Press Release

iOnctura initiates Phase Ib pancreatic cancer trial of next-generation autotaxin inhibitor IOA-289

Geneva, Switzerland, 8 December 2022 -- iOnctura SA a clinical-stage biotech developing selective cancer therapies against targets that play critical roles in multiple tumor survival pathways, announces today the first patient has been dosed in a Phase Ib clinical trial of IOA-289 in metastatic pancreatic cancer.

"We are excited to progress clinical development of our autotaxin (ATX) inhibitor IOA-289, the second most advanced product in our pipeline," said Catherine Pickering, PhD, CEO of iOnctura. "Our preclinical research has uncovered a central role for ATX as a tumor survival factor, especially in highly fibrotic malignancies such as pancreatic, liver, colorectal, ovarian and breast cancers. To our knowledge, this is the first time an ATX inhibitor will be investigated in cancer patients. The learnings from this study will serve as a prototype to explore the therapeutic potential of IOA-289 in further fibrotic cancers."

The Phase Ib AION-02 study (NCT05586516) is a dose-escalation study of IOA-289 in combination with standard-of-care gemcitabine/nab-paclitaxel chemotherapy in first-line metastatic pancreatic cancer. Patients will be dosed with IOA-289 monotherapy for 7 days before commencing combination treatment of IOA-289 and chemotherapy.

Fibrotic cancers, including pancreatic cancer, are characterized by the deposition of thick layers of extracellular matrix containing collagen fibers and pro-tumorigenic factors. This microenvironment impedes the entry of immune cells and drugs, making the tumors difficult to treat.

"IOA-289 is an orally dosed small molecule that has been shown preclinically to have a multi-pronged approach to treating cancer, acting directly to prevent proliferation of tumor cells and indirectly to potentiate the actions of the immune system and chemotherapy in the fibrotic microenvironment." said David Brindley, Professor of Biochemistry, University of Alberta, and member of iOnctura's clinical advisory board. "We hypothesize that the lead-in of IOA-289 will reduce the expression of collagen and other pro-tumorigenic secreted factors rendering the tumor microenvironment susceptible to chemotherapy and unveiling the tumor to the immune system."

The trial's primary endpoint is to evaluate the safety and tolerability of the ascending doses of IOA-289. Secondary endpoints include biomarker changes and efficacy endpoints. The trial will be conducted in sites in Italy and the UK. The principal investigators of the trial are Professor Davide Melisi, University of Verona, Professor Michele Maio, University of Siena and Professor Jeff Evans, University of Glasgow.

IOA-289 is the first autotaxin (ATX) inhibitor in clinical development for cancer. It is an oral small molecule non-competitive inhibitor with novel binding chemistry and a safe clinical profile. It has been shown that inhibiting ATX with IOA-289 directly prevents the proliferation of cancer cells[1]. Furthermore, IOA-289 interrupts resistance to cancer therapy by reducing fibrotic scar tissue, unveiling the tumor and enabling the immune system to recruit infiltrating lymphocytes into the tumor[2]. Thanks to this multi-pronged mode of attack, IOA-289 reduced tumor burden in mouse pancreatic cancer models[1].

Pancreatic cancer (PDAC): Pancreatic ductal adenocarcinoma (PDAC) is the most common form of pancreatic cancer accounting for approximately 90% of cases. PDAC has a poor prognosis, with less

than 5% of patients surviving beyond five years after diagnosis. There are over 50,000 diagnoses of pancreatic cancer each year in the United States and over 65,000 in the EU5.

iOnctura SA is a clinical-stage biotech developing selective cancer therapies against targets that play critical roles in multiple tumor survival pathways such as cellular proliferation; escape from immune detection; and drug resistance. iOnctura's pioneering approach to drug development is expected to offer significant clinical benefits over the traditional approach of targeting a single pathway alone. iOnctura has progressed two therapeutic candidates into mid-stage clinical development: IOA-244, a highly selective allosteric inhibitor of PI3Kδ; and IOA-289, a highly selective, non-competitive autotaxin (ATX) inhibitor. iOnctura is backed by specialist institutional investors including M Ventures, Inkef Capital, VI Partners, Schroders Capital, and 3B Future Health Fund.

- ENDS -

Contacts

iOnctura	**Press Relations**
Catherine Pickering	Chris Maggos
Chief Executive Officer	BioConfidant Sàrl
T : +41 79 952 72 52	T: +41 79 367 6254
E: c.pickering@iOnctura.com	E: maggos@bioconfidant.ch