



## BioNTech Announces Positive Topline Phase 2 Results for mRNA Immunotherapy Candidate BNT111 in Patients with Advanced Melanoma

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- Primary endpoint met in a Phase 2 trial evaluating the investigational mRNA immunotherapy BNT111 in combination with the PD-1 checkpoint inhibitor cemiplimab
- Data demonstrated a statistically significant improvement of overall response rate (“ORR”) compared to historical control in patients with anti-PD-(L)1 relapsed/refractory advanced melanoma
- BioNTech and Regeneron plan to present data from this trial at a forthcoming medical conference; the BNT111 program received a Fast Track designation and an Orphan Drug designation from the U.S. Food and Drug Administration (“FDA”) in 2021
- BNT111 is based on BioNTech’s fully owned FixVac platform and proprietary uridine mRNA-LPX technology

**MAINZ, Germany, July 30, 2024 (GLOBE NEWSWIRE)** -- [BioNTech SE](#) (Nasdaq: BNTX, “BioNTech” or “the Company”) today announced positive topline data from the ongoing Phase 2 clinical trial (EudraCT No.: [2020-002195-12](#); [NCT04526899](#)) in patients with unresectable stage III or IV melanoma whose disease had progressed following anti-PD-(L)1-containing treatment. The randomized trial evaluates the clinical activity and safety of the investigational mRNA cancer immunotherapy BNT111 in combination with Libtayo® (cemiplimab), an anti-PD-1 monoclonal antibody being developed by Regeneron, and assesses the two single agents alone.

The trial met its primary efficacy outcome measure, demonstrating a statistically significant improvement in ORR in patients treated with BNT111 in combination with cemiplimab as compared to historical control in this indication and treatment setting. Both randomized monotherapy arms showed clinical activity. The ORR in the cemiplimab monotherapy arm was in line with the historical control of anti-PD-(L)1 or anti-CTLA-4 treatments in this patient group. The treatment was well tolerated and the safety profile of BNT111 in combination with cemiplimab in this trial was consistent with previous clinical trials assessing BNT111 in combination with anti-PD-(L)1-containing treatments. The Phase 2 trial will continue as planned to further assess the secondary endpoints, which were not mature at the time of the primary analysis.

“These Phase 2 results mark a significant step towards our vision of personalized cancer medicine. We envision mRNA as a centerpiece in future treatment paradigms for cancer, helping to address unmet medical needs, such as for patients with anti-PD-(L)1 refractory or resistant melanoma,” said **Prof. Özlem Türeci, M.D., Chief Medical Officer and Co-Founder at BioNTech**. “These data are a proof of concept for us in three dimensions: First, for our decade-long improved mRNA cancer vaccine technology that uses uridine mRNA chemistry, a non-coding backbone that is engineered for optimal translational performance and our proprietary lipoplex formulation for delivery. Second, for our computational approaches for selecting suitable tumor antigens for our cancer indication-specific FixVac platform candidates. Third, for our strategy to combine synergistic modalities, in this case BNT111 with an established immune checkpoint treatment.”

BioNTech and Regeneron plan to present data from this trial at a forthcoming medical conference. Further, the companies also intend to submit these data for publication in a peer reviewed scientific journal.

BNT111 is based on BioNTech’s fully owned FixVac platform that utilizes a fixed combination of four mRNA-encoded, tumor-associated antigens designed to trigger an innate and tumor-antigen-specific immune response against cancer cells expressing one or more of the respective tumor antigens. In 2021, BNT111 in combination with cemiplimab received [Fast Track designation](#) by the FDA for the treatment of anti-PD-1-refractory/relapsed, unresectable Stage III or IV melanoma. In the same year, the FDA granted Orphan Drug designation for BNT111 the treatment of stage IIB through IV melanoma.

### About BioNTech’s oncology mRNA platforms

BioNTech has developed a range of mRNA platforms to establish a novel class of therapeutics and vaccines aimed at improving the health of people worldwide. In oncology, BioNTech utilizes five mRNA platforms. Each platform is designed with the aim to address unique challenges in oncology. BioNTech’s fully owned FixVac (Fix Combination Vaccine) platform candidates target specific cancer indications focusing on tumor-associated antigens which are shared by many cancer patients, while iNeST (Individualized Neoantigen Specific Immunotherapy) platform candidates are personalized immunotherapies tailored to the patient’s individual tumor profile. Both platforms utilize BioNTech’s proprietary optimized uridine mRNA (“uRNA”) technology and the lipoplex (“LPX”) delivery technology that the scientific founders and the researchers at BioNTech have pioneered over decades of scientific discoveries and technological advancements. These technologies are optimized for immunotherapy applications aiming to boost the immunostimulatory effect of the investigational immunotherapies and to trigger targeted immune responses against cancer cells expressing one or more of the respective encoded tumor antigens. Currently, six programs based on the Company’s FixVac and iNeST platforms are being evaluated in randomized Phase 2 trials in various solid tumor indications.

In addition to the FixVac and iNeST platforms, BioNTech is leveraging mRNA to deliver the building plan for targeted antibody, cytokine or immunomodulating protein approaches directly to the patient based on the Company’s RiboMab, RiboCytokine and Intratumoral Immunotherapy platforms aiming to help the body to produce its own therapeutic.

### About advanced melanoma

Melanoma is amongst the leading causes of cancer-related deaths globally, responsible for roughly 58,000 deaths yearly.<sup>1</sup> Anti-PD-1 refractory/relapsed unresectable Stage III or IV melanoma is an aggressive form of melanoma, which remains particularly lethal. Current standard of care includes checkpoint inhibitor therapies that substantially improve the life expectancy of patients with melanoma.<sup>2,3</sup> Despite advances in treatment, a high proportion of patients exhibit resistance to approved therapies, leading to limited options for those who progress on targeted or immunotherapy.<sup>4</sup> The 5-year survival rate for patients with distant metastatic melanoma is approximately 35%.<sup>5</sup> This underscores the significant unmet medical need.

## About BNT111

BNT111 is an mRNA-based off-the-shelf cancer immunotherapy candidate for intravenous administration encoding a fixed set of four non-mutated melanoma-associated antigens (NY-ESO-1, MAGE-A3, tyrosinase, and TPTE) delivered as uridine mRNA-lipoplex formulation. Over 90% of patients with cutaneous melanomas express at least one of these antigens.<sup>6</sup> Data of the Lipo-MERIT Phase 1 clinical trial have shown that BNT111 alone or in combination with blockade of the checkpoint inhibitor PD-1 induces novel antigen-specific anti-tumor immune responses and enhances pre-existing immune responses against the encoded melanoma-associated antigens in checkpoint inhibitor-experienced patients with unresectable melanoma.<sup>7</sup> Further, these data have shown that the candidate can prime and activate T cells against the vaccine antigens that persisted for more than one year under continuous monthly vaccination.<sup>7</sup> BNT111 is one of three clinical-stage FixVac product candidates within BioNTech's development pipeline. The candidate is currently being evaluated in a Phase 2 clinical trial in combination with cemiplimab, in patients with anti-PD-1 refractory/relapsed unresectable Stage III or IV melanoma.

## About the BNT111-01 trial

The BNT111-01 trial (EudraCT No.: [2020-002195-12](https://www.eudract.eu/number/2020-002195-12); [NCT04526899](https://www.clinicaltrials.gov/ct2/show/study/NCT04526899)) is an open-label, randomized Phase 2 trial evaluating the efficacy of BNT111 and cemiplimab and the contribution of the single components in patients with anti-PD-1/PD-L1-refractory or relapsed, unresectable Stage III or IV cutaneous melanoma. Conducted across approximately 60 sites in 7 countries, this multi-site trial aims to demonstrate anti-tumor activity and ORR of the combination therapy as well as each agent alone. Additional endpoints include duration of response (DOR), disease control rate (DCR), overall survival (OS), safety, and tolerability. Patients were randomized in a 2:1:1 ratio to Arm 1 (BNT111 + cemiplimab), Arm 2 (BNT111 monotherapy), and Arm 3 (cemiplimab monotherapy), with up to 24 months of active treatment. More information on this trial can be found at [www.clinicaltrialsregister.eu](https://www.clinicaltrialsregister.eu).

## About BioNTech

Biopharmaceutical New Technologies (BioNTech) is a global next generation immunotherapy company pioneering novel therapies for cancer and other serious diseases. BioNTech 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 and specialized pharmaceutical collaborators, including Biotheus, DualityBio, Fosun Pharma, Genentech, a member of the Roche Group, Genevant, Genmab, MediLink, OncoC4, Pfizer and Regeneron.

For more information, please visit [www.BioNTech.com](https://www.BioNTech.com).

## 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 initiation, timing, progress and results of BioNTech's research and development plans in oncology, including its collaboration with Regeneron and FixVac program candidates BNT111, BNT113 and BNT116; the nature and characterization of and timing for release of clinical data across BioNTech's platforms, including any data readouts of the Phase 2 trial of BNT111 in combination with cemiplimab in patients with anti-PD-(L)1 refractory/relapsed unresectable Stage III or IV melanoma, which is subject to peer review, regulatory review and market interpretation; the planned next steps in BioNTech's pipeline programs, including, but not limited to, statements regarding timing or plans for initiation or enrollment of clinical trials, or submission for and receipt of product approvals and potential commercialization 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; and the potential safety and efficacy of BioNTech's product candidates. 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 based on BioNTech's current expectations and beliefs of future events, and are neither promises nor guarantees. 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 and adversely 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 clinical data, which is subject to ongoing peer review, regulatory review and market interpretation; the ability to produce comparable clinical results in future clinical trials; the timing of and BioNTech's ability to obtain and maintain regulatory approval for its product candidates; discussions with regulatory agencies regarding timing and requirements for additional clinical trials; 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, its product candidates, if approved; BioNTech's ability to manage its development and expansion; regulatory developments in the United States and other countries; BioNTech's ability to effectively scale its production capabilities and manufacture its products and 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 March 31, 2024, and in subsequent filings made by BioNTech with the SEC, which are available on the SEC's website at [www.sec.gov](https://www.sec.gov). These forward-looking statements speak only as of the date hereof. 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.

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<sup>1</sup> Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, Bray F. CA Cancer J Clin.2021 Feb 4. Epub ahead of print.

<sup>2</sup> Nogrady B. Nature 580, S14-S16 (2020). Available at <https://www.nature.com/articles/d41586-020-01038-9>

<sup>3</sup> Huang AC, Zappasodi R. Nat Immunol 23, 660–670 (2022).

<sup>4</sup> Hassel JC, et al. Cancers (Basel). 2023 Jul; 15(13): 3448.

<sup>5</sup> National Cancer Institute. Cancer Stat Facts: Melanoma of the Skin. Available from: <https://seer.cancer.gov/statfacts/html/melan.html>. Last accessed 15.07.2024

<sup>6</sup> Data on file.

<sup>7</sup> Sahin, U., Oehm, P., Derhovanessian, E. et al. Nature 585, 107–112 (2020). Available from: <https://www.nature.com/articles/s41586-020-2537-9>