Juniper Biologics signs exclusive license agreement with Helsinn for infigratinib (INN) for the emerging markets*

Lugano, Switzerland, and Singapore, 04 May 2022 – Juniper Biologics Pte Ltd , a science-led healthcare company focused on researching, developing and commercializing novel therapies, and Helsinn Group, a fully integrated, global biopharma company with a diversified pipeline of innovative oncology assets and strong track-record of commercial execution, announced today the signing of an exclusive license agreement to develop and commercialise infigratinib (INN) in Australia, New Zealand, Southeast Asia and certain markets in the Middle East and Africa (see full list below) for the treatment of adults with previously treated, unresectable locally advanced or metastatic cholangiocarcinoma (CCA) with a fibroblast growth factor receptor 2 (FGFR2) fusion or other rearrangement.

In 2021 infigratinib obtained accelerated approval from the U.S. Food and Drug Administration (FDA) under the brand name "TRUSELTIQ"® for the treatment of adults with previously treated, unresectable locally advanced or metastatic cholangiocarcinoma with a fibroblast growth factor receptor 2 (*FGFR2*) fusion or other rearrangement as detected by an FDA-approved test. This indication is based on overall response rate and duration of response. Additionally, infigratinib received conditional approval by Health Canada and provisional approval by the Therapeutics Goods Association in Australia for the treatment of adults with previously treated, unresectable locally advanced or metastatic cholangiocarcinoma with a *FGFR2* fusion or other rearrangement. Continued approval in the U.S., Canada and Australia for this indication may be contingent upon verification and description of clinical benefit in confirmatory trial(s).

Infigratinib is not FDA-, Health Canada- or Therapeutics Goods Association-approved for any other indication in the United States, Canada and Australia, and is not approved for use by any other health authority.

Raman Singh, CEO of Juniper Biologics, **commented**: "The acquisition of infigratinib is an important addition to our oncology portfolio and a much-needed treatment for patients whose cancer has spread or cannot be removed by surgery. Our mission is to increase access to proven

treatments and we trust that infigratinib will help advance the treatment of patients in markets, where there remains an unmet patient need."

Giorgio Calderari, Helsinn CEO commented: "This agreement with Juniper is another example of our Fully Integrated Targeted Therapy (FITT) Strategy in action as we continue to widen our network of partners for infigratinib. Helsinn's renewed strategic focus is on developing highly innovative oncology assets to address unmet needs, and this license agreement with our trusted partner, Juniper Biologics, will ensure that this important treatment is accessible to patients in Australia, Southeast Asia and certain markets in Middle East and Africa."

*The full list of countries covered by the license agreement includes: Algeria, Angola, Australia, Bahrain, Brunei, Cambodia, Egypt, India, Indonesia, Ivory Coast, Jordan, Kenya, Kuwait, Laos, Lebanon, Libya, Malaysia, Mauritius, Morocco, Myanmar, Nepal, New Zealand, Nigeria, Oman, Pakistan, Philippines, Qatar, Saudi Arabia, Seychelles, Singapore, South Africa, South Korea, Taiwan, Tanzania, Thailand, Tunisia, Sri Lanka, United Arab Emirates, Vietnam, Zimbabwe.

About Infigratinib

Infigratinib is an orally administered, selective, ATP-competitive, kinase inhibitor of FGFR 1, 2, and 3. The therapy is currently under investigation as a potential first-line treatment for individuals with unresectable locally advanced or metastatic cholangiocarcinoma (bile duct cancer) with *FGFR2* fusion/rearrangement and in the adjuvant setting for individuals with invasive urothelial carcinoma (bladder cancer) with susceptible *FGFR3* genetic alterations.

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 <20%. *FGFR2* genetic alterations are present in approximately 15% to 20% of CCA patients and represent potential targets for

treatments.[1,2]

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 fibroblast growth factor receptor 2 (*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

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

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.

For more information, please visit www.Helsinn.com and follow us on Twitter and LinkedIn.

About Juniper Biologics

Backed by The Sylvan Group, Juniper Biologics is a science-led healthcare company focused on delivering novel therapies to improve the health and quality of life of patients, by building a growing presence in Oncology, Rare/Orphan Diseases and Gene Therapy. It was founded on a vision to provide treatments for unmet medical needs focused on specialist therapy areas in which it can make the most difference. Through bold and transformative science, Juniper Biologics is committed to creating possibilities that have the potential to become the next generation of life-changing medicines for patient communities in China, Japan, Asia, Australia, New Zealand, Middle East and Africa.

References

[1]Banales, J., Cardinale, V., Carpino, G. et al. Cholangiocarcinoma: current knowledge and future perspectives consensus statement from the European Network for the Study of Cholangiocarcinoma (ENS-CCA). Nat Rev Gastroenterol Hepatol 13, 261–280 (2016). https://doi.org/10.1038/nrgastro.2016.51

[2]Banales, J.M., Marin, J.J.G., Lamarca, A. et al. Cholangiocarcinoma 2020: the next horizon in mechanisms and management. Nat Rev Gastroenterol Hepatol 17, 557–588 (2020). https://doi.org/10.1038/s41575-020-0310-z

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