

Press Release

iOnctura data at AACR demonstrates unique mechanism of action for clinical stage autotaxin inhibitor IOA-289

Geneva, Switzerland, 8 April 2022: iOnctura SA, a clinical-stage oncology company targeting core resistance and relapse mechanisms at the tumor-stroma-immune interface, has preclinical data that shows its autotaxin inhibitor IOA-289 both inhibits pancreatic cells directly and inhibits the cancer-promoting activity of secreted factors from Cancer-Associated Fibroblasts (CAFs). The data will be shared via a poster (#2636) at the annual meeting of the American Association for Cancer Research (AACR) taking place on April 8-13, 2022 in New Orleans, Louisiana.

Autotaxin (ATX) is a secreted glycoprotein that hydrolyzes Lysophosphatidylcholine (LPC) to Lysophosphatidic Acid (LPA). LPA is a tumor cell growth activator and survival promotor. The AACR presentation demonstrates that by preventing LPA production, IOA-289 has a direct effect on pancreatic cancer cell lines (PDAC cells), inhibiting their growth *in vitro*.

LPA also modulates the tumor stroma which enables tumors to evade host immunity and impairs patients' responses to therapy. Cancer Associated Fibroblasts (CAFs) are particularly important drivers of this effect and are responsible for supporting and promoting the growth of cancer cells via the secretion of soluble mediators such as lipids (eg LPC) and cytokines. iOnctura's data shows that addition of IOA-289 to CAF cultures inhibits the ability of these secreted factors to promote cancer cell growth *in vitro*. Further experiments with activated fibroblasts show that IOA-289 inhibits IL-6 and PAI-1 secretion, and likely contributes to the *in vivo* anti-tumorigenic nature of IOA-289.

These results provide further evidence for the mode of action of IOA-289 which acts directly on tumor cells and also modulates the immunosuppressive fibrotic microenvironment. IOA-289 represents a novel therapeutic strategy for the treatment of highly fibrotic, immunosuppressive ("cold") cancer indications such as pancreatic cancer that are resistant to therapy. A Phase I clinical study of IOA-289 in pancreatic cancer is in planning.

The poster presentation (#2636) at AACR is entitled "Targeting Autotaxin to Suppress Stromal Signaling in the Tumor Microenvironment to Improve Outcome to Therapy in Fibrotic Tumor Types." The poster will be presented on Tuesday Apr 12, 2022 between 9:00 AM and 12:30 PM in New Orleans Convention Center, Exhibit Halls D-H, Poster Section 24. The abstract is available in the AACR Online Proceedings planner and will also be published in the online supplement to the AACR journal Cancer Research approximately eight weeks after the AACR annual meeting.

The e-poster presentation will be available on [iOnctura's website](#) following the meeting.

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iOnctura SA is clinical stage oncology company targeting core resistance and relapse mechanisms at the tumor-stroma-immune interface. iOnctura's best-in-class drug development programs combine immune-mediated and direct anti-tumor activity to deliver molecules with superior clinical efficacy and safety in oncology. Its lead program, IOA-244 is the only semi-allosteric PI3K δ specific, orally dosed, small molecule inhibitor that is being developed in solid and hematological malignancies to address tumor and stroma induced immune suppression. IOA-244 is currently in Part B of a Phase 1 study. iOnctura's second program, IOA-289, is an oral small molecule that inhibits the cross-talk between the tumor and its stroma and is in a Phase 1 clinical study. iOnctura is backed by blue chip investors including M Ventures, Inkef Capital, VI Partners, Schrodgers Capital, and 3B Future Health Fund. For more information, please visit [iOnctura's website](#).

IOA-289, originally licensed from Cancer Research UK, is a next generation oral small molecule autotaxin inhibitor that has been investigated in healthy volunteers in study AION 01 trial (ClinicalTrials.gov Identifier: NCT05027568). A phase 1 clinical study in pancreatic cancer patients is in preparation. iOnctura has undertaken extensive validation of the autotaxin inhibition mechanism in multiple solid tumor preclinical models.

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.