A FIRST-IN-HUMAN PHASE 1 STUDY OF NL-201 IN PATIENTS WITH RELAPSED OR REFRACTORY CANCER

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Background NL-201 is a selective and long-acting computationally designed alpha-independent agonist of the IL-2 and IL-15 receptors, which share beta and gamma signaling subunits. NL-201 is being developed as a potent activator of CD8 + T cells and NK cells for cancer immunotherapy. Binding to the beta and gamma subunits selectively stimulates dose-dependent expansion and tumor infiltration of cytotoxic CD8 + T cells and NK cells, thereby enhancing the immune response in the tumor. The absence of binding to the IL-2 alpha subunit reduces the undesirable effects of traditional IL-2 therapies, such as vascular leak syndrome and expansion of immunosuppressive regulatory T cells. As such, NL-201 is designed to promote the desired immunomodulatory anti-tumor effects of IL-2 with an improved safety profile.

Methods NL201-101 is a Phase 1 first-in-human, open-label, dose-escalation, and cohort expansion study consisting of two parts. Part 1 is an adaptive monotherapy dose escalation study in up to 60 adult patients with advanced and/or refractory solid tumors to determine the safety profile and the recommended phase 2 dose (RP2D) and schedule of NL-201. During dose escalation, two different schedules will be evaluated: dosing every 21 days or on days 1 and 8 of each 21-day cycle. Tumor response to treatment will be assessed by Response Evaluation Criteria in Solid Tumours (RECIST) 1.1 and/or RECIST for use in cancer immunotherapy trials (iRECIST). In Part 2, patients with pathologically proven diagnosis of indication-specific cohorts (up to N=30/cohort), who have advanced and/or refractory measurable disease and have failed at least one line of treatment, which may include checkpoint inhibitors, will be enrolled. Key exclusion criteria include history of brain cancer, carcinomatous meningitis, neurologic autoimmune disease, or active central nervous system metastases; patients previously receiving CAR-T or IL-2-based therapies are not eligible. Recruitment of Part 1 began in April 2021, and the trial is actively enrolling. Clinicaltrials.gov identifier: NCT04659629.

Trial Registration ClinicalTrials.gov identifier: NCT04659629.

Ethics Approval All relevant documents have been or will be submitted to an Institutional Review Board (IRB)/Independent Ethics Committee (IEC) by the investigator and reviewed and approved by the IRB/IEC before the study is initiated. Site 1001: Belberry HREC, application number 2020-09-925 (Belberry does not provide an approval number); Site 1003: Austin Health HREC, approval number HREC/69340/Austin-2020; Site 2003: MDACC Office of Human Subjects Protection, approval number 2020-0383.

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