A PHASE I, DOSE ESCALATION AND EXPANSION STUDY OF PT199, A NEXT GENERATION CD73 MONOCLONAL ANTIBODY, ADMINISTERED ALONE AND IN COMBINATION WITH A PD-1 INHIBITOR IN ADULT PATIENTS WITH ADVANCED SOLID TUMORS

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Background PT199 is an anti-CD73 monoclonal antibody (mAb) with a differentiated mechanism of action. PT199 is designed to counter the adenosine-mediated immunosuppressive tumor microenvironment, rendering antitumor immune cells more responsive to checkpoint immunotherapies, such as PD-1/PD-L1 inhibitors. PT199 fully inhibits both soluble and membrane-bound CD73, unlike some other CD73 inhibitors which may inhibit only one form of enzyme or exhibit incomplete inhibition. Moreover, at higher concentrations no loss of inhibition or “hook effect” is observed with PT199, unlike with some other CD73 inhibitors in clinical development. Hence, PT199 addresses the limitations of current CD73 inhibitors and is expected to increase antitumor immune activation, especially in combination with PD-1 pathway inhibition, and thus offers a new treatment option for cancer patients.

Methods This study is evaluating the safety, tolerability, pharmacokinetics, pharmacodynamics, and preliminary efficacy of PT199 alone and in combination with a PD-1 inhibitor, in patients with locally advanced or metastatic solid tumors that have progressed after all available standard therapy or for which standard therapy has proven to be ineffective, intolerable, or is considered inappropriate. Approximately 32-38 patients will be enrolled. The study consists of 3 parts: Monotherapy Dose Escalation, Combination Therapy Dose Escalation, and Combination Dose Expansion. The dose escalation study of PT199 will be guided by a standard 3+3 dose escalation study design to determine the maximum tolerated dose (MTD) and/or the dose recommended for dose expansion (DRDE). The MTD and/or DRDE will be further evaluated in a dose expansion cohort and a recommended phase II dose (RP2D) may be determined based on the totality of the safety, pharmacokinetics (PK), pharmacodynamics (PD), and efficacy data obtained from both dose escalation and expansion cohorts. Each enrolled patient will receive PT199 as a monotherapy (10, 20, or 30 mg/kg QW) as an intravenous infusion continuously in 21-day cycles or in combination with a PD-1 inhibitor.

Results The primary endpoints are Dose Limiting Toxicity and MTD, if reached, and RP2D of PT199 as a single agent and/or in combination with a PD-1 inhibitor. PD assessments will include measurements of CD73 enzyme activity and cytokines in serum and CD73/PD-L1 expression in tumor tissues.

Conclusions The study is currently enrolling. Preliminary safety and efficacy data is anticipated the middle of next year.

Trial Registration NCT05431270

Ethics Approval The study obtained ethics approval through a central IRB (Advara IRB: Pro00063442). All participants have given informed consent before taking part in this trial.