NATURE MEDICINE REPORTS ELIMINATION OF LARGE TUMORS IN MICE BY MESSENGER RNA-ENCODED BISPECIFIC ANTIBODIES

Novel mRNA-based antibody drug class holds promise for fast development of potent immunotherapies

Mainz, Germany – June 12 , 2017 – BioNTech AG, a fully-integrated biotechnology company pioneering individualized cancer immunotherapy, reported preclinical data featuring a novel class of mRNA-encoded antibody drugs called RiboMABs®. In *Nature Medicine,* BioNTech presents the application of this technology for mRNA-based *in vivo* delivery of T cell engaging bispecific antibodies. The study entitled "Elimination of large tumors in mice by mRNA-encoded bispecific antibodies" can be found here: http://nature.com/articles/doi:10.1038/nm.4356.

Bispecific antibodies act by connecting human immune cells to tumor cells for highly efficient killing and have demonstrated great promise as immunotherapy agents. However, the challenges that go along with demanding procedures of production, purification and formulation of a recombinant protein hinder the development of new drugs in this class.

Administering the mRNA encoding the bispecific antibody, thus enabling the patient's body to synthesize the therapeutic protein, may profoundly reduce complexity of drug development.

BioNTech researchers achieved this aim by incorporating modified nucleosides into the pharmacologically optimized mRNA and using liver targeting nanoparticles to ensure prolonged production *in vivo*. Intravenously injecting a few micrograms of mRNA resulted in bispecific RiboMAB production in the liver cells that rapidly secreted into the circulation, reaching peak level within hours and remaining at therapeutically effective plasma concentrations for a week.

To demonstrate universality of this novel approach, bispecific RiboMABs targeting different tumor antigens were generated, and their therapeutic potency was tested in mice bearing human tumors and repopulated with human immune cells. Weekly application of any of the bispecific RiboMAB, directed against cancer antigens that are present in many human cancers, resulted in elimination of aggressively growing, large tumors. This is the first preclinical study to demonstrate *in vivo* application of mRNA-encoded antibodies for successful treatment of cancer.

"Our data show that with low doses of mRNA encoding a bispecific antibody, we get sustained production of RiboMAB comparable to those of naturally produced immunoglobulin proteins and capable of curing advanced cancers in mice," said Prof. Ugur Sahin, founder and CEO of BioNTech, who led the study. "What we have learned about RiboMAB pharmacology provides a sound basis for moving towards first clinical testing of this approach in cancer patients."

The extension to other antibody formats as well as to biomedical fields such as infectious disease is conceivable especially as the feasibility to generate mRNA encoding IgG against infectious disease has been reported very recently (Nature Communications 8, Article number: 14630 (2017)).

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About BioNTech AG

BioNTech is Europe's largest privately held biopharmaceutical company pioneering the development of individualized therapies for cancer and other diseases. The Company combines all building blocks for individualized immunotherapy under one roof – from diagnostics and drug development to manufacturing. Its cutting-edge technologies range from individualized mRNA-based medicines through innovative chimeric antigen receptors and T-cell receptor-based products to novel checkpoint immunomodulators. BioNTech's approach is validated by five top-tier corporate partnerships with Genentech, Genmab, Eli Lilly and Company, Sanofi and Bayer Animal Health. Founded in 2008, BioNTech's financial shareholders include the MIG Fonds, Salvia and the Strüngmann Family Office, with the Strüngmann Family Office as the majority shareholder.

More information about BioNTech is available at www.biontech.de.