Herantis Announces Inconclusive Results from Phase II Study with Lymfactin in Breast Cancer Related Lymphedema®

Herantis Pharma Plc
Company release, inside information, 2 March 2021 at 2:00 p.m. Eastern European Time

Herantis Pharma Plc ("Herantis"), an innovative clinical stage biotech company pioneering new disease modifying and regenerative biologic and gene therapies, today announced that clinical trial results from its Phase II study investigating Herantis' patented gene therapy Lymfactin®, for the treatment of Breast Cancer Related Lymphedema (BCRL), were inconclusive. Lymfactin® is a unique gene therapy that induces expression of VEGF-C, an endogenous protein that is responsible for driving the growth and regeneration of lymphatic vessels. The primary purpose of the trial was to determine whether there was an additional benefit of Lymfactin® treatment in combination with lymph node transfer surgery, compared to surgery alone. While both treatment groups experienced clear clinical benefits, the trial did not establish additional treatment benefit for Lymfactin® in combination with surgery, compared to surgery alone.

The results unexpectedly showed differences between the treatment groups at the start of the study (baseline), in terms of arm volume and quality of life, making it unfeasible to draw conclusions on the treatment effect of Lymfactin® in combination with surgery, compared to surgery alone. In addition, the outcome measures used for the study were inconsistent which was surprising and made it difficult to accurately assess treatment response. These factors reflect the pioneering nature of the study in a novel indication where there will be inevitable learnings with regard to study design and suitable outcome measures to assess treatment effect.

Dr Anne Saarikko, Coordinating Principal Investigator of the study, commented "Herantis is at the forefront of finding a treatment for BCRL. This has been a ground-breaking study for the treatment of BCRL, and I commend the Herantis team for pushing the boundaries of science in an effort to help patients suffering from this debilitating condition. The overall results of the treatment appear promising for the majority of patients; however, we need to ascertain and assess the effect of Lymfactin® specifically, which has not been possible in this challenging study."

The key findings of the analysis at 12 months post treatment indicate that approximately half of the patients obtained a clinically meaningful response, over 25% reduction in the affected arm volume compared with the normal arm in both Lymfactin® and placebo treatment groups. Improvement in quality of life of most patients in the study was also seen across both treatment groups. However, for a meaningful statistical analysis to be conducted, it is essential that the two groups - placebo and active treatment groups - are comparable at baseline in terms of the primary outcome measures and other disease characteristics, which was not the case in this trial at the study start. The imprecision of the outcome measures further complicated demonstration of a therapeutic effect of Lymfactin®. The company will continue to analyse and review the data to gain additional insight from the study including the baseline differences, adequacy of dosing, outcome measures, measurement tools, other signals in the data, and other potentially applicable target indications. The company expects to be able to announce any further findings and decisions on the program in Q2 2021.

From a safety perspective, Lymfactin® was generally safe and well tolerated. Adverse events were mild and transient. The incidence of adverse events reported in patients treated with Lymfactin® was comparable to the incidence for patients in the placebo group.

Craig Cook CEO commented "We are very grateful to the patients who participated in this pioneering study of our innovative gene therapy Lymfactin® for the treatment of BCRL. While the efficacy of the overall treatment regime i.e. lymph node transfer surgery plus Lymfactin® – is encouraging, we are disappointed that the study design did not allow for meaningful conclusions to be drawn about Lymfactin® specifically. The novel nature of the Lymfactin® program generally, and this study specifically, means there have been a number of clear and important learnings, and we will now continue our analysis of the data and review of the strategic options for the program moving forward. In parallel, the

company's CDNF and xCDNF programs continue at pace, with the dedicated funds raised in recent fundraise December 2020 enabling planned development activities for these programs."

The study is a randomized, double-blinded, placebo-controlled, Phase II clinical trial conducted in 39 patients across 5 sites in Finland and Sweden. Patients selected according to strict inclusion criteria were enrolled into the study and randomized to receive either one dose of placebo or Lymfactin®, together with lymph node transfer surgery. The study was unblinded after all patients were monitored for 12 months post-surgery. Primary endpoints were volume reduction in the affected arm, changes in quality of life (QoL) and changes in lymphatic flow assessed by quantitative lymphoscintigraphy. The patients will continue to be monitored for efficacy and safety endpoints for 36 months and 60 months post-operation, respectively.

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About Lymfactin®
Lymfactin® is the world's first and only clinical stage gene therapy that repairs damages of the lymphatic system. It expresses the human growth factor VEGF-C, which is naturally associated with the development of lymphatic vessels. Based on preclinical studies, Lymfactin® triggers the growth of new functional lymphatic vasculature in the injured area and thus repairs the underlying cause of secondary lymphedema. The first target indication for Lymfactin® is Breast Cancer Associated Lymphedema; Herantis believes that Lymfactin® may also be suitable for the treatment of other forms of secondary lymphedema if its safety and efficacy are established in the first indication.

Lymfactin®, patented by Herantis, is based on the internationally renowned scientific research of academy professor Kari Alitalo and his research group, a national center of excellence at the University of Helsinki.

About Breast Cancer Associated Lymphedema
Approximately 20% of breast cancer patients who undergo axillary lymph node dissection develop secondary lymphedema: a progressive, disabling, and disfiguring disease that severely affects the quality of life. Symptoms include a chronic swelling of an upper limb, thickening and hardening of skin, loss of mobility and flexibility, pain, and susceptibility to secondary infections. Secondary lymphedema is currently treated with compression garments, special massage, and exercises. While these therapies may relief the symptoms in some patients, they do not address the underlying cause of lymphedema, which results from damage to the lymphatic system. There are currently no approved medicines for the treatment of secondary lymphedema.

About Herantis Pharma Plc
Herantis Pharma Plc is an innovative drug development company looking to break the boundaries of standard therapeutic approaches. Our regenerative medicine drug candidates include i. CDNF biological therapy that acts on the proteostatic mechanisms of disease for the treatment of Parkinson's disease and other neurodegenerative diseases, and ii. Lymfactin® VEGF-C gene therapy for restoring lymphatic structure and function for the treatment of oncology related secondary Lymphedema and other lymphatic based diseases. The Herantis programs are potentially disease modifying that treat the cause as well as symptoms of disease, and bring the innovation necessary to provide further treatment options in underserved diseases. The shares of Herantis are listed on the Nasdaq First North Growth Market Finland and Nasdaq First North Growth Market Sweden.

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.