Press release

iOnctura provides development update on first-in-class semi-allosteric PI3Kδ inhibitor program

- *Updated clinical data demonstrates a prolonged and sustained favorable safety profile for roginolisib (IOA-244)*
- *Clinical data shows a comparable safety profile in both solid and hematologic malignancies*
- *Clinical responses seen in both solid and hematologic malignancies*
- *US FDA grants Orphan Drug Designation for IOA-244 in uveal melanoma*

Geneva, Switzerland and Amsterdam, The Netherlands, 5 January - iOnctura, a clinical-stage biotech developing selective cancer therapies against targets that play critical roles in multiple tumor survival pathways, today provides an update on IOA-244, its lead cancer drug, which is in development for solid and hematologic malignancies including uveal melanoma, a rare cancer arising within the uveal tract of the eye.

After assessing the novel chemical and biological properties of IOA-244, and the promising signals of clinical activity seen to date in patients with uveal melanoma, the US FDA granted Orphan Drug Status for IOA-244. This grants certain benefits during development and commercialization. Uveal melanoma is a disease in which cancer originates in the tissues of the eye, causing symptoms such as blurred vision or a dark spot on the iris. When the cancer metastases, which it does in approximately 50% of patients, there are limited treatment options and projected overall survival is only a year.

A PI3Kδ inhibitor, IOA-244 recently received the proposed name roginolisib and is being investigated in the DIONE-01 trial, a two-part, first-in-human Phase I study (ClinicalTrials.gov, identifier NCT04328844). Part A of the study investigated the safety and pharmacokinetics of continuous daily dosing of IOA-244 at 10, 20, 40 and 80mg. Part B is an ongoing cohort-expansion of the biologically-effective dose (BED) of 80mg in solid and hematologic malignancies including a recently opened non-Hodgkin´s lymphoma cohort.

As of December 2022, 38 patients (including 23 with metastatic uveal melanoma and eight patients with follicular lymphoma) have been treated with IOA-244. Across all patients treated to date, roginolisib given at the BED showed less than 5% Grade 3 or Grade 4 toxicities, with these toxicities being transient in nature. There have been no dose-limiting drug reductions or interruptions and long-term (over six months) administration of IOA-244 is well tolerated.

Clinical activity, including partial and complete responses, are being seen in patients with both solid and hematologic malignancies. Further details on clinical responses will be released at a future international clinical conference in 2023. Fourteen of 38 patients (including 11 of 23 uveal melanoma patients) are still on treatment, with two patients having been on treatment for more than two years. The one-year OS rate is currently 70%; median OS has not been reached.

Catherine Pickering, Chief Executive Officer of iOnctura, said: "We are delighted to provide these positive updates on IOA-244, our lead clinical program. These important new data, taken together with previous findings, show a drug with a game-changing clinical safety and activity profile. These data demonstrate for the first time that a semi-allosteric inhibitor of PI3Kδ can be given to patients safely for long durations with no serious adverse events. We are excited to take IOA-244 forwards into a monotherapy registration study in uveal melanoma and to further explore its potential both in lymphoma and solid tumors such as NSCLC."

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About iOnctura

iOnctura 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 first-in-class semi-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. iOnctura BV is headquartered in Amsterdam, The Netherlands with its wholly owned Swiss subsidiary, iOnctura SA, located in Geneva, Switzerland.

About IOA-244

IOA-244 is a first-in-class semi-allosteric, non-ATP competitive, small molecule PI3Kδ inhibitor. Its unique structural and selectivity features drive a unique way of inhibiting PI3Kδ which translates into a highly beneficial tolerability and clinical benefit profile. PI3Kδ over-expression stimulates multiple cancer mechanisms and has an oncogenic role in many tumor types. IOA-244 has a multi-modal effect on cancer; directly preventing cancer cell proliferation, harnessing an anti-tumor immune response via an effect on regulatory T-cells and cytotoxic T cells and potentiating the effect of immunotherapy. 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 (NCT04328844).

Uveal melanoma

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 for metastatic patients refractory to immunotherapy, the population included in the DIONE-01 trial, is approximately seven months.