Summit Therapeutics Reports Financial Results and Operational Progress for the Fourth Quarter and Twelve Months Ended December 31, 2024

Clinical Trial Collaboration with Pfizer Evaluating Ivonescimab in Combination with Several Vedotin ADCs in Unique Solid Tumor Settings; Clinical Trials Expected to Start Mid-2025

Enrollment Completed for Global, Multi-Regional Phase III HARMONi Trial in 2L+ EGFRm Advanced NSCLC; Top-Line Data Expected Mid-2025; Received Fast Track Designation from FDA

HARMONi-3 Global Phase III Trial Expanded to Include Patients with Squamous and Non-Squamous Histologies

Initial Trial Sites Activated for Global Phase III HARMONi-7 Trial in 1L PD-L1 High, Advanced NSCLC

Miami, Florida, February 24, 2025 - Summit Therapeutics Inc. (NASDAQ: SMMT) ("Summit," "we," or the "Company") today reports its financial results and provides an update on operational progress for the fourth quarter and year-ended December 31, 2024.

Operational & Corporate Updates

Operational progress continues with ivonescimab (SMT112), an investigational, potentially first-in-class 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:

- In January 2023, we closed our Collaboration and License Agreement with Akeso Inc. (Akeso, HKEX Code: 9926.HK) for ivonescimab (SMT112), with which over 2,300 patients have been treated in clinical studies globally. Summit has rights to develop and commercialize ivonescimab in 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 while Akeso retains development and commercialization rights for the rest of the world, including China.

- Since in-licensing ivonescimab, we have begun our development for ivonescimab in non-small cell lung cancer (“NSCLC”), specifically launching Phase III clinical trials in the following proposed indications:

    - *HARMONi*: Ivonescimab combined with chemotherapy in patients with epidermal growth factor receptor (EGFR)-mutated, locally advanced or metastatic non-squamous NSCLC who have progressed after treatment with a third-generation EGFR tyrosine kinase inhibitor (TKI)

    - *HARMONi-3*: Ivonescimab combined with chemotherapy in first-line metastatic NSCLC patients

- In addition, we have begun to activate clinical trial sites in the United States for a Phase III clinical study in the following proposed indication:

    - *HARMONi-7*: Ivonescimab monotherapy in first-line metastatic NSCLC patients with high PD-L1 expression

- In October 2024, we completed enrollment in our HARMONi clinical trial. We expect to disclose topline results from HARMONi in mid-2025, depending upon maturation of the data per the protocol.

    - The U.S. Food and Drug Administration ("FDA") has granted Fast Track designation for the proposed use of ivonescimab in combination with platinum-based chemotherapy for the treatment of adult patients with locally advanced or metastatic NSCLC with EGFR mutation, who have experienced disease progression following EGFR-TKI therapy.

- In the fourth quarter of 2024, we amended the HARMONi-3 protocol to, amongst other changes, include patients with both squamous and non-squamous histologies, significantly increasing the population of patients eligible for treatment in the proposed indication. Enrollment has begun in all regions for patients with squamous tumors; the protocol amendment is effective and enrollment has begun in United States for patients with non-squamous tumors.

- Recently, we announced a clinical trial collaboration with Pfizer in which Pfizer will contribute multiple antibody drug conjugates (ADCs) to be evaluated in combination with ivonescimab in unique solid tumor settings. The goal of the collaboration is to accelerate the advancement of potentially landscape-changing therapeutic combinations, which seek to improve the standards of care for patients facing serious unmet needs.

    - Under the terms of the agreement, Summit will provide ivonescimab for use in the proposed studies, and Pfizer will be responsible for conducting the operations of the studies, including associated costs. The studies will be overseen by both Summit and Pfizer. Both parties retain their respective rights to their products. The studies combining ivonescimab with Pfizer's vedotin ADCs are planned to begin in the middle of this year. Further details on the clinical trials will be announced at a later date.

- We intend to explore further clinical development of ivonescimab in solid tumor settings outside of metastatic non-small cell lung cancer, Additionally, institutions with whom we have collaborated have begun opening investigator-sponsored trials across multiple oncology settings. We plan to review the data generated from these clinical trials as a part of our consideration for advancing our clinical development for ivonescimab beyond non-small cell lung cancer.

Financial Highlights

Cash and Cash Equivalents & Short-term Investments

- Aggregate cash and cash equivalents and short-term investments were $412.3 million and $186.2 million at December 31, 2024 and December 31, 2023, respectively.

GAAP and Non-GAAP Research and Development (R&D) Expenses

- GAAP R&D expenses according to generally accepted accounting principles in the U.S. ("GAAP") were $150.8 million for the full year of 2024, compared to $59.4 million for the full year of 2023.

- Non-GAAP R&D expenses were $134.8 million for the full year of 2024, compared to $55.0 million for the full year of 2023.

GAAP and Non-GAAP General and Administrative (G&A) Expenses

- GAAP G&A expenses were $60.5 million for the full year of 2024, compared to $30.3 million for the full year of 2023.

- Non-GAAP G&A expenses were $25.5 million for the full year of 2024, compared to $20.6 million for the full year of 2023.

GAAP and Non-GAAP Operating Expenses

- GAAP operating expenses were $226.3 million for the full year of 2024, compared to $610.6 million for the full year of 2023.

- Non-GAAP operating expenses were $175.3 million for the full year of 2024, compared to $596.5 million for the full year of 2023. The decrease is primarily related to the decrease in acquired in-process R&D expenses of $505.9 million, offset by the increase in R&D expenses due to expansion of clinical studies and development costs related to ivonescimab and increases in people costs as we continue to build out our team.

GAAP and Non-GAAP Net Loss

- GAAP net loss in the full year of 2024 and 2023 was $221.3 million or $(0.31) per basic and diluted share, and $614.9 million or $(0.99) per basic and diluted share, respectively.

- Non-GAAP net loss in the full year of 2024 and 2023 was $170.3 million or $(0.24) per basic and diluted share, and $600.8 million or $(0.97) per basic and diluted share, respectively.

Use of Non-GAAP Financial Measures

This release includes measures that are not in accordance with U.S. generally accepted accounting principles ("Non-GAAP measures"). These Non-GAAP measures should be viewed in addition to, and not as a substitute for, Summit's reported GAAP results, and may be different from Non-GAAP measures used by other companies. In addition, these Non-GAAP measures are not based on any comprehensive set of accounting rules or principles. Summit management uses these non-GAAP measures for internal budgeting and forecasting purposes and to evaluate Summit's financial performance. Summit management believes the presentation of these Non-GAAP measures is useful to investors for comparing prior periods and analyzing ongoing business trends and operating results. For further information regarding these Non-GAAP measures, please refer to the tables presenting reconciliations of our Non-GAAP results to our U.S. GAAP results and the "Notes on our Non-GAAP Financial Information" that accompany this press release.

Fourth Quarter 2024 Earnings Call

Summit will host an earnings call this morning, Monday, February 24, 2025, at 9:00am ET. The conference call will be accessible by dialing (800) 715-9871 (toll-free domestic) or (646) 307-1963 (international) using conference code 3934052. A live webcast and instructions for joining the call are accessible through Summit's website www.smmttx.com. An archived edition of the webcast will be available on our website after the call.

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 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 (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 2,300 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, and the Company has begun to activate clinical trial sites in the United States for HARMONi-7.

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).

Enrollment in HARMONi was completed in the second-half of 2024, and top-line results are expected to be announced in the middle of this year.

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 NSCLC.

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.

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.

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. Ivonescimab was granted Fast Track designation by the US Food & Drug Administration (FDA) for the HARMONi clinical trial setting.

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, 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" 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.

Summit Therapeutics Inc.
GAAP Condensed Consolidated Statements of Operations
(in millions, except per share data)

	Three Months Ended December 31,		Twelve Months Ended December 31,	
	2024	**2023**	**2024**	**2023**
Operating expenses:				
Research and development	$ 51.4	$ 24.8	$ 150.8	$ 59.4
Acquired in-process research and development	—	—	15.0	520.9
General and administrative	14.4	11.6	60.5	30.3
Total operating expenses	65.8	36.4	226.3	610.6
Other operating income, net	0.2	0.2	0.3	1.0
Operating loss	(65.6)	(36.2)	(226.0)	(609.6)
Other income, net	4.4	2.5	13.4	11.2
Interest expense	—	(2.9)	(8.7)	(16.5)
Loss before income tax	(61.2)	(36.6)	(221.3)	(614.9)
Net loss	$ (61.2)	$ (36.6)	$ (221.3)	$ (614.9)
Net loss per share attributable to common shareholders per share, basic and diluted	$ (0.08)	$ (0.05)	$ (0.31)	$ (0.99)

Summit Therapeutics Inc.
GAAP Condensed Consolidated Balance Sheet Information
(in millions)

	December 31, 2024	December 31, 2023
Cash and cash equivalents and short-term investments	$ 412.3	$ 186.2
Total assets	$ 435.6	$ 202.9
Total liabilities	$ 46.8	$ 125.3
Total stockholders' equity	$ 388.7	$ 77.7

Summit Therapeutics Inc.
GAAP Condensed Consolidated Statement of Cash Flows Information
(in millions)

	Twelve Months Ended December 31,	
	2024	**2023**
Net cash used in operating activities	$ (142.1)	$ (76.8)
Net cash used in investing activities	(205.3)	(587.8)
Net cash provided by financing activities	381.2	86.5
Effect of exchange rates on cash and cash equivalents	—	0.8
Increase (decrease) in cash, cash equivalents and restricted cash	$ 33.8	$ (577.3)

Summit Therapeutics Inc.
Schedule Reconciling Selected Non-GAAP Financial Measures
(in millions, except per share data)

	Three Months Ended December 31,		Twelve Months Ended December 31,	
	2024	**2023**	**2024**	**2023**
Reconciliation of GAAP to Non-GAAP Research and Development Expense				
GAAP Research and development	$ 51.4	$ 24.8	$ 150.8	$ 59.4
Stock-based compensation (Note 1)	(4.3)	(2.4)	(16.0)	(4.4)
Non-GAAP Research and development	$ 47.1	$ 22.4	$ 134.8	$ 55.0
Reconciliation of GAAP to Non-GAAP General and Administrative Expenses				
GAAP General and administrative	$ 14.4	$ 11.6	$ 60.5	$ 30.3
Stock-based compensation (Note 1)	(6.7)	(6.3)	(35.0)	(9.7)
Non-GAAP General and administrative	$ 7.7	$ 5.3	$ 25.5	$ 20.6
Reconciliation of GAAP to Non-GAAP Operating Expenses				
GAAP Operating expenses	$ 65.8	$ 36.4	$ 226.3	$ 610.6
Stock-based compensation (Note 1)	(11.0)	(8.7)	(51.0)	(14.1)
Non-GAAP Operating expense (Note 2)	$ 54.8	$ 27.7	$ 175.3	$ 596.5
Reconciliation of GAAP Net Loss to Non-GAAP Net Loss				
GAAP Net Loss	$ (61.2)	$ (36.6)	$ (221.3)	$ (614.9)
Stock-based compensation (Note 1)	11.0	8.7	51.0	14.1
Non-GAAP Net Loss (Note 2)	$ (50.2)	$ (27.9)	$ (170.3)	$ (600.8)
Reconciliation of GAAP Net Loss to Non-GAAP Net Loss Per Common Share				
GAAP Net Loss Per Basic and Diluted Common Share	$ (0.08)	$ (0.05)	$ (0.31)	$ (0.99)
Stock-based compensation (Note 1)	0.01	0.01	0.07	0.02
Non-GAAP Net loss Per Basic and Diluted Common Share (Note 2)	$ (0.07)	$ (0.04)	$ (0.24)	$ (0.97)
Basic and Diluted Common Shares	737.5	700.6	718.5	619.6

Summit Therapeutics Inc.
Schedule Reconciling Selected Non-GAAP Financial Measures
(in millions)

	Three Months Ended				
	December 31, 2024	September 30, 2024	June 30, 2024	March 31, 2024	December 31, 2023
Reconciliation of GAAP to Non-GAAP Operating Expenses					
GAAP Operating expenses	$ 65.8	$ 58.1	$ 59.8	$ 42.6	$ 36.4
Stock-based compensation (Note 1)	(11.0)	(19.4)	(11.1)	(9.5)	(8.7)
Non-GAAP Operating Expense (Note 2)	$ 54.8	$ 38.7	$ 48.7	$ 33.1	$ 27.7
Reconciliation of GAAP Net Loss to Non-GAAP Net Loss					
GAAP Net Loss	$ (61.2)	$ (56.3)	$ (60.4)	$ (43.5)	$ (36.6)
Stock-based compensation (Note 1)	11.0	19.4	11.1	9.5	8.7
Non-GAAP Net Loss (Note 2)	$ (50.2)	$ (36.9)	$ (49.3)	$ (34.0)	$ (27.9)

Summit Therapeutics Inc.
Notes on our Non-GAAP Financial Information

Non-GAAP financial measures adjust GAAP financial measures for the items listed below. These Non-GAAP measures should be viewed in addition to, and not as a substitute for Summit's reported GAAP results, and may be different from Non-GAAP measures used by other companies. In addition, these Non-GAAP measures are not based on any comprehensive set of accounting rules or principles. Summit management uses these non-GAAP measures for internal budgeting and forecasting purposes and to evaluate Summit's financial performance. Summit management believes the presentation of these Non-GAAP measures is useful to investors for comparing prior periods and analyzing ongoing business trends and operating results.

Each of non-GAAP Research and Development Expense, non-GAAP General and Administrative Expenses, non-GAAP Operating Expenses, Non-GAAP Net Loss and Non-GAAP EPS differ from GAAP in that such measures exclude the non-cash charges and costs associated with stock-based compensation.

Note 1: Stock-based compensation is a non-cash charge and costs calculated for this expense can vary year-over-year depending on the stock price of awards on the date of grant as well as the timing of compensation award arrangements.

Note 2: Beginning in the fourth quarter of 2024, the Company's non-GAAP financial measures will no longer exclude acquired in-process research and development expenses ("IPR&D"). Previously reported non-GAAP financial measures for the twelve months ended December 31, 2023 excluded $520.9 million of IPR&D which represented the upfront payment made to Akeso under the Collaboration and License Agreement. Non-GAAP financial measures for the three months ended June 30, 2024 previously excluded $15.0 million of IPR&D which represented an upfront payment made to Akeso under an amendment to the Collaboration and License Agreement. Prior period amounts have been revised to conform to the current period presentation.

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.

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]

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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.

[6] Cleveland Clinic. https://my.clevelandclinic.org/health/body/24630-t-cells. Accessed April 2024.

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]

[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.