Helsinn announces publication of anamorelin ROMANA 1 and ROMANA 2 Phase III studies in *The Lancet Oncology*

- ***Pivotal data from anamorelin ROMANA 1 and ROMANA 2 Phase III studies published in world-leading, peer-reviewed medical journal***
- ***Study showed anamorelin significantly improved lean body mass, body weight and symptom burden including appetite in NSCLC patients with cachexia***

Lugano, Switzerland, 23 February, 2016 – Helsinn, the Swiss pharmaceutical Group focused on building quality cancer care, today announces that on February 19th the journal, *The Lancet Oncology,* published the results from the pivotal ROMANA Phase III trials assessing efficacy and safety of the ghrelin receptor agonist anamorelin in patients with Cancer Anorexia-Cachexia in non-small cell lung cancer (NSCLC). The lead author was Dr. Jennifer Temel, from the Massachusetts General Hospital in Boston (USA).

The paper, "*Anamorelin in patients with non-small-cell lung cancer and cachexia (ROMANA 1 and ROMANA 2): results from two randomised, double-blind, phase 3 trials*", can be accessed here: [www.thelancet.com/journals/lanonc/onlinefirst] and an executive summary of the Lancet Oncology article is available below.

Cancer Anorexia-Cachexia is a frequent condition in patients with advanced cancer, in particular in those with lung cancer. A combination of reduced food intake and altered metabolism leads to loss of lean body mass and body weight in patients affected by this condition. There are few therapeutic options and no standard of care for the management of Cancer Anorexia-Cachexia. Despite the fact that some of the currently available drugs can improve patient's appetite or increase body weight, none can substantially affect lean body mass.

The ROMANA 1 and ROMANA 2 phase III studies clinically demonstrated that anamorelin significantly improved, in respect to placebo, lean body mass and body weight, in addition to symptom burden, including appetite, in NSCLC patients with Cancer Cachexia. No differences between patients treated with anamorelin or placebo were observed for handgrip strength, one

of the co-primary endpoint of the study. Improvements in patients' weight and symptom burden were rapid (as early as three weeks) and progressive, which is important in a debilitated population. Most participants in the trials were receiving chemotherapy, indicating that Cancer Anorexia-Cachexia can occur also in patients undergoing active treatment.

Ken Fearon, co-author of the paper, commented *"This represents a landmark study in providing a potential key building block for the development of a comprehensive approach for the supportive care of weight-losing cancer patients."*

Riccardo Braglia, Vice Chairman and Helsinn Group CEO, commented: "*Cancer Anorexia-Cachexia is a debilitating disease for which there are currently few treatment options available, making these findings relevant. At Helsinn, we are committed to helping to improve quality of life for people with cancer and we are pleased that this research has been recognized by* The Lancet Oncology*, medical journal.*"

Study design of the ROMANA trials

ROMANA 1 and ROMANA 2 were two international, double-blind, randomized, placebo-controlled Phase III trials evaluating the efficacy and safety of anamorelin in patients with Stage III/IV NSCLC and cachexia (≥5% weight loss within six months or BMI <20 kg/m^2). ROMANA 1 enrolled 484 patients and ROMANA 2 enrolled 495 patients. Patients were randomized (2:1) to 100 mg anamorelin or placebo, given daily orally for 12 weeks, and were permitted to receive chemotherapy while on study. Efficacy was assessed through the change from baseline over 12 weeks in the co-primary endpoints, lean body mass (measured by dual-energy X-ray absorptiometry) and handgrip strength, and in the secondary endpoints, which included body weight, and the anorexia-cachexia symptoms and concerns.

Key highlights from ROMANA 1 and 2

- Over 12 weeks, anamorelin significantly increased median lean body mass versus placebo in ROMANA 1 (0.99 vs -0.47 kg; p<0.001) and ROMANA 2 (0.65 vs -0.98 kg; p<0.0001); in both studies changes in handgrip strength were not different between patients receiving anamorelin or placebo.

- Anamorelin-treated patients also significantly improved compared to placebo Cancer Anorexia-Cachexia symptoms and concerns (ROMANA 1: 4.12 vs 1.92; p=0.0004; and ROMANA 2: 3.48 vs 1.34; p=0.0016), and significantly gained body weight (ROMANA 1: 2.20 vs 0.14 kg; p<0.0001; and ROMANA 2: 0.95 vs -0.57 kg; p<0.0001).

- There were no differences in grade 3-4 drug-related adverse events between study arms. Hyperglycemia was the most common grade 3-4 drug-related adverse event occurring in ≤1% of patients receiving anamorelin.

Lancet Oncology Executive Summary

- Background: Patients with advanced cancer frequently experience anorexia and cachexia, which are associated with reduced food intake, altered body composition, and decreased functionality. We assessed anamorelin, a novel ghrelin-receptor agonist, on cachexia in patients with advanced non-small-cell lung cancer and cachexia.

- Methods: ROMANA 1 and ROMANA 2 were randomised, double-blind, placebo-controlled phase 3 trials done at 93 sites in 19 countries. Patients with inoperable stage III or IV non-small-cell lung cancer and cachexia (defined as ≥5% weight loss within 6 months or body-mass index <20 kg/m^2) were randomly assigned 2:1 to anamorelin 100 mg orally once daily or placebo, with a computer-generated randomisation algorithm stratified by geographical region, cancer treatment status, and weight loss over the previous 6 months. Co-primary efficacy endpoints were the median change in lean body mass and handgrip strength over 12 weeks and were measured in all study participants (intention-to-treat population). Both trials are now completed and are registered with ClinicalTrials.gov, numbers NCT01387269 and NCT01387282.

- Findings: From July 8, 2011, to Jan 28, 2014, 484 patients were enrolled in ROMANA 1 (323 to anamorelin, 161 to placebo), and from July 14, 2011, to Oct 31, 2013, 495 patients were enrolled in ROMANA 2 (330 to anamorelin, 165 to

placebo). Over 12 weeks, lean body mass increased in patients assigned to anamorelin compared with those assigned to placebo in ROMANA 1 (median increase 0·99 kg [95% CI 0·61 to 1·36] vs –0·47 kg [–1·00 to 0·21], p<0·0001) and ROMANA 2 (0·65 kg [0·38 to 0·91] vs –0·98 kg [–1·49 to –0·41], p<0·0001). We noted no difference in handgrip strength in ROMANA 1 (–1·10 kg [–1·69 to –0·40] vs –1·58 kg [–2·99 to –1·14], p=0·15) or ROMANA 2 (–1·49 kg [–2·06 to –0·58] vs –0·95 kg [–1·56 to 0·04], p=0·65). There were no differences in grade 3–4 treatment-related adverse events between study groups; the most common grade 3–4 adverse event was hyperglycaemia, occurring in one (<1%) of 320 patients given anamorelin in ROMANA 1 and in four (1%) of 330 patients given anamorelin in ROMANA 2.

- Interpretation: Anamorelin significantly increased lean body mass, but not handgrip strength in patients with advanced non-small-cell lung cancer. Considering the unmet medical need for safe and effective treatments for cachexia, anamorelin might be a treatment option for patients with cancer anorexia and cachexia.

The print edition of the Lancet report will be made available in April 2016.

Notes for editors:

NSCLC

Non-small cell lung cancer accounts for roughly 85% of all lung cancer cases. Lung cancer has some of the poorest survival rates comparing to other types of cancer, based on epidemiological data, and is the most common form of cancer globally.

About anamorelin and ghrelin

Anamorelin is an investigational agent that has not yet been approved by any regulatory authority. The marketing authorization application is under review by the European Medicines Agency

Anamorelin HCl is an investigational selective, novel, orally active ghrelin receptor agonist that is under development for the treatment of Anorexia, Cachexia, and Unintended Weight Loss in NSCLC patients. Ghrelin is an endogenous peptide primarily secreted by the stomach. Upon

binding to its receptor, ghrelin stimulates multiple pathways in the positive regulation of body weight, lean body mass, appetite and metabolism.

The information discussed in this release is not intended to convey conclusions about its efficacy and safety.

About Helsinn Group

Helsinn is a privately owned cancer supportive care pharmaceutical group with an extensive portfolio of marketed products and a broad development pipeline. Since 1976, Helsinn has been improving the everyday lives of patients, guided by core family values of respect, integrity and quality, through a unique integrated licensing business model working with long standing partners in pharmaceuticals, medical devices and nutritional supplement products. Helsinn is headquartered in Lugano, Switzerland, with operating subsidiaries in Ireland and the US (Helsinn Therapeutics), a representative office in China, as well as a product presence in about 90 countries globally.

In 2016, our 40th anniversary year, you can meet representatives from Helsinn at:

- NCCN Annual Conference (Hollywood, FL, USA, 31 March-2 April)
- ASCO Annual Meeting (Chicago, USA, 3-7 June)
- MAASC Annual Meeting (Adelaide, Australia, 23-25 June)
- ChemOutsourcing Conference (Parsippany, New Jersey, 19-21 September)
- CPhI Worldwide (Barcelona, Spain, 4-6 October)
- ESMO Congress (Copenhagen, Denmark, 7-11 October)
- BioEurope (Köln, Germany, 4-6 November)

For more information, please visit www.helsinn.com

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