Background INCB099318 is an orally administered small-molecule inhibitor of programmed cell death ligand 1 (PD-L1). This is an ongoing phase 1, open-label, multicenter study.

Methods Eligible patients are aged ≥18 years with advanced solid tumors and Eastern Cooperative Oncology Group performance status of 0–1. Patients had disease progression after treatment with available therapies or were ineligible for or without access to standard treatment. The study is conducted in 2 parts: in part 1, a Bayesian optimal interval design is being used to identify the maximum tolerated dose (MTD) of INCB099318. In part 2, selected doses will be expanded for patients who are immunotherapy-naive with various tumor types. The primary endpoints are safety and tolerability measured by monitoring frequency and severity of adverse events (AEs) and to determine a pharmacologically active dose and/or MTD. Antitumor activity is assessed using Response Evaluation Criteria in Solid Tumors (RECIST) v1.1.

Results As of April 22, 2022, 32 patients received INCB099318 in part 1 in 6 dose-escalation cohorts ranging from 100 mg twice daily (bid) to 600 mg bid; median age was 60 years (range, 34–78), 56.3% were women, 81.3% were white, 56.3% had ≥2 lines of previous therapy, and 15.6% had prior exposure to immunotherapy. Eleven patients (34.4%) discontinued treatment, 10 of whom discontinued for disease progression. Treatment-emergent AEs (TEAEs) occurring in >20% of patients were fatigue and nausea. Seven serious TEAEs (SAEs) occurred in 5 patients (15.6%) and consisted of abdominal pain, cerebrovascular accident, migraine, neck pain, pleural infection, pneumonia, and sepsis (n=1 each). Three grade ≥3 treatment-related TEAEs occurred in one patient (abdominal pain, fatigue, and insomnia). No dose-limiting toxicities occurred. Several responses have been observed, and updated results will be presented.

Conclusions INCB099318 was generally well tolerated at total daily doses up to 600 mg bid. Unlike with the first-generation oral PD-L1 inhibitor, INCB086550, no dose-limiting immune-mediated peripheral neuropathy has occurred with INCB099318 to date. Preliminary safety warrants continued investigation and further development. Dose escalation is ongoing, and dose expansion is planned to further characterize the safety, tolerability, pharmacokinetics, pharmacodynamics, and antitumor activity of INCB099318.

Trial Registration NCT04272034

Ethics Approval This study was reviewed and approved by the institutional review boards of the participating institutions. Approval numbers are: Comité d’éthique Institut Jules Bordet (Belgium), CE3326; Ethics Committee Research UZ/Leuven (Belgium), S65537; Ethics Comite UZA/Antwerpen (Belgium), 2021-0592-Edge 001759; Medical Ethics Committee UZ Brussel – VUB (Belgium) EC-2021-285; UZ Gent Ethische Commissie (Belgium), BC-10108 CE3326; National Videnskabssetisk komite (Denmark), 2110272; HUS Hospital District of Helsinki and Uusimaa (Finland), HUS/2452/2021; REK South-East Kulmu A (Norway), 253989; Linkoping Department Medicine EC (Sweden), 2021-02574; NHS Fast Track REC (United Kingdom), 21/FT/0058; WIRB (USA), 20201315; Vanderbilt IRB (USA), 211153; WCG IRB (USA), 20201315, 1300136, 1308493. All patients provided written informed consent.