TPS3182 **Poster Session**

A phase 1/2 study of JK06, a 5T4 antibody drug conjugate, in patients with unresectable locally advanced or metastatic cancer.

Nuria Kotecki, Sylvie Rottey, Brant Delafontaine, Vladimir Galvao, Maria J. de Miguel, Omar Saavedra, Valentina Boni, Hans Prenen, Bernd Dekeyser, Judit Johnson, Jonathan P. McNally, Jennifer Lindelien, Alice Drumheller, Jijun Dong, Samuel Murphy, Shalabh Singhal, Naimish Pandya; Université libre de Bruxelles (ULB), Hôpital Universitaire de Bruxelles (H.U.B), Institut Jules Bordet, Brussels, Belgium; Gent University Hospital, Gent, Belgium; Universitair Ziekenhuis Ghent, Ghent, Belgium; Vall d'Hebron Institute of Oncology (VHIO), Barcelona, Spain; START Madrid - CIOCC, Madrid, Spain; Next Oncology, Madrid, Spain; NEXT Madrid Universitary Hospital Quironsalud Madrid, Madrid, Spain; University Hospital Gasthuisberg, Leuven, Belgium; University Hospital Antwerp, Antwerp, Belgium; Salubris Biotherapeutics, Inc., Gaithersburg, MD; Salubris Biotherapeutics, Inc., Gathersburg, MD; Salubris Biotherapeutics, Gaithersburg, MD

Background: 5T4, a Type I transmembrane glycoprotein, plays a pivotal role in neonatal development, but its expression in normal adult tissues is limited. In contrast, 5T4 emerges prominently in a broad spectrum of solid tumors, including but not limited to NSCLC, breast, ovarian, endometrial, bladder, pancreatic, esophageal, gastric and colorectal cancers. Furthermore, the expression of 5T4 is confirmed to be associated with advanced disease and worse clinical outcomes in multiple solid tumors. These features make 5T4 an attractive, but as of yet unexploited, target for cancer therapeutics. JK06 is an antibody-drug-conjugate (ADC) targeting 5T4-expressing cancer cells. The antibody moiety of JK06 has a high-affinity tetravalent binding capacity, compensating for generally low 5T4 expression levels. Further, the JK06 binding specificity is biparatopic, targeting two non-overlapping epitopes on 5T4 antigens. In this way, JK06 cross-links 5T4 on the surface of cancer cells, which enhances internalization and increases intracellular release of the cytotoxic payload. The cytotoxic payload of JK06 is the clinically proven microtubule-disrupting agent, MMAE, that inhibits cell division by preventing the polymerization of tubulin, leading to cell cycle arrest and apoptosis. JK06 mediates cytotoxicity in vitro, in a 5T4 receptor density dependent manner, and anti-tumor activity has been demonstrated in several murine xenograft models. JK06 has been shown to bind to recombinant human and cynomolgus 5T4, supporting the translation of pre-clinical toxicology studies. Preclinical toxicology studies showed no toxicity with JK06 at dose levels up to 17 mg/kg single dose and 9 mg/kg repeat dose. Toxicokinetic analysis and PK modeling suggest that a Q3W dosing regimen should provide adequately sustained exposure in clinical studies. In summary, preclinical studies support clinical development of JK06 for the treatment of multiple 5T4 expressing solid tumors. **Methods:** The Phase 1/2 study of JK06 will enroll patients with advanced relapsed/refractory solid tumors. The study will employ a 3+3 escalation design to explore the safety, PK and preliminary anti-tumor activity of JK06. Back-fill enrollment at specific dose levels is permitted but mandates fresh tumor biopsy. Patients will receive treatment with JK06 intravenously once every three weeks until confirmed disease progression or intolerable toxicity. Tumor specific expansion cohorts will be initiated once dose and schedule are established from dose escalation; fresh tumor biopsies will also be collected from patients enrolled in expansion cohorts. Response will be assessed every 9 weeks per RECIST v1.1. Clinical trial information: NCT06667960. Research Sponsor: None.