Promising Anti-Tumor Activity and Safety of Ivonescimab in Combination Therapies in CRC, TNBC, and HNSCC Featured at ESMO 2024

Two Oral Presentations Featured Updated Ivonescimab Data from Phase II Studies in CRC and TNBC in Addition to Poster Presentation on HNSCC

Encouraging Phase II Data Supports the Continuing Expansion of the Clinical Development of Ivonescimab Outside of Metastatic Non-Small Cell Lung Cancer

Miami, Florida, September 16, 2024 – Summit Therapeutics Inc. (NASDAQ: SMMT) ("Summit," "we," or the "Company") today announced that data for the novel, potential first-in-class investigational bispecific antibody, ivonescimab, was presented at the 2024 European Society for Medical Oncology Annual Meeting (ESMO 2024) in Barcelona, Spain, including two presentations and one poster featuring updated ivonescimab data in advanced triple-negative breast cancer (TNBC), recurrent / metastatic head and neck squamous cell carcinoma (HNSCC), and metastatic microsatellite-stable (MSS) colorectal cancer (CRC). Each trial from which the data was generated was a Phase II study conducted in China sponsored by Akeso Inc. (HKEX Code: 9926.HK) with data generated and analyzed by Akeso.

Based on the results of these Phase II data sets as well as data announced earlier in 2024, including early-stage non-small cell lung cancer and biliary tract cancer, Summit intends to explore further clinical development of ivonescimab in solid tumor settings outside of metastatic non-small cell lung cancer, the Company's current area of focus in its Phase III clinical trials.

Metastatic MSS Colorectal Cancer

The first oral presentation was presented by Dr. Yanhong Deng, Sun Yat-Sen University. The presentation was entitled, *The efficacy and safety of ivonescimab with or without ligufalimab in combination with FOLFOXIRI (chemotherapy) as first-line treatment for metastatic CRC,* presenting the current data from AK112-206, included data from this single-region (China), multicenter, open-label, Phase II randomized study of patients with first-line metastatic MSS CRC (NCT05382442).

The study was designed to assess patients who were randomly assigned to receive ivonescimab plus FOLFOXIRI with or without ligufalimab (anti-CD47 monoclonal antibody). Note that ligufalimab, or AK117, is Akeso's proprietary, investigational product that is not approved by any regulatory authority, and to which Summit does not have any license or ownership rights.

As of February 29, 2024, 22 patients received ivonescimab plus FOLFOXIRI ("Group A" with median follow-up time of 9 months); 18 patients received ivonescimab plus ligufalimab plus FOLFOXIRI ("Group B" with median follow-up time of 9.6 months).

	Ivonescimab + Chemo (Group A) (n = 22)	**Ivonescimab + Ligufalimab + Chemo (Group B) (n = 18)[a]**
Overall response rate	81.8% (95% CI: 59.7, 94.8)	88.2% (95% CI: 63.6, 98.5)
Disease control rate	100% (95% CI: 84.6, 100)	100% (95% CI: 80.5, 100)
Median PFS	NR	NR

9-month PFS rate	81.4% (95% CI: 52.1, 93.7)	86.2% (95% CI: 55.0, 96.4)
Serious TRAE	22.7%	11.1%
TRAEs Leading to Permanent Discontinuation	0	5.6%

[a] As of data cutoff, one patient in Group B had not yet had a post-baseline tumor assessment; Group B response and control rates based on n=17.

All patients in both Group A and Group B experienced a reduction in their tumor burden compared to their baseline tumor assessment. The overall response rate and the disease control rate for the 39 patients who had a least one post-baseline tumor assessment was 84.6% and 100%, respectively. Median progression-free survival was not reached in either group at the time of this analysis.

The safety profile in this Phase II study was acceptable and manageable. No patients receiving ivonescimab plus FOLFOXIRI and one patient receiving ivonescimab plus ligufalimab plus FOLFOXIRI permanently discontinued drug treatment due to treatment-related adverse events. The most common TRAEs were anemia, proteinuria, white blood cell count decreases, and neutrophil count decreases in this Phase II data set.

Advanced Triple Negative Breast Cancer

The second oral presentation was presented by Dr. Xiaojia Wang, Zhejiang Cancer Hospital. The presentation was entitled, *The safety and efficacy of ivonescimab in combination with chemotherapy as first-line (1L) treatment for triple-negative breast cancer (TNBC),* presenting the current data from AK117-203, included data from this single-region (China), multicenter, open-label, Phase II study (NCT05227664).

The results presented were from the portion of the study intended to assess patients who received ivonescimab plus chemotherapy (either paclitaxel or nab-paclitaxel) with locally advanced or metastatic TNBC.

As of May 31, 2024, 30 patients received ivonescimab plus chemotherapy with median follow-up time of 10.2 months. Sixty percent of patients had previously received taxane-based chemotherapy in either the neoadjuvant or adjuvant setting in this Phase II data set.

	Overall (n = 30)[a]
Overall response rate	72.4%
Disease control rate	100%
Median PFS	9.3 months (95% CI: 6.24, NE)
Serious TRAE	30%
TRAEs Leading to Permanent Discontinuation	0

	PD-L1 CPS ≥10 (n = 6)	PD-L1 CPS <10 (n = 24)[a]	PD-L1 CPS <1 (n = 16)[a]
Overall response rate	83.3%	69.6%	86.7%
Disease control rate	100%	100%	100%
Median PFS	NR (5.36, NE)	9.3 months (5.55, NE)	9.3 months (5.26, NE)

[a] As of data cutoff, one patient with a PD-L1 CPS expression of 0 had not yet had a post-baseline tumor assessment; Overall patients, PD-L1 CPS <10, and PD-L1 CPS <1 response and control rates based on n=29, n=23, and n=15, respectively.

All patients experienced a reduction in their tumor burden compared to their baseline tumor assessment. The overall response rate and the disease control rate for the 29 patients who had at least one post-baseline tumor assessment were 72.4% and 100%, respectively. Median progression-free survival was 9.30 months as the time of this analysis.

The safety profile in this Phase II study was acceptable and manageable. No patients receiving ivonescimab plus chemotherapy permanently discontinued drug treatment due to treatment-related adverse events. The most common TRAEs were white blood cell count decreases, ALT increases, alopecia, AST increases, and neutrophil count decreases in this Phase II data set.

Recurrent / Metastatic Head and Neck Squamous Cell Carcinoma

The third data presentation was a poster from Dr. Xiaozhong Chen, *et al*. The poster was entitled, *Evaluation of the safety and efficacy of ivonescimab in combination with ligufalimab (anti-CD47) as first-line treatment for PD-L1 positive recurrent/metastasis HNSCC,* presenting current data from a portion of AK117-201. The data is from a single-region (China), multicenter, open-label, Phase II study (NCT05229497).

The results presented were from the portion of the study intended to assess patients who received ivonescimab with or without ligufalimab (anti-CD47) with PD-L1 positive, locally advanced or metastatic recurrent / metastatic head and neck squamous cell carcinoma.

As of March 19, 2024, 10 patients received ivonescimab (median follow-up: 3.3 months) and 20 patients received ivonescimab plus ligufalimab (median follow-up 4.1 months). Four of 10 patients receiving ivonescimab had a PD-L1 CPS of 1-20; nine of 20 patients administered ivonescimab plus ligufalimab had a PD-L1 CPS of 1-20; the remaining patients in each arm had a PD-L1 CPS ≥20.

	Ivonescimab (n=10)	Ivonescimab + Ligufalimab (n = 20)
Overall response rate	30.0%	60.0%
Disease control rate	80.0%	90.0%
Median PFS	5.0 months	7.1 months

6-month PFS rate	NR	71.8%
Serious TRAE	0	5.0%
TRAEs Leading to Permanent Discontinuation	0	0

The overall response rate and the disease control rate for the 30 patients was 50.0% and 86.7%, respectively.

The safety profile in this Phase II study was acceptable and manageable. No patients receiving ivonescimab or ivonescimab plus ligufalimab in this data set permanently discontinued drug treatment due to treatment-related adverse events. The most common TRAEs in this Phase II data set were proteinuria, dermatitis acneiform (each observed in both arms), and hypothyroidism (observed only in the ivonescimab plus ligufalimab arm).

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 ≥ 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., 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.

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.

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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.

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.