Background

Anti-programmed cell death-1 (PD-1)/PD ligand 1 (PD-L1) checkpoint blockade has not been effective for all solid tumors and alternative therapies are needed for patients who do not respond to currently approved checkpoint inhibitors. Sialic acid binding immunoglobulin like lectin-15 (Siglec-15) is an immunomodulatory pathway independent of PD-1/PD-L1. Siglec-15 is expressed on tumor cells and macrophages and has been shown to play a role in the inhibition of T cells. Blocking Siglec-15 overcomes T cell inhibition and limits tumor growth.

PYX-106 is an investigational, fully human, anti Siglec-15 immunoglobulin G1 kappa (IgG1k) monoclonal antibody that binds to human Siglec-15 with high affinity and cross-reacts to cynomolgus monkey, rat, and mouse Siglec-15. PYX-106 potently reverses Siglec-15-mediated suppression of CD4+ and CD8+ proliferation and induces IFN-gamma secretion in an ex vivo model. The PYX-106–101 clinical trial is in progress in participants with advanced cancers.

Methods

PYX-106 is being evaluated in a first-in-human, open-label, non-randomized, Phase 1 dose-escalation (Part 1) study in participants with advanced solid tumors known to have expression of Siglec-15 (NCT05718557). The phase 1 study utilizes a Bayesian optimal interval design to explore ascending doses of PYX-106 administered as an intravenous infusion to identify the recommended phase 2 dose(s). The study is designed to characterize safety and pharmacokinetics and incorporates a robust translational biomarker plan. Upon completion of Part 1 and depending upon the data obtained, a Part 2 Dose Expansion part of the study may be initiated. The PYX-106–101 study began enrolling participants in February 2023 and will be conducted in the US and Europe. Adverse events are assessed according to National Cancer Institute Common Terminology Criteria for Adverse Events Version 5.0. Tumor response is determined according to Response Evaluation Criteria in Solid Tumors 1.1 criteria and safety findings are reviewed by the dose escalation steering committee, which monitors the safety and recommends dose(s) for Part 2. The study population includes participants with histologically or cytologically confirmed solid tumors including non-small cell lung cancer (without driver mutations/translocations), breast cancer, endometrial cancer, thyroid cancer, kidney cancer, cholangiocarcinoma, bladder cancer, colorectal cancer, and head and neck squamous cell carcinoma. Clinical Trial Information: NCT05718557

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