TPS8670 **Poster Session**

A global phase 2/3, randomized, open-label trial of BNT327/PM8002 in combination with chemotherapy (chemo) in first-line (1L) non-small cell lung cancer (NSCLC).

Solange Peters, Stephen V. Liu, Vinod Ganju, Suzanne Kosmider, Se-Hoon Lee, Mehmet Ali Nahit Sendur, Yvonne J. Summers, Nicolas Girard, Yotsawaj Runglodvatana, Hasna Bouchaab, Ilhan Celik, Ulug Mutlu Gunaydin, René Bartz, Sarita Koride, Li Li, Claudia-Nanette Gann, Ugur Sahin, Özlem Türeci, Shun Lu; Centre Hospitalier Universitaire Vaudois Lausanne (CHUV), Lausanne, Switzerland; Georgetown University, Washington, DC; PASO Medical, Frankston, Australia; Western Health Sunshine Hospital, Melbourne, Australia; Samsung Medical Center, Seoul, South Korea; Ankara Yıldırım Beyazıt University and Ankara City Hospital, Cankaya/Ankara, Turkey; The Christie NHS Foundation Trust, Manchester, United Kingdom; Institut Curie - Centre de Recherche, Paris, France; Vajira Hospital, Bangkok, Thailand; BioNTech SE, Mainz, Germany; BioNTech US Inc., Cambridge, MA; Shanghai Lung Cancer Center, Shanghai Chest Hospital, Shanghai Jiao Tong University, Shanghai, China

Background: The introduction of immune checkpoint inhibition for the treatment of 1L NSCLC has improved survival, however long-term outcomes remain suboptimal, highlighting the need for more efficacious treatments. BNT327 is an investigational bispecific antibody, targeting both PD-L1 and VEGF-A in the tumor and tumor microenvironment (TME). By binding to PD-L1 on tumor cells it is designed to restore effector T-cell function and by binding to VEGF-A within the TME it also reverses the negative impact of VEGF signaling on immune cell infiltration and activation. In addition, via VEGF-A neutralization, it normalizes tumor vasculature. This dual targeting of PD-L1 and VEGF-A aims to deliver better efficacy and safety. Data published on BNT327 has indicated a tolerable safety profile and encouraging anti-tumor activity in patients (pts) with NSCLC (ASCO 2023, ASCO and ESMO 2024). This global Phase 2/3 trial will further assess safety and efficacy of BNT327 plus chemo (Phase 2) and BNT327 plus chemo versus pembrolizumab plus chemo (Phase 3) in pts with advanced NSCLC. **Methods:** This Phase 2/3, multisite, randomized, open-label trial will enroll ~982 pts with stage IIIB/C and stage IV non-squamous cell (NSQ) NSCLC (Substudy A) and squamous (SQ) NSCLC (Substudy B) without actionable EGFR mutations or ALK rearrangements. Each substudy consists of a Phase 2 and a Phase 3 part. During the Phase 2 part, pts will be randomized 1:1 to receive BNT327 at either 1400 mg (Arm 1) or 2000 mg (Arm 2) plus chemo (carboplatin + pemetrexed for Substudy A, carboplatin + paclitaxel for Substudy B) Q3W IV for four cycles, followed by Q3W IV maintenance BNT327 at previously administered doses (with maintenance pemetrexed for Substudy A). In the Phase 3 part, pts will be randomized 1:1 to receive BNT327 at the selected dose (based on the Phase 2 part) plus chemo (carboplatin + pemetrexed for Substudy A, carboplatin + paclitaxel for Substudy B) or pembrolizumab 200 mg plus chemo Q3W IV, followed by Q3W IV maintenance BNT327 or pembrolizumab (both with maintenance pemetrexed for Substudy A). Chemo will be administered at approved doses. Primary endpoints include occurrence of adverse events (AE) and serious AEs, rates of dose interruption, reduction and discontinuation due to treatment-emergent (TE) AEs, objective response rate (ORR) and best percentage change from baseline in tumor size (Phase 2), and both progression free survival (PFS) per blinded independent central review and overall survival (OS) (Phase 3). Secondary endpoints include duration of response, disease control rate (Phase 2), PFS per investigator, ORR, landmark PFS and OS, patient reported outcomes and occurrence of AEs, and rates of dose interruption, reduction and discontinuation due to TEAEs (Phase 3); with efficacy endpoints per RECIST 1.1; safety per CTCAE v5.0. The trial is enrolling. Clinical trial information: NCT06712316. Research Sponsor: BioNTech SE.