**TPS3159** **Poster Session**

# A phase 1, open-label, multi-center study of the safety, tolerability, and efficacy of IPH4502 as a single agent in advanced solid tumors.

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**Background:** Nectin-4 is a cell adhesion molecule frequently overexpressed across multiple solid tumor types, including urothelial carcinoma (UC), esophageal cancer, non-small cell lung cancer, and triple-negative breast cancer. It plays a significant role in carcinogenesis and cancer progression and is associated with poor survival in several tumor indications. Targeting Nectin-4 with enfortumab vedotin (EV), an antibody-drug conjugate (ADC) with a monomethyl auristatin E (MMAE) payload, demonstrated clinical benefit in UC, which exhibits the highest Nectin-4 expression among all solid tumor types. EV is now approved for the treatment of UC. IPH4502 is a differentiated Nectin-4 ADC conjugated with exatecan, a topoisomerase-1 inhibitor payload with a drug-to-antibody ratio of 8 via a cleavable hydrophilic linker. IPH4502 has been developed to address the unmet medical need of UC patients who have progressed on, or are ineligible for EV, as well as to treat tumor types with lower Nectin-4 expression beyond UC. In preclinical models, internalization capability and bystander effect of IPH4502 enable an efficient antitumor activity in Nectin-4 expressing tumor models, independent of Nectin-4 expression level, as well as in models resistant to EV. Finally, IPH4502 shows antitumor activity in patient-derived xenograft models from UC and other tumor types. **Methods:** This is a first-in-human, open-label, multicenter, single-arm Phase 1 study to assess the safety profile (DLTs and MTD), tolerability according to NCI-CTCAE v5.0, and RP2D of IPH4502 in patients with advanced solid tumors. Secondary objectives aim to characterize the pharmacokinetic profile and evaluate the immunogenicity and preliminary efficacy of IPH4502. The study is being conducted in participants aged ≥18 years withhistologically confirmed, unresectable, locally advanced, or metastatic solid tumors known to express Nectin-4, including, but not limited to non-small cell lung, triple-negative breast, ovarian, esophageal, gastric, and colorectal cancers, as well as UC. Part 1 (Dose Escalation) will use a Bayesian Optimal Interval Design (BOIN) with backfilling of safety-cleared dose levels. This approach will guide dose escalation and help establish the MTD/MAD. Part 2 (Dose Optimization)will begin after identifying the MTD/MAD, to select the RP2D. It will enroll participants with selected tumor indications (up to 2), for whom a clinical benefit was observed in Part 1. Participants will be randomized at a 1:1 ratio to 2 dose levels, to determine the RP2D. A maximum of 105 participants will receive treatment with IPH4502 in France and the US. Clinical trial information: NCT06781983. Research Sponsor: None.