



NEWS RELEASE

Summit Therapeutics Announces Expansion of Ivonescimab Global Phase III Development Program with HARMONi-GI3 Study in 1L Colorectal Cancer

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HARMONi-GI3 is the Fourth Global Phase III Study of Ivonescimab and First Global Study beyond NSCLC

Clinical Trial Site Activations Planned to Begin This Quarter in the United States

Conference Call to be Held at 8:00am ET on Monday, October 20, 2025

MIAMI--(BUSINESS WIRE)-- Summit Therapeutics Inc. (NASDAQ: SMMT) ("Summit," "we," or the "Company") today announced the expansion of its Phase III clinical development program of the novel, potential first-in-class investigational bispecific antibody, ivonescimab, into colorectal cancer (CRC) with the initiation of the global Phase III HARMONi-GI3 trial.

Summit is starting a Phase III clinical study, HARMONi-GI3, to evaluate ivonescimab plus chemotherapy compared to bevacizumab plus chemotherapy as first line therapy in patients with unresectable metastatic colorectal cancer (CRC).

Clinical trial sites for HARMONi-GI3 are planned to begin activating in the United States prior to the end of the year. The multiregional study intends to enroll approximately 600 patients. The primary endpoint for this study is progression-free survival.

Each year, approximately 48,000 patients are estimated to be diagnosed with or have unresectable recurrent metastatic MSS CRC (also known as mismatch repair-proficient colorectal cancer, or pMMR CRC).¹ There have been limited options approved in the United States in the last 20 years for those first-line patients whose tumors are not positive for certain biomarkers or other activating mutations.

MSS CRC is a setting where monoclonal PD-1 inhibitors such as pembrolizumab and nivolumab have failed to show a clinically meaningful benefit. Anti-VEGF therapy (e.g., bevacizumab) plus chemotherapy is the standard of care for many patients with 1L metastatic MSS CRC.

At the 2024 Annual Congress of the European Society of Medical Oncology (ESMO 2024), Akeso Inc. (Akeso) presented encouraging Phase II data of ivonescimab in combination with FOLFOXIRI chemotherapy demonstrating an objective response rate (ORR) of 81.8% (95% CI: 59.7% – 94.8%) and a disease control rate (DCR) of 100% (95% CI: 84.6% – 100.0%) in 22 patients. This Phase II study, AK112-206, was conducted in China and sponsored by Akeso with all relevant data exclusively generated, managed, and analyzed by Akeso. In the ivonescimab plus FOLFOXIRI chemotherapy arm, there were no treatment emergent adverse events that led to permanent discontinuation of ivonescimab as of the data cutoff from the ESMO 2024 presentation.

Subsequently, AK112-206 was expanded to include additional patients from the United States and China to study ivonescimab in combination with FOLFOX chemotherapy. FOLFOX in combination with a monoclonal antibody such as bevacizumab represents a preferred treatment regimen for physicians treating patients in the United States and other western territories. The data from the initial patient cohort presented at ESMO 2024 have continued to mature, in addition to the global Phase II data generated in combination with FOLFOX in the United States and China, which support the Phase III HARMONi-G13 study design using FOLFOX.

“As promised earlier in the year, we sought to expand the ivonescimab clinical development program beyond non-small cell lung cancer in order to continue to explore the potential benefits of its specifically-engineered, novel design and mechanism of action, including its cooperative binding attributes,” stated Robert W. Duggan and Dr. Maky Zanganeh, Co-Chief Executive Officers of Summit. “Microsatellite stable colorectal cancer represents a global unmet need whereby ivonescimab has the potential to bring the benefits of immunotherapy to solid tumors where PD-1 monoclonal antibodies have not been able to successfully improve upon existing standards of care. We are thrilled by the potential of ivonescimab to make a significant difference to these patients with few front-line options available today.”

Conference Call

Summit Therapeutics Inc. will host a conference call and live webcast to discuss recent updates related to

ivonescimab, including data released at ESMO, on Monday, October 20, 2025, at 8:00am ET. Conference call and webcast information will be accessible through our website www.smmmtx.com.

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, North America, South America, Europe, the Middle East, Africa, 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 multi-fold higher affinity to PD-1 when in the presence of 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 specifically engineered tetravalent structure (four binding sites) enables higher avidity (accumulated strength of multiple binding interactions) in the TME (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 after the first dose (Zhong, et al., SITC, 2023) increasing to approximately 10 days at steady state dosing, 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 3,000 patients have been treated with ivonescimab in clinical studies globally.

Summit began its clinical development of ivonescimab in non-small cell lung cancer (NSCLC), commencing enrollment in 2023 in two multiregional Phase III clinical trials, HARMONi and HARMONi-3. In early 2025, the Company began enrolling patients in the United States for HARMONi-7. Summit intends to open clinical trial sites in the United States for the Phase III study in colorectal cancer (CRC) by the end of 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 were previously treated with a 3rd generation EGFR TKI (e.g., osimertinib). Enrollment in HARMONi was completed in the second half of 2024, top-line results were announced in May of 2025, with detailed results provided in September 2025.

HARMONI-3 is a Phase III clinical trial which is intended to evaluate ivonescimab combined with chemotherapy compared to pembrolizumab combined with chemotherapy in patients with first-line metastatic, squamous or non-squamous NSCLC, irrespective of PD-L1 expression.

HARMONI-7 is a 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.

HARMONI-GI3 is a planned Phase III clinical trial evaluating ivonescimab in combination with chemotherapy compared with bevacizumab plus chemotherapy in patients with first-line unresectable metastatic CRC.

In addition, Akeso has recently had positive read-outs in three single-region (China), randomized Phase III clinical trials for ivonescimab in NSCLC: HARMONI-A, HARMONI-2, and HARMONI-6.

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.

HARMONI-6 is a Phase III clinical trial evaluating ivonescimab in combination with platinum-based chemotherapy compared with tislelizumab, an anti-PD-1 antibody, in combination with platinum-based chemotherapy in patients with locally advanced or metastatic squamous NSCLC, irrespective of PD-L1 expression.

Akeso is actively conducting multiple Phase III clinical studies in settings outside of NSCLC, including biliary tract cancer, colorectal cancer, breast cancer, pancreatic cancer, small cell lung cancer, and head and neck cancer.

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 initially 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.

¹ Malla, Midhun, et al.; Journal of the National Comprehensive Cancer Network: JNCCN, 01 May 2023, Vol. 21, Issue

5.5, pages 567 – 571; Buchler T.; Microsatellite Instability and Metastatic Colorectal Cancer - A Clinical Perspective. *Front Oncol.* 2022 Apr 28;12:888181; Cohen R, Platell CF. Metachronous colorectal cancer metastasis: who, what, when and what to do about it. *J Surg Oncol.* 2024; 129: 71-77; SEER data (provided by the US Department of Health and Human Services; US National Institutes of Health; US National Cancer Institute).

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.smmmtx.com> and follow us on X @SMMT_TX.

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, 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, the Company's estimates regarding stock-based compensation, 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, 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, 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" and "Management's Discussion and Analysis of Financial Condition and Results of Operations" sections 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.

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Contact Summit Investor Relations:

Dave Gancarz

Chief Business & Strategy Officer

Nathan LiaBraaten

Senior Director, Investor Relations

investors@smmmtx.com

media@smmmtx.com

Source: Summit Therapeutics