Ivonescimab Monotherapy Decisively Beats Pembrolizumab Monotherapy Head-to-Head, Achieves Statistically Significant Superiority in PFS in First-Line Treatment of Patients with PD-L1 Positive NSCLC in China

Unprecedented: Ivonescimab Is the First Drug to Achieve Clinically Meaningful Benefit over Pembrolizumab in Randomized Phase III Clinical Trial in NSCLC

Monotherapy Ivonescimab Achieved Clinically Meaningful PFS Benefit in HARMONi-2 Trial Conducted by Akeso

PFS Improvement Was Observed Broadly in Patients Across Subgroups, including PD-L1 Low and PD-L1 High Expressing Tumors, Squamous and Non-Squamous Histologies

Full Data Set to be Presented at an Upcoming Major Medical Conference Planned for Later This Year

Conference Call to be Held at 8:00am ET on Monday, June 3, 2024

Miami, Florida, May 30, 2024 – Summit Therapeutics Inc. (NASDAQ: SMMT) ("Summit," "we," or the "Company") today announced that the Phase III clinical trial, HARMONi-2 or AK112-303, met its primary endpoint of progression-free survival (PFS). HARMONi-2 evaluated monotherapy ivonescimab against monotherapy pembrolizumab in patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) whose tumors have positive PD-L1 expression (PD-L1 TPS $\geq$1%). HARMONi-2 is a single region, multi-center, double-blinded Phase III study conducted in China sponsored by Akeso, Inc. (Akeso, HKEX Code: 9926.HK) with data generated and analyzed by Akeso.

At a prespecified interim analysis conducted by an independent Data Monitoring Committee, ivonescimab demonstrated a statistically significant and clinically meaningful improvement in PFS by blinded independent central radiology review committee (BICR) compared to pembrolizumab. The PFS benefit was demonstrated across clinical subgroups, including those with PD-L1 low expression (PD-L1 TPS 1-49%), PD-L1 high expression (PD-L1 TPS $\geq$50%), squamous and non-squamous histologies, as well as other high-risk patients.

There are no known Phase III clinical trials in NSCLC which have shown a statistically significant improvement compared to pembrolizumab in a head-to-head setting.

The Phase III HARMONi-2 study, along with the approval of ivonescimab in China in combination with chemotherapy based on the results of the HARMONi-A trial, provides clear evidence supporting the purposefully-engineered, differentiated mechanism of action of ivonescimab, a PD-1 / VEGF bispecific antibody evidencing cooperative binding characteristics, and its opportunity to improve upon the existing standards of care for solid tumors.

"HARMONi-2 clearly demonstrates that ivonescimab is the next generation in PD-1 directed immunotherapy, and its potential to make a significant difference in the lives of patients with lung cancer and prospectively other solid tumors," stated Dr. Maky Zanganeh, Chief Executive Officer and President of Summit. "We want to congratulate our partners at Akeso for this incredible result and their work to advance the patient-friendly standards of care today and well into the future. This result validates Team Summit's present-time intention to execute a development plan worthy of ivonescimab's emergent potential – including clinical trials in both NSCLC and other tumors where ivonescimab can improve upon existing standards of care."

"This is an historic moment for ivonescimab, Team Summit, our partners at Akeso, and most importantly, we believe this is the beginning of a paradigm change for treatment options for patients living with cancer," added Robert W. Duggan, Chairman and Chief Executive Officer of Summit. "We are incredibly proud of our partnership with Akeso and their accomplishment with the HARMONi-2 trial."

Conference Call

Summit Therapeutics Inc. will host a conference call to discuss recent updates related to ivonescimab, including data released at ASCO, on Monday June 3, 2024, before the market opens.

Summit will host a live webcast of the conference call at 8:00am ET, which will be accessible through our website www.smmttx.com. An archived edition of the session will be available on our website.

About Ivonescimab

Ivonescimab, known as SMT112 in Summit's license territories, the United States, Canada, Europe, and Japan, 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 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 tumor microenvironment 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*.[1] 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,[1] is to improve upon previously established efficacy thresholds, in addition to side effects and safety profiles associated with these targets.

Ivonescimab was discovered by Akeso Inc. (HKEX Code: 9926.HK) and is currently engaged in multiple Phase III clinical trials. Over 1,600 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 Phase III clinical trials, HARMONi and HARMONi-3.

The safety profile of ivonescimab is manageable and consistent with known risks for PD-1 and VEGF inhibiting drugs. In the first Phase III study to be presented at ASCO, "Ivonescimab combined with chemotherapy in patients with EGFR-mutant non-squamous NSCLC who progressed on EGFR TKI treatment (HARMONi-A): A randomized, double-blind, multi-center, phase 3 trial," 5.6% of patients discontinued ivonescimab due to adverse events.

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

[1] Zhong, et al, SITC 2023

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.

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.

About Lung Cancer
Lung cancer is believed to impact approximately 600,000 people across the United States, United Kingdom, Spain, France, Italy, Germany, and Japan.[2] NSCLC is the most prevalent type of lung cancer and represents approximately 80% to 85% of all incidences.[3] Among patients with non-squamous NSCLC, approximately 15% have EGFR-sensitizing mutations in the United States and Europe.[4] Patients with squamous histology represent approximately 25% to 30% of NSCLC patients.[5]

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 @summitplc.

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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 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,

[2] American Cancer Society: www.cancer.org/cancer/types/lung-cancer/about/key-statistics.html. Accessed April 2024; World Health Organization: International Agency for Research on Cancer, Globocan data by country (UK, Spain, France, Italy, Germany); Japan National Cancer Registry.

[3] Schabath MB, Cote ML. Cancer Progress and Priorities: Lung Cancer. Cancer Epidemiology, Biomarkers & Prevention. (2019).

[4] About EGFR-Positive Lung Cancer | Navigating EGFR (lungevity.org).

[5] Schabath MB, Cote ML. Cancer Progress and Priorities: Lung Cancer. Cancer Epidemiology, Biomarkers & Prevention. (2019).

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 use 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.[6]

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.[7]

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.[8]

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.[9]

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.[10]

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

PFS – Progression-Free Survival.

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

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[6] 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

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

[8] 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.

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

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

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.[11]

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.[12]

VEGF – Vascular Endothelial Growth Factor is a signaling protein that promotes angiogenesis.[13]

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

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

[13] 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.