



Domain Therapeutics announces nomination of first-in-class PAR2 NAM candidate, DT-9045, to unlock new cancer treatment possibilities

- DT-9045 is a unique drug candidate due to its competitive differentiating pharmacological features
- Start of Phase 1 ascending dose studies in recurrent or metastatic solid tumors with DT-9045 is expected by mid-2025
- DT-9045 builds upon the Company's growing pipeline which includes the clinical-stage drug candidates, M1069 (A2a/A2b antagonist) and DT-9081 (EP4 receptor antagonist)

Strasbourg, France – Montreal, Canada, [June 5th, 2023] – Domain Therapeutics (“Domain” or “the Company”), a clinical-stage biopharmaceutical company developing innovative drug candidates in immuno-oncology targeting G Protein-Coupled Receptors (GPCRs), today announces the nomination of a drug candidate, a Negative Allosteric Modulator (NAM) of protease-activated receptor 2 (PAR2), DT-9045, with first-in-class potential for immuno-oncology, particularly for fibrotic tumors.

Domain carefully selects its immuno-oncology assets using its proprietary cross-validation platform that includes preclinical and clinical data to identify and validate GPCR targets involved in immunosuppressive mechanisms. Through this precision research strategy, backed by two decades of deep-expertise in understanding GPCRs, the Company has developed a novel series of potent and selective PAR2 NAMs. PAR2 is a novel therapeutic target in oncology and immuno-oncology, involved in several processes such as tumor proliferation, resistance to immunotherapy and fibrosis.

Domain nominated DT-9045 as a first-in-class PAR2 NAM clinical candidate based on its added-value, unique properties and greater therapeutic potential in comparison to biologics targeting PAR2 currently in the clinic by several competitors. DT-9045 has demonstrated proof-of-concept efficacy in syngeneic models potentiating the anti-tumor activity of an anti-PD1 treatment.

The Company's PAR2 NAM approach is particularly advantageous compared to competitors due to its unique pharmacological features:

- G-protein biased NAM activity on PAR2 (with no impact on the β -Arrestin pathway and ligand-induced receptor internalization),
- unsurmountable property enabling preservation of efficacy even at high concentrations of ligand that could be found in the tumor microenvironment
- activity maintained at acidic pH, typical to inflammatory and tumoral environment

Domain has established a clear biomarker strategy guiding the clinical positioning for DT-9045 and with pre-IND studies in progress, the Company's expectations are for Phase I ascending dose studies in recurrent or metastatic solid tumors to start by mid-2025.

Dr. Pascal Neuville, CEO of Domain Therapeutics, commented: “The nomination of our first-in-class PAR2 NAM drug candidate, DT-9045, is an exciting step forward for Domain Therapeutics and for cancer treatment in general. With its unique features of modulating the immune system response and playing a role in immunosuppression triggered by the tumor, this asset shows unmatched potential to expand the responsiveness of immunotherapy and increase the success rate of non-responding patients. Applying our precision research, we are making steady progress in building our portfolio of assets with best-in-class and

first-in-class potential. We look forward to bringing DT-9045 to the clinic by mid-2025 as we work to unlock new cancer treatment possibilities.”

Dr. John Stagg, Principal investigator at the Centre Hospitalier de l’Université de Montréal (CHUM), Canada and Member of Domain Therapeutic’s Scientific Advisory Board, commented: “Working closely with Domain, we were able to identify the PAR2 therapeutic target that can potentially pave the way to new GPCR-based immunotherapies and deliver more efficient therapeutic strategies for cancer patients. I look forward to advising the team through the next stages to progress the clinical development of DT-9045 through our fruitful collaboration.”

Furthermore, Cancer Associated Fibroblasts (CAF) are involved in fibrosis mediated immunoresistance leading to failure of several therapies in the clinic. The role of PAR2 in CAF modulation opens a novel therapeutic avenue for the treatment of solid tumors, including those involving fibrosis such as pancreatic or lung cancers.

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About Domain Therapeutics

Domain Therapeutics, a clinical-stage biopharmaceutical company operating in France and Canada, focuses on developing innovative immunotherapies targeting G Protein-Coupled Receptors (GPCRs), one of the most important drug target classes, 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 ensures rigorous GPCR target identification and selection as well as thorough analysis of tumor complexity and mechanisms to deliver the next generation of immunotherapies.

Domain’s clinical-stage programs include M1069, an A2aR/A2b receptor antagonist identified during a research collaboration with Merck KGaA, DT-9081, its fully owned EP4 receptor antagonist and DT-9045 its PAR2 NAM antagonist, alongside a rich, optimized pipeline of first-in-class GPCR targets selected through Domain’s drug discovery platform.

The Company raised €39m (\$42m) in early 2022 to develop high-value drug candidates to address GPCR-mediated immunosuppression in immuno-oncology. 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