BioNTech Expands Late-Stage Clinical Oncology Portfolio with Initiation of further Phase 2 Trial with mRNA-based Individualized Neoantigen Specific Immunotherapy in New Cancer Indication

October 19, 2023

- *Initiation of Phase 2 builds on data from a Phase 1 clinical trial evaluating the safety and tolerability of autogene cevumeran (BNT122, RO7198457) in combination with the anti-PD-L1 immune checkpoint inhibitor atezolizumab and standard of care chemotherapy in patients with resected pancreatic ductal adenocarcinoma (PDAC)*
- *The Phase 2 trial is expected to enroll approximately 260 patients with PDAC at clinical trial sites initially in the United States, followed by Europe and Asia Pacific region*
- *This is the third later-stage trial with a product candidate based on BioNTech's individualized cancer vaccine platform iNeST aimed at treating patients with solid tumors in a high unmet need indication*

MAINZ, Germany, October 19, 2023 (GLOBE NEWSWIRE) – BioNTech SE (Nasdaq: BNTX, "BioNTech" or "the Company") today announced that the first patient has been treated in a Phase 2 clinical trial evaluating the mRNA-based individualized neoantigen-specific immunotherapy (iNeST) candidate autogene cevumeran (also known as BNT122, RO7198457) in resected pancreatic ductal adenocarcinoma (PDAC). PDACs are solid tumors with a poor prognosis reflected in a 5-year overall survival rate of only 8-10%[1,2], high recurrence rates[3] and limited treatment options.

Autogene cevumeran, which is being jointly developed by BioNTech and Genentech, a member of the Roche Group, is a therapeutic, individualized cancer vaccine candidate encoding up to 20 patient-specific cancer mutations selected for their proficiency to serve as neoantigens. Neoantigens are proteins that are produced by cancer cells that differ from the proteins produced by healthy cells. The investigational treatment aims to induce a neoantigen-directed immune response against the patient's individual tumor.

The open-label, multicenter, randomized Phase 2 trial (NCT05968326), sponsored by Genentech, will evaluate the efficacy and safety of autogene cevumeran in combination with anti-PD-L1 immune checkpoint inhibitor atezolizumab and chemotherapy compared to the current standard-of-care chemotherapy (mFOLFIRINOX). The Phase 2 study is expected to enroll 260 patients with resected PDAC, who have not received prior systemic anti-cancer treatment and showed no evidence of disease after surgery. The trial will be conducted at various sites in the United States, followed by Europe and Asia Pacific region. The primary endpoint is disease-free survival. Secondary endpoints include disease-free survival rates, overall survival, overall survival rate and safety profile.

The Phase 2 initiation is based on data from an investigator-initiated, single-center Phase 1 trial (NCT04161755) evaluating the combination of autogene cevumeran (BNT122, RO7198457), atezolizumab, and chemotherapy (mFOLFIRINOX) in patients with resected PDAC. Preliminary data of the Phase 1 trial were presented at the American Society of Clinical Oncology ("ASCO") Annual Meeting in June 2022 and complete study results were recently published in *Nature*, demonstrating a favorable safety profile and substantial vaccine-induced T cell responses that may correlate with delayed PDAC recurrence.

"PDAC is a tumor type for which the relapse rate after surgery is extremely high at nearly 80%. The recent Phase 1 study has shown that individualized neoantigen vaccination is feasible for this tumor type with low mutational burden and an immunosuppressive microenvironment[3]. We have been evaluating cancer mutations since the start of the first clinical trial based on our mRNA technology in 2014 with the hypothesis that they could be suitable targets for individualized cancer vaccines," said **Prof. Özlem Türeci, M.D., Co-Founder and Chief Medical Officer at BioNTech**. "The Phase 2 study will provide additional data whether our approach with autogene cevumeran has the potential to provide a benefit for patients in this high unmet medical need setting. Our aim is to prevent relapses and thus ensure that the disease is managed at the earliest possible stage."

Autogene cevumeran (BNT122, RO7198457) is part of BioNTech's and Genentech's worldwide strategic collaboration to develop, manufacture and commercialize novel mRNA-based, individualized cancer vaccines, which was initiated in 2016. Autogene cevumeran is currently being evaluated in various solid tumor indications, including a Phase 2 trial (NCT04486378) in the adjuvant treatment of surgically resected colorectal cancer, a Phase 2 proof-of-concept study (NCT03815058) of autogene cevumeran in combination with pembrolizumab in the first-line treatment of advanced melanoma and a Phase 1a/b trial in locally advanced or metastatic tumors (NCT03289962). The Phase 2 trial of autogene cevumeran in patients with PDAC is the third later-stage trial based on BioNTech's individualized cancer vaccine platform iNeST.

About resected pancreatic ductal adenocarcinoma (PDAC)

PDAC is amongst the leading causes of cancer-related deaths in the United States[4] with approximately 90% of patients dying within two years of their diagnosis[5]. A combination of surgical removal and systemic cytotoxic chemotherapy has shown to improve clinical outcomes, however, even with surgical resection, the relapse rate remains high, and the 5-year overall survival is only approximately 20%[6] in patients who undergo surgery followed by adjuvant chemotherapy ("ACT") and only 8-10% [1,2] in those who do not receive ACT. Thus, there is a high unmet medical need for novel therapies for patients with resected PDAC. The individualized neoantigen specific immunotherapy ("iNeST") candidate autogene cevumeran (BNT122, RO7198457) provides a novel treatment strategy aimed to induce de-novo immune responses against cancer-specific neoantigens, recognize residual cancer cells and to prevent relapse.

About iNeST (individualized Neoantigen Specific immunoTherapy)

iNeST immunotherapies are individualized cancer therapies tailored to a specific patient's tumor. They contain unmodified, pharmacologically optimized mRNA encoding up to 20 patient-specific neoantigens, identified using real-time next generation sequencing and bioinformatic neoantigen discovery. Neoantigens are proteins that are produced by cancer cells that differ from the proteins produced by healthy cells and are recognized by immune cells. The mRNA is encapsulated in BioNTech's proprietary intravenous RNA-lipoplex delivery formulation which is designed to enhance stability as well as enable targeted delivery to dendritic cells. By analyzing each patient's tumor, BioNTech is able to identify the cancer mutations that may act as neoantigens. Each individual cancer vaccine encodes for neoantigen candidates with the highest likelihood to help the immune system to recognize the cancer. For this purpose, BioNTech has developed an on-demand manufacturing process, following Good Manufacturing Practice

(GMP) conditions.

An iNeST Fact Sheet and images from the iNeST manufacturing process are available in the newsroom section on BioNTech's website at this link.

About BioNTech
Biopharmaceutical New Technologies (BioNTech) is a next generation immunotherapy company pioneering novel therapies for cancer and other serious diseases. The Company exploits a wide array of computational discovery and therapeutic drug platforms for the rapid development of novel biopharmaceuticals. Its broad portfolio of oncology product candidates includes individualized and off-the-shelf mRNA-based therapies, innovative chimeric antigen receptor (CAR) T cells, several protein-based therapeutics, including bispecific immune checkpoint modulators, targeted cancer antibodies and antibody-drug conjugate (ADC) therapeutics, as well as small molecules. Based on its deep expertise in mRNA vaccine development and in-house manufacturing capabilities, BioNTech and its collaborators are developing multiple mRNA vaccine candidates for a range of infectious diseases alongside its diverse oncology pipeline. BioNTech has established a broad set of relationships with multiple global pharmaceutical collaborators, including Duality Biologics, Fosun Pharma, Genentech, a member of the Roche Group, Genevant, Genmab, OncoC4, Regeneron, Sanofi and Pfizer.

For more information, please visit www.BioNTech.com.

BioNTech Forward-Looking Statements
This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, as amended, including, but not be limited to, statements concerning: The collaboration between BioNTech and Genentech to jointly clinical develop the iNeST program candidate autogene cevumeran (BNT122); timing for commencement of a Phase 2 trial as well as any subsequent data readouts; the registrational potential of any trial we may initiate for BNT122; the nature and characterization of and timing for release of clinical data across BioNTech's platforms, which is subject to peer review, regulatory review and market interpretation; the planned next steps in BioNTech's pipeline programs and specifically including, but not limited to, statements regarding timing or plans for initiation of clinical trials, enrolment or submission for and receipt of product approvals with respect to BioNTech's product candidates; the ability of BioNTech's mRNA technology to demonstrate clinical efficacy outside of BioNTech's infectious disease platform; the potential safety and efficacy of our other product candidates; BioNTech's anticipated market opportunity and size for its product candidates. Any forward-looking statements in this press release are based on BioNTech's current expectations and beliefs of future events and are subject to a number of risks and uncertainties that could cause actual results to differ materially and adversely from those set forth in or implied by such forward-looking statements. These risks and uncertainties include but are not limited to discussions with regulatory agencies regarding timing and requirements for additional clinical trials; and the ability to produce comparable clinical results in future clinical trials. In some cases, forward-looking statements can be identified by terminology such as "will," "may," "should," "expects," "intends," "plans," "aims," "anticipates," "believes," "estimates," "predicts," "potential," "continue," or the negative of these terms or other comparable terminology, although not all forward-looking statements contain these words. The forward-looking statements in this press release are neither promises nor guarantees, and you should not place undue reliance on these forward-looking statements because they involve known and unknown risks, uncertainties, and other factors, many of which are beyond BioNTech's control and which could cause actual results to differ materially from those expressed or implied by these forward-looking statements. These risks and uncertainties include, but are not limited to: the uncertainties inherent in research and development, including the ability to meet anticipated clinical endpoints, commencement and/or completion dates for clinical trials, regulatory submission dates, regulatory approval dates and/or launch dates, as well as risks associated with preclinical and clinical data, including the data discussed in this release, and including the possibility of unfavorable new preclinical, clinical or safety data and further analyses of existing preclinical, clinical or safety data; the nature of the clinical data, which is subject to ongoing peer review, regulatory review and market interpretation; the timing of and BioNTech's ability to obtain and maintain regulatory approval for BioNTech's product candidates; BioNTech's and its counterparties' ability to manage and source necessary energy resources; BioNTech's ability to identify research opportunities and discover and develop investigational medicines; the ability and willingness of BioNTech's third-party collaborators to continue research and development activities relating to BioNTech's development candidates and investigational medicines; unforeseen safety issues and potential claims that are alleged to arise from the use of products and product candidates developed or manufactured by BioNTech; BioNTech's and its collaborators' ability to commercialize and market, if approved, its product candidates; BioNTech's ability to manage its development and expansion; regulatory developments in the United States and other countries; BioNTech's ability to effectively scale BioNTech's production capabilities and manufacture BioNTech's products and BioNTech's product candidates; risks relating to the global financial system and markets; and other factors not known to BioNTech at this time.

You should review the risks and uncertainties described under the heading "Risk Factors" in BioNTech's Report on Form 6-K for the period ended June 30, 2023, and in subsequent filings made by BioNTech with the U.S. Securities and Exchange Commission ("SEC"), which are available on the SEC's website at www.sec.gov. Except as required by law, BioNTech disclaims any intention or responsibility for updating or revising any forward-looking statements contained in this press release in the event of new information, future developments or otherwise. These forward-looking statements are based on BioNTech's current expectations and speak only as of the date hereof.

CONTACTS

BioNTech
Investor Relations
Victoria Meissner, M.D.
+1 617 528 8293
Investors@biontech.de

Media Relations
Jasmina Alatovic
+49 (0)6131 9084 1513
Media@biontech.de

[1] Oettle, H. et al. Adjuvant chemotherapy with gemcitabine and long-term outcomes among patients with resected pancreatic cancer: the CONKO-001 randomized trial. JAMA 310, 1473–1481 (2013).

[2] Neoptolemos, J. P. et al. A randomized trial of chemoradiotherapy and chemotherapy after resection of pancreatic cancer. N. Engl. J. Med. 350, 1200–1210 (2004).

[3] Rojas, L.A., Sethna, Z., Soares, K.C. et al. Personalized RNA neoantigen vaccines stimulate T cells in pancreatic cancer. Nature 618, 144–150 (2023).

[4] Siegel R.L., Miller K.D., Jemal A. Cancer statistics 2017. CA Cancer J. Clin. 2017;67:7–30.

[5] Stott, MC et al. Recent advances in understanding pancreatic cancer. Fac Rev. 2022; 11: 9.

[6] Strobel, O., Neoptolemos, J., Jäger, D. & Büchler, M. W. Optimizing the outcomes of pancreatic cancer surgery. Nat. Rev. Clin. Oncol. 16, 11–26 (2018).