Domain Therapeutics to present latest data on DT-9045,
a first-in-class Negative Allosteric Modulator of PAR2 for immuno-oncology,
at AACR 2024 annual meeting, highlighting clear competitive advantages of this candidate

- *DT-9045 is a game-changer in immuno-oncology with competitive pharmacological properties and unique therapeutic potential to unlock new cancer treatment possibilities*
- *Preclinical studies highlight the efficacy of DT-9045 in overcoming resistance to EGFR-targeting therapies and immunotherapy in cancer models*
- *IND-enabling studies are currently ongoing*

Strasbourg, France – Montreal, Canada - Boston, United States, March 26, 2024 – Domain Therapeutics ("Domain" or "the Company"), a global clinical-stage biopharmaceutical company developing innovative drug candidates in immuno-oncology targeting G Protein-Coupled Receptors (GPCRs), today announces that latest preclinical data on DT-9045, a novel protease-activated receptor 2 (PAR2) Negative Allosteric Modulator candidate, will be presented at the American Association for Cancer Research (AACR) Annual Meeting 2024 in San Diego, California.

Date/Time: 7 April 2024 1:30 PM - 5:00 PM PST – Section 27
Abstract number: 684 / 30
Poster session: PO.ET09.05 - Novel Antitumor Agents 2
Title: DT-9045, a novel PAR2 inhibitor with best-in-class properties that reduces resistance to both EGFR-targeting therapies and immunotherapy in oncology models
The abstract will be made available in the online Proceedings of the AACR.

PAR2 is one of the genes most significantly linked to resistance against immune checkpoint blockage (ICB) and T cells dysfunction in cancer patients. Its upregulation across a variety of cancer types and expression on diverse cells within the tumor microenvironment underscore PAR2's critical role in cancer development.

Leveraging its integrated precision research approach, backed by over 20 years of solid GPCR expertise, Domain has developed a novel highly potent and selective PAR2 inhibitor, DT-9045. This first-in-class Negative Allosteric Modulator has shown unparalleled potential in oncology and immuno-oncology. Remarkably, when compared to its most advanced competitors positioned in other therapeutic areas, this candidate has demonstrated clear differentiated features. Moreover, several proof-of-concept studies have shown strong potency in models resistant to EGFR-targeting therapies and immunotherapy opening solid perspectives of strategic clinical positioning and revenues generation in tumor types that constitute a high medical unmet need.

DT-9045 is a small molecule, orally available, insurmountable, biased, and active in tumor-like conditions (high concentration of activating proteases and acidic pH). IND-enabling studies are currently ongoing to advance the candidate toward the clinic.

Stephan Schann, Chief Scientific Officer of Domain Therapeutics, commented: "We are excited to present our newest findings on DT-9045 at AACR. The results not only confirm the immense potential of our PAR2 inhibitor to change the way we treat cancer, but also emphasize its high potency and efficacy against several drug resistance, offering cancer patients a clear therapeutic perspectives in immuno-oncology. More broadly, they reflect our deep commitment to precision research, pioneering innovative new GPCR targets in immunosuppression, designing clear competitive properties to deliver game-changing candidates. We eagerly anticipate advancing this groundbreaking research, with a focus on addressing a

substantial unmet medical need for cancer patients."

This progress, follows the announcement in June 2023 when DT-9045 was nominated as a first-in-class clinical PAR2 antagonist. It has shown great therapeutic potential in enhancing the efficacy to immunotherapy aiming to substantially improve treatment outcomes for non-responding cancer patients.

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About Domain Therapeutics

Domain Therapeutics, a global clinical-stage biopharmaceutical company, is developing innovative immunotherapies targeting G Protein-Coupled Receptors (GPCRs), one of the most important drug target classes, to unlock new possibilities in cancer. As the leading GPCR immuno-oncology company, Domain aims to beat resistance to immune modulation within the tumor microenvironment by unveiling therapeutic potential of GPCRs to defeat cancer. Two decades of solid GPCR expertise, validated through multiple pharma partnerships across various therapeutic areas and associated to a world-class drug discovery platform, enable the Company to deepen the understanding of cancer biology and deliver the next-generation of immunotherapies to patients.

Domain's proprietary programs include DT-7012, a Treg-depleting CCR8 antibody, DT-9045, a first-in-class PAR2 negative allosteric modulator, and DT-9081, an EP4 receptor antagonist alongside the M1069, an A2aR/A2b receptor antagonist identified in partnership with Merck KGaA. The company has also an optimized pipeline of best-in-class and first-in-class GPCR targets selected through Domain's proprietary cross-validation drug discovery and development platform.

Since 2022, the Company raised €51m ($55m) in series A to progress preclinical and clinical development of its high-value drug candidates to address GPCR-mediated immunosuppression. Domain is supported by leading international venture capital firms from Europe (3B Future Health Fund, Seventure, Schroders, Omnes, Turenne, Theodorus), Asia (Panacea and Viva) and North America (CTI Life Science, adMare).

For more information, please visit: www.domaintherapeutics.com