New data on Helsinn's oncology pipeline presented at American Society of Clinical Oncology (ASCO) Annual Meeting 2022

Lugano, Switzerland, June 02, 2022 - Helsinn Group ("Helsinn"), a fully integrated, global biopharma company with a diversified pipeline of innovative oncology assets, announces its participation in the upcoming 2022 American Society of Clinical Oncology (ASCO) Annual Meeting which will be held from 3-7 June.

In alignment with Helsinn's new Fully Integrated Target Therapy (FITT) strategy in oncology, two abstracts have been accepted for poster presentation.

The first abstract shares results of a preclinical study exploring the brain penetrability of vepafestinib (TAS0953/HM06), Helsinn's investigational oral treatment targeting rearranged during transfection (RET) abnormalities in solid tumors.

Title: **Comparison of TAS0953/HM06 and selpercatinib in RET Fusion-driven Preclinical Disease Models of Intracranial Metastases**

- Author: Igor Odintsov, MD, Memorial Sloan Kettering Cancer Center
- Session: Central Nervous System Tumors
- Abstract ID: 2024

The second abstract provides an overview of the ongoing PROOF 301 trial of infigratinib, a kinase inhibitor targeting cancers driven by fibroblast growth factor receptor 2 (*FGFR2)* fusions or other rearrangements. Details are as follows:

Title: **PROOF 301: a multicenter, open-label, randomized, phase 3 trial of infigratinib vs gemcitabine + cisplatin in patients with advanced cholangiocarcinoma with an *FGFR2* gene fusion/rearrangement**

- Author: Ghassan K. Abou-Alfa, MD, MBA, Memorial Sloan Kettering Cancer Center, Weill Cornell Medical College

- Session: Gastrointestinal Cancer—Gastroesophageal, Pancreatic, and Hepatobiliary
- Abstract ID: TPS4171

Sergio Cantoreggi, Helsinn Group Chief Scientific Officer and Head of R&D, commented: *"We are excited that the abstracts on two of our investigational products, vepafestinib and infigratinib, have been accepted for presentation at ASCO. In line with our Fully Integrated Targeted Therapy strategy, we are dedicated to progressing our pipeline of products to treat rare oncological diseases. More broadly, we are increasingly convinced of the importance of adequate screening for genetic alterations, through the use of comprehensive biomarker testing, to expand disease treatment options, thus ensuring that patients can receive the most appropriate and targeted treatment."*

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 an innovative pipeline of cancer therapeutics.

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. It operates a unique licensing business model with integrated drug development and manufacturing capabilities. Helsinn 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. Corporate social responsibility 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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About vepafestinib (TAS0953/HM06)

Vepafestinib (also known as TAS0953/HM06 in partnership with Taiho Pharmaceutical) is an investigational, potent, orally administered, highly selective RET inhibitor[1,2]. Relative to first generation RET inhibitors, vepafestinib is pharmacologically distinct, exhibits a distinct binding mode to RET, and has shown evidence of enhanced brain penetrability characteristics in preclinical models[3]. Vepafestinib is currently being evaluated in a phase 1 /2 study (the margaRET study, NCT04683250) in individuals with advanced solid cancers with RET abnormalities, including those resistant to first-generation selective RET inhibitors. Taiho and Helsinn signed a co-development and commercialization agreement for TAS0953/HM06 in 2017 and will continue to pursue together all preclinical, clinical and CMC developments.

About RET

RET is a transmembrane receptor tyrosine kinase. Abnormalities in the RET gene, such as fusions and point mutations, are oncogenic drivers of multiple human cancers. RET fusions are present in 1-2 % of patients with non-small cell lung cancer (NSCLC) and are associated with a high incidence of brain metastasis at diagnosis. Patients are typically young and non-smokers. Although treatment for these patients has significantly improved in recent years, acquired resistance to first generation RET inhibitors has emerged. Overcoming this resistance and addressing the CNS progression in these patients are important areas of unmet need[4,5].

About infigratinib

Infigratinib (BGJ398) is an oral, selective, small molecule kinase inhibitor of FGFR 1, 2, and 3. Infigratinib has received regulatory approval in the USA, Canada, and Australia for the treatment of adults with previously treated locally advanced or metastatic cholangiocarcinoma (bile duct cancer) with a *FGFR2* fusion or rearrangement. All three approvals were conditional and will require further evidence of efficacy. (See below for full US FDA-approved indication). The therapy is currently under investigation as a potential first-line treatment for adult patients with unresectable locally advanced or metastatic cholangiocarcinoma with *FGFR2* fusion/rearrangement (PROOF 301 Trial, NCT03773302), in the adjuvant setting for adult patients with invasive urothelial carcinoma (bladder cancer) with susceptible *FGFR3* genetic alterations

(PROOF 302 trial, NCT04197986), and in pediatric patients with advanced solid and central nervous system tumors with selected *FGFR1-3* alterations (NEWEL Trial, NCT05222165).

U.S. Indication and Important Safety Information for TRUSELTIQ® (infigratinib)

TRUSELTIQ® (infigratinib) is indicated for the treatment of adults with previously treated, unresectable, locally advanced or metastatic cholangiocarcinoma with a *FGFR2* fusion or other rearrangement as detected by an FDA-approved test.

Accelerated approval was granted based on overall response rate and duration of response. Continued approval for this indication may be contingent upon verification of clinical benefit in confirmatory trial(s).

The recommended dosage of TRUSELTIQ is 125 mg (one 100 mg capsule and one 25 mg capsule) orally once daily for 21 consecutive days followed by 7 days off therapy, in 28-day cycles.

Warnings and precautions

- **Ocular toxicity**: Retinal pigment epithelial detachment (RPED), which may cause blurred vision, occurred in 11% of 351 patients treated with TRUSELTIQ, including patients with asymptomatic RPED, with a median onset of 26 days. Perform comprehensive ophthalmological exam including optical coherence tomography prior to initiating, at 1 month, at 3 months, and then every 3 months during treatment with TRUSELTIQ. Urgently evaluate patients for onset of visual symptoms and follow up every 3 weeks until resolved or TRUSELTIQ is discontinued. Withhold TRUSELTIQ as recommended. Dry eye occurred in 29% of 351 patients; treat with ocular demulcents as needed
- **Hyperphosphatemia and soft tissue mineralization**: Hyperphosphatemia, which can lead to soft tissue mineralization, cutaneous calcinosis, non-uremic calciphylaxis, vascular calcification, and myocardial calcification, occurred in 82% of 351 patients treated with TRUSELTIQ, with a median time to onset of 8 days (range 1-349); 83% of 351 patients treated with TRUSELTIQ received phosphate binders. Monitor for hyperphosphatemia throughout treatment. Initiate phosphate-lowering therapy for serum phosphate >5.5 mg/dL; withhold TRUSELTIQ and

initiate phosphate-lowering therapy for serum phosphate >7.5 mg/dL; withhold, reduce the dose, or permanently discontinue TRUSELTIQ based on duration and severity of hyperphosphatemia

- **Embryo-fetal toxicity**: TRUSELTIQ can cause fetal harm. Advise pregnant women of the potential risk to the fetus; advise females of reproductive potential and men who are partnered with women of reproductive potential to use effective contraception during treatment with TRUSELTIQ and for 1 month after the final dose.

Adverse reactions

- **Most common adverse reactions (incidence ≥20%, all grades)**: nail toxicity, stomatitis, dry eye, fatigue, alopecia, palmar-plantar erythrodysesthesia syndrome, arthralgia, dysgeusia, constipation, abdominal pain, dry mouth, eyelash changes, diarrhea, dry skin, decreased appetite, blurred vision, and vomiting.
- **Most common laboratory abnormalities (incidence ≥20%, all grades)**: increased creatinine, increased phosphate, decreased phosphate, increased alkaline phosphatase, decreased hemoglobin, increased alanine aminotransferase, increased lipase, increased calcium, decreased lymphocytes, decreased sodium, increased triglycerides, increased aspartate aminotransferase (AST), increased urate, decreased platelets, decreased leukocytes, decreased albumin, increased bilirubin, and decreased potassium.

Drug interactions

- **CYP3A inhibitors**: Avoid use with strong and moderate CYP3A inhibitors
- **CYP3A inducers**: Avoid use with strong and moderate CYP3A inducers
- **Gastric acid–reducing agents**: Avoid coadministration with proton pump inhibitors, histamine-2 receptor antagonists (H2RA), and locally acting antacids. If coadministration of H2RA or locally acting antacids cannot be avoided, separate TRUSELTIQ administration
    - H2RA: Take TRUSELTIQ 2 hours before or 10 hours after
    - Locally-acting antacid: Take TRUSELTIQ 2 hours before or 2 hours after

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Dosage and administration

- **Prior to initiating TRUSELTIQ**: Confirm FGFR2 fusion or rearrangement; perform comprehensive ophthalmic exam including OCT; confirm negative pregnancy test in females of reproductive potential.
- **Starting dose**: Take TRUSELTIQ orally once daily on Days 1-21 of 28-day cycles; continue treatment until disease progression or unacceptable toxicity. Take TRUSELTIQ on an empty stomach with a glass of water at least 1 hour before or 2 hours after food at approximately the same time each day.
    - No renal or hepatic impairment
        - 125 mg (one 100 mg capsule and one 25 mg capsule)
    - Mild and moderate renal impairment (creatinine clearance 30-89 mL/min)
        - 100 mg (one 100 mg capsule)
    - Mild hepatic impairment (total bilirubin >upper limit of normal [ULN] to 1.5 x ULN or AST > ULN)
        - 100 mg (one 100 mg capsule)
    - Moderate hepatic impairment (total bilirubin >1.5 to 3 x ULN with any AST)
        - 75 mg (three 25 mg capsules)
- **Dose modification**: Consult the TRUSELTIQ full Prescribing Information for dose modifications and monitoring recommendations for RPED, hyperphosphatemia, and other Grades 3-4 adverse reactions.

For additional information, please see the:

U.S. Full Prescribing Information for TRUSELTIQ

Canada Patient Medication Information for TRUSELTIQ™ infigratinib capsules

Australia Product Information for TRUSELTIQ™ infigratinib hard capsules

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About Cholangiocarcinoma (CCA)

CCA represents an aggressive group of malignancies that form in the bile ducts. Although rare in most countries (with a worldwide estimated incidence of <6 per 100,000 people), the incidence of this malignancy is increasing worldwide. Because the disease is usually asymptomatic at early-stages, diagnosis may be delayed until advanced stages, when CCA typically presents as locally advanced or metastatic disease. Despite continuing advances in treatments, the prognosis for this disease remains poor, with a 5-year survival rate of 7-20%[9]. Cholangiocarcinoma is currently classified into intrahepatic and extrahepatic, on the basis of the anatomical site of origin. *FGFR2* alterations are present in approximately 10-16%[6,7] of CCA patients with intrahepatic disease and represent potential targets for treatments.[8,9]

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