Ivonescimab Monotherapy Reduced the Risk of Disease Progression or Death by 49% Compared to Pembrolizumab Monotherapy in First-Line Treatment of Patients with PD-L1 Positive Advanced NSCLC in China

Summit to Initiate HARMONi-7, a Phase III Trial in First-Line PD-L1 High, Advanced NSCLC, in Early 2025

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

Median PFS of 11.14 Months vs. 5.82 Months, Respectively, for Patients Receiving Ivonescimab vs. Pembrolizumab; PFS Improvement Was Observed Broadly in Patients Across Subgroups, including PD-L1 High and Low Expressing Tumors, Squamous and Non-Squamous Histologies

Comparable Serious Treatment-Related Adverse Events and TRAE-Led Discontinuation Rates Were Observed; Serious TRAEs were 20.8% vs. 16.1%, Respectively, in Ivonescimab and Pembrolizumab Arms

Encouraging Perioperative NSCLC Phase II Data Also Featured in an Oral Presentation at WCLC 2024

Three Additional Phase II Solid Tumor Settings beyond NSCLC Featuring Ivonescimab to be Presented at ESMO 2024

Conference Call to be Held at 8:30am ET on Monday, September 9, 2024

Miami, Florida, September 8, 2024 – Summit Therapeutics Inc. (NASDAQ: SMMT) ("Summit," "we," or the "Company") today announced data from the primary analysis of the Phase III HARMONi-2 trial featuring the novel, potential first-in-class investigational bispecific antibody, ivonescimab. The data was presented this morning as part of the Presidential Symposium at the International Association for the Study of Lung Cancer's (IASLC) 2024 World Conference on Lung Cancer (WCLC 2024) in San Diego, California.

The HARMONi-2 presentation, *Phase 3 Study of Ivonescimab (AK112) vs. Pembrolizumab as First-line Treatment for PD-L1-positive Advanced NSCLC: Primary Analysis of 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 ≥1%). HARMONi-2 is a single region, multi-center, double-blinded Phase III study conducted in China sponsored by our collaboration partner, Akeso, Inc. (Akeso, HKEX Code: 9926.HK), with data generated and analyzed by Akeso.

The trial results were presented by Professor Caicun Zhou, MD, PhD, Chief Physician and Director of the Department of Medical Oncology at Shanghai Pulmonary Hospital, Tongji University School of Medicine, and President-Elect of IASLC.

Clinically Meaningful Efficacy

In the HARMONi-2 primary analysis, ivonescimab monotherapy demonstrated a statistically significant improvement in the trial's primary endpoint, progression-free survival (PFS) by Independent Radiologic Review Committee (IRRC), when compared to monotherapy pembrolizumab, achieving a hazard ratio (HR) of 0.51 (95% CI: 0.38, 0.69; p<0.0001). A clinically meaningful 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 ≥ 50%), squamous and

non-squamous histologies, as well as other high-risk patients. Both the overall response rate (ORR) measured according to RECIST v1.1 criteria as well as the disease control rate (DCR) were higher in patients treated with ivonescimab compared to those treated with pembrolizumab.

HARMONi-2 ITT (n=398); *Median Follow-up: 8.67 mos*	**Ivonescimab (n=198)**	**Pembrolizumab (n=200)**
Median PFS	11.14 mos (95% CI: 7.33, NE)	5.82 mos (95% CI: 5.03, 8.21)
PFS Stratified HR	0.51 (95% CI: 0.38, 0.69; p<0.0001)	
ORR	50.0% (95% CI: 42.8%, 57.2%)	38.5% (95% CI: 31.7%, 45.6%)
DCR	89.9% (95% CI: 84.8%, 93.7%)	70.5% (95% CI: 63.7%, 76.7%)

HARMONi-2 Subgroup Analyses	**Ivonescimab vs. Pembrolizumab**
PD-L1 High (PD-L1 TPS ≥50%) PFS stratified HR *Ivonescimab n=83; Pembrolizumab n=85*	0.46 (95% CI: 0.28, 0.75)
PD-L1 Low (PD-L1 TPS 1-49%) PFS stratified HR *Ivonescimab n=115; Pembrolizumab n=115*	0.54 (95% CI: 0.37, 0.79)
Squamous histology PFS stratified HR *Ivonescimab n=90; Pembrolizumab n=91*	0.48 (95% CI: 0.31, 0.74)
Non-Squamous histology PFS stratified HR *Ivonescimab n=108; Pembrolizumab n=109*	0.54 (95% CI: 0.36, 0.82)

Overall survival data was not yet mature at the time of the data cutoff and will be evaluated in the future.

Manageable Safety Profile

Ivonescimab demonstrated an acceptable and manageable safety profile, which was consistent with previous studies. There were three patients (1.5%) who discontinued ivonescimab due to TRAEs compared to six patients (3.0%) who discontinued pembrolizumab due to TRAEs. There was one patient in the ivonescimab arm and two patients in the pembrolizumab arm who died as a result of TRAEs in this Phase III study. The most frequent treatment-related adverse events (TRAEs) for ivonescimab treatment were proteinuria (Grade 3+: ivonescimab, 3.0%; pembrolizumab 0.0%), hypertension (Grade 3+: ivonescimab, 5.1%; pembrolizumab 0.5%), and various laboratory abnormalities, including AST increases, hypercholesterolemia, anemia, and bilirubin increases. Grade 3 or higher immune-related adverse events occurred in 7.1% of patients receiving ivonescimab and 8.0% of patients receiving pembrolizumab. Grade 3 or higher adverse events that were possibly VEGF-related in the ivonescimab monotherapy arm were 10.2% vs. 1.0% for pembrolizumab, all of which were classified as Grade 3. Of note, Grade 3 hemorrhage events were observed in two patients in the ivonescimab arm (both were of non-squamous histology) compared to one patient in the pembrolizumab arm in this study.

HARMONi-2 (n=396)	Ivonescimab (n=197)	Pembrolizumab (n=199)
TRAEs Grade 3+	29.4%	15.6%
Serious TRAEs (TRSAEs)	20.8%	16.1%
TRAEs Leading to Drug Discontinuation	1.5%	3.0%
TRAEs Leading to Death	0.5%	1.0%
Grade 3+ Immune-related	7.1%	8.0%
Grade 3+ Possibly VEGF-related*	10.2%	1.0%

**All Grade 3+ adverse events that were possibly VEGF-related were classified as Grade 3 events in both arms; there were no Grade 4 or 5 adverse events that were possibly VEGF-related observed in either arm.*

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

Based on the results of HARMONi-2, Summit announced its intention to initiate HARMONi-7 in early 2025. HARMONi-7 is currently planned as a multi-regional Phase III clinical trial that will compare ivonescimab monotherapy to pembrolizumab monotherapy in patients with metastatic NSCLC whose tumors have high PD-L1 expression (PD-L1 TPS $\geq$ 50%).

"HARMONi-2 clearly demonstrates that ivonescimab has the potential to be the next generation in PD-1 directed immunotherapy, and potentially make a significant difference in the lives of patients with lung cancer and prospectively other tumors," added Dr. Maky Zanganeh, Chief Executive Officer and President of Summit. "We want to again congratulate Akeso for this incredible result and their work to advance the patient-friendly standards of care today and well into the future. We look forward to initiating HARMONi-7 and sharing additional details about our expanded clinical development plan in early 2025."

Phase II Perioperative NSCLC

In addition to the HARMONi-2 data presentation, a second oral presentation featuring ivonescimab was presented by Xiaoliang Zhao, MD, Deputy Chief Physician, Department of Lung Cancer at Tianjin Medical University Cancer Institute & Hospital, and Visiting Scholar at the Lombardi Comprehensive Cancer Center at Georgetown University in Washington, D.C. The presentation was entitled, *A Phase II Study of Perioperative Ivonescimab Alone or Combined with Chemotherapy in Resectable Non-Small Cell Lung Cancer*, presenting the results from AK112-205, a single-region (China), multi-center, open-label Phase II study of patients with Stage II or III resectable NSCLC.

The study is designed to assess patients receiving either ivonescimab monotherapy or ivonescimab plus chemotherapy prior to surgical resection and then ivonescimab monotherapy after surgery. Due to the maturity of the data and the timing of the data cutoff, the results were limited to the neo-adjuvant, or pre-surgery, portion of the clinical trial. At the time of data cutoff, 49 patients had been enrolled into the ivonescimab plus chemotherapy arm in the neo-adjuvant setting; of these 49 patients, 39 went on to complete surgery.

Of the 39 patients who received ivonescimab plus chemotherapy in the neo-adjuvant stage and completed surgery, 71.8% of patients experienced a major pathological response (MPR) and 43.6% of patients experienced a pathological complete response (pCR). In the 49 patients enrolled in this cohort, median event-free survival (EFS) was not yet reached after 8.9 months of median follow-up time; the 12-month EFS rate was 80.3% (95% CI: 59.6, 91.1). These results are encouraging compared to the historical data that has been observed in global pivotal studies in a similar setting. The safety profile was manageable: of the 49 patients who received ivonescimab plus chemotherapy in the neo-adjuvant setting, Grade 3 or higher adverse events were observed in 32.7% of patients; there was one patient who experienced a treatment-related serious adverse event. There were no TRAEs leading to delayed or cancelled surgery or that led to the death of a patient.

Additional Phase II Data to be Presented at ESMO 2024

Beyond the data recently featured at WCLC 2024, Phase II data featuring ivonescimab will be presented at the European Society of Medical Oncology (ESMO) Congress 2024. ESMO 2024 will take place in Barcelona, Spain, from September 13 – 17, 2024.

These presentations, which will feature data from studies sponsored by Akeso including first-line treatment for triple-negative advanced breast cancer (TNBC), first-line treatment for advanced head and neck squamous cell carcinoma (HNSCC), and first-line treatment of advanced colorectal cancer (CRC).

About the ESMO 2024 Presentations

Presentation Title: The efficacy and safety of ivonescimab with or without ligufalimab in combination with FOLFOXIRI (chemotherapy) as first-line treatment for metastatic colorectal cancer (mCRC)

ESMO Presentation No.: 514MO

Session Date & Time: Saturday, September 14, 3:50 to 3:55pm CET

Presentation Title: The safety and efficacy of ivonescimab in combination with chemotherapy as first-line treatment for triple-negative breast cancer (TNBC)

ESMO Presentation No.: 347MO

Session Date & Time: Monday, September 16, 8:30 to 8:35pm CET

Poster Title: Evaluation of the safety and efficacy of ivonescimab in combination with ligufalimab as first-line treatment for PD-L1 positive recurrent/metastasis head and neck squamous cell carcinoma (R/M HNSCC)

ESMO Poster No.: 876P

Poster Display Date & Time: Saturday, September 14, 12:00 to 1:00pm CET

Conference Call

Summit Therapeutics Inc. will host a conference call to discuss recent updates related to ivonescimab, including data released at WCLC, on Monday September 9, 2024, before the market opens.

Summit will host a live webcast of the conference call at 8:30am ET, which will be accessible through our website www.smmttx.com, and can also be accessed via the following link: https://events.q4inc.com/attendee/904766612.

The dial-in information for US attendees is toll-free at (800) 715-9871. Additionally, all attendees may access through the toll number, (646) 307-1963. The Conference ID is 9820029.

An archived edition of the webcast will be available on our website later in the day on Monday.

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 ≥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.

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., including the expected benefits of the amendment to the collaboration and license agreement, the intended use of the net proceeds from the private placement, 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.

Monotherapy – a medical treatment that consists of a single drug or therapy.

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.

Perioperative – around the time of surgery, typically considered to mean both before and after a surgery.

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[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.

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.

RECIST v1.1 – A generally-accepted way to measuring and evaluating the response of a tumor in clinical trials. The criteria is designated by an international group of experienced physicians in drug development from academic research backgrounds, government backgrounds and industry backgrounds, as well as imaging specialists and statisticians, referred to as the RECIST Working Group.[6]

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.[7]

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.[8]

VEGF – Vascular Endothelial Growth Factor is a signaling protein that promotes angiogenesis.[9]

[6] Eisenhauer, *et. al.* New response evaluation criteria in solid tumours: Revised RECIST guideline (version 1.1), Eur J Cancer. 2009 Jan;45(2):228-47.
[7] Cleveland Clinic. https://my.clevelandclinic.org/health/body/24630-t-cells. Accessed April 2024.
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[9] 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.