Press Release
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Medivir's phase 1 study of fostrox monotherapy published in Journal of Hepatocellular Carcinoma

- *The study provides clinical proof-of-concept for fostrox monotherapy in patients with cancer in the liver.*
- *The results show that fostrox is safe and tolerable with preliminary anti-tumor activity.*
- *Confirmation of fostrox' liver-targeted mechanism inducing DNA damage selectively in tumor cells.*

Stockholm, Sweden — Medivir AB (Nasdaq Stockholm: MVIR), a pharmaceutical company focused on developing innovative treatments for cancer in areas of high unmet medical need, today announced that the phase 1 study of fostrox monotherapy in patients with cancers in the liver has been published in the Journal of Hepatocellular Carcinoma (online first doi: https://doi.org/10.2147/JHC.S481410). The title of the article is "*A phase 1a/1b study of fostroxacitabine bralpamide (fostrox) monotherapy in hepatocellular carcinoma and solid tumor liver metastases*", author Plummer R et al. Fostrox is currently in the final phase of the ongoing phase 1b/2a combination study with Lenvima in advanced liver cancer.

The published study evaluated safety and preliminary efficacy of fostrox as a novel, oral drug candidate designed to maximise exposure in the liver while minimizing systemic adverse events. The study established safety and tolerability with clinical proof-of-concept for fostrox monotherapy, including biopsy confirmed selective induction of DNA damage in tumor cells.

"Primary liver cancer (HCC) has a particularly poor prognosis, and the incidence is projected to increase dramatically, attributed to life style factors such as obesity and fatty liver disease. Despite progress in development of new treatments, there are currently no approved second line treatments in liver cancer post immunotherapy. Fostrox, with its liver-targeted mechanism has, in this first monotherapy study, shown to be safe and tolerable with preliminary anti-tumor activity", says Dr Jeff Evans, Beatson West of Scotland Cancer Centre, one of the investigators in the study.

Study results confirmed that fostrox had a liver targeted distribution. Most patients could stay on the recommended phase 2 dose of 40 mg without dose modification or discontinuation. In liver cancer patients, the clinical benefit rate was 63%, establishing preliminary efficacy with fostrox monotherapy in patients that had exhausted all approved treatment options. The data supported the next step in clinical development of fostrox in combination with other modes of action in HCC.

"In primary liver cancer, it is critical to maximize the anti-tumor effect locally in the liver as the combination of tumor burden and underlying liver disease increases the risk of liver failure. Fostrox has been designed with this challenge in mind and the study results confirm a liver-directed delivery where fostrox induces DNA damage selectively in tumors cells, to ensure optimal efficacy and safety.

This targeted mechanism is unique to fostrox and enables patients to stay on treatment long-term as it avoids harming healthy liver cells. The data reinforces our confidence in fostrox as a potential treatment option for patients with advanced liver cancer. Fostrox in combination with Lenvima is currently being investigated in a phase 1b/2a study", says Dr. Pia Baumann, CMO at Medivir.

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About fostrox
Fostrox is a liver-targeted inhibitor of DNA replication that delivers the cell-killing compound selectively to the tumor while minimizing the harmful effect on normal cells. This is achieved by coupling an active chemotherapy (troxacitabine) with a prodrug tail. This design enables fostrox to be administered orally and travel directly to the liver where the active substance is released locally in the liver. With this unique mechanism, fostrox has the potential to become the first liver-targeted, orally administered drug that can help patients with various types of liver cancer. A phase 1b monotherapy study with fostrox has been completed and a phase 1b/2a combination study in HCC is ongoing where it has shown encouraging anti-cancer efficacy with a good safety and tolerability profile (ref Chon et al., ESMO 2024, Poster 986).

About primary liver cancer
Primary liver cancer is the third leading cause of cancer-related deaths worldwide. Hepatocellular carcinoma (HCC) is the most common cancer that arises in the liver and it is the fastest growing cancer in the USA. Although existing therapies for advanced HCC can extend the lives of patients, treatment benefits are insufficient and death rates remain high. There are approximately 660,000 patients diagnosed with primary liver cancer per year globally and current five-year survival is less than 20 percent [1], [2]. HCC is a heterogeneous disease with diverse etiologies, and lacks defining mutations observed in many other cancers. This has contributed to the lack of success of molecularly targeted agents in HCC. The limited overall benefit, taken together with the poor overall prognosis for patients with intermediate and advanced HCC, results in a large unmet medical need.

1) Rumgay et al.,European Journal of Cancer 2022 vol.161, 108-118.
*2) Yang, J.D., Hainaut, P., Gores, G.J. et al. A global view of hepatocellular carcinoma: trends, risk, prevention and management. Nat Rev Gastroenterol Hepatol **16**, 589–604 (2019).*

About Medivir
Medivir develops innovative drugs with a focus on cancer where the unmet medical needs are high. The drug candidates are directed toward indication areas where available therapies are limited or missing and there are great opportunities to offer significant improvements to patients. Medivir is focusing on the development of fostroxacitabine bralpamide (fostrox), a drug candidate designed to selectively treat cancer cells in the liver and to minimize side effects. Collaborations and partnerships are important parts of Medivir's business model, and the drug development is conducted either by Medivir or in partnership. Medivir's share (ticker: MVIR) is listed on Nasdaq Stockholm's Small Cap list. www.medivir.com.