manifest as neurodegenerative diseases.

- **CDNF:** Independent research has demonstrated that CDNF is essential for enteric dopamine neuron development and survival. Dopaminergic neurons occur in highest concentration in brain and gut areas of body, hence the role of CDNF can be observed in both brain and gut dopamine neurons. Convincing research by <sup>1)</sup> Chalazonitis et al. and <sup>2)</sup> Lindahl et al., demonstrated that CDNF deficient mice show marked degeneration of gut dopamine neurons, thus supporting the key role of CDNF in dopaminergic neurons of Parkinson's patients.
- **xCDNF (HER-096):** Multiple pre-clinical experiments conducted in 2021 have confirmed that HER-096 is a very potent neuroprotective molecule. This was observed in preventative models where HER-096 is given at same time as disease is induced, as well as in therapeutic models where HER-096 is given after disease is well established. Both these scenarios represent key clinical questions that need to be answered for any Parkinson's Disease therapy in development. HER-096's neuroprotective effects consistently show between 50% - 75% improvement of dopaminergic neuronal survival versus non-treated control groups. Similar impressive results were seen in HER-096's ability to eliminate alpha-synuclein, a key pathology in Parkinson's Disease, to almost normal levels. This confirms that HER-096 has been successfully engineered to both cross the BBB as well as deliver potent neuroprotection, after being administered by simple skin injection.

<sup>1)</sup>Chalazonitis et al. CDNF is essential for enteric neuronal development, maintenance, and regulation of gastrointestinal transit. J. Comp. Neurol. 528: 2420-2444, 2020.

<sup>2)</sup>Lindahl M, Chalazonitis A, Palm E, Pakarinen E, Danilova T, Pham TD, Setlik W, Rao M, Vöikar V, Huotari J, Kopra J, Andressoo JO, Piepponen PT, Airavaara M, Panhelainen A, Gershon MD, Saarma M. [Cerebral dopamine neurotrophic factor-deficiency leads to degeneration of enteric neurons and altered brain dopamine neuronal function in mice.](#) Neurobiol Dis. 134: 104696, 2020.

**For more information, please contact:**

Julie Silber/Gabriela Urquilla

Tel: +46 (0)7 93 486 277/+46 (0)72-396 72 19

Email: [ir@herantis.com](mailto:ir@herantis.com)

**Certified Advisor: UB Securities Ltd, Finland: +358 9 25 380 225, Sweden: +358 40 5161400**

**Company website: [www.herantis.com](http://www.herantis.com)**

**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. CDNF (a biological protein) is Herantis' lead program and a clinical stage asset; and xCDNF (HER-096) (a synthetic peptide version of CDNF) 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 CDNF and xCDNF (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.