NEWS RELEASE

Ivonescimab Plus Chemotherapy Global Phase III HARMONi Primary Analysis Results Published in The Lancet Oncology

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First Immunotherapy-Based Regimen to Show Statistically Significant and Clinically Meaningful PFS Benefit in a Global Phase III Study of EGFR-Mutated NSCLC after Third-Generation EGFR TKI Progression

Updated OS Data to Be Presented at WCLC 2026

MIAMI--(BUSINESS WIRE)-- Summit Therapeutics Inc. (NASDAQ: SMMT) today announced the publication of primary analysis results from the global Phase III HARMONi clinical trial in The Lancet Oncology. In HARMONi, ivonescimab in combination with platinum-doublet chemotherapy demonstrated a statistically significant and clinically meaningful improvement in progression-free survival (PFS) compared to placebo plus platinum-doublet chemotherapy in patients with epidermal growth factor receptor (EGFR)-mutated, locally advanced or metastatic non-squamous non-small cell lung cancer (NSCLC) whose disease progressed following treatment with a third-generation EGFR tyrosine kinase inhibitor (TKI).

The manuscript, titled “Ivonescimab plus chemotherapy versus placebo plus chemotherapy in patients with advanced EGFR-mutated non-small cell lung cancer after EGFR-TKI progression (HARMONi): a randomised, double-blind, multi-centre phase 3 trial,” reports primary efficacy and safety results from the study conducted at 114 cancer centers and hospitals across Asia, Europe, and North America. The study was designed to evaluate whether

ivonescimab plus chemotherapy could improve clinical outcomes in a setting where treatment options remain limited after progression on EGFR-directed therapy.

“Once a patient with EGFR-mutated lung cancer progresses after a third-generation EGFR TKI, there are limited treatment options for those patients and the survival may be limited,” said Xiuning Le, M.D., Ph.D., Associate Professor, Department of Thoracic/Head and Neck Medical Oncology, The University of Texas MD Anderson Cancer Center, and lead author of the HARMONi manuscript. “In this patient population, traditional anti-PD-(L)1 therapies have not established a clear benefit in prior Phase III studies. The HARMONi results suggest that ivonescimab’s mechanism of action, targeting of PD-1 and VEGF simultaneously in one construct, may offer a clinically meaningful strategy with the potential to improve outcomes for patients.”

HARMONi Primary Analysis Results

At the primary analysis, ivonescimab in combination with chemotherapy demonstrated a statistically significant and clinically meaningful improvement in PFS, as assessed by independent radiographic review committee, compared to placebo plus chemotherapy. Median PFS was 6.8 months in the ivonescimab-plus-chemotherapy arm compared to 4.4 months in the placebo-plus-chemotherapy arm, with a hazard ratio of 0.52 (95% CI: 0.41–0.66; $p<0.0001$). The PFS benefit was consistent across preplanned subgroups. At the time of the primary overall survival (OS) analysis, ivonescimab plus chemotherapy showed a positive OS trend but did not reach statistical significance. The safety profile observed with ivonescimab plus chemotherapy was manageable and consistent with prior clinical experience; treatment-related grade 3–5 hemorrhage events occurred in less than 1% of patients in the ivonescimab-plus-chemotherapy arm.

“The publication of HARMONi in The Lancet Oncology provides peer-reviewed support for the scientific rationale behind ivonescimab and its dual targeting of PD-1 and VEGF in a Phase III setting with high unmet need,” said Dr. Maky Zanganeh, President and Co-Chief Executive Officer of Summit Therapeutics. “In a patient population where outcomes after EGFR TKI progression remain challenging, these data further support our ongoing development of ivonescimab, and we continue to evaluate longer-term results from HARMONi as the data mature. Our commitment remains focused on bringing meaningful new options to patients with significant unmet medical need.”

“The publication of the HARMONi primary analysis data is a meaningful milestone for the patients, caregivers, investigators, and clinical teams who contributed to this global study,” said Robert W. Duggan, Chairman and Co-Chief Executive Officer of Summit Therapeutics. “Together with Akeso, we remain focused on advancing ivonescimab with urgency, discipline, and purpose as we work to translate promising science into meaningful impact for patients.”

Additional HARMONi OS Follow-Up Data to Be Presented at WCLC 2026

On July 22, 2026, Summit **announced** an updated OS analysis from HARMONi based on a June 2026 data cut-off that showed ivonescimab plus chemotherapy continued to demonstrate a positive OS trend and a consistent efficacy and safety profile in Asian and western patients compared with chemotherapy alone; western patients achieved an OS hazard ratio of 0.76, consistent with the global study population. Additional details from the updated HARMONi data analysis will be presented at the International Association for the Study of Lung Cancer's (IASLC) 2026 World Conference on Lung Cancer (WCLC 2026) on September 15, 2026, at 1:02–1:12 p.m. KST (12:02–12:12 a.m. EDT), in the session entitled, "OA14 The Breakthrough Immunotherapy for Advanced NSCLC" (abstract #OA14.04).

As previously communicated, the FDA has assigned a Prescription Drug User Fee Act goal action date of November 14, 2026, for Summit's Biologics License Application for ivonescimab in combination with platinum-doublet chemotherapy for the treatment of patients with epidermal growth factor receptor (EGFR)-mutated, locally advanced or metastatic non-squamous non-small cell lung cancer (NSCLC) whose disease has progressed following treatment with a third-generation EGFR tyrosine kinase inhibitor (TKI).

About EGFR-Mutated NSCLC

Lung cancer is the second most commonly diagnosed cancer worldwide and remains the leading cause of cancer-related death globally, with an estimated 2.6 million new cases and 1.9 million deaths in 2024.[1] In the United States, the American Cancer Society estimates that approximately 230,000 new lung cancer cases will be diagnosed and nearly 125,000 deaths from lung cancer will occur in 2026.[2] Non-small cell lung cancer (NSCLC) is the most common type of lung cancer, representing approximately 80% to 85% of all cases.[1,3]

EGFR mutations are among the most common actionable oncogenic drivers in non-squamous NSCLC, occurring in approximately 10-15% of patients in western populations and 40-50% of patients in Asia.[4,5] Activating EGFR mutations can drive tumor growth through aberrant EGFR signaling.[6] EGFR tyrosine kinase inhibitors (TKIs), including third-generation EGFR TKIs, are an important treatment approach for patients with advanced EGFR-mutated NSCLC.[4]

Despite advances with EGFR-targeted therapy, most patients with locally advanced or metastatic EGFR-mutated NSCLC eventually experience disease progression after treatment with a third-generation EGFR TKI.[7] In patients with EGFR-mutated, locally advanced or metastatic non-squamous NSCLC previously treated with a third-generation EGFR TKI, treatment options remain limited, underscoring the need for new therapeutic approaches after progression on EGFR-targeted therapy.[7]

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 outside of Summit's license territories, 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. By design, ivonescimab displays unique cooperative binding to each of its intended targets with multifold higher affinity to PD-1 when in the presence of VEGF.

This design is intended to 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. Summit believes ivonescimab's specifically engineered tetravalent structure (four binding sites) enables higher avidity (accumulated strength of multiple binding interactions) in the TME (Zhong, et al, iScience, 2025). 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, iScience, 2025) increasing to approximately 10 days at steady state dosing, is to improve upon previously established efficacy thresholds, side effects, and safety profiles associated with prior approved drugs to these targets.

Ivonescimab was engineered by Akeso Inc. (HKEX Code: 9926.HK) and is currently utilized in multiple Phase III clinical trials. Over 4,000 patients have been treated with ivonescimab in clinical studies globally, and over 70,000 patients when considering those treated in a commercial setting in China, as noted by Akeso.

There are currently 16 Phase III clinical studies that are either announced, ongoing, or have been completed studying ivonescimab, five of which are Summit-sponsored global studies, one of which is a multiregional study sponsored by a cooperative group, and 10 of which are being or have been conducted in China by Akeso. Summit began its clinical development of ivonescimab in NSCLC, commencing enrollment in 2023 in two multiregional Phase III clinical trials, HARMONi and HARMONi-3. In 2025, Summit began enrolling patients in HARMONi-7. Summit expanded its Phase III clinical development program into colorectal cancer (CRC) in the fourth quarter of 2025 by initiating enrollment in HARMONi-GI3. In 2026, Summit announced initiation of HARMONi-GU1, a Phase II/III study in urothelial carcinoma (bladder cancer) with global clinical trial site activations planned to begin by the fourth quarter of 2026.

HARMONi is a Phase III clinical trial evaluating 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 third-generation EGFR TKI (e.g., osimertinib). Detailed results of the study were provided in September 2025, and a Biologics License Application (BLA) was submitted to the United States Food and Drug Administration (FDA) for marketing authorization, which the FDA accepted for filing in January 2026; the goal Prescription Drug User Fee Act (PDUFA) date is November 14, 2026.

HARMONi-3 is a Phase III clinical trial evaluating 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. The clinical trial is evaluating the two histologies as individual, separately powered cohorts with independent statistical powering.

HARMONi-7 is a Phase III clinical trial evaluating ivonescimab monotherapy compared to pembrolizumab monotherapy in patients with first-line metastatic NSCLC whose tumors have high PD-L1 expression.

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

HARMONi-GU1 is a Phase II/III clinical trial evaluating ivonescimab plus the antibody drug conjugate (ADC) enfortumab vedotin (EV) compared to pembrolizumab plus EV as first-line therapy in patients with previously untreated locally advanced or metastatic urothelial carcinoma (la/mUC).

ILLUMINE is a Phase III study being conducted by GORTEC, a cooperative group dedicated to Head and Neck Oncology, in recurrent / metastatic head and neck squamous cell carcinoma (r/m HNSCC). ILLUMINE is a three-arm Phase III clinical trial designed to evaluate ivonescimab monotherapy, as well as ivonescimab in combination with ligufalimab, Akeso's proprietary anti-CD47 monoclonal antibody, compared to monotherapy pembrolizumab in patients with PD-L1 positive r/m HNSCC.

Four Phase III ivonescimab clinical trials have read out to date, all four with positive data, in NSCLC. In addition to Summit's positive HARMONi study, Akeso has had positive read-outs in three single-region (China), randomized Phase III clinical trials, HARMONi-A, HARMONi-2, and HARMONi-6, for ivonescimab in NSCLC, including a statistically significant overall survival benefit in both the HARMONi-A and HARMONi-6 studies. A manageable, consistent safety profile was achieved in each of these studies.

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, triple-negative breast cancer, head and neck squamous cell carcinoma, small cell lung cancer, colorectal cancer, and pancreatic 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.

About Summit Therapeutics Inc.

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 the company's shares are listed on the Nasdaq Global Market (symbol "SMMT"). Summit is headquartered in Miami, Florida, with additional offices in Palo Alto, California, Princeton, New Jersey, Dublin, Ireland, and Oxford, UK.

For more information, please visit **https://www.smmttx.com** and follow Summit 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. and other collaborations, 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, the expected timing of BLA submissions or FDA decisions, 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, including the effects of geopolitical developments, domestic and foreign trade policies, and monetary policies, 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. Summit defines a "positive study" as a clinical study with one or more prespecified primary endpoints in which one of those endpoints achieves a statistically significant benefit according to the protocol or statistical analysis plan. 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.

References

1. Sung H, Filho AM, Siegel RL, Laversanne M, Ferlay J, Soerjomataram I, et al. Global cancer statistics 2024: GLOBOCAN estimates of incidence and mortality worldwide for 34 cancers in 186 countries. CA Cancer J Clin. 2026. doi:10.3322/caac.70090.
2. American Cancer Society. **Lung Cancer Statistics: How Common Is Lung Cancer?** Accessed August 20, 2026.
3. American Cancer Society. **What Is Lung Cancer? Types of Lung Cancer**. Accessed August 20, 2026.

4. National Cancer Institute. **Non-Small Cell Lung Cancer Treatment (PDQ®)–Health Professional Version**. Accessed August 20, 2026.
5. Midha A, Dearden S, McCormack R. EGFR mutation incidence in non-small-cell lung cancer of adenocarcinoma histology: a systematic review and global map by ethnicity (mutMapII). Am J Cancer Res. 2015;5(9):2892-2911.
6. Pao W, Chmielecki J. Rational, biologically based treatment of EGFR-mutant non-small-cell lung cancer. Nat Rev Cancer. 2010;10(11):760-774. doi:10.1038/nrc2947.
7. Zhou Q, Zhao H, Lu S, et al. Consensus on the lung cancer management after third-generation EGFR-TKI resistance. Lancet Reg Health West Pac. 2024;53:101260. doi:10.1016/j.lanwpc.2024.101260.

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