# InteRNA Demonstrates Preclinical Proof-of-Concept for Lead microRNA Candidate INT-1B3 in a Range of Cancer Models at 2018 AACR Annual Meeting

--INT-1B3 targets multiple hallmarks of cancer as a single agent resulting in immune-system activation, tumor regression and pronounced long term immunity--

**Utrecht, The Netherlands, April 18, 2018** – InteRNA Technologies presented proof-of concept data on lead microRNA candidate INT-1B3 highlighting its distinct mode of action that combines anti-tumor activity, modulation of the immunosuppressive tumor microenvironment and long-term immunity against cancer. INT-1B3 is a lipid nanoparticle (LNP) formulated, chemically modified microRNA 193a-3p mimic that can be delivered systemically to cancer cells. MicroRNAs are naturally occurring small RNA interfering molecules which represent a part of the body's arsenal to regulate gene expression, each targeting a specific set of genes. MicroRNA 193a-3p is a known tumor suppressor microRNA that is downregulated in many cancers and the reintroduction of the synthetic mimic aims to restore its function and generate biological responses relevant to key hallmarks of cancer. The results were presented in a poster at the American Association for Cancer Research (AACR) Annual Meeting, held in Chicago, IL, from April 14-18, 2018.

"Overall these data strongly support the unique potential of microRNAs, and INT-1B3 in specific, as a novel therapeutic modality in cancer that acts as a 'combination treatment in one drug'. It is an important milestone for InteRNA because it validates our microRNA platform and demonstrates the focus and commitment of the team over the last years," said Dr. Roel Schaapveld, CEO of InteRNA. "Our lead candidate stands out through a unique mode of action and an advanced delivery technology to achieve effective tumor tissue delivery. We are preparing to move this exciting program towards clinical assessment."

The study investigated multiple biological effects as well as the underlying mechanism of action of INT-1B3 in both tumor cell-based assays and experimental tumor models. The data show that INT-1B3 specifically targets pivotal oncogenes including MCL1, CCND1 and KRAS to induce cell death and apoptosis. In addition, it targets ENTPD1 (CD39) and NT5E (CD73), two crucial enzymes in the ATP to adenosine degradation pathway which has been linked to evasion of tumor immune surveillance. Importantly, INT-1B3 showed a good safety and tolerability profile in all animal studies with no treatment-related adverse events.

The most striking results were observed in a syngeneic mouse model of triple negative breast cancer (TNBC 4T1) in which INT-1B3-treated animals survived significantly longer than control or anti-PD-1 treated mice. The INT-1B3-treated mice showed a significant modulation of the immunosuppressive tumor microenvironment, illustrated by an increase in T cell function and a subsequent increase in cytotoxic T-cell frequency. In addition, the number of immunosuppressive regulatory T cells decreased, indicating a transition from an immunosuppressive to an immune stimulatory tumor microenvironment. To investigate the long-term immunity potential, the surviving INT-1B3-treated mice were challenged with the same tumor cells (4T1) and followed up for 28 days in the absence of any further treatment. Although three of the eight mice showed an initial tumor take and growth, a rapid and complete tumor regression with 100% of the animals being tumor-free was achieved by the completion of the study, suggesting a long-term immunization against the 4T1 cancer cells. The same mice were then re-challenged with mouse liver cancer cells (H22) to investigate the long-term immunity potential against an unrelated cancer cell type.

Despite an initial and efficient (100%) tumor take in all mice, complete tumor regression was seen within the 28-day follow-up period providing an indication that INT-1B3 can induce a long-term broad cancer immunity. Furthermore, INT-1B3 demonstrated pronounced tumor growth inhibition in human xenograft melanoma and liver cancer models.

The poster, titled "Pharmacologic profile of INT-1B3: a novel synthetic microRNA 193a-3p mimic for therapeutic intervention in oncology" was presented by InteRNA's Senior Research Scientist, Dr. Sanaz Yahyanejad and Chief Development Officer, Dr. Michel Janicot and is available on InteRNA's website through the following link: https://interna-technologies.com/technology/scientific-publications/.

## About InteRNA Technologies

InteRNA is developing potent microRNA drug candidates designed to mount a coordinated anti-cancer attack by simultaneously engaging multiple signal transduction targets. The company's focused anti-cancer pipeline has demonstrated proof-of-concept in key *in vivo* models showing effective target engagement and strong anti-tumor response. Lead candidate INT-1B3 induces immune system activation, tumor regression and pronounced long-term immunity by targeting the adenosine-dependent signaling pathways as well as key targets involved in tumor cell proliferation and survival, and cell-cycle modulation. Founded by Aglaia Oncology Fund, the company aims to harness its expertise in RNA delivery technologies and manufacturing to bring microRNA therapeutics to cancer patients.

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