Zanidatamab, a HER2-Targeted Bispecific Antibody, in Combination with Docetaxel as First-Line Therapy for Patients with Advanced HER2-Positive Breast Cancer: Updated Results from a Phase Ib/II Study

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Background: Despite human epidermal growth factor receptor 2 (HER2)-targeted agents improving outcomes in HER2-positive (+) breast cancer (BC), some patients (pts) develop resistance, relapse, or do not respond to current first-line (1L) therapies. Zanidatamab (zani; ZW25) is a novel HER2-targeted bispecific antibody that binds to two distinct extracellular domains of HER2. Preliminary results from this Phase Ib/II trial (NCT04276493) showed that zani plus docetaxel had a manageable safety profile and demonstrated promising antitumour activity in pts with advanced HER2+ BC. Here, we present updated data following enrollment completion.

Methods: Cohort 1 of this open-label study is evaluating zani plus docetaxel as a 1L therapy in adult females with advanced HER2+ BC who may have received prior neoadjuvant/adjuvant therapy. Pts enrolled in Cohort 1a received zani 30 mg/kg intravenously (IV), pts enrolled in Cohort 1b received zani 1800 mg IV, both with docetaxel 75 mg/m^2 IV every 3 weeks. The primary endpoints were safety and investigator (INV)-assessed objective response rate (ORR) per Response Evaluation Criteria in Solid Tumors version 1.1. Secondary endpoints included INV-assessed duration of response (DoR) and disease control rate (DCR).

Results: As of Nov 22, 2022, 37 pts (median age 55 years [range: 33-80]) were assigned to Cohort 1a (n=10) or 1b (n=27). Median study follow-up was 15.5 months (range: 1.1-29.3); pts received a median of 13 treatment cycles (range: 1-37) and 18 (48.6%) pts remained on treatment. Of 33 efficacy-evaluable (EE) pts, the confirmed (c) ORR was 90.9% (95% confidence interval [CI]: 75.7, 98.1); 2 (6.1%) pts had complete responses, 28 (84.8%) pts had partial responses, 2 (6.1%) pts had stable disease, and 1 (3.0%) had progressive disease. The cORR was 100% (95% CI: 63.1, 100) for Cohort 1a (n=8) and 88.0% (95% CI: 68.6, 97.5) for Cohort 1b (n=25). In EE pts, the overall cDCR was 97.0% (95% CI: 84.2, 99.9) and median DoR was not estimable (NE; 95% CI: 12.1, NE). Median DoR was 12.4 months in Cohort 1a (95% CI: 5.5, NE) and was NE (95% CI: 12.1, NE) in Cohort 1b. In total, 36 (97.3%) pts experienced ≥1

treatment-related adverse event (TRAE); 25 (67.6%) experienced ≥grade 3 TRAEs. The most common ≥grade 3 TRAEs were decreased neutrophil count (n=18 pts [48.6%]) and decreased white blood cell count (n=7 [18.9%]). Serious TRAEs occurred in 6 (16.2%) pts. No TRAEs led to death.

Conclusions: Zani with docetaxel demonstrated promising antitumor activity as 1L therapy for advanced HER2+ BC, with a manageable safety profile.