Helsinn publishes results from a secondary analysis of a Phase 3 trial in patients with CINV in *The Oncologist*

Lugano, Switzerland, January 4, 2023 - Helsinn Group ("Helsinn"), a fully integrated global biopharma company with a track record of over forty years of commercial execution and a strong focus in oncology and rare diseases, announces results from a secondary analysis of a Phase 3 multicenter pivotal trial in patients with breakthrough chemotherapy-induced nausea and vomiting (CINV) receiving antiemetic prophylaxis (oral or IV NEPA) have been published in *The Oncologist*.

The objectives of this analysis were to assess the rate of complete response (CR, no nausea/vomiting or rescue medications), and to evaluate the association between the duration of CINV in the first chemotherapy cycle and the risk of CINV in subsequent cycles in patients receiving chemotherapy.

Using data from a previously reported phase 3 trial, the analysis classified patients into 3 groups based on their response during the first chemotherapy cycle: CR, short-term CINV (1-2 days), and extended CINV (3-5 days). The analysis indicated that patients who experienced CR in their first cycle had a 93% or higher CR rates in subsequent cycles. Comparing patients with short-term CINV and extended CINV in cycle 1, recurrent CINV occurred in 30.6% and 69.5% of subsequent cycles, respectively ($p<0.001$). With close monitoring during the first chemotherapy cycle, clinicians can use the patient's response data to optimize antiemetic prophylaxis when extended CINV does occur.

Details of the publication:

- **Title:** "Duration of chemotherapy-induced nausea and vomiting (CINV) as a predictor of recurrent CINV in later cycles"
- **Authors:** Rudolph Navari, MD PhD; Gary Binder, MBA; Alex Molassiotis, PhD; Jørn

Herrstedt, MD; Eric J Roeland, MD; Kathryn J. Ruddy, MD MPH; Thomas W LeBlanc, MD; Dwight D Kloth, PharmD; Kelsey A Klute, MD; Eros Papademetriou, MA; Luke Schmerold, BS; Lee Schwartzberg, MD

- **Journal**: *The Oncologist*
- **Link**: Duration of Chemotherapy-Induced Nausea and Vomiting (CINV) as a Predictor of Recurrent CINV in Later Cycles | The Oncologist | Oxford Academic (oup.com)

Dr. Rudolph Navari, MD, PhD, hematologist oncologist, commented: "From the results of this analysis we can see that the duration of CINV in the first cycle of chemotherapy predicts CINV outcomes for the remainder of the patient's course. This may potentially have significant implications when treating patients in the future, meaning that clinicians should consider monitoring the duration of breakthrough CINV and optimizing antiemetic prophylaxis when this occurs."

About AKYNZEO® in the EU

AKYNZEO® is the first and only 5-HT_3 and NK_1 receptor antagonist fixed combination approved in adults for the prevention of acute and delayed nausea and vomiting associated with cisplatin-based highly emetogenic chemotherapy and moderately emetogenic chemotherapy. A single dose of AKYNZEO® given with dexamethasone has been shown to prevent chemotherapy-induced nausea and vomiting for up to 5 days.

For additional information please see the EU Summary of Product Characteristics.

About AKYNZEO® in the US

INDICATION

AKYNZEO® (netupitant 300mg/palonosetron 0.5mg) capsules was approved in October 2014 in the United States and is indicated in combination with dexamethasone in adults for the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of cancer chemotherapy, including, but not limited to, highly emetogenic chemotherapy.

AKYNZEO® (fosnetupitant 235mg/palonosetron 0.25) for injection was approved in April 2018 and

AKYNZEO® injection was approved in May 2020 in the United States. Each is indicated in combination with dexamethasone in adults for the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of highly emetogenic cancer chemotherapy.

Limitations of Use:

AKYNZEO® for injection and AKYNZEO® injection have not been studied for the prevention of nausea and vomiting associated with anthracycline plus cyclophosphamide chemotherapy.

AKYNZEO® is a combination of palonosetron, a serotonin-3 ($5\text{-}HT_3$) receptor antagonist, and netupitant or fosnetupitant, substance P/neurokinin-1 (NK_1) receptor antagonists: palonosetron prevents nausea and vomiting during the acute phase and netupitant/fosnetupitant prevents nausea and vomiting during both the acute and delayed phase after cancer chemotherapy.

IMPORTANT SAFETY INFORMATION

Warnings and Precautions:

Hypersensitivity reactions, including anaphylaxis, have been reported in patients receiving palonosetron, one of the components of AKYNZEO®, with or without known hypersensitivity to other 5-HT3 receptor antagonists.

Serotonin syndrome has been reported with 5-HT3 receptor antagonists alone but particularly with concomitant use of serotonergic drugs. Serotonin syndrome can be life threatening. Symptoms associated with serotonin syndrome may include the following combination of signs and symptoms: mental status changes, autonomic instability, neuromuscular symptoms, seizures, and gastrointestinal symptoms. Patients should be monitored for the emergence of serotonin syndrome, and if symptoms occur, discontinue AKYNZEO® and initiate supportive treatment. Patients should be informed of the increased risk of serotonin syndrome, especially if AKYNZEO® is used concomitantly with other serotonergic drugs.

Adverse Reactions:

Most common adverse reactions for AKYNZEO®: headache, asthenia, dyspepsia, fatigue, constipation and erythema.

Drug-drug Interactions:

Use with caution in patients receiving concomitant medications primarily metabolized by CYP3A4 isoenzyme. The plasma concentrations of CYP3A4 substrates can increase when co-administered with AKYNZEO®. The inhibitory effect on CYP3A4 can last for multiple days.

Dexamethasone doses should be reduced when given with AKYNZEO®. A more than two-fold increase in the systemic exposure of dexamethasone was observed 4 days after a single dose of netupitant or a single infusion of fosnetupitant.

Consider the potential effects of increased plasma concentrations of midazolam or other benzodiazepines metabolized via CYP3A4 (alprazolam, triazolam) when administering with AKYNZEO®. When administered with netupitant, the systemic exposure to midazolam was significantly increased.

Avoid concomitant use of AKYNZEO® in patients on chronic use of a strong CYP3A4 inducer such as rifampin as this may decrease the efficacy of AKYNZEO®.

Use in Specific Populations:

Avoid use of AKYNZEO® in patients with severe hepatic impairment, severe renal impairment, or end-stage renal disease.

Avoid use in pregnancy, limited data is available, may cause fetal harm.

For more information about AKYNZEO® please see the full US Prescribing Information

About Helsinn

Helsinn is a fully integrated global biopharma company headquartered in Lugano, Switzerland. It is focused on improving the lives of cancer patients all over the world with a leading position in cancer supportive care and a focus on cancer therapeutics and rare diseases.

Helsinn is a third-generation family-owned company, that since 1976 has been focused on improving the lives of patients, guided by core values of respect, integrity and quality. Helsinn's unique business model enables it to in-license or acquire assets at a late stage of development. It has a commercial presence in 190 countries either directly, with operating subsidiaries in the U.S. and China, or via its network of long-standing trusted partners. Helsinn also has a fully integrated supply chain and product development through its subsidiary in Ireland, Helsinn Birex

Pharmaceuticals Ltd.

Helsinn plays an active and central role in promoting social transformation in favor of people and the environment. Sustainability is at the heart of everything we do, which is reinforced in the company's strategic plan by a commitment to sustainable growth.

To learn more about Helsinn please visit: www.helsinn.com

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