Domain Therapeutics announces first patient dosed with DT-9081 in phase I clinical study in patients with advanced, recurrent or metastatic solid tumors: the EPRAD study

- *EP4R antagonist is Domain Therapeutics' first fully-owned immuno-oncology asset to enter clinic*
- *Unique clinical strategy focused on unlocking new possibilities in the treatment of cancer*

Strasbourg, France – Montreal, Canada, January 5, 2023 – Domain Therapeutics ("Domain" or "the Company"), a drug discovery and development company focused on G Protein-Coupled Receptors (GPCRs) in immuno-oncology (IO), today announces that the first patient has been dosed with DT-9081, Domain's proprietary IO asset, in a first-in-human Phase I study.

DT-9081 is an oral small molecule product which, by blocking the EP4 receptor present on immune cells, is able to reverse the prostaglandin E2 (PGE2)-mediated immunosuppression triggered by some tumors to bypass the immune system. In preclinical studies, the asset demonstrated strong anti-tumor effects and synergies with immune checkpoint inhibitors in multiple models. The Phase I study, named EPRAD, is a multi-center, open-label study that will evaluate the safety, tolerability, pharmacokinetics, pharmacodynamics, and preliminary efficacy of DT-9081 in adult patients with advanced, recurrent or metastatic solid tumors who have failed standard of care therapies. Domain has developed a precise biomarker strategy that is being applied in the clinical study to track target engagement and signs of activity and to optimize the selection of patients and, ultimately, deliver improved clinical outcomes.

Dr. Pascal Neuville, CEO of Domain Therapeutics, commented: "The successful initiation of this first-in-human study is a significant milestone for Domain. Our differentiated approach to tackling cancer with GPCR-based drug candidates is built on the premise that every cancer is unique. By treating patients based on their individual cancer signatures we can deliver targeted, scientifically validated therapies. We look forward to progressing this clinical study as we continue to demonstrate the potential of our optimized pipeline of GPCR assets that we believe will unlock new possibilities in the treatment of cancer."

Professor Jean-Pascal Machiels, Saint-Luc Hospital Brussels and Lead Investigator of the study, commented: "Innate or acquired immunosuppression is a complex and significant challenge in the clinic and remains an unmet need in many patient populations. By blocking the EP4 receptor, I believe that DT-9081 has the potential to address this challenge and offer new hope for patients. The findings from the preclinical studies of DT-9081 are clearly encouraging and we are pleased to progress such a promising product with multi-tumor potential through clinical development."

The overall objectives of the EPRAD study are to determine the maximum tolerated dose and/or the recommended clinical dose of DT-9081 and to evaluate its safety and preliminary efficacy. The study comprises two parts with the first part focusing on dose-escalation with the ultimate aim of establishing the recommended clinical dose, and the second part consisting of an expansion phase to validate the dose and schedule of administration in addition to assessing the preliminary efficacy of the asset. For further details about the study, please refer to clinicaltrials.gov NCT05582850.

Four expert clinical investigators are contributing this clinical study; in Brussels, Belgium, Prof Jean-Pascal Machiels from Saint Luc Hospital and Dr Nuria Kotecki from Institut Jules Bordet, in France, Prof Christophe

Le Tourneau from Institut Curie in Paris and Prof Jean-Pierre Delord from Institut Claudius Regaud in Toulouse.

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About Domain Therapeutics
Domain Therapeutics is developing innovative immunotherapies targeting G Protein-Coupled Receptors (GPCRs) to unlock new possibilities in cancer. As a leader in GPCRs in immuno-oncology, Domain sees cancer differently, using a precise biomarker strategy to address the specific needs of patients based on unique signatures of individual cancers. Backed by decades of research and validated by multiple pharma partnerships, the Company's unrivalled discovery engine enables rigorous GPCR target identification and selection.

Domain has a clinical stage portfolio with its A2aR/A2bR asset in development through a partnership with Merck KGaA and its fully owned EP4R antagonist, DT-9081, recently entering Phase I trials. The Company is also progressing an anti-CCR8 asset alongside a rich, optimized pipeline of first-in-class GPCR targets selected through Domain's drug discovery engine. Domain is backed by a syndicate of leading international venture capital funds from Europe, Asia and North America. For more information, please visit:
www.domaintherapeutics.com