



NEWS RELEASE

Ivonescimab Plus Chemotherapy Demonstrates Overall Survival Superiority Compared to Durvalumab Plus Chemotherapy in First-Line Treatment of Patients with Advanced Biliary Tract Cancer in HARMONi-GI1 Study Conducted by Akeso in China

2026-10-25

First Regimen to Achieve a Statistically Significant and Clinically Meaningful Overall Survival Benefit over an Anti-PD-(L)1 Antibody Combined with Chemotherapy in a Phase III Clinical Trial in BTC

Ivonescimab Plus Chemotherapy Reduced the Risk of Death by 25% Compared to Durvalumab Plus Chemotherapy;
OS Hazard Ratio 0.75

Tolerable Safety Profile Consistent with Prior Clinical Trial Results

U.S. Registration-Enabling Phase II / III Study of Ivonescimab in BTC starting in Q4 2026 through Summit's ECOG-ACRIN Collaboration

MIAMI--(BUSINESS WIRE)-- Summit Therapeutics Inc. (Nasdaq: SMMT) today noted that its partner Akeso Inc. announced positive results from the Phase III HARMONi-GI1 study evaluating the novel, potential first-in-class investigational bispecific antibody ivonescimab plus chemotherapy compared with durvalumab plus chemotherapy as a first-line treatment for patients with advanced biliary tract cancer (BTC). These data are featured in today's

Presidential Symposium II at the European Society for Medical Oncology 2026 Congress (ESMO 2026) in Madrid, Spain.

The HARMONi-GI1 presentation is entitled “Ivonescimab plus chemotherapy versus durvalumab plus chemotherapy as first-line treatment for advanced biliary tract cancer: A randomized, controlled, double-blinded, phase 3 trial (HARMONi-GI1).” The HARMONi-GI1 study is a single-region, multi-center, Phase III study conducted in China and sponsored by Akeso, with all relevant data exclusively generated, managed, and analyzed by Akeso. The primary endpoint of the HARMONi-GI1 trial is overall survival (OS) and, as Akeso previously **announced**, a prespecified analysis showed the ivonescimab-based regimen achieved statistically significant and clinically meaningful superiority in OS compared to the durvalumab-based regimen.

Clinically Meaningful Efficacy

In the HARMONi-GI1 interim analysis of OS, ivonescimab in combination with chemotherapy demonstrated a statistically significant improvement when compared to durvalumab in combination with chemotherapy, with a hazard ratio (HR) of 0.75 (95% CI: 0.61, 0.92; one-sided $p=0.0031$). A clinically meaningful benefit was demonstrated across clinical subgroups, including age. Median follow-up time of the current data cut was 14.3 months.

HARMONi-GI1 ITT (n=682): Median Follow-up: 14.3 mos.	Ivonescimab + Chemo (n=340)	Durvalumab + Chemo (n=342)
Median OS	14.9 mos. (95% CI: 12.9, NE)	12.1 mos. (95% CI: 11.0, 13.4)
OS Stratified HR	0.75 (95% CI: 0.61, 0.92; $p = 0.0031$ [one-sided])	
12-Month OS Rates	59.7%	50.7%
18-Month OS Rates	44.0%	32.5%

ITT = intention-to-treat; n = number; mos.: months; CI=confidence interval; NE: not established

Key secondary endpoints in the HARMONi-GI1 study were also met. Ivonescimab in combination with chemotherapy demonstrated a statistically significant improvement in progression-free survival (PFS) when compared with durvalumab in combination with chemotherapy, with an HR of 0.61 (95% CI: 0.51, 0.72; one-sided $p<0.0001$). Objective response rate (ORR) and disease control rate (DCR) were 53.8% and 91.5%, respectively, in the ivonescimab-containing arm, compared with 32.5% and 77.8%, respectively, in the durvalumab-containing arm.

HARMONi-GI1 ITT (n=682): Median Follow-up: 14.3 mos.	Ivonescimab + Chemo (n=340)	Durvalumab + Chemo (n=342)
Median PFS	8.4 mos. (95% CI: 7.5, 9.3)	5.8 mos. (95% CI: 5.6, 7.2)
PFS Stratified HR	0.61 (95% CI: 0.51, 0.72; $p < 0.0001$ [one-sided])	

6-Month PFS Rates	68.7%	49.3%
9-Month PFS Rates	49.3%	31.7%
ORR	53.8% (95% CI: 48.4%, 59.2%)	32.5% (95% CI: 27.5%, 37.7%)
DCR	91.5% (95% CI: 88.0%, 94.2%)	77.8% (95% CI: 73.0%, 82.1%)

ITT=intention-to-treat; n = number; mos.: months; CI=confidence interval

“HARMONi-GI1 marks an important milestone for patients with advanced biliary tract cancer and for the continued development of ivonescimab,” said Dr. Maky Zanganeh, President and Co-Chief Executive Officer of Summit. “This is the first known Phase III study in advanced biliary tract cancer to demonstrate overall survival superiority over an anti-PD-(L)1 therapy combined with chemotherapy. Moreover, as the first Phase III readout for ivonescimab beyond non-small cell lung cancer, the HARMONi-GI1 results further reinforce the potential of ivonescimab to deliver meaningful survival improvements across multiple tumor types and support our commitment to advancing its development for patients with cancers where significant unmet need remains.”

Manageable Safety Profile

In the HARMONi-GI1 study, ivonescimab plus chemotherapy demonstrated an acceptable and manageable safety profile, which was accompanied by longer treatment exposure of ivonescimab compared to durvalumab, and the safety profile was consistent with previous Phase III studies of ivonescimab plus chemotherapy. No additional safety signals were identified.

The most common adverse events of any Grade and of Grade ≥ 3 were hematologic toxicities (namely, decreased neutrophil count, decreased platelet count, decreased white blood cell count, and anemia). Treatment-emergent serious adverse events occurred in 43.4% of patients receiving ivonescimab in combination with chemotherapy and 43.7% of patients receiving durvalumab in combination with chemotherapy. The incidence of immune-related adverse events (irAEs) of all Grades and Grade ≥ 3 was similar between the two arms. The most common possibly VEGF-related adverse events occurring in the ivonescimab plus chemotherapy arm were proteinuria, hypertension, and hemorrhage, with most classified as Grade 1 or 2 in this study. Treatment-emergent adverse events leading to discontinuation of ivonescimab or durvalumab in this study occurred in 3.5% of patients in the ivonescimab arm compared to 5.6% for those in the durvalumab arm.

“These results represent another significant step in realizing the broad potential of ivonescimab to transform outcomes for patients facing some of the most difficult-to-treat cancers,” said Robert W. Duggan, Chairman and Co-Chief Executive Officer of Summit. “Overall survival is the gold-standard measurement of benefit for patients, and the efficacy superiority and safety profile demonstrated in HARMONi-GI1 reinforces our conviction in ivonescimab and its innovative design. We look forward to building upon these findings through our planned registration-enabling Phase II / III study in biliary tract cancer in collaboration with ECOG-ACRIN, as we work to bring this investigational therapy to patients in the United States and beyond.”

On October 21, 2026, Summit **announced** a clinical trial collaboration with ECOG-ACRIN Cancer Research Group (ECOG-ACRIN) to evaluate the safety and efficacy of ivonescimab with chemotherapy compared to pembrolizumab or durvalumab plus chemotherapy in a registration-enabling Phase II / III study (**EA2251**), in the first-line treatment of patients with advanced BTC. The primary endpoint for the study is OS. Activation of U.S. clinical trial sites is expected to begin in the fourth quarter of 2026.

In China, ivonescimab is approved and commercially available for indications in non-small cell lung cancer (NSCLC). Ivonescimab remains investigational and is not approved by any regulatory authority in Summit's license territories, including the United States and Europe.

About Biliary Tract Cancer

Biliary tract cancer (BTC) is a rare and aggressive group of gastrointestinal (GI) cancers that includes intrahepatic, perihilar, and distal cholangiocarcinoma as well as gallbladder cancer.¹ Because BTC often develops with few clear early symptoms, approximately 30% to 50% of patients are diagnosed after the disease has spread, when curative surgery is often no longer an option.² Prognosis remains poor, with five-year survival rates estimated to be less than 5% for patients diagnosed with distant-stage BTCs.^{3,4} Despite recent progress in the treatment of advanced BTC, there remains a significant need for additional therapeutic approaches that can improve outcomes for patients facing this difficult-to-treat disease.⁵

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 ivonescimab's 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 invented by Akeso Inc. (HKEX Code: 9926.HK) and is currently utilized in multiple Phase III clinical trials. Over 5,000 patients have been treated with ivonescimab in clinical studies globally and over 100,000 patients when considering those treated in a commercial setting in China, as noted by Akeso.

There are currently 17 Phase III clinical studies that are either announced, ongoing, or have been completed studying ivonescimab, five of which are Summit-sponsored global studies, two of which are studies sponsored by cooperative groups, and 10 of which are being or have been conducted in China by Akeso. Summit began its clinical development of ivonescimab in NSCLC (HARMONi, HARMONi-3, HARMONi-7) and expanded its sponsored Phase III clinical development program into colorectal cancer (CRC; HARMONi-GI3) and urothelial carcinoma (bladder cancer; HARMONi-GU1). The two cooperative studies are in head and neck squamous cell carcinoma (HNSCC; ILLUMINE) and biliary tract cancer (BTC; EA2251).

EA2251 is a Phase II/III study being conducted by the ECOG-ACRIN Cancer Research Group, an expansive membership-based scientific organization known for advancing precision oncology through its leadership of major national clinical trials. The randomized, open-label study is designed to evaluate the safety and efficacy of ivonescimab with chemotherapy compared to pembrolizumab or durvalumab plus chemotherapy in the first-line treatment of patients with advanced BTC.

Five Phase III ivonescimab clinical trials have read out to date, all five with positive data. Four of these five studies are in NSCLC, and one is in BTC. In addition to Summit's positive HARMONi study in NSCLC, Akeso has had positive read-outs in four single-region (China), randomized Phase III clinical trials: HARMONi-A, HARMONi-2, HARMONi-6 (each in NSCLC), and HARMONi-GI1 (in BTC) for ivonescimab, including a statistically significant overall survival benefit in all four studies from China.

Akeso is actively conducting additional Phase III clinical studies in settings outside of NSCLC and biliary-tract cancer, including 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.smmmtx.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"), or the AstraZeneca private placement; the expected proceeds and uses thereof, dilution to existing stockholders and potential adverse effects on the market price of the Company's common stock, including from future sales by AstraZeneca, the Company's broad discretion over the use of proceeds, and the possibility that the proceeds will not be sufficient to fund operations as long as anticipated, AstraZeneca's ownership and contractual rights, including Third Party acquisition participation, and registration rights, and potential conflicts of interest, the completion of the Private Placement does not depend on the parties entering into a definitive collaboration agreement, the Company's reliance on AstraZeneca for the supply of AstraZeneca's products and other contributions to the clinical trials, 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.

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