BioNTech and OncoC4 Initiate Pivotal Phase 3 Trial of BNT316/ONC-392 Program in Metastatic NSCLC

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- *Initiation of pivotal Phase 3 trial in non-small cell lung cancer (NSCLC) marks the first landmark in BioNTech's and OncoC4's strategic collaboration initiated in March 2023 with the aim to evaluate BNT316/ONC-392 in various solid tumor indications*
- *The randomized Phase 3 trial is expected to enroll approximately 600 patients with metastatic, immunotherapy-resistant NSCLC at clinical trial sites initially in the United States, followed by Europe and other countries and regions*
- *The trial initiation follows the FDA Fast Track Designation granted in 2022, based on Phase 1/2 safety and efficacy data for the monotherapy in metastatic, immunotherapy-resistant NSCLC*
- *BNT316/ONC-392 is entering the pivotal clinical evaluation as part of BioNTech's strategy to initiate multiple trials with registrational potential in 2023 and 2024*

MAINZ, Germany, and ROCKVILLE, Maryland, USA, June 29, 2023 (GLOBE NEWSWIRE) — BioNTech SE (Nasdaq: BNTX, "BioNTech") and OncoC4, Inc. ("OncoC4") today announced that the first patient with non-small cell lung cancer (NSCLC) has been treated in a pivotal Phase 3 trial evaluating the companies' next-generation anti-CTLA-4 antibody candidate BNT316/ONC-392 (gotistobart). The trial is part of BioNTech's strategy to initiate multiple pivotal trials in 2023 and 2024.

The two-stage, open-label, randomized Phase 3 trial, PRESERVE-003 (NCT05671510), will assess the efficacy and safety of BNT316/ONC-392 as monotherapy compared to the standard-of-care chemotherapy (docetaxel) in patients with metastatic NSCLC that progressed under previous PD-(L)1-inhibitor treatment. Approximately 600 patients are planned to be enrolled at clinical sites in the United States, Europe and other countries and regions, including Belgium, Germany, Italy, Spain, and Türkiye. The primary endpoint measure will be overall survival. Secondary endpoints include overall response rate, progression-free survival and adverse event profile. The program received Fast Track Designation from the U.S. Food and Drug Administration (FDA) in 2022 and represents an innovative approach which aims to leverage the full potential of CTLA-4-targeting therapies.

"We believe this investigational treatment has the potential to become a new option for patients with late-stage NSCLC who have an otherwise poor prognosis. Given its specific mode of action, this treatment approach may also be applicable in a synergistic combination with other immunotherapeutic modalities to provide benefit to further patient populations," said **Prof. Özlem Türeci, M.D., Chief Medical Officer and Co-Founder at BioNTech**. "We are committed to rapidly advancing our oncology pipeline towards late-stage development for multiple product candidates in cancer indications with high unmet medical need."

"Today represents a significant landmark for the differentiated program we developed with BNT316/ONC-392, aiming to overcome current challenges of CTLA-4-targeting cancer therapeutics and in particular the very narrow therapeutic window that restricts them from delivering on their full potential," said **Pan Zheng, M.D., Ph.D., Chief Medical Officer and Co-Founder at OncoC4.** "With less than three years from first-in-human dosing to Phase 3 initiation, we are hopeful these results will build on the responses we have seen so far."

The initiation of the Phase 3 trial is based on positive safety and efficacy data from an ongoing Phase 1/2 study (NCT04140526) with BNT316/ONC-392 alone and in combination with pembrolizumab in patients with advanced solid tumors. Follow-up data recently presented at the ASCO 2023 Annual Meeting demonstrate an encouraging anti-tumor activity and a manageable safety profile for BNT316/ONC-392 in a patient cohort with metastatic, anti-PD-(L)1-resistant NSCLC.

The Phase 3 trial initiation marks the first landmark of BioNTech's and OncoC4's strategic collaboration initiated in March 2023. Under the terms of the collaboration agreement, OncoC4 received a $200 million upfront payment and is eligible to receive development, regulatory and commercial milestone payments as well as double-digit tiered royalties. BioNTech and OncoC4 will jointly develop BNT316/ONC-392 as monotherapy and in combination with anti-PD-(L)-1 antibodies in a range of solid tumor indications until regulatory authorization, with the parties equally sharing development costs for such studies. Combinations outside of PD-1 inhibition, in particular all combinations with a compound in BioNTech's pipeline, will be solely developed by BioNTech. BioNTech will hold the exclusive worldwide commercialization rights for any of these products with participation of OncoC4 in certain markets to be negotiated in the future.

About BNT316/ONC-392 (gotistobart)
BNT316/ONC-392 (gotistobart) is a next-generation anti-CTLA-4 antibody candidate jointly developed by BioNTech and OncoC4. BNT316/ONC-392 is currently in late-stage clinical development as monotherapy or combination therapy in various cancer indications. The immune checkpoint receptor CTLA-4 inhibits T cell immune response and reduces the activity of T cells in recognizing and eliminating cancer cells[1]. This mechanism is also exploited by cancer cells to prevent them from being eliminated by T cells[2]. Blocking CTLA-4 may help to preserve T cell activity and enhance anti-tumor activity. BNT316/ONC-392 was designed with the aim to address this mechanism while preserving CTLA-4 recycling and thus the immunosuppressive T cell (regulatory T cells, or "Tregs") function in the peripheral tissues. This approach, which is currently in clinical evaluation, aims to give rise to fewer immune-related adverse effects and a more favorable safety profile. BNT316/ONC-392 is currently being evaluated in an ongoing Phase 1/2 trial, PRESERVE-001, (NCT04140526) in patients with advanced solid tumors as single agent or in combination with pembrolizumab. An ongoing registrational Phase 3 trial, PRESERVE-003 (NCT05671510) evaluates the candidate as monotherapy in patients with metastatic, immunotherapy-resistant non-small cell lung cancer (NSCLC). In addition, the candidate is also being evaluated in a Phase 2 trial as a combination therapy with pembrolizumab in platinum-resistant ovarian cancer (NCT05446298).

About NSCLC
Non-small cell lung cancer (NSCLC) covers all epithelial lung cancers other than small cell lung cancer and includes squamous cell carcinoma, large cell carcinoma, and adenocarcinoma of the lung. It is the most common type of lung cancer, accounting for up to 85% of cases[3], with risk factors

ranging from smoking to asbestos exposure and pulmonary fibrosis[4]. With a 5-year relative survival rate of 23% in the United States (2012-2018), NSCLC is a devastating disease with limited treatment options depending on the stage and location of the tumor[4]. Current standard of care includes surgery, radiotherapy in combination with chemotherapy and immunotherapy[5].

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 T cells, bispecific immune checkpoint modulators, targeted cancer antibodies and 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 DualityBio, Fosun Pharma, Genentech, a member of the Roche Group, Genevant, Genmab, OncoC4, Regeneron, Sanofi, and Pfizer.

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

About OncoC4

Based in Rockville, Maryland, OncoC4 is a privately held, late clinical-stage biopharmaceutical company that is actively engaged in the discovery and development of novel biologicals for cancer treatment. Its lead clinical candidate is BNT316/ONC-392, a next generation anti-CTLA-4 antibody that allows CTLA-4 to recycle and maintain its protective function against autoimmune diseases while enhancing anti-tumor activity at the same time. In addition, OncoC4 has a pipeline of first-in-class preclinical product candidates focusing on the CD24-Siglecs cancer immune evasion pathway.

More information: www.oncoc4.com.

BioNTech Forward-Looking Statements
This press release contains “forward-looking statements” of BioNTech within the meaning of the Private Securities Litigation Reform Act of 1995. These forward-looking statements may include, but may not be limited to, statements concerning: BioNTech’s collaboration with OncoC4, Inc; the ability of the anti-CTLA-4 monoclonal antibody candidate BNT316/ONC-392 to eliminate immunosuppressive regulatory T cells and enhance anti-tumor activity in various cancer indications; the development of BNT316/ONC-392 as a monotherapy or combination therapy in various cancer indications; the timing, size and success of a Phase 3 study evaluating BNT316/ONC-392 as a monotherapy against the current standard of care in PD-1-resistant NSCLC; the timing and success of a Phase 2 trial of BNT316/ONC-392 as a combination therapy with pembrolizumab in platinum-resistant ovarian cancer; and the timing of BioNTech’s strategy to initiate trials with registrational potential for multiple oncology candidates in 2023 and 2024. 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: the ability of BioNTech to develop and, if approved, commercialize these potential immunotherapies.

For a discussion of these and other risks and uncertainties, see BioNTech’s Quarterly Report on Form 6-K for the quarter ended March 31, 2023, filed with the U.S. Securities and Exchange Commission (“SEC”) on May 8, 2023, which is available on the SEC’s website at www.sec.gov. All information in this press release is as of the date of the release, and BioNTech undertakes no duty to update this information unless required by law.

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