Background Overexpression of Prostaglandin E2 (PGE2) in tumour tissues suppresses anti-tumour immunity in the tumour microenvironment and can lead to disease progression. DT-9081 is a small molecule, orally administered, highly selective antagonist of prostaglandin E receptor 4 (EP4R) developed to overcome the immune-suppressive effects of PGE2, and to reverse the resistance to immune checkpoint blockers. DT-9081 has recently demonstrated significant anti-tumor activity in vivo as monotherapy and in combination with immunotherapeutic agents in several mouse tumor models.

Methods This first-in-human phase 1, multicentre, open label trial is evaluating the safety, tolerability, pharmacokinetics (PK), pharmacodynamics (PD), and preliminary efficacy of DT-9081 in adult patients with recurrent and/or metastatic solid tumors who failed standard of care therapies (EudraCT Number 2022-000092-40). Patients will be dosed orally once daily. The schedule might be adjusted in case of toxicities or based on PK parameters.

This Phase 1 consists of 2 parts. The first part will consist in an initial dose-escalation phase using a 3+3 design up to 6 dose escalation cohorts at increasing levels are planned. The primary objectives will be to determine the dose-limiting toxicities, maximal tolerated dose, and the toxicity profile (NCI CTCAE v5.0) to establish the recommended phase II dose (RP2D) as single agent. Adjustment of the doses will be based on toxicities, pharmacokinetics data and pharmacodynamics effects of DT-9081.

The second part will be an expansion phase at the RP2D in a homogeneous patient population to validate the dose/schedule of administration as well as to assess preliminary efficacy of DT-9081 according to RECIST1.1.

Ethics Approval UNDER REVIEW