As filed with the Securities and Exchange Commission on September 19, 2024

Registration No. 333-

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM S-3
REGISTRATION STATEMENT
UNDER
THE SECURITIES ACT OF 1933

Summit Therapeutics Inc.
(Exact name of registrant as specified in its charter)

Delaware	**37-1979717**
(State or Other Jurisdiction of Incorporation or Organization)	**(I.R.S. Employer Identification No.)**

601 Brickell Key Drive, Suite 1000
Miami, FL 33131
(305) 203-2034
(Address, including zip code, and telephone number, including area code, of registrant's principal executive offices)

Robert W. Duggan	**Mahkam Zanganeh**
Chairman and Chief Executive Officer	**Chief Executive Officer and President**
Summit Therapeutics Inc.	**Summit Therapeutics Inc.**
601 Brickell Key Drive, Suite 1000	**601 Brickell Key Drive, Suite 1000**
Miami, FL 33131	**Miami, FL 33131**
(305) 203-2034	**(305) 203-2034**

(Name, address, including zip code, and telephone number, including area code, of agent for service)

With copies to:

Adam Finerman, Esq.
Baker & Hostetler LLP
45 Rockefeller Plaza
New York, NY 10111
(212) 589-4233

Approximate date of commencement of proposed sale to the public: From time to time after the effective date of this Registration Statement.

If the only securities being registered on this Form are being offered pursuant to dividend or interest reinvestment plans, please check the following box: ☐

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, other than securities offered only in connection with dividend or interest reinvestment plans, check the following box: ☒

If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, please check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ☐

If this Form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ☐

If this Form is a registration statement pursuant to General Instruction I.D. or a post-effective amendment thereto that shall become effective upon filing with the Commission pursuant to Rule 462(e) under the Securities Act, check the following box. ☒

If this Form is a post-effective amendment to a registration statement filed pursuant to General Instruction I.D. filed to register additional securities or additional classes of securities pursuant to Rule 413(b) under the Securities Act, check the following box. ☐

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company" and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer	☐	Accelerated filer	☐
Non-accelerated filer	☒	Smaller reporting company	☒
		Emerging growth company	☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 7(a)(2)(B) of the Securities Act. ☐

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PROSPECTUS

10,352,418 Shares of Common Stock

This prospectus relates to the proposed resale from time to time by the selling stockholders named herein, together with any of such stockholders' transferees, pledgees, donees or successors, an aggregate of 10,352,418 shares (the "Shares") of our common stock, par value $0.01 per share ("common stock"), issued to the selling stockholders pursuant to those certain securities purchase agreements, each dated as of September 11, 2024 (the "Purchase Agreements"), by and among us and the selling stockholders (the "Selling Stockholders").

We are registering the offer and sale of the Shares from time to time by the Selling Stockholders to satisfy registration rights the Selling Stockholders were granted in connection with the Purchase Agreements. We are not selling any of our common stock pursuant to this prospectus, and we will not receive any proceeds from the sale of our common stock offered by this prospectus by the Selling Stockholders.

The Selling Stockholders may offer and sell or otherwise dispose of the Shares described in this prospectus from time to time through public or private transactions at prevailing market prices, at prices related to prevailing market prices or at privately negotiated prices. The Selling Stockholders will bear all underwriting fees, commissions and discounts, if any, attributable to the sales of Shares and any transfer taxes. We will bear all other costs, expenses and fees in connection with the registration of the Shares. See "Plan of Distribution" for more information about how the Selling Stockholders may sell or dispose of the Shares.

Our common stock is listed on The Nasdaq Global Market under the trading symbol "SMMT." On September 18, 2024, the last reported sales price of our common stock on The Nasdaq Global Market was $24.56 per share.

Investing in our common stock involves a high degree of risk. You should review carefully the risks and uncertainties described under the heading "Risk Factors" on page 8 of this prospectus, and under similar headings in any amendment or supplement to this prospectus or in the other documents that are incorporated by reference into this prospectus.

NEITHER THE SECURITIES AND EXCHANGE COMMISSION NOR ANY STATE SECURITIES COMMISSION HAS APPROVED OR DISAPPROVED OF THESE SECURITIES OR DETERMINED IF THIS PROSPECTUS IS TRUTHFUL OR COMPLETE. ANY REPRESENTATION TO THE CONTRARY IS A CRIMINAL OFFENSE.

The date of this prospectus is September 19, 2024.

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ABOUT THIS PROSPECTUS

This prospectus is part of an automatically effective registration statement on Form S-3 that we filed with the Securities and Exchange Commission (the "SEC") as a "well-known seasoned issuer" as defined in Rule 405 under the Securities Act of 1933, as amended (the "Securities Act"), using a "shelf" registration process. Under this shelf registration process, the Selling Stockholders may from time to time sell Shares described in this prospectus in one or more offerings or otherwise as described under "Plan of Distribution."

Neither we nor the Selling Stockholders have authorized anyone to provide you with any information other than that contained in, or incorporated by reference into, this prospectus. We take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. This prospectus is an offer to sell only the shares of our common stock offered hereby, but only under circumstances and in jurisdictions where it is lawful to do so. You should not assume that the information contained in or incorporated by reference in this prospectus is accurate as of any date other than their respective dates. Our business, financial condition, results of operations and prospects may have changed since those dates.

This prospectus may be supplemented from time to time by one or more prospectus supplements. Such prospectus supplement may add to, update or change the information contained in this prospectus. If there is any inconsistency between the information in this prospectus and the applicable prospectus supplement, you must rely on the information in the prospectus supplement. You should read both this prospectus and any applicable prospectus supplement together with additional information described below under the heading "Where You Can Find Additional Information."

Throughout this prospectus, when we refer to the Selling Stockholders, we are referring to the Selling Stockholders identified in this prospectus and, as applicable, their permitted transferees or other successors-in-interest that may be identified in a supplement to this prospectus or, if required, a post-effective amendment to the registration statement of which this prospectus is a part.

This prospectus contains summaries of certain provisions contained in some of the documents described herein, but reference is made to the actual documents for complete information. All of the summaries are qualified in their entirety by the actual documents. Copies of some of the documents referred to herein have been filed, will be filed or will be incorporated by reference as exhibits to the registration statement of which this prospectus is a part, and you may obtain copies of those documents as described below under the section titled "Where You Can Find Additional Information."

Unless the context indicates otherwise, as used in this prospectus, the terms "Company," "we," "us," "our," and "Summit," and similar designations, except where context requires otherwise, refer collectively to Summit Therapeutics Inc. and its consolidated subsidiaries.

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus, each prospectus supplement and the information incorporated by reference in this prospectus and each prospectus supplement contain "forward-looking statements" within the meaning of Section 27A of the Securities Act and Section 21E of the Exchange Act. These forward-looking statements speak only as of the date of this prospectus or the documents incorporated by reference in this prospectus, as applicable, and are subject to a number of risks, uncertainties and assumptions described under the sections in this prospectus and the documents incorporated by reference herein entitled "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations" and elsewhere in this prospectus and the documents incorporated by reference herein.

In some cases, you can identify forward-looking statements by terminology such as "anticipate," "believe," "continue," "could," "estimate," "expect," "forecast," "intends," "may," "might," "plan," "possible," "potential," "predict," "project," "should," "target," "will," "would" or the negative of such terms or other similar expressions. These forward-looking statements are based on our management's current expectations, assumptions, hopes, beliefs, intentions and strategies regarding future events and are based on currently available information as to the outcome and timing of future events. Although we believe such expectations and assumptions to be reasonable, they are inherently uncertain and involve a number of risks and uncertainties that are beyond our control. In addition, management's assumptions about future events may prove to be inaccurate. All readers are cautioned that these forward-looking statements are not guarantees of future performance and we cannot assure any reader that such statements will be realized or that the forward-looking events and circumstances will occur.

Forward-looking statements in this prospectus and the documents incorporated by reference herein include, but are not limited to, statements about:

- our ability to develop a successful product candidate under the Collaboration and License Agreement, as amended (the "License Agreement"), with Akeso, Inc. and its affiliates ("Akeso");
- our ability to raise sufficient additional funds to make payments under the License Agreement, and fund ongoing operations and capital needs;
- the timing of and the ability to effectively execute clinical development of ivonescimab;
- the timing, costs, conduct and outcomes of clinical trials for any product candidates;
- our plans with respect to possible future collaborations and partnering arrangements;
- the potential benefits of possible future acquisitions or investments in other businesses, products or technologies;
- our plans to pursue research and development of other future product candidates;
- our estimates regarding the potential market opportunity and patient population for commercializing our product candidates, if approved for commercial use;
- our sales, marketing and distribution capabilities and strategy;
- our ability to establish and maintain arrangements with third parties, such as contract research organizations, contract manufacturing organizations, suppliers, and distributors;
- the costs and timing of preparing, filing and prosecuting patent applications, maintaining and protecting our intellectual property rights and defending against any intellectual property-related claims;
- our estimates regarding expenses, future revenues, capital requirements and needs for additional financing;
- the impact of government laws and regulations in the United States and in foreign countries;
- the timing and likelihood of regulatory filings and approvals for our product candidates;

- whether regulatory authorities determine that additional trials or data are necessary in order to accept a new drug application for review and/or approval;
- our competitive position;
- our use of our existing cash, cash equivalents and marketable securities;
- our ability to attract and retain key scientific or management personnel; and
- the impact of public health epidemics, the response to such epidemics and the potential effects of such epidemics on our clinical trials, business, financial results, supply chain and market.

Because forward-looking statements are inherently subject to risks and uncertainties, some of which cannot be predicted or quantified and some of which are beyond our control, you should not rely on these forward-looking statements as predictions of future events. The events and circumstances reflected in our forward-looking statements may not be achieved or occur and actual results could differ materially from those projected in the forward-looking statements. Moreover, we operate in an evolving environment. New risk factors and uncertainties may emerge from time to time, and it is not possible for our management to predict all risk factors and uncertainties. Except as required by applicable law, we undertake no obligation to publicly update or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise. You should, however, review the factors and risks we describe in the reports we will file from time to time with the SEC after the date of this prospectus. See the section entitled “Where You Can Find Additional Information” in this prospectus.

PROSPECTUS SUMMARY

This summary highlights selected information contained elsewhere in this prospectus or incorporated by reference in this prospectus, and does not contain all of the information that you need to consider in making your investment decision. You should carefully read the entire prospectus, including the risks of investing in our securities discussed under the heading "Risk Factors" contained in this prospectus and under similar headings in the other documents that are incorporated by reference into this prospectus. You should also carefully read the information incorporated by reference into this prospectus, including our consolidated financial statements, and the exhibits to the registration statement of which this prospectus is a part.

Company Overview

We are a biopharmaceutical 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. The Company's pipeline of product candidates is designed with the goal to become the patient-friendly, new-era standard-of-care medicines, in the therapeutic area of oncology.

Our current lead development candidate is ivonescimab, a novel, potential first-in-class bispecific antibody intending to combine the effects of immunotherapy via a blockade of PD-1 with the anti-angiogenesis effects of an anti-VEGF compound into a single molecule. On December 5, 2022, we entered into a Collaboration and License Agreement (the "License Agreement") with Akeso, Inc. and its affiliates ("Akeso") pursuant to which we have in-licensed ivonescimab. Through the License Agreement, we obtained the rights to develop and commercialize ivonescimab in the United States, Canada, Europe, and Japan. The License Agreement and transaction closed in January 2023 following customary waiting periods. On June 3, 2024, we entered into an amendment to the License Agreement with Akeso to expand our territories covered under the License Agreement to also include the Latin America, Middle East and Africa regions (collectively, and as expanded, the "Licensed Territory"). Our operations are focused on the development of ivonescimab and other future activities, as we determine.

We have begun our development for ivonescimab in non-small cell lung cancer ("NSCLC"), specifically launching Phase III clinical trials in the following indications:

a) 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"); and

b) ivonescimab combined with chemotherapy in first-line metastatic squamous NSCLC patients ("HARMONi-3").

As of the date of this prospectus, both studies are enrolling and treating patients.

The entry into the License Agreement with Akeso represented a significant change in our strategy and our future operations will be focused on the development of ivonescimab and other future activities as we determine. Our portfolio also includes ridinilazole, a product candidate for treating patients suffering from Clostridioides difficile infection, also known as C. difficile infection ("CDI"), and SMT-738, the first of a novel class of precision antibiotics for combating multidrug resistant infections, specifically carbapenem-resistant Enterobacteriaceae ("CRE") infections. All prior development activities related to ridinilazole and SMT-738 have been terminated; we may explore partnership opportunities for both assets.

Akeso Collaboration and License Agreement

Pursuant to the License Agreement with Akeso, we received the rights to develop and commercialize ivonescimab in the United States, Canada, Europe, and Japan. Akeso will retain development and

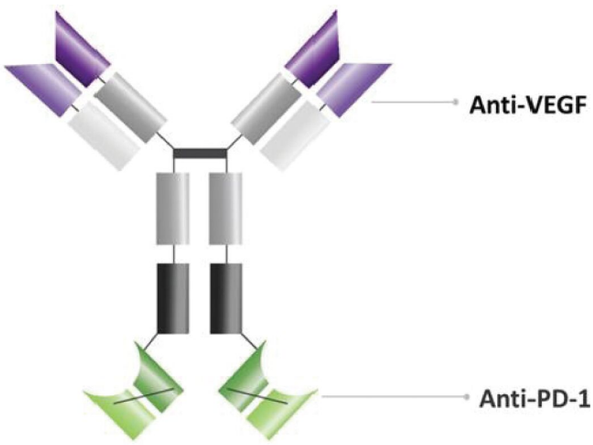
commercialization rights for the rest of the world excluding such licensed territories. In exchange for these rights, we made an upfront payment during the first quarter of 2023 comprised of $474.9 million cash and the issuance of 10 million shares of our common stock in lieu of $25.1 million cash pursuant to a share transfer agreement. Furthermore, on June 3, 2024, we entered into an amendment to the License Agreement with Akeso to expand our territories covered under the License Agreement to also include the Latin America, Middle East and Africa regions (collectively, and as expanded, the "Licensed Territory"), for which we have paid an upfront payment of $15.0 million cash. In addition, we will potentially owe Akeso (a) milestone payments tied to achievement of regulatory approval of ivonescimab with various regulatory authorities in the Licensed Territory (b) milestone payments tied to achievement of annual revenue from ivonescimab in the Licensed Territory and (c) royalty payments equal to low-double-digit percentage of annual revenues from ivonescimab in the Licensed Territory.

Pursuant to the terms of the License Agreement, we will have final decision-making authority with respect to clinical development strategy and execution in the Licensed Territory. For co-joined studies in which both we and Akeso participate, mutual agreement is required for material decisions; we retain the exclusive decision making with respect to participating in, and continuing its participation in, co-joined studies. In connection with the License Agreement, we agreed to enter into a Supply Agreement with Akeso (the "Supply Agreement"). Pursuant to the Supply Agreement, Summit agreed to purchase a certain portion of drug substance for clinical and commercial supply. Pursuant to the terms of the License Agreement, we will have final decision-making authority with respect to commercial strategy, pricing and reimbursement and other commercialization matters in the Licensed Territory.

We have not assumed any liabilities (including contingent liabilities), nor acquired any physical assets or trade names, or hired or acquired any employees from Akeso in connection with the License Agreement.

Ivonescimab

Ivonescimab is a novel potential first-in-class PD-1 / VEGF bispecific antibody, believed to be the most advanced in clinical development in the Licensed Territory; there are no known PD-1 / VEGF bispecific antibodies approved in our Licensed Territory. Engineered with Akeso's unique Tetrabody technology, ivonescimab, as a single molecule, blocks programmed cell death protein 1 ("PD-1") from binding to PD-L1 and PD-L2, and blocks vascular endothelial growth factor ("VEGF") from binding to VEGF receptors. Ivonescimab is designed to potentially allow cooperative binding of the intended targets, such that the binding of PD-1 increases the binding affinity of VEGF and the binding of VEGF increases the affinity towards PD-1. In view of the co-expression of VEGF and PD-1 in the tumor micro-environment ("TME"), ivonescimab may block these two pathways more effectively and enhance the antitumor activity, as compared to combination therapy through what is believed to be a differentiated cooperative binding mechanism.



This could differentiate ivonescimab as there is potentially higher expression (presence) of both PD-1 and VEGF in tumor tissue and the TME as compared to normal tissue in the body. As shown in Akeso's *in-vitro* studies, ivonescimab's tetravalent structure (four binding sites) enables higher avidity (accumulated strength of multiple binding interactions) in the tumor microenvironment 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*. 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 six to seven days, is to improve upon previously established efficacy thresholds, in addition to side effects and safety profiles associated with these targets.

In addition to the two Phase III clinical trials sponsored by us, ivonescimab is also being developed in China and Australia by Akeso in multiple solid tumors and has been dosed in more than 1,800 patients globally.

Based on data published by Akeso at the 2024 Annual Meeting of the American Society of Clinical Oncology (ASCO 2024) in the HARMONi-A study, in a single-region (China), randomized, double-blinded Phase III study in patients with NSCLC who have progressed following an EGFR-TKI, ivonescimab achieved its primary endpoint of Progression-free Survival (PFS) when combined with doublet chemotherapy (pemetrexed and carboplatin). Patients experienced a 54% reduction in disease progression or death as compared to placebo plus doublet-chemotherapy (hazard ratio (HR): 0.46, 95% CI: 0.34 - 0.62; $p<0.001$). In a pre-specified subgroup analysis of patients who received a previous third-generation TKI, a hazard ratio of 0.48 was observed. A median Overall Survival (mOS) in this study of 17.1 months was observed, reflecting a 20% reduction in death as compared to placebo plus chemotherapy in the study (HR: 0.80, 95% CI: 0.59 - 1.08). The Phase III study was considered to have demonstrated a tolerable safety profile and a low discontinuation rate for adverse events.

In addition to the HARMONi-A data, Akeso announced at ASCO 2024 the results from AK117-202, a single-region (China), multi-center, open-label Phase II study, conducted by Akeso, of patients with advanced biliary tract cancer, with data generated and analyzed by Akeso.

Data published by Akeso in March 2024 at the 2024 European Lung Cancer Conference showed that, in AK112-201 (Cohort 1), a Phase II study conducted in China, for first-line advanced or metastatic NSCLC patients with squamous histology (n=63) patients administered, ivonescimab, combined with carboplatin and paclitaxel, experienced a median PFS of 11.1 months. Median overall survival was not reached after a median follow-up period of 22.1 months. This Phase II study was considered to have demonstrated a tolerable safety profile and a low discontinuation rate for adverse events.

We plan to conduct our current clinical trials, as well as design and conduct additional clinical trial activities for ivonescimab within our Licensed Territory, to support and submit relevant regulatory filings. We also plan to support additional study activities through its investigator initiated study program.

Product Pipeline

Summit sponsored ivonescimab trials: Ivonescimab is currently being investigated in global Phase III clinical trials. Phase I and II trials were completed by our partner Akeso. This pipeline reflects clinical trials that have been initiated by us in our Licensed Territory.

Trial	Indication	Histology/Population	Regimen	Phase III
HARMONi	NSCLC	**EGFRm+** 2L+ Advanced or Metastatic	Combo ivonescimab + chemo vs. placebo + chemo	
HARMONi-3	NSCLC	**Squamous** 1L Metastatic	Combo ivonescimab + chemo vs. pembro + chemo	

HARMONi study is a multi-regional, potentially registration-enabling clinical trial that we joined with Akeso, and for which we started initiating and activating sites in North America and Europe during 2023. The first patient in our Licensed Territory was enrolled during the second quarter of 2023. We expect to complete enrollment during the second half of 2024. The co-primary endpoints for this study are progression free survival ("PFS") and overall survival ("OS"), and the study compares ivonescimab plus doublet-platinum chemotherapy versus placebo plus platinum-based doublet chemotherapy.

HARMONi-3 study is a Phase III, multi-regional, potentially registration-enabling clinical trial for which we initiated activating sites in North Americas and China during fourth quarter of 2023. We plan to initiate additional sites in North America, China, Europe, Japan, and other countries through early 2025. Our plan to initiate in new countries and sites is dependent upon the timing and requirements for getting the regulatory approval of the clinical trial applications with the respective regulatory authorities and approvals from central or local independent review boards. We may decide to modify our plans to go into certain regions or countries based on the timelines and requirements from the respective regulatory regions. We commenced patient enrollment in the HARMONi-3 study during fourth quarter of 2023. The primary endpoint for this study is OS, and the study compares ivonescimab plus platinum-based doublet chemotherapy versus pembrolizumab plus platinum-based doublet chemotherapy.

In the fourth quarter of 2023, we began collaborating with multiple institutions globally and opened our investigator-initiated study program across several disease areas. In July 2024, we entered into a collaboration agreement with The University of Texas M.D. Anderson Cancer Center with the intent to further accelerate the development of ivonescimab through pre-clinical and clinical studies.

In addition, our partners at Akeso are sponsoring multiple, ongoing Phase II and III clinical trials in NSCLC and other cancers outside of our Licensed Territory. We plan to review the data generated from these clinical trials as a part of our consideration for advancing our clinical development pipeline for ivonescimab in our Licensed Territory.

Recent Developments

After announcing qualitative results for the HARMONi-2 trial on May 30, 2024, on September 8, 2024, Akeso announced the quantitative data from the primary analysis of the Phase III HARMONi-2 trial featuring ivonescimab that was presented as part of the Presidential Symposium at the International Association for the Study of Lung Cancer's (IASLC) 2024 World Conference on Lung Cancer (WCLC 2024). The HARMONi-2 presentation evaluated monotherapy ivonescimab compared to monotherapy pembrolizumab in patients with locally advanced or metastatic NSCLC whose tumors have positive PD-L1 expression (PD-L1 TPS $\geq$1%). HARMONi-2 is a single region, multi-center, double-blinded Phase III study conducted in China sponsored by Akeso, with data generated and analyzed by Akeso.

In the HARMONi-2 primary analysis, ivonescimab monotherapy demonstrated a statistically significant improvement in the trial's primary endpoint, PFS by Independent Radiologic Review Committee (IRRC), when compared to monotherapy pembrolizumab, achieving a hazard ratio of 0.51 (95% CI: 0.38, 0.69; $p<0.0001$). A clinically meaningful benefit was demonstrated across clinical subgroups, including patients with tumors with high PD-L1 expression (PD-L1 TPS $\geq$ 50%). Overall survival data was not yet mature at the time of the data cutoff and will be evaluated in the future.

Ivonescimab demonstrated an acceptable and manageable safety profile, which was consistent with previous studies. There were three patients (1.5%) who discontinued ivonescimab due to treatment-related adverse events (TRAEs) compared to six patients (3.0%) who discontinued pembrolizumab due to TRAEs. There was one patient in the ivonescimab arm and two patients in the pembrolizumab arm who died as a result of TRAEs in this Phase III study.

Based on the results of HARMONi-2, Summit announced its intention to initiate HARMONi-7 in early 2025. HARMONi-7 is currently planned as a multi-regional Phase III clinical trial that will compare ivonescimab monotherapy to pembrolizumab monotherapy in patients with metastatic NSCLC whose tumors have high PD-L1 expression (PD-L1 TPS > 50%).

In addition to the HARMONi-2 data, on September 8, 2024, Akeso announced the results from AK112-205, a single-region (China), multi-center, open-label Phase II study, conducted by Akeso, of patients with Stage II or III resectable NSCLC, with data generated and analyzed by Akeso. Further, data for ivonescimab was presented as a part of the 2024 European Society for Medical Oncology Annual Meeting (ESMO 2024) 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, with data generated and analyzed by Akeso.

Based on the results of these recent Phase II data sets as well as previously presented data, we intend to explore further clinical development of ivonescimab in solid tumor settings outside of metastatic non-small cell lung cancer, our current area of focus in its Phase III clinical trials.

Private Placement

On September 11, 2024, we entered into the Purchase Agreements with multiple leading biotech institutional and individual accredited investors (the "Investors"), for the sale by us in a private placement (the "Private Placement") of an aggregate of 10,352,418 shares (the "Shares") of our common stock, at purchase price of $22.70 per Share, which was the closing price of the common stock on September 11, 2024, for aggregate gross proceeds to us of approximately $235.0 million (the "Private Placement"). The closing of the Private Placement occurred on September 13, 2024. The proceeds of the Private Placement are expected to be used for working capital and general corporate purposes, including, without limitation, the repayment of principal in the amount of approximately $75.5 million of the $100 million promissory note issued by the Company to Robert W. Duggan, due April 1, 2025.

Our Chief Executive Officer, Executive Chairman and majority stockholder, Robert W. Duggan, Chief Executive Officer, President and member of our Board of Directors (the "Board"), Dr. Mahkam Zanganeh, Chief Operating Officer, Chief Financial Officer and member of the Board, Manmeet Soni, Chief Accounting Officer, Bhaskar Anand, and member of the Board, Jeff Huber, through his controlled entity Caspian Capital LLC, each participated as Investors in the Private Placement, purchasing an aggregate of 3,480,173 shares of common stock.

The offer and sale of shares of common stock issued to the Investors were not initially registered under the Securities Act or any state securities laws. We relied on the exemption from the registration requirements afforded by Section 4(a)(2) of the Securities Act and/or Regulation D promulgated thereunder for the Private Placement. In connection with their execution of the respective Purchase Agreements, each of the Investors represented to us that such Investor is either (i) an "accredited investor" as defined in Regulation D of the Securities Act, or (ii) a qualified institutional buyer (as defined in Rule 144A of the Securities Act), and that the securities purchased by such Investor were being acquired solely for its own account and for investment purposes and not with a present view to its future public sale or distribution.

On September 11, 2024, in connection with the Purchase Agreements, we entered into Registration Rights Agreements with the Investors (the "Registration Rights Agreements"). The Registration Rights Agreements provide, among other things, that we will as soon as reasonably practicable file with the Securities and Exchange Commission (the "SEC") a registration statement registering the resale of the Shares. We agreed to use our

reasonable best efforts to have such registration statement declared effective as soon as practicable after the filing thereof. The registration statement to which this prospectus forms a part is intended to satisfy such requirements under the Registration Rights Agreements.

Corporate Information

Summit Therapeutics Inc. was incorporated in Delaware on July 17, 2020. Our principal executive office is located at 601 Brickell Key Drive, Suite 1000, Miami, FL 33131 and our phone number is (305) 203-2034. Our website is https://www.smmttx.com. Information contained on or accessible through our website is not incorporated by reference into this prospectus and should not be considered a part of this prospectus. We have included our website in this prospectus solely as an inactive textual reference.

This prospectus contains references to our trademarks and to trademarks belonging to other entities. Solely for convenience, trademarks and trade names referred to in this prospectus, including logos, artwork and other visual displays, may appear without the ® or ™ symbols, but such references are not intended to indicate, in any way, that their respective owners will not assert, to the fullest extent under applicable law, their rights thereto. We do not intend our use or display of other companies' trade names or trademarks to imply a relationship with, or endorsement or sponsorship of us by, any other companies.

THE OFFERING	
Common stock offered by the Selling Stockholders	10,352,418 shares.
Use of Proceeds	We will not receive any proceeds from the sale of the Shares covered by this prospectus. See “Use of Proceeds.”
Risk Factors	An investment in our common stock involves a high degree of risk. See “Risk Factors” on page 7 of this prospectus, and under similar headings in the other documents that are incorporated by reference into this prospectus for a discussion of the factors you should consider before deciding to invest in shares of our common stock.
Nasdaq Global Market symbol	SMMT

RISK FACTORS

Investing in our common stock involves a high degree of risk. Before deciding whether to invest in our common stock, you should consider carefully the risks and uncertainties described under the heading "Risk Factors" contained in our most recent Annual Report on Form 10-K, as updated and supplemented by subsequent Quarterly Reports on Form 10-Q and Current Reports on Form 8-K that we have filed with the SEC, and by our other filings we make with the SEC which are incorporated by reference into this prospectus, together with other information in this prospectus and the documents incorporated by reference into this prospectus. The risks described in these documents are not the only ones we face, but those that we consider to be material. Additional risks not presently known to us or that we currently deem immaterial may also impair our business operations. Our business, financial condition, or results of operations could be materially adversely affected by the materialization of any of these risks. The trading price of our common stock could decline due to the materialization of any of these risks and you may lose all or part of your investment.

For more information about our SEC filings, please see "Where You Can Find More Information" and "Incorporation of Certain Information by Reference."

USE OF PROCEEDS

We are registering the resale of the Shares by the Selling Stockholders. We will not receive any proceeds from the sale or other disposition of the Shares offered by this prospectus.

The Selling Stockholders will bear all fees, commissions and discounts, if any, attributable to the sale of the Shares. We will bear all other costs, expenses and fees in connection with the registration of the Shares to be sold by the Selling Stockholders pursuant to this prospectus.

SELLING STOCKHOLDERS

We have prepared this prospectus to allow the Selling Stockholders to offer and sell from time to time up to 10,352,418 Shares. We are registering the offer and sale of the Shares to satisfy certain registration obligations that we granted the Selling Stockholders in the Private Placement.

The following table sets forth (i) the name of each Selling Stockholder; (ii) the number of shares of common stock beneficially owned by each Selling Stockholder; (iii) the number of Shares that may be offered under this prospectus; and (iv) the number of shares of common stock beneficially owned by each Selling Stockholder assuming all of the Shares covered hereby are sold. We do not know how long the Selling Stockholders will hold the Shares before selling them. We currently have no agreements, arrangements or understandings with the Selling Stockholders regarding the sale or other disposition of any Shares. Other than as set forth below, the Selling Stockholders do not have, or within the past three years has not had, any material relationship with us or any of our or affiliates.

Beneficial ownership is determined in accordance with the rules of the SEC and includes voting or investment power with respect to our common stock. Generally, a person "beneficially owns" shares of common stock if the person has or shares with others the right to vote those shares or to dispose of them, or if the person has the right to acquire voting or disposition rights within 60 days.

The information set forth in the table below is based upon information obtained from the Selling Stockholders. The percentage of shares beneficially owned prior to, and after, the offering is based on 735,160,424 shares of our common stock outstanding as of September 13, 2024, after giving effect to the closing of the Private Placement, and assumes the Selling Stockholders dispose of all of the Shares covered by this prospectus and do not acquire beneficial ownership of any additional shares of common stock. The registration of the Shares does not necessarily mean that the Selling Stockholders will sell all or any portion of the Shares covered by this prospectus.

As used in this prospectus, the term "Selling Stockholders" includes the Selling Stockholders listed in the table below, together with any additional Selling Stockholders listed in a prospectus supplement, and their donees, pledgees, assignees, transferees, distributees and successors-in-interest that receive Shares in any non-sale transfer after the date of this prospectus. Unless otherwise noted below, the address for the Selling Stockholders is 601 Brickell Key Drive, Suite 1000, Miami, FL 33131.

	Shares of Common Stock beneficially owned before this offering		Shares of Common Stock offered pursuant to this prospectus	Shares of Common Stock beneficially owned after this offering[2]	
Name of Selling Stockholder	Number of shares	Percentage of outstanding shares	Number of shares [1]	Number of shares	Percentage of shares
Baker Bros. Advisors LP [3]	24,424,865	3.3%	2,202,643	22,222,222	3.0%
Fidelity Mt. Vernon Street Trust: Fidelity Series Growth Company Fund [4]	243,283	*	99,283	144,000	*
Fidelity Mt. Vernon Street Trust: Fidelity Growth Company Fund[4]	952,056	*	376,818	575,238	*
Fidelity Growth Company Commingled Pool[4]	1,278,848	*	507,242	771,606	*
Fidelity Mt. Vernon Street Trust: Fidelity Growth Company K6 Fund[4]	299,234	*	117,978	181,256	*
Fidelity Select Portfolios: Biotechnology Portfolio[4]	3,800,458	*	440,529	3,359,929	*
Fidelity Select Portfolios: Pharmaceuticals Portfolio[4]	264,317	*	264,317	—	*

Name of Selling Stockholder	Shares of Common Stock beneficially owned before this offering		Shares of Common Stock offered pursuant to this prospectus	Shares of Common Stock beneficially owned after this offering(2)	
	Number of shares	Percentage of outstanding shares	Number of shares (1)	Number of shares	Percentage of shares
T. Rowe Price Health Sciences Fund, Inc. (5)	5,597,468	*	1,943,821	3,653,647	*
TD Mutual Funds – TD Health Sciences Fund (5)	462,761	*	163,986	298,775	*
T. Rowe Price Health Sciences Portfolio (5)	262,117	*	94,836	167,281	*
Rock Springs Capital Master Fund LP (6)	1,060,762	*	660,792	400,000	*
Robert W. Duggan (7)	555,736,060	75.2%	3,325,991	552,410,069	74.7%
Mahkam Zanganeh (8)	43,496,455	5.9%	44,052	43,452,403	5.9%
Manmeet S. Soni (9)	9,714,961	1.3%	44,052	9,670,909	1.3%
Jeff Huber (10)	50,052	*	44,052	6,000	*
Bhaskar Anand (11)	131,426	*	22,026	109,400	*

* Less than one percent (1%)

(1) Represents all of the Shares that each Selling Stockholder may offer and sell from time to time under this prospectus.

(2) Assumes each Selling Stockholder sells the maximum number of Shares possible in this offering.

(3) Consists of (i) 2,061,013 shares of common stock held directly by 667, L.P. (“667”) and (ii) 22,363,852 shares of common stock held directly by Baker Brothers Life Sciences, L.P. (“Life Sciences”, and together with 667, the “BBA Funds”). Shares offered pursuant to this prospectus in consists of (i) 186,380 shares of common stock purchased by 667 in the Private Placement and (ii) 2,016,263 shares of common stock purchased by Life Sciences in the Private Placement. Baker Bros. Advisors LP (“BBA”) is the investment adviser to the BBA Funds and has the sole voting and investment power with respect to the securities held by the BBA Funds and thus may be deemed to beneficially own such securities. Baker Bros. Advisors (GP) LLC (“BBA GP”) is the sole general partner of BBA and thus may be deemed to beneficially own the securities held by the BBA Funds. The managing members of BBA GP are Julian C. Baker and Felix J. Baker, who may be deemed to beneficially own the securities held by the BBA Funds. Julian C. Baker, Felix J. Baker, BBA and BBA GP disclaim beneficial ownership of all shares held by the BBA Funds, except to the extent of their indirect pecuniary interest therein. The business address of BBA, BBA GP, Julian C. Baker and Felix J. Baker is 860 Washington Street, 3rd Floor, New York, NY 10014.

(4) Shares offered pursuant to this prospectus consists of: (i) 99,283 shares of common stock purchased in the Private Placement by Fidelity Mt. Vernon Street Trust: Fidelity Series Growth Company Fund, (ii) 376,818 shares of common stock purchased in the Private Placement by Fidelity Mt. Vernon Street Trust: Fidelity Growth Company Fund, (iii) 507,242 shares of common stock purchased in the Private Placement by Fidelity Growth Company Commingled Pool, (iv) 117,978 shares of common stock purchased in the Private Placement by Fidelity Mt. Vernon Street Trust: Fidelity Growth Company K6 Fund, (v) 440,529 shares of common stock purchased in the Private Placement by Fidelity Select Portfolios: Biotechnology Portfolio and (vi) 264,317 shares of common stock purchased in the Private Placement by Fidelity Select Portfolios: Pharmaceuticals Portfolio. These funds and accounts are managed by direct or indirect subsidiaries of FMR LLC. Abigail P. Johnson is a Director, the Chairman and the Chief Executive Officer of FMR LLC. Members of the Johnson family, including Abigail P. Johnson, are the predominant owners, directly or through trusts, of Series B voting common shares of FMR LLC, representing 49% of the voting power of FMR LLC. The Johnson family group and all other Series B shareholders have entered into a shareholders’ voting agreement under which all Series B voting common shares will be voted in accordance with the majority vote of Series B voting common shares. Accordingly, through their ownership of voting common shares and the execution of the shareholders’ voting agreement, members of the Johnson family may be

deemed, under the Investment Company Act of 1940, to form a controlling group with respect to FMR LLC. The address of these funds and accounts is 245 Summer Street, Boston, MA 02210.

(5) Shares offered pursuant to this prospectus consists of: (i) 1,943,821 shares of common stock purchased in the Private Placement by T. Rowe Price Health Sciences Fund, Inc., (ii) 163,986 shares of common stock purchased in the Private Placement by TD Mutual Funds - TD Health Sciences Fund and (iii) 94,836 shares of common stock purchased in the Private Placement by T. Rowe Price Health Sciences Portfolio. These funds and accounts are advised or subadvised by T. Rowe Price Associates, Inc. ("TRPA"). TRPA, as investment adviser, has dispositive and voting power with respect to the securities held by these funds and accounts. TRPA may be deemed to be the beneficial owner of these securities, however, TRPA expressly disclaims that it is, in fact, the beneficial owner of such securities. TRPA is a wholly owned subsidiary of T. Rowe Price Group, Inc., which is a publicly traded financial services holding company. The principal business address of the selling stockholders is T. Rowe Price Associates, Inc., 100 East Pratt Street, Baltimore, MD 21202.

(6) Shares offered pursuant to this prospectus consists of 660,792 shares of common stock purchased in the Private Placement by Rock Springs Capital Master Fund ("Rock Springs Fund"). Rock Springs Capital Management LP ("RSCM") is the investment adviser of Rock Springs Fund. The general partner of RSCM is Rock Springs Capital LLC ("RSC"). RSC and RSCM may therefore be deemed to have or share beneficial ownership of the shares held directly by Rock Springs Fund. The address of this selling stockholder is 650 S. Exeter Street, Suite 1070, Baltimore, MD 21202.

(7) Shares beneficially owned prior to the offering to which the prospectus relates is based solely on the Schedule 13-D/A filed by Robert W. Duggan filed with the Securities and Exchange Commission on September 13, 2024, and consists of (i) 551,695,096 shares of common stock owned directly by Mr. Duggan, (ii) 3,985,055 shares of common stock issuable pursuant to outstanding warrants held by Mr. Duggan, which are exercisable until December 24, 2029, and (iii) 55,909 shares of common stock issuable pursuant to outstanding options that are exercisable within 60 days of September 13, 2024. Shares offered pursuant to this prospectus consists of 3,325,991 shares of common stock purchased in the Private Placement by Mr. Duggan. Mr. Duggan serves as the Company's Chief Executive Officer and Executive Chairman.

(8) Shares beneficially owned prior to the offering to which this prospectus relates is based upon a Schedule 13D/A filed by Dr. Zanganeh with the Securities and Exchange Commission on March 13, 2023, updated by information known to the Company and Form 4s filed on December 13, 2023, March 27, 2024, August 23, 2024 and September 13, 2024. The shares of common stock beneficially owned consist of (i) 24,967,852 shares of common stock owned by the Mahkam Zanganeh Revocable Trust, (ii) 9,884,095 shares of common stock owned by the Shaun Zanganeh Irrevocable Trust, (iii) 315,681 shares of common stock issuable pursuant to outstanding warrants held by the Shaun Zanganeh Irrevocable Trust that are exercisable until December 24, 2029, (iv) 7,758,013 shares of common stock issuable pursuant to outstanding options that are exercisable within 60 days of September 13, 2024 and (v) 50,000 shares purchased by an immediate family member. Shares offered pursuant to this prospectus consists of 44,052 shares of common stock purchased in the Private Placement by the Mahkam Zanganeh Revocable Trust. Dr. Zanganeh is the trustee of each of the Mahkam Zanganeh Revocable Trust and the Shaun Zanganeh Irrevocable Trust. Dr. Zanganeh serves as the Company's Chief Executive Officer, President and member of the Company's Board of Directors.

(9) Shares beneficially owned prior to the offering to which this prospectus relates is based upon Form 4s filed by Mr. Soni with the Securities and Exchange Commission on August 23, 2024 and September 13, 2024 and information known to the Company. The shares of common stock beneficially owned consists of (i) 3,020,242 shares of common stock owned by Mr. Soni and (ii) 6,694,719 shares of common stock issuable pursuant to outstanding options that are exercisable within 60 days of September 13, 2024. Shares offered pursuant to this prospectus consists of 44,052 shares of common stock purchased in the Private Placement by Mr. Soni. Mr. Soni serves as the Company's Chief Financial Officer, Chief Operating Officer and member of the Company's Board of Directors.

(10) Shares beneficially owned prior to the offering to which this prospectus relates consists of (i) 6,000 shares of common stock held by an Estate Plan Living Trust (the "Huber Trust") and (ii) 44,052 shares held Caspian Capital LLC ("Caspian Capital"). Shares offered pursuant to this prospectus consists of 44,052 shares of common stock purchased in the Private Placement by Caspian Capital. Mr. Huber is a trustee of the Huber Trust and is a manager and member of Caspian Capital. Mr. Huber serves a member of the Company's Board of Directors.

(11) Shares beneficially owned prior to the offering to which this prospectus relates is based upon the Form 3 and Form 4s by Mr. Anand on April 4, 2024 and September 13, 2024. The shares of common stock beneficially owned consists of 131,426 shares owned by Mr. Anand. Shares offered pursuant to this prospectus consists of 22,026 shares of common stock purchased in the Private Placement by Mr. Anand. Mr. Anand serves as Chief Accounting Officer of the Company.

PLAN OF DISTRIBUTION

We are registering the resale of the shares of our common stock held by the Selling Stockholders from time to time after the date of this prospectus. We will not receive any of the proceeds from the sale by the Selling Stockholders of the shares of our common stock. The Selling Stockholders will bear all fees, commissions and discounts, if any, attributable to the sales of shares and any transfer taxes. We will bear all other costs, expenses and fees in connection with the registration of shares of our common stock to be sold by the Selling stockholders pursuant to this prospectus.

The term "Selling Stockholders" includes donees, pledgees, transferees or other successors in interest selling securities received after the date of this prospectus from the Selling Stockholders as a gift, pledge, partnership distribution or other transfer. The Selling Stockholders will act independently of us in making decisions with respect to the timing, manner and size of each sale. Such sales may be made on the principal trading market for our common stock or any other stock exchange, market or trading facility on which our common stock is traded or in private transactions. These sales may be at fixed or negotiated prices. The Selling Stockholders may use any one or more of the following methods when selling securities:

- ordinary brokerage transactions and transactions in which the broker dealer solicits purchasers;
- block trades in which the broker dealer will attempt to sell the common stock as agent but may position and resell a portion of the block as principal to facilitate the transaction;
- purchases by a broker dealer as principal and resale by the broker dealer for its account;
- an exchange distribution in accordance with the rules of the applicable exchange;
- directly to one or more purchasers;
- settlement of short sales;
- distribution to employees, members, limited partners or stockholders of the Selling Stockholders;
- in transactions through broker dealers that agree with the Selling Stockholders to sell a specified number of such common stock at a stipulated price per security;
- through the writing or settlement of options or other hedging transactions, whether through an options exchange or otherwise;
- by pledge to secured debts and other obligations;
- delayed delivery arrangements;
- to or through underwriters, broker-dealers or agents; provided that in no event shall any resales by the Selling Stockholders take the form of an underwritten offering (as the term "underwritten public offering" is commonly understood, which for clarity does not include a transaction that does not involve the purchase by such broker-dealer of securities with a view to public resale thereby, but which transaction may be treated similarly to an underwritten public offering in terms of the procedures to be followed thereby as a matter of law or customary practice) without our prior consent;
- in "at the market" offerings, as defined in Rule 415 under the Securities Act, at negotiated prices, at prices prevailing at the time of sale or at prices related to such prevailing market prices, including sales made directly on a national securities exchange or sales made through a market maker other than on an exchange or other similar offerings through sales agents;
- in privately negotiated transactions;
- in options transactions;
- a combination of any such methods of sale; or
- any other method permitted pursuant to applicable law.

The Selling Stockholders may also sell the shares of our common stock under Rule 144 or any other exemption from registration under the Securities Act, if available, rather than under this prospectus.

In addition, each Selling Stockholders that is an entity may elect to make a pro rata in-kind distribution of securities to its members, partners or stockholders pursuant to the registration statement of which this prospectus is a part by delivering a prospectus with a plan of distribution. Such members, partners or stockholders would thereby receive freely tradeable securities pursuant to the distribution through a registration statement. To the extent a distributee is our affiliate (or to the extent otherwise required by law), we may, at our option, file a prospectus supplement in order to permit the distributees to use the prospectus to resell the securities acquired in the distribution.

Broker-dealers engaged by the Selling Stockholders may arrange for other brokers-dealers to participate in sales. Broker-dealers may receive commissions or discounts from the selling stockholder (or, if any broker-dealer acts as agent for the purchaser of our common stock, from the purchaser) in amounts to be negotiated, but, except as set forth in a supplement to this prospectus, in the case of an agency transaction not in excess of a customary brokerage commission in compliance with Financial Industry Regulatory Authority, or FINRA, Rule 5110; and in the case of a principal transaction a markup or markdown in compliance with FINRA Rule 2121.

To the extent required, this prospectus may be amended or supplemented from time to time to describe a specific plan of distribution. In connection with the sale of our common stock or interests therein, the Selling Stockholders may enter into hedging transactions with broker-dealers or other financial institutions, which may in turn engage in short sales of our common stock in the course of hedging the positions they assume. The Selling Stockholders may also sell our common stock short and deliver these shares to close out their short positions, or loan or pledge the securities to broker-dealers that in turn may sell these shares. The Selling Stockholders may also enter into option or other transactions with broker-dealers or other financial institutions or create one or more derivative securities which require the delivery to such broker-dealer or other financial institution of securities offered by this prospectus, which securities such broker-dealer or other financial institution may resell pursuant to this prospectus (as supplemented or amended to reflect such transaction). The Selling Stockholders may also pledge securities to a broker-dealer or other financial institution, and, upon a default, such broker-dealer or other financial institution, may effect sales of the pledged securities pursuant to this prospectus (as supplemented or amended to reflect such transaction).

In effecting sales, broker-dealers or agents engaged by the Selling Stockholders may arrange for other broker-dealers to participate. Broker-dealers or agents may receive commissions, discounts or concessions from the Selling Stockholders in amounts to be negotiated immediately prior to the sale.

The Selling Stockholders have informed us that they do not have any written or oral agreement or understanding, directly or indirectly, with any person to distribute the shares of our common stock.

We will pay certain fees and expenses incurred by us incident to the registration of the resale of the Shares. We have agreed to indemnify the selling stockholder against certain losses, claims, damages and liabilities, including liabilities under the Securities Act, and the Selling Stockholders may be entitled to contribution. We may be indemnified by the Selling Stockholders against certain losses, claims, damages and liabilities, including liabilities under the Securities Act that may arise from any written information furnished to us by the Selling Stockholders specifically for use in this prospectus, or we may be entitled to contribution.

The resale securities will be sold only through registered or licensed brokers or dealers if required under applicable state securities laws. In addition, in certain states, the resale securities covered hereby may not be sold unless they have been registered or qualified for sale in the applicable state or an exemption from the registration or qualification requirement is available and is complied with.

Under applicable rules and regulations under the Exchange Act, any person engaged in the distribution of the resale shares of our common stock may not simultaneously engage in market making activities with respect

to our common stock for the applicable restricted period, as defined in Regulation M, prior to the commencement of the distribution. In addition, the Selling Stockholders will be subject to applicable provisions of the Exchange Act and the rules and regulations thereunder, including Regulation M, which may limit the timing of purchases and sales of our common stock by the Selling Stockholders or any other person. We will make copies of this prospectus available to the Selling Stockholders and have informed them of the need to deliver a copy of this prospectus to each purchaser at or prior to the time of the sale (including by compliance with Rule 172 under the Securities Act).

At the time a particular offer of securities is made, if required, a prospectus supplement will be distributed that will set forth the number of securities being offered and the terms of the offering, including the name of any underwriter, dealer or agent, the purchase price paid by any underwriter, any discount, commission and other item constituting compensation, any discount, commission or concession allowed or reallowed or paid to any dealer, and the proposed selling price to the public.

We have agreed with the Selling Stockholders to keep the registration statement of which this prospectus forms a part effective until the earlier of (i) the date on which the Selling Stockholders cease to hold any Shares issued pursuant to Purchase Agreement, and (iii) all the Shares held by the Selling Stockholders may be sold without registration under Rule 144 and without being subject to any volume, manner of sale or publicly available information requirements.

LEGAL MATTERS

Baker & Hostetler LLP, Los Angeles, California, will pass upon the validity of the shares of our common stock offered by this prospectus.

EXPERTS

The financial statements incorporated in this prospectus by reference to the Annual Report on Form 10-K for the year ended December 31, 2023 have been so incorporated in reliance on the report (which contains an explanatory paragraph relating to the Company's ability to continue as a going concern as described in Note 3 to the consolidated financial statements) of PricewaterhouseCoopers LLP, an independent registered public accounting firm, given on the authority of said firm as experts in auditing and accounting.

WHERE YOU CAN FIND MORE INFORMATION

We file annual, quarterly and other reports, proxy statements and other information with the SEC. Our SEC filings are available to the public over the Internet at the SEC's website at www.sec.gov. Our Annual Report on Form 10-K, Quarterly Reports on Form 10-Q, and Current Reports on Form 8-K, including any amendments to those reports, and other information that we file with or furnish to the SEC pursuant to Section 13(a) or 15(d) of the Exchange Act can also be accessed free of charge through the Internet. These filings will be available as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC.

This prospectus is part of a registration statement that we filed with the SEC. This prospectus omits some information contained in the registration statement in accordance with SEC rules and regulations. You should review the information and exhibits in the registration statement for further information about us and our subsidiaries and the securities we are offering. Statements in this prospectus concerning any document we filed as an exhibit to the registration statement or that we otherwise filed with the SEC are not intended to be comprehensive and are qualified by reference to these filings. You should review the complete document to evaluate these statements.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to incorporate by reference the information and reports we file with it, which means that we can disclose important information to you by referring you to these documents. The information incorporated by reference is an important part of this prospectus, and information that we file after the date hereof with the SEC will automatically update and supersede the information already incorporated by reference. We are incorporating by reference the documents listed below:

- Our Annual Report on Form 10-K for the fiscal year ended December 31, 2023, as filed on February 20, 2024;
- Our Quarterly Reports on Form 10-Q for the quarter ended March 31, 2024, filed on May 1, 2024 and for the quarter ended June 30, 2024, filed on August 6, 2024;
- Our Current Reports on Form 8-K filed on January 3, 2024, February 8, 2024, March 5, 2024, March 22, 2024, April 3, 2024, April 11, 2024, May 13, 2024, May 24, 2024, May 30, 2024, June 3, 2024, June 3, 2024, June 17, 2024, June 27, 2024; September 9, 2024 and September 12, 2024; and
- The description of our Common Stock contained on our Current Report on Form 8-K dated September 18, 2020, including any amendment or report filed for the purpose of updating such description.

All documents we file with the SEC pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act shall be deemed incorporated by reference in this prospectus and to be a part of this prospectus from the date of filing of those documents, with the exception of any portion of any report or document that is not deemed "filed" under such provisions on or after the date of this prospectus, until the earlier of the date on which: (1) all of the securities, the offer and resale of which are registered hereunder, have been sold; or (2) the registration statement of which this prospectus is a part has been withdrawn.

Under no circumstances will any information filed under current items 2.02 or 7.01 of Form 8-K be deemed incorporated herein by reference unless such Form 8-K expressly provides to the contrary.

Upon written or oral request, we will provide without charge to each person to whom a copy of the prospectus is delivered a copy of the documents incorporated by reference herein (other than exhibits to such documents unless such exhibits are specifically incorporated by reference herein). You may request a copy of these filings, at no cost, by writing, calling or emailing us at the contact information set forth below. We have authorized no one to provide you with any information that differs from that contained in this prospectus. Accordingly, we take no responsibility for any other information that others may give you. You should not assume that the information in this prospectus is accurate as of any date other than the date of the front cover of this prospectus

Summit Therapeutics Inc.
601 Brickell Key Drive, Suite 1000
Miami, FL 33131
Attention: Investor Relations
(305) 203-2034

PART II
INFORMATION NOT REQUIRED IN THE PROSPECTUS

Item 14. Other Expenses of Issuance and Distribution.

The following table sets forth an estimate of the fees and expenses payable by us in connection with the issuance and distribution of the securities being registered (other than the underwriting discounts and commissions and expenses incurred by the Selling Stockholders in disposing of its Shares). All the amounts shown are estimates, except for the SEC registration fee.

	Amount
SEC registration fee	$ 38.690
Legal fees and expenses	15,000
Accounting fees and expenses	35,000
Miscellaneous fees and expenses	10,000
Total	$ 98,690

Item 15. Indemnification of Directors and Officers.

Section 145(a) of the DGCL provides, in general, that a corporation may indemnify any person who was or is a party to or is threatened to be made a party to any threatened, pending or completed action, suit or proceeding, whether civil, criminal, administrative or investigative (other than an action by or in the right of the corporation), because he or she is or was a director, officer, employee or agent of the corporation, or is or was serving at the request of the corporation as a director, officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise, against expenses (including attorneys' fees), judgments, fines and amounts paid in settlement actually and reasonably incurred by the person in connection with such action, suit or proceeding, if he or she acted in good faith and in a manner he or she reasonably believed to be in or not opposed to the best interests of the corporation and, with respect to any criminal action or proceeding, had no reasonable cause to believe his or her conduct was unlawful.

Section 145(b) of the DGCL provides, in general, that a corporation may indemnify any person who was or is a party or is threatened to be made a party to any threatened, pending or completed action or suit by or in the right of the corporation to procure a judgment in its favor because the person is or was a director, officer, employee or agent of the corporation, or is or was serving at the request of the corporation as a director, officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise, against expenses (including attorneys' fees) actually and reasonably incurred by the person in connection with the defense or settlement of such action or suit if he or she acted in good faith and in a manner he or she reasonably believed to be in or not opposed to the best interests of the corporation, except that no indemnification shall be made with respect to any claim, issue or matter as to which he or she shall have been adjudged to be liable to the corporation unless and only to the extent that the Court of Chancery or other adjudicating court determines that, despite the adjudication of liability but in view of all of the circumstances of the case, he or she is fairly and reasonably entitled to indemnity for such expenses that the Court of Chancery or other adjudicating court shall deem proper.

Section 145(g) of the DGCL provides, in general, that a corporation may purchase and maintain insurance on behalf of any person who is or was a director, officer, employee or agent of the corporation, or is or was serving at the request of the corporation as a director, officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise, against any liability asserted against such person and incurred by such person in any such capacity, or arising out of his or her status as such, whether or not the corporation would have the power to indemnify the person against such liability under Section 145 of the DGCL.

The registrant's Certificate of Incorporation provides that the registrant will indemnify each person who was or is a party or threatened to be made a party to or is involved in any threatened, pending or completed action,

suit or proceeding, whether civil, criminal, administrative or investigative (other than an action by or in the right of the registrant) by reason of the fact that he or she is or was a director or officer of the registrant, or is or was serving at the registrant's request as a director or officer of another corporation, partnership, joint venture, trust or other enterprise to the fullest extent permitted by the DGCL. The registrant's Certificate of Incorporation provides that any reasonable, documented, out-pocket expenses must be advanced to these indemnitees under certain circumstances.

The indemnification provisions contained in the registrant's Certificate of Incorporation are not exclusive. In addition, the registrant has entered into indemnification agreements with each of its directors and executive officers. Each indemnification agreement provides that the registrant will indemnify the director or executive officer to the fullest extent permitted by law for claims arising in his or her capacity as a director or executive officer, provided that he or she acted in good faith and in a manner that he or she reasonably believed to be in, or not opposed to, the registrant's best interests and, with respect to any criminal proceeding, had no reasonable cause to believe that his or her conduct was unlawful. In the event that the registrant does not assume the defense of a claim against a director or executive officer, the registrant is required to advance his or her expenses in connection with his defense, provided that he or she undertakes to repay all amounts advanced if it is ultimately determined that he or she is not entitled to be indemnified by the registrant.

In addition, the registrant maintains standard policies of insurance under which coverage is provided to the registrant's directors and officers against losses arising from claims made by reason of breach of duty or other wrongful act, and to the registrant with respect to payments which may be made by the registrant to such directors and officers pursuant to the above indemnification provisions or otherwise as a matter of law.

Item 16. Exhibits.

Exhibit No.	Description
3.1	Restated Certificate of Incorporation of the Registrant (incorporated by reference to Exhibit 3.1 to the Registrant's Current Report on Form 8-K (File No. 001-36866), filed with the Securities and Exchange Commission on September 18, 2020)
3.2	Amendment to Restated Certificate of Incorporation of the Registrant (incorporated by reference to Exhibit 3.1 to the Registrant's Current Report on Form 8-K (File No. 001-36866), filed with the Securities and Exchange Commission on July 29, 2022)
3.3	Amendment No. 2 to Restated Certificate of Incorporation (incorporated by reference to Exhibit 5.1 to Registrant's Current Report on Form 8-K (File No. 001-36866), filed with the Securities and Exchange Commission on January 20, 2023)
3.4	Amended and Restated Bylaws (incorporated by reference to Exhibit 3.2 to the Registrant's Current Report on Form 8-K (File No. 001-36866), filed with the Securities and Exchange Commission on September 18, 2020)
5.1*	Opinion of Baker & Hostetler LLP
23.1*	Consent of PricewaterhouseCoopers LLP, an independent registered public accounting firm for the Registrant
23.2*	Consent of Baker & Hostetler LLP (included in Exhibit 5.1)
24.1*	Powers of Attorney (included on signature page hereto)
107*	Filing Fee Table

* Filed herewith.

Item 17. Undertakings.

(a) The undersigned registrant hereby undertakes:

(1) To file, during any period in which offers or sales are being made, a post-effective amendment to this registration statement:

(i) To include any prospectus required by Section 10(a)(3) of the Securities Act of 1933;

(ii) To reflect in the prospectus any facts or events arising after the effective date of the registration statement (or the most recent post-effective amendment thereof) which, individually or in the aggregate, represent a fundamental change in the information set forth in the registration statement. Notwithstanding the foregoing, any increase or decrease in volume of securities offered (if the total dollar value of securities offered would not exceed that which was registered) and any deviation from the low or high end of the estimated maximum offering range may be reflected in the form of prospectus filed with the SEC pursuant to Rule 424(b) if, in the aggregate, the changes in volume and price represent no more than a 20% change in the maximum aggregate offering price set forth in the "Calculation of Registration Fee" table in the effective registration statement; and

(iii) To include any material information with respect to the plan of distribution not previously disclosed in the registration statement or any material change to such information in the registration statement;

provided, however, that paragraphs (a)(1)(i), (a)(1)(ii) and (a)(1)(iii) do not apply if the information required to be included in a post-effective amendment by those paragraphs is contained in reports filed with or furnished to the SEC by the registrant pursuant to Section 13 or Section 15(d) of the Securities Exchange Act of 1934 that are incorporated by reference in the registration statement, or is contained in a form of prospectus filed pursuant to Rule 424(b) that is part of the registration statement;

(2) That, for the purpose of determining any liability under the Securities Act of 1933, each such post-effective amendment shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

(3) To remove from registration by means of a post-effective amendment any of the securities being registered which remain unsold at the termination of the offering.

(4) That, for the purpose of determining liability under the Securities Act of 1933 to any purchaser::

(i) Each prospectus filed by the registrant pursuant to Rule 424(b)(3) shall be deemed to be part of the registration statement as of the date the filed prospectus was deemed part of and included in the registration statement; and

(ii) Each prospectus required to be filed pursuant to Rule 424(b)(2), (b)(5), or (b)(7) as part of a registration statement in reliance on Rule 430B relating to an offering made pursuant to Rule 415(a)(1)(i), (vii), or (x) for the purpose of providing the information required by Section 10(a) of the Securities Act of 1933 shall be deemed to be part of and included in the registration statement as of the earlier of the date such form of prospectus is first used after effectiveness or the date of the first contract of sale of securities in the offering described in the prospectus. As provided in Rule 430B, for liability purposes of the issuer and any person that is at that date an underwriter, such date shall be deemed to be a new effective date of the registration statement relating to the securities in the registration statement to which that prospectus relates, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof. Provided, however, that no statement made in a registration statement or prospectus that is part of the registration statement or made in a document incorporated or deemed incorporated by reference into the registration statement or prospectus that is part of the registration statement will, as to a purchaser with a time of contract of sale prior to such effective date, supersede or modify any statement that was made in the registration statement or prospectus that was part of the registration statement or made in any such document immediately prior to such effective date.

(b) The undersigned registrant hereby undertakes that, for purposes of determining any liability under the Securities Act of 1933, each filing of the registrant's annual report pursuant to section 13(a) or section 15(d) of the Securities Exchange Act of 1934 (and, where applicable, each filing of an employee benefit plan's annual report pursuant to section 15(d) of the Securities Exchange Act of 1934) that is incorporated by reference in the registration statement shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

(c) Insofar as indemnification for liabilities arising under the Securities Act of 1933 may be permitted to directors, officers and controlling persons of the registrant pursuant to the foregoing provisions, or otherwise, the registrant has been advised that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Securities Act of 1933 and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the registrant of expenses incurred or paid by a director, officer or controlling person of the registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Securities Act of 1933 and will be governed by the final adjudication of such issue.

SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, the registrant certifies that it has reasonable grounds to believe that it meets all of the requirements for filing on Form S-3 and has duly caused this registration statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of Miami, State of Florida, on September 19, 2024.

SUMMIT THERAPEUTICS INC.

By: /s/ Robert W. Duggan
Name: Robert W. Duggan
Title: Chief Executive Officer and Executive Chairman; Principal Executive Officer

By: /s/ Dr. Mahkam Zanganeh
Name: Dr. Mahkam Zanganeh
Title: Chief Executive Officer; President and member of the Board; Principal Executive Officer

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below hereby constitutes and appoints Robert W. Duggan, Dr. Mahkam Zanganeh and Manmeet Soni, and each of them singly, as the undersigned's true and lawful attorneys-in-fact and agents, with full power of substitution, for the undersigned in any and all capacities, to sign any or all amendments to this Registration Statement (including post-effective amendments), and to file the same, with all exhibits thereto, and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents full power and authority to do and perform each and every act and thing requisite and necessary to be done in connection therewith, as fully for all intents and purposes as the undersigned might or could do in person, hereby and about the premises hereby ratifying and confirming all that said attorneys-in-fact and agent, proxy and agent, or their substitute, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Act of 1933, this registration statement has been signed below by the following persons in the capacities and on the dates indicated.

Name	Title	Date
/s/ Robert W. Duggan Robert W. Duggan	Chief Executive Officer and Executive Chairman *(Principal Executive Officer)*	September 19, 2024
/s/ Dr. Mahkam Zanganeh Dr. Mahkam Zanganeh	Chief Executive Officer, President and Director *(Principal Executive Officer)*	September 19, 2024
/s/ Manmeet S. Soni Manmeet S. Soni	Chief Operating Officer, Chief Financial Officer and Director *(Principal Financial and Accounting Officer)*	September 19, 2024
/s/ Dr. Robert Booth Dr. Robert Booth	Director	September 19, 2024

Name	Title	Date
/s/ Dr. Alessandra Cesano Dr. Alessandra Cesano	Director	September 19, 2024
/s/ Kenneth Clark Kenneth Clark	Director	September 19, 2024
/s/ Jeff Huber Jeff Huber	Director	September 19, 2024
/s/ Dr. Mostafa Ronaghi Dr. Mostafa Ronaghi	Director	September 19, 2024
/s/ Dr. Yu Xia Dr. Yu Xia	Director	September 19, 2024

BakerHostetler

Baker&Hostetler LLP
45 Rockefeller Plaza
New York, NY 10111

T 212.589.4200
F 212.589.4201
www.bakerlaw.com

September 19, 2024

Summit Therapeutics Inc.
601 Brickell Key Drive, Suite 1000
Miami, FL 33131

Ladies and Gentlemen:

We have acted as counsel to Summit Therapeutics Inc., a Delaware corporation (the "**Company**"), in connection with the filing of the Company's Registration Statement on Form S-3 (the "**Registration Statement**") with the Securities and Exchange Commission (the "**Commission**") under the Securities Act of 1933, as amended (the "**Act**"), covering the registration for resale of up to an aggregate of 10,352,418 shares (the "**Shares**") of the Company's common stock, par value $0.01 per share (the "**Common Stock**"), held by the selling stockholders identified in the Registration Statement.

We have examined such documents and such matters of fact and law as we deem necessary to render the opinion contained herein. In our examination, we have assumed, but have not independently verified, the genuineness of all signatures, the conformity to original documents of all documents submitted to us as certified facsimile or other copies, and the authenticity of all such documents. As to questions of fact material to this opinion, we have relied on certificates or comparable documents of public officials and of officers and representatives of the Company.

Based on such examination, we are of the opinion that the Shares are validly issued, fully paid and nonassessable.

The opinion expressed herein is limited to the General Corporation Law of the State of Delaware and we express no opinion as to the effect on the matters covered by this letter of the laws of any other jurisdiction.

We hereby consent to the filing of this letter as Exhibit 5.1 to the Registration Statement and to the reference to our firm under the heading “Legal Matters” in the prospectus included in the Registration Statement. In giving such consent, we do not hereby admit that we are in the category of persons whose consent is required under Section 7 of the Act or the rules and regulations of the Commission.

Very truly yours,

/s/ Baker & Hostetler LLP

BAKER & HOSTETLER LLP

Exhibit 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We hereby consent to the incorporation by reference in this Registration Statement on Form S-3 of Summit Therapeutics Inc. of our report dated February 20, 2024 relating to the financial statements, which appears in Summit Therapeutics Inc.'s Annual Report on Form 10-K for the year ended December 31, 2023. We also consent to the reference to us under the heading "Experts" in such Registration Statement.

/s/ PricewaterhouseCoopers LLP

San Jose, California
September 19, 2024

Exhibit 107

Calculation of Filing Fee Tables

Form S-3
(Form Type)

Summit Therapeutics Inc.
(Exact Name of Registrant as Specified in its Charter)

Table 1: Newly Registered and Carry Forward Securities

	Security Type	Security Class Title	Fee Calculation or Carry Forward Rule	Amount Registered (1)	Proposed Maximum Offering Price Per Unit (2)	Maximum Aggregate Offering Price	Fee Rate	Amount of Registration Fee
Fees to Be Paid	Equity	Common Stock, par value $0.01 per share	Other	10,352,418	$25.32	$262,123,223.76	0.00014760	$38,689.39
	Total Offering Amounts					$262,123,223.76		$38,689.39
	Total Fees Previously Paid							—
	Total Fee Offsets							—
	Net Fee Due							$38,689.39

(1) The shares of common stock, par value $0.01 per share ("Common Stock"), of the Registrant will be offered for resale by the selling stockholders. Pursuant to Rule 416 under the Securities Act of 1933, as amended (the "Securities Act"), the shares being registered hereunder include such indeterminate number of shares of Common Stock as may be issuable with respect to the shares being registered hereunder as a result of stock splits, stock dividends or similar transactions.

(2) Estimated solely for the purpose of calculating the amount of the registration fee pursuant to Rule 457(c) of the Securities Act. The proposed maximum offering price per share and maximum aggregate offering price are calculated using the average of the high ($26.67) and low ($23.96) prices of the Common Stock as reported on the Nasdaq Global Market on September 18, 2024, which date is within five business days prior to the filing of this registration statement.