

Domain Therapeutics Doses First Patients in Phase I/II Trial of DT-7012 Targeting CCR8 in Solid Tumors

- DT-7012 is a proprietary, differentiated Treg-depleting anti-CCR8 monoclonal antibody
- Differentiated binding capacities and competitive properties position it as a promising therapeutic to boost anti-tumor immunity, overcoming immunosuppression

Strasbourg, France – Montreal, Canada – Boston, United States, October 28, 2025: Domain Therapeutics ("Domain" or "the Company"), the GPCR experts harnessing deep receptor biology to develop breakthrough treatments for patients, today announced that the first patients have been dosed in its Phase I/II DOMISOL clinical study of <u>DT-7012</u>, a differentiated Treg-depleting anti-CCR8 monoclonal antibody for the treatment of solid tumors.

The DOMISOL study is an open-label, multicenter Phase I/II, first-in-human dose-escalation and cohort-expansion trial evaluating the safety, tolerability, pharmacokinetics, pharmacodynamics, and preliminary anti-tumor activity of DT-7012 in adult patients with selected advanced solid tumors. The trial is being conducted in Australia, with initial clinical sites including Peninsula and Southeast Oncology (PASO) and Cabrini Health in Melbourne. Additional centers are expected to come online in the coming months. For more information on the trial, visit: NCT06819735.

Stephan Schann, Chief Scientific Officer of Domain Therapeutics, said: "CCR8 has rapidly emerged as a highly competitive target, drawing significant interest across the industry, including from leading pharmaceutical companies. DT-7012 stands out with its unique and differentiating properties, offering unprecedented selectivity in depleting intratumoral Tregs while simultaneously improving overall immune system function. These features are critical for effective cancer immunotherapy, positioning DT-7012 as a promising candidate to overcome immune resistance and bring hope to patients with limited treatment options."

Professor Vinod Ganju, Principal Investigator at PASO, commented: "Immune checkpoint inhibitors (ICIs) have revolutionized cancer treatment, yet a significant unmet need remains as Tregs suppress immune response, driving resistance to ICIs and limiting their effectiveness. We are excited to participate in this important trial and offer patients access to a highly promising therapeutic candidate that could make Treg depletion a reality in cancer therapy. DT-7012 adds to the growing momentum around CCR8, complementing another CCR8-targeting asset currently undergoing significant patient expansion."

"Dosing of the first patients in the DOMISOL trial represents a significant milestone, as DT-7012 becomes our second fully proprietary asset to enter the clinic, underscoring our proven ability to translate cutting-edge GPCR biology into high value differentiated products", added Sean A. MacDonald, Chief Executive Officer of Domain Therapeutics. "Initiating this trial in Australia aligns with our strategy to accelerate clinical development and strengthens momentum behind our pipeline of drug candidates. As we continue to advance our programs and deliver value for stakeholders, we are proud to contribute to the introduction of a potentially groundbreaking therapeutic solution that could transform lives of cancer patients worldwide."

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About Domain Therapeutics

Domain Therapeutics is a clinical-stage biopharmaceutical company developing highly differentiated therapeutic strategies targeting G protein-coupled receptors (GPCRs), a crucial class of drug targets. Its robust regulatory and clinical pipeline aims to address significant unmet medical needs, offering novel solutions for patients, particularly in immuno-oncology and inflammation. Domain's key programs include a best-in-class Treg-depleting anti-CCR8 antibody and a first-in-class biased antagonist of PAR2. These innovative therapies are driving value creation, positioning the company in competitive and fast-expanding markets.

Domain leverages its proprietary drug discovery and development approach, founded on a unique platform and unmatched knowledge of GPCR receptor biology, to successfully unlock very challenging GPCR targets, including intractable and orphan receptors. The team's expertise, developed over two decades, is reflected in its solid track record of collaboration with major pharma, KOLs and physicians worldwide. By integrating detailed biological understanding of GPCRs at each step of the drug discovery and development process, Domain creates highly effective and differentiated drugs that target specific pathways, thereby therapeutic improving efficacy. For more information, please visit https://www.domaintherapeutics.com/

About DT-7012

DT-7012 is a novel immunotherapy candidate designed to selectively deplete intratumoral regulatory T cells (Tregs) by targeting CCR8, a receptor predominantly expressed on Tregs within the tumor microenvironment (TME). Leveraging potent ADCC and ADCP mechanisms, DT-7012 effectively eliminates these immunosuppressive cells, transforming the TME into a more immunocompetent state. By disrupting CCR8-mediated immunosuppressive environment, DT-7012 promotes tumor regression, offering a potential new treatment option to patients unresponsive to existing immunotherapies.

Distinct from other CCR8-targeting therapies currently in clinical development, DT-7012 exhibits broader binding across CCR8 variants, extending its therapeutic reach across diverse immunosuppressive populations. Additionally, DT-7012 maintains depletion efficiency even in CCL1-rich environments, preventing CCR8 internalization and ensuring sustained Treg depletion in challenging TMEs.

About GPCRs

G Protein-Coupled Receptors (GPCRs) are at the top of complex signaling cascades and are responsible for translating extracellular messages into intracellular actions, making them critical for various biological processes and attractive for therapeutic intervention. Despite being the most validated drug target family, with 30-35% of all marketed drugs acting on them, they remain challenging to drug, with existing drugs targeting only 10% of the total potential GPCR targets. While most efforts in GPCR drug discovery and development have traditionally focused on central nervous system and cardio-metabolic disorders, Domain recognizes the untapped potential of GPCRs in immuno-oncology and inflammatory diseases, areas where GPCRs have not been as extensively explored.