Summit Therapeutics Announces Completion of Enrollment in Its Phase III HARMONi Trial in 2L+ EGFRm NSCLC

FDA Grants Fast Track Designation for Ivonescimab in 2L+ EGFRm NSCLC

HARMONi Completed Enrollment for Summit's First Sponsored Study Evaluating Ivonescimab

Topline data from the HARMONi Trial Is Expected in Mid-2025

Miami, Florida, October 03, 2024 – Summit Therapeutics Inc. (NASDAQ: SMMT) ("Summit," "we," or the "Company") today announced that we have completed enrollment in our HARMONi clinical trial, a multi-regional Phase III study sponsored by Summit evaluating ivonescimab plus platinum-doublet chemotherapy vs. placebo plus platinum-doublet chemotherapy with epidermal growth factor receptor (EGFR)-mutated, locally advanced or metastatic non-squamous non-small cell lung cancer (NSCLC) who have progressed after treatment with a 3rd generation EGFR tyrosine kinase inhibitor (TKI). HARMONi completed enrolling patients from sites in North America, Europe, and China. This is a clinical setting with a patient population where PD-1 monoclonal antibodies have previously been unsuccessful in Phase III global clinical trials.

"I would like to sincerely thank the investigators, site coordinators, Team Summit, and, most importantly, the patients around the world who are participating in the HARMONi study," said Dr. Maky Zanganeh, Chief Executive Officer and President of Summit. "Completing enrollment in the first global study for ivonescimab is a credit to the growing belief in the potential for ivonescimab to make a significant difference in the lives of patients around the world."

In addition, the U.S. Food and Drug Administration (FDA) has granted Fast Track designation for the proposed use of ivonescimab in combination with platinum-based chemotherapy for the treatment of adult patients with locally advanced or metastatic NSCLC with EGFR mutation, who have experienced disease progression following EGFR-TKI therapy.

The FDA's Fast Track designation is designed to facilitate the development and expedite the review of drugs to treat serious conditions and fill an unmet medical need. According to the FDA, the purpose is to get important new drugs to patients earlier. A drug that receives Fast Track designation is eligible for some of the following: more frequent meetings with the FDA to discuss the drug's development plan, more frequent written communication from the FDA, and a rolling review process, allowing the sponsor to submit completed sections of its Biologic License Application (BLA) for review rather than every section at once, though the review by FDA typically begins when the entire application has been submitted. Per the FDA, once a drug receives Fast Track designation, early and frequent communication with the FDA is encouraged throughout the entire drug development and review process; the frequency of communication assures that questions and issues are resolved quickly, often leading to earlier drug approval and access by patients.

"Completing enrollment in the HARMONi study represents another step towards our goal of bringing to patients a drug that is intended to improve the quality and potential duration of life for those facing serious unmet medical needs," stated Robert W. Duggan, Chairman & Chief Executive Officer of Summit. "As our belief in the potential

for ivonescimab to make a meaningful, positive difference continues to grow, we are pleased that the FDA has granted Fast Track designation for ivonescimab."

As a reminder, the HARMONi analysis will include all patients from the HARMONi-A trial who previously received a 3rd generation TKI. HARMONi-A was a single-region, multi-center Phase III clinical trial evaluating ivonescimab plus platinum-doublet chemotherapy vs. placebo plus platinum-doublet chemotherapy with EGFR-mutated, locally advanced or metastatic non-squamous NSCLC who have progressed after treatment with an EGFR TKI. HARMONi-A was sponsored by our collaboration partner, Akeso, Inc. (Akeso, HKEX Code: 9926.HK), with data generated and analyzed by Akeso. On May 24, 2024, our partner, Akeso, received marketing authorization in China from the National Medical Products Administration (NMPA) based on the positive dataset associated with HARMONi-A. HARMONi-A was designed with a primary endpoint of progression-free survival. HARMONi is designed with dual primary endpoints of progression-free survival and overall survival.

About Ivonescimab

Ivonescimab, known as SMT112 in Summit's license territories, the United States, Canada, Europe, Japan, Latin America, including Mexico and all countries in Central America, South America, and the Caribbean, the Middle East, and Africa, and as AK112 in China and Australia, is a novel, potential first-in-class investigational bispecific antibody combining the effects of immunotherapy via a blockade of PD-1 with the anti-angiogenesis effects associated with blocking VEGF into a single molecule. Ivonescimab displays unique cooperative binding to each of its intended targets with multifold higher affinity when in the presence of both PD-1 and VEGF.

This could differentiate ivonescimab as there is potentially higher expression (presence) of both PD-1 and VEGF in tumor tissue and the tumor microenvironment (TME) as compared to normal tissue in the body. Ivonescimab's tetravalent structure (four binding sites) enables higher avidity (accumulated strength of multiple binding interactions) in the TME with over 18-fold increased binding affinity to PD-1 in the presence of VEGF *in vitro*, and over 4-times increased binding affinity to VEGF in the presence of PD-1 *in vitro* (Zhong, *et al*, SITC, 2023). This tetravalent structure, the intentional novel design of the molecule, and bringing these two targets into a single bispecific antibody with cooperative binding qualities have the potential to direct ivonescimab to the tumor tissue versus healthy tissue. The intent of this design, together with a half-life of 6 to 7 days (Zhong, *et al*, SITC, 2023), is to improve upon previously established efficacy thresholds, in addition to side effects and safety profiles associated with these targets.

Ivonescimab was engineered by Akeso Inc. (HKEX Code: 9926.HK) and is currently engaged in multiple Phase III clinical trials. Over 1,800 patients have been treated with ivonescimab in clinical studies globally.

Summit has begun its clinical development of ivonescimab in non-small cell lung cancer (NSCLC), commencing enrollment in 2023 in two multi-regional Phase III clinical trials, HARMONi and HARMONi-3, with a plan to initiate HARMONi-7 in early 2025.

HARMONi is a Phase III clinical trial which intends to evaluate ivonescimab combined with chemotherapy compared to placebo plus chemotherapy in patients with EGFR-mutated, locally advanced or metastatic non-squamous NSCLC who have progressed after treatment with a 3rd generation EGFR TKI (e.g., osimertinib).

HARMONi-3 is a Phase III clinical trial which is designed to evaluate ivonescimab combined with chemotherapy compared to pembrolizumab combined with chemotherapy in patients with first-line metastatic squamous NSCLC.

HARMONi-7 is a planned Phase III clinical trial which is intended to evaluate ivonescimab monotherapy compared to pembrolizumab monotherapy in patients with first-line metastatic NSCLC whose tumors have high PD-L1 expression (PD-L1 TPS $\geq$ 50%).

In addition, Akeso has recently had positive read-outs in two single-region (China), randomized Phase III clinical trials for ivonescimab in NSCLC, HARMONi-A and HARMONi-2.

HARMONi-A was a Phase III clinical trial which evaluated ivonescimab combined with chemotherapy compared to placebo plus chemotherapy in patients with EGFR-mutated, locally advanced or metastatic non-squamous NSCLC who have progressed after treatment with an EGFR TKI.

HARMONi-2 is a Phase III clinical trial evaluating monotherapy ivonescimab against monotherapy pembrolizumab in patients with locally advanced or metastatic NSCLC whose tumors have positive PD-L1 expression (PD-L1 TPS $\geq$1%).

Ivonescimab is an investigational therapy that is not approved by any regulatory authority in Summit's license territories, including the United States and Europe. Ivonescimab was approved for marketing authorization in China in May 2024. Ivonescimab was granted Fast Track designation by the US Food & Drug Administration (FDA) for the HARMONi clinical trial setting.

About Summit Therapeutics
Summit Therapeutics Inc. is a biopharmaceutical oncology company focused on the discovery, development, and commercialization of patient-, physician-, caregiver- and societal-friendly medicinal therapies intended to improve quality of life, increase potential duration of life, and resolve serious unmet medical needs.

Summit was founded in 2003 and our shares are listed on the Nasdaq Global Market (symbol "SMMT"). We are headquartered in Miami, Florida, and we have additional offices in Menlo Park, California, and Oxford, UK.

For more information, please visit https://www.smmttx.com and follow us on X @SMMT_TX.

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Summit Forward-looking Statements

Any statements in this press release about the Company's future expectations, plans and prospects, including but not limited to, statements about the clinical and preclinical development of the Company's product candidates, entry into and actions related to the Company's partnership with Akeso Inc., the intended use of the net proceeds from the private placements, the Company's anticipated spending and cash runway, the therapeutic potential of the Company's product candidates, the potential commercialization of the Company's product candidates, the timing of initiation, completion and availability of data from clinical trials, the potential submission of applications for marketing approvals, potential acquisitions, statements about the previously disclosed At-The-Market equity offering program ("ATM Program"), the expected proceeds and uses thereof, and other statements containing the words "anticipate," "believe," "continue," "could," "estimate," "expect," "intend," "may," "plan," "potential," "predict," "project," "should," "target," "would," and similar expressions, constitute forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995. Actual results may differ materially from those indicated by such forward-looking statements as a result of various important factors, including the Company's ability to sell shares of our common stock under the ATM Program, the conditions affecting the capital markets, general economic, industry, or political conditions, including the results of our evaluation of the underlying data in connection with the development and commercialization activities for ivonescimab, the outcome of discussions with regulatory authorities, including the Food and Drug Administration, the uncertainties inherent in the initiation of future clinical trials, availability and timing of data from ongoing and future clinical trials, the results of such trials, and their success, and global public health crises, that may affect timing and status of our clinical trials and operations, whether preliminary results from a clinical trial will be predictive of the final results of that trial or whether results of early clinical trials or preclinical studies will be indicative of the results of later clinical trials, whether business development opportunities to expand the Company's pipeline of drug candidates, including without limitation, through potential acquisitions of, and/or collaborations with, other entities occur, expectations for regulatory approvals, laws and regulations affecting government contracts and funding awards, availability of funding sufficient for the Company's foreseeable and unforeseeable operating expenses and capital expenditure requirements and other factors discussed in the "Risk Factors" section of filings that the Company makes with the Securities and Exchange Commission. Any change to our ongoing trials could cause delays, affect our future expenses, and add uncertainty to our commercialization efforts, as well as to affect the likelihood of the successful completion of clinical development of ivonescimab. Accordingly, readers should not place undue reliance on forward-looking statements or information. In addition, any forward-looking statements included in this press release represent the Company's views only as of the date of this release and should not be relied upon as representing the Company's views as of any subsequent date. The Company specifically disclaims any obligation to update any forward-looking statements included in this press release.

Appendix: Glossary of Critical Terms Contained Herein

Affinity – Affinity is the strength of binding of a molecule, such as a protein or antibody, to another molecule, such as a ligand.

Avidity – Avidity is the accumulated strength of multiple binding interactions.

Angiogenesis – Angiogenesis is the development, formation, and maintenance of blood vessel structures. Without sufficient blood flow, tissue may experience hypoxia (insufficient oxygen) or lack of nutrition, which may cause cell death.[1]

Cooperative binding – Cooperative binding occurs when the number of binding sites on the molecule that can be occupied by a specific ligand (e.g., protein) is impacted by the ligand's concentration. For example, this can be due to an affinity for the ligand that depends on the amount of ligand bound or the binding strength of the molecule to one ligand based on the concentration of another ligand, increasing the chance of another ligand binding to the compound.[2]

Immunotherapy – Immunotherapy is a type of treatment, including cancer treatments, that help a person's immune system fight cancer. Examples include anti-PD-1 therapies.[3]

Intracranial - Within the cranium or skull.

PD-1 – Programmed cell Death protein 1 is a protein on the surface of T cells and other cells. PD-1 plays a key role in reducing the regulation of ineffective or harmful immune responses and maintaining immune tolerance. However, with respect to cancer tumor cells, PD-1 can act as a stopping mechanism (a brake or checkpoint) by binding to PD-L1 ligands that exist on tumor cells and preventing the T cells from targeting cancerous tumor cells.[4]

PD-L1 – Programmed cell Death Ligand 1 is expressed by cancerous tumor cells as an adaptive immune mechanism to escape anti-tumor responses, thus believed to suppress the immune system's response to the presence of cancer cells.[5]

PD-L1 TPS – PD-L1 Tumor Proportion Score represents the percentage of tumor cells that express PD-L1 proteins.

PFS – Progression-Free Survival.

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[1] Shibuya M. Vascular Endothelial Growth Factor (VEGF) and Its Receptor (VEGFR) Signaling in Angiogenesis: A Crucial Target for Anti- and Pro-Angiogenic Therapies. Genes Cancer. 2011 Dec;2(12):1097-105

[2] Stefan MI, Le Novère N. Cooperative binding. PLoS Comput Biol. 2013;9(6)

[3] US National Cancer Institute, a part of the National Institute of Health (NIH). https://www.cancer.gov/about-cancer/treatment/types/immunotherapy. Accessed April 2024.

[4] Han Y, *et al.* PD-1/PD-L1 Pathway: Current Researches in Cancer. Am J Cancer Res. 2020 Mar 1;10(3):727-742.

[5] Han Y, *et al.* PD-1/PD-L1 Pathway: Current Researches in Cancer. Am J Cancer Res. 2020 Mar 1;10(3):727-742.

RANO – Response Assessment in Neuro-Oncology, the standard for assessing the response of a brain or spinal cord tumor to therapy.

SQ-NSCLC – Non-small cell lung cancer tumors of squamous histology.

T Cells – T cells are a type of white blood cell that is a component of the immune system that, in general, fights against infection and harmful cells like tumor cells.[6]

Tetravalent – A tetravalent molecule has four binding sites or regions.

Tumor Microenvironment – The tumor microenvironment is the ecosystem that surrounds a tumor inside the body. It includes immune cells, the extracellular matrix, blood vessels and other cells, like fibroblasts. A tumor and its microenvironment constantly interact and influence each other, either positively or negatively.[7]

VEGF – Vascular Endothelial Growth Factor is a signaling protein that promotes angiogenesis.[8]

[6] Cleveland Clinic. https://my.clevelandclinic.org/health/body/24630-t-cells. Accessed April 2024.

[7] MD Anderson Cancer Center. https://www.mdanderson.org/cancerwise/what-is-the-tumor-microenvironment-3-things-to-know.h00-159460056.html. Accessed April 2024.

[8] Shibuya M. Vascular Endothelial Growth Factor (VEGF) and Its Receptor (VEGFR) Signaling in Angiogenesis: A Crucial Target for Anti- and Pro-Angiogenic Therapies. Genes Cancer. 2011 Dec;2(12):1097-105.