**Background**

**Key Eligibility Criteria**
- **Histology:** histologically confirmed BTC, including GBC, ICC, or ECC.
- **Locally advanced or metastatic BTC:** disease not eligible for curative resection, transplantation, or ablative therapies.
- **Patient must have progressed after treatment with a gemcitabine-based chemotherapy regimen.**
- **Patient must have experienced disease progression after the most recent prior therapy.**
- **Patients must test positive for HER2 amplification by IHC (i.e., IHC 2+ or 3+).**
- **Patients must have not received any prior HER2-targeted therapy.**
- **Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1.**

**Treatment**
- **Enrolled patients will receive zanidatamab 20 mg/kg intravenously (Q2W) until at least 1 treatment discontinuation criterion is met: investigator-determined radiographic disease progression per RECIST 1.1, unequivocal clinical progression, unacceptable toxicity, consent withdrawal, physician decision, pregnancy, start of subsequent anticancer therapy, or study termination by the sponsor.**

**Assessments**
- **CT or MRI scans will be performed at baseline and every 6 weeks during treatment.**
- **Primary and secondary endpoints will be assessed according to RECIST 1.1 and independent central review (primary endpoint) and by the investigator (secondary endpoints).**

**Key Safety Results**
- **In a 28-day treatment cycle, related reactions (33%). A single treatment cycle was associated with a maximum of 4 days of related toxicity.**
- **Atrial fibrillation was reported by 2 patients (6%).**

**Zanidatamab: A Bispecific HER2-targeted Antibody**
- **A bispecific antibody that simultaneously binds to two distinct sites on HER2: EC14 (targeted by trastuzumab) and EC23 (targeted by pertuzumab).**
- **Unique binding results in multiple mechanisms of action: zanidatamab leads to improved binding, clustering, and receptor internalization and downregulation, inhibition of ligand-dependent and -independent proliferation, and potent activation of antibody-dependent cellular cytotoxicity**

**Results from the Ongoing Phase 1 Study (ZW25-101; NCT02892123) demonstrate that zanidatamab is well-tolerated and has single-agent activity in patients with advanced HER2-expressing cancers, including BTC, that have progressed after standard of care therapies.**

**Key Safety Results:**
- **Zanidatamab-related adverse events (AEs) occurred in 71% (37/52) of patients, and included predominantly of diarrhea (43%) and infusion-related reactions (34%). A single treatment-related grade 3 diarrhea was reported.**
- **Key Efficacy Results:**
  - **8% of enrolled patients achieved radiographic disease control.**

**The ZW25-101 study has been planned in the following 5 countries: Canada, United States, Chile, United Kingdom, Spain, France, Italy, China and South Korea.**

charted studies have been planned in the following 5 countries: Canada, United States, Chile, United Kingdom, Spain, France, Italy, China and South Korea.**

**ZW25-203 (NCT04466891): Global Phase 2b Study of Zanidatamab Monotherapy in HER2-amplified BTC**

**Primary & Secondary Objectives:**
- **To evaluate the anti-tumor activity of zanidatamab in patients with advanced or metastatic HER2-amplified BTC in the second-line and later setting.**
- **Primary Endpoint:**
  - **Objective response rate**
- **Key Secondary Endpoints:**
  - **Duration of response**
  - **Progression-free survival**
  - **Overall survival**
  - **Frequency & severity of AEs**
  - **Frequency of SAEs and deaths**

**Zanidatamab Clinical Trials**
- **ZW25-203 Study Design & Key Endpoints**

**Data Supporting the Phase 2b Registrational Trial**

**References**

**Acknowledgments**

We acknowledge the contributions of the investigators, patients, and their families. This study was funded by Zymeworks Inc. and BeiGene, Ltd. The ZW25-203 study is sponsored by Zymeworks Inc. and BeiGene, Ltd. The ZW25-203 study is an investigator-initiated protocol approved by the Institutional Review Board (IRB) and Data Safety Monitoring Board (DSMB) in accordance with the applicable laws, regulations, and guidelines. For more information, please refer to the ZW25-203 Study Protocol and ZW25-203 Study Investigator-Initiated Trial Report. The authors of this paper have no conflicts of interest to disclose.