InteRNA Technologies Publishes Preclinical Data from Investigational microRNA INT-1B3 Program in *Molecular Therapy – Nucleic Acids* and *Oncotarget*

-- Results further support the potential of lead candidate, INT-1B3, as novel option for therapeutic intervention in oncology --

Utrecht, The Netherlands, March 24, 2021 – InteRNA Technologies, a clinical-stage biotech company developing microRNA (miRNA)-based therapeutics with a focus on cancer, today announced that preclinical data investigating the Company's lead candidate, INT-1B3, have been published in the peer-reviewed journals *Molecular Therapy – Nucleic Acids* and *Oncotarget.* INT-1B3 is a mimic of the tumor suppressor miRNA-193a-3p and has the potential to address multiple hallmarks of cancer at the same time. The published results include data from tumor cell lines and experimental tumor models and support the high therapeutic potential of INT-1B3 in solid tumor indications.

"Publications of our preclinical data with INT-1B3 in two highly-ranked, peer-reviewed journals represent a major milestone for our research and development team, and recognition of the innovative scientific research conducted at InteRNA in the last few years," said Dr. Michel Janicot, Chief Development Officer of InteRNA Technologies. "Documenting the molecular mechanism of action of our miR-193a-3p mimic and consequent downstream biology in cancer cells strongly supports INT-1B3 as novel promising candidate for therapeutic intervention in oncology."

In the publication in *Molecular Therapy – Nucleic Acids*, results of extended RNA-sequencing and transcriptome-wide analysis after transfection of the miR-193a-3p mimic (1B3) in human tumor cell lines were presented, revealing insights into the underlying molecular pathways of 1B3's tumor suppressor functions. Differentially expressed genes mapped by Ingenuity Pathway Analysis strongly indicated upregulation of the tumor suppressive PTEN pathway as well as downregulation of many oncogenic growth factor signaling pathways. Furthermore, the analysis pointed to an extensive link of 1B3 with cancer, based on predicted negative effects on tumor cell survival, proliferation and migration as well as induction of cell death in tumor cells. These data strongly suggest that 1B3 is a potent tumor suppressor agent which targets various key hallmark pathways across cancer types.

In the publication in *Oncotarget*, preclinical data from different tumor cell-based assays demonstrated multi-modal effects of 1B3 on cancer cells. 1B3 was shown to efficiently reduce target gene expression in tumor cells, leading to diminished cell proliferation and survival, induction of cell cycle arrest and apoptosis, increased cell senescence, DNA damage and inhibition of cell migration. In addition, the novel lipid nanoparticle (LNP)-based formulation of 1B3, INT-1B3, demonstrated pronounced anti-tumor activity as a single agent upon systemic administration in tumor-bearing mice at well-tolerated doses.

These preclinical results contributed to the decision by InteRNA to initiate a first-in-human clinical study with INT-1B3 in patients with advanced solid tumors. The first patient in the study was dosed in February 2021. The trial is conducted in clinical study centers in the Netherlands and Belgium and topline results from the dose escalation part of the study are expected by the end of 2021.

About INT-1B3

INT-1B3's unique mechanism of action addresses multiple hallmarks of cancer simultaneously. It directly targets tumor cells and the tumor microenvironment by specific modulation of multiple signaling pathway components across the PTEN tumor suppressor pathway and the oncogenic PI3K/Akt and Ras/MAPK pathways resulting in inhibition of proliferation and migration and induction of cell cycle arrest and apoptosis. The triggering of the immunogenic tumor cell death (ICD) process as well as downregulation of the adenosine-A2A receptor pathway through inhibition of CD39/CD73 leads to a decrease in immunosuppressive FoxP3/Lag3 regulatory T cells and monocytic myeloid-derived suppressor cells (mMDSCs), and maturation of dendritic cells. As a result, the immune system is activated, and long-term immunity is triggered by recruitment of CD8+ effector T cells leading to decreased metastasis development and improved animal survival compared to anti-PD1 treatment.

About InteRNA Technologies

InteRNA is a Dutch clinical-stage biotech company developing a pipeline of proprietary microRNA (miRNA) therapeutics targeting key processes in initiation and progression of human diseases, with a focus on cancer. Selected through InteRNA's leading miRNA discovery and functional validation platform and enabled with a 3rd-generation drug delivery formulation, these miRNA compounds can mount a coordinated anti-cancer attack by engaging multiple signal transduction targets simultaneously. With this approach, we address the high need for novel therapeutics with improved efficacy and less prone to drug-acquired resistance that will benefit cancer patients.

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