iOnctura announces publication of pioneering research describing the unique biological features of roginolisib

Preclinical data on roginolisib, an oral first-in-class non-ATP competitive allosteric modulator of PI3Kδ, for the potential treatment of solid and hematological tumors

Geneva, Switzerland and Amsterdam, The Netherlands, 16 March - iOnctura, a clinical stage biotechnology company developing breakthrough therapies for patients suffering with cancer, today announces the publication of non-clinical research on roginolisib in the AACR journal Cancer Research Communications. Roginolisib is a first-in-class, non-ATP-competitive, allosteric modulator of PI3Kδ which prevents tumor proliferation and breaks immune tolerance in patients with solid and hematological tumors.

PI3Kδ inhibition in solid tumors has recently emerged as a novel approach to treating cancer because of its potential in targeting multiple tumor survival pathways. First-generation PI3Kδ inhibitors are used to treat hematological tumors, but safety concerns and limited target selectivity have curbed their clinical usefulness. Safety concerns are even more aggravated in patients with solid malignancies where rapid onset of toxicities have been observed. Conversely, roginolisib has a favorable toxicity profile with less than 5% Grade 3/4 toxicities at the biologically effective dose. Importantly, these toxicities were transient in nature without the need for dose reductions.

The research published in Cancer Research Communications reinforces the conclusion that roginolisib inhibits regulatory T cell proliferation while having limited anti-proliferative effects on conventional CD4+ T cells and no effect on CD8+ T cells. This process unveils the tumor to the immune system whilst retaining normal immune function. Importantly, treatment of CD8+ T cells with roginolisib during activation favors the differentiation of memory-like, long-lived CD8+ T cells, known to have increased antitumor capacity. Consistent with first-generation PI3Kδ inhibitors, roginolisib inhibits the *in vitro* growth of lymphoma cells. In contrast to these other PI3Kδ inhibitors, roginolisib activity is correlated with the expression levels of PIK3CD, suggesting cancer cell-intrinsic effects of the drug.

Professor Francesco Bertoni, Head of the Lymphoma Genomics group at Institute of Oncology Research in Bellinzona, Switzerland, said: "This research differentiates roginolisib from other PI3Kδ inhibitors and adds to the growing body of nonclinical and clinical evidence that modulation of PI3Kδ through an allosteric non-ATP competitive mechanism can be achieved safely and effectively."

The research also highlights roginolisib has immune-modulatory properties that can be exploited in solid tumors. In CT26 colorectal and LLC lung cancer models, roginolisib sensitized the tumors to anti-PD-1 (Programmed cell death protein 1) treatment, with similar activity in the Pan-02 pancreatic and A20 lymphoma syngeneic mouse models. Roginolisib reshaped the balance of tumor infiltrating cells, favoring infiltration of CD8+ and NK cells, while decreasing suppressive immune cells. Roginolisib presented no safety concerns in animal studies, or in Phase I human studies, and is currently in clinical Phase Ib/II investigation in solid and hematological tumors.

Catherine Pickering, Chief Executive Officer of iOnctura, said: "We are excited that our ground-breaking research has been published by Cancer Research Communications highlighting the potential of our lead clinical program, roginolisib in both solid and hematological cancers. We anticipate returning this key anti-tumor mechanism to physician's tool-boxes for hematological cancers as well as offering new value for patients with solid tumors."

The research was published in the open access peer-reviewed journal Cancer Research Communications, part of the prestigious AACR stable of journals, which aims to accelerate the pace of discovery and stimulate innovation in cancer science, by giving rapid open publication of hypotheses, methods, results, data resources and cutting-edge knowledge.

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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 (proposed name roginolisib), a first-in-class allosteric modulator 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 roginolisib
Roginolisib is a first-in-class non-ATP competitive, small molecule, allosteric PI3Kδ modulator. 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. Roginolisib 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. Roginolisib is currently in the cohort expansion phase of the DIONE-01 trial, a two-part, first-in-human dose study evaluating roginolisib in advanced cancers and as a combination partner for conventional and immune- therapies (NCT04328844).

About Professor Francesco Bertoni
Prof. Francesco Bertoni is the head of the Lymphoma Genomics group at Institute of Oncology Research in Bellinzona, Switzerland, the Institute deputy director, and Adjunct Professor at the Università della Svizzera italiana (USI). Prof. Bertoni's research topics are the development of new anti-lymphoma compounds and lymphoma genomics. He actively participates in the Swiss Cancer Research Group (SAKK), where he is the President of the Project Group Lymphoma and member of the Project Group Developmental Therapeutics. Prof. Bertoni is the author or co-author of over 200 original papers, over 50 editorials or invited reviews, 20 book sections, one edited book and several abstracts at national and international meetings.