

iOnctura to present at ASCO encouraging Phase Ib refractory uveal melanoma data for first semi-allosteric PI3K δ inhibitor, IOA-244

Geneva, Switzerland, 17 May 2022: [iOnctura SA](#), a clinical-stage oncology company targeting key resistance mechanisms in solid tumors, announced today that it will present Phase Ib data on its lead pipeline asset, IOA-244, the highly differentiated novel phosphoinositide 3-kinase delta (PI3K δ) inhibitor, at the 2022 ASCO (American Society of Clinical Oncology) Annual Meeting, taking place June 3-7 in Chicago.

“We believe IOA-244 has a wider therapeutic window than other molecules in the PI3K δ inhibitor class because of its unique semi-allosteric binding properties,” said Catherine Pickering, PhD, CEO of iOnctura. “The data presented at ASCO will show that IOA-244 has potentially best-in-class tolerability and impressive overall survival in refractory uveal melanoma patients. We are looking forward to presenting the data and accelerating development of IOA-244 to treat uveal melanoma and other solid tumors.”

High expression of PI3K δ in both cancer cells and in the tumor immune landscape is a contributing factor to many solid tumor types escaping the host’s immune response. This is achieved by tumors, in part, through PI3k δ -mediated upregulation of T regulatory (Treg) cells, making the tumors “cold”, or difficult to detect by the body’s immune system. IOA-244 inhibition of PI3k δ blocks proliferation of Treg cells, thus making “cold” tumors “hot”, unveiling them to immune system detection and facilitating an anti-tumor immune response.

Exquisite selectivity for PI3K δ over other subtypes, including the closely related PI3K γ , taken together with IOA-244’s unique semi-allosteric mechanism, which is achieved through differentiated binding to the PI3k δ protein’s kinase domain, represents a unique first-in-class mechanism in solid tumors. This mechanism may allow IOA-244 to lock the kinase in its resting state, completely preventing initiation of downstream cell signalling pathways normally triggered when it is activated at the cell membrane.

“We believe IOA-244’s semi-allosteric non-ATP competitive mechanism may block Treg upregulation and simultaneously avoid initiating other signalling cascades that may lead to toxicities,” explained Lars Van Der Veen, PhD, CTO of iOnctura. “Other PI3k δ inhibitors are thought to act on PI3k δ by blocking the ATP pocket without preventing the kinase from being activated at the cell membrane.”

IOA-244 is being investigated in the DIONE-01 Phase I trial in metastatic cancers. The objective of Part A, now complete, was to determine the safety, tolerability, and dosage of IOA-244 in cancer patients to determine the biologically effective dose range. The continuing Part B of the study consists of expansion cohorts of patients with different tumor types, including patients with metastatic uveal melanoma. The poster at ASCO will include Phase Ib data from DIONE-01 in refractory uveal melanoma patients.

Details of the presentation:

- Title: First-in-human (FIH) phase I study of the highly selective phosphoinositide 3-kinase inhibitor delta (PI3K δ) inhibitor IOA-244 in patients with advanced cancer: Safety, activity, pharmacokinetic (PK), pharmacodynamic (PD) results.
- Type: Poster
- Session: Developmental Therapeutics-Molecularly Targeted Agents and Tumor Biology
- Time: Sunday, June 5, 2022, 8:00 AM-11:00 AM CDT

IOA-244 is a PI3K δ specific, orally dosed, small molecule inhibitor that overcomes tumor and stroma induced immune suppression. Its unique chemistry, semi allosteric binding mode and mechanism of action contribute to its unprecedented clinical profile. IOA-244 is currently in the cohort expansion phase of the DIONE-01 trial, a two-part, first-in-human dose study evaluating IOA-244 in advanced cancers and as a combination partner for conventional and immune-therapies (ClinicalTrials.gov Identifier: NCT04328844).

Uveal melanoma (UM) is a rare malignancy arising within the uveal tract of the eye. There are approximately 7,000 newly diagnosed cases of uveal melanoma each year (around 2,000 in the United States). Over 50% of patients will progress to metastatic disease. Median overall survival is approximately 1 year for metastatic uveal melanoma and there are no approved therapies.

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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](#).