Summit Therapeutics Presents Breakthrough Research Data from Ph II Studies, including Evidence Validating Microbiome Preservation, Potential Benefit for the Control of Antimicrobial Resistance, and a Novel Mechanism of Action, for its Investigational Drug Ridinilazole

Cambridge, MA, July 12, 2021 - Summit Therapeutics Inc. (NASDAQ: SMMT) ("Summit" or the "Company") is today displaying three preeminent ePosters at the prestigious 31st European Congress of Clinical Microbiology & Infectious Diseases (ECCMID). Two ePosters bring increased awareness and understanding of the significance of data generated using shotgun metagenomic analyses to compare ridinilazole and vancomycin treated patients with *Clostridioides difficile* infection (CDI) from our Phase II CoDIFy clinical trial. Vancomycin, discovered in the 1950's, is the current standard of care for the treatment of *C. difficile* infection. Highlights of the ePosters include data demonstrating the relative impact on the gut microbiota as well as the gut resistome of ridinilazole and vancomycin. Ridinilazole's recently discovered novel mechanism of action is also described.

Ridinilazole is Summit Therapeutics' investigational first-in-class drug currently in two pivotal Phase III Ri-CoDIFy clinical trials. The objective of these trials is to obtain approval for ridinilazole as a first-line therapy for the treatment of initial *C. difficile* infection, and to show superiority in sustained clinical response (cure at initial response and no recurrence within 30 days after end of treatment). Ridinilazole is currently under investigation for use by several regulatory authorities including the FDA and the EMA.

Summit's poster presentations provide demonstrable scientific evidence of the following:

- **Ridinilazole showed no increase in the gut resistome.** Ridinilazole demonstrated no impact on the gut resistome as compared to vancomycin, which displayed an expansion of the presence of Enterobacteriaceae (potentially bad bacteria) in the gut and corresponding increase in antibiotic resistance genes in the gut resistome in a Phase II study.

- **Ridinilazole showed evidence of preservation and minimal impact to the gut microbiome.** In a Phase II study, treatment with ridinilazole compared to vancomycin demonstrated a significant sparing effect on the gut microbiome, supporting the production of protective secondary bile acids. Secondary bile acids are a key component in preventing recurrence of *C. difficile* infection. It was found that vancomycin treatment was associated with significant changes to the gut microbiome, impacting the microbiome's ability to produce protective secondary bile acids, increasing the risk of *C. difficile* infection recurrence.

- **Ridinilazole has the potential to be the first novel mechanism of action antibiotic approved in over ten years.** Ridinilazole's novel mechanism of action involves binding to the minor groove of *Clostridioides difficile* bacteria's DNA. This is believed to be the primary mechanism through which ridinilazole elicits its bactericidal action against *C. difficile* bacteria.

"The gut microbiome is a critical ecosystem that plays an important role in the overall health of the human body," stated Dr. Maky Zanganeh, the Chief Operating Officer of Summit. "The results of our shotgun metagenomic analyses evidencing how ridinilazole preserved the gut microbiome, including its ability to produce secondary bile acids, provides further scientific support for our confidence in ridinilazole's value for the treatment of *C. difficile* infection and, particularly, in ridinilazole's ability to reduce relative CDI recurrence. These results provide a strong mechanistic rationale as to why a lower rate of recurrence of *C. difficile* infection

was observed in our Phase II study for patients taking ridinilazole as compared to vancomycin. The combination of these studies and discoveries provide us with further data in support of the intended efficacy of ridinilazole."

"There is the promise in ridinilazole for a new antibiotic drug to significantly impact the *C. difficile* infection treatment market in a material and positive manner. The need exists now. In our opinion, upon FDA and worldwide regulatory approval, a new era for friendly patient and physician infectious disease management is upon us. This journey has not been easy. It is not yet over. But it is a worthwhile journey, and Team Summit is pleased to be playing a leadership role," said Bob Duggan, Summit's Chairman and Chief Executive Officer. "*C. difficile* infection is an especially insidious disease that remains an unmet medical need, as emphasized by the US Centers for Disease Control and Prevention (CDC) listing it as one of five pathogens that is currently an urgent threat to public health. The results of these metagenomic analyses add to the increasing body of data supporting ridinilazole. Summit Therapeutics intends for ridinilazole to provide high therapeutic efficacy while minimizing antibacterial resistance and disease recurrence. We believe ridinilazole continues to be well-positioned to achieve these stated goals."

Our three ePosters can be viewed as follows:

- *ECCMID-designated Top Rated ePoster:* Metagenomic Analysis of the Impact of the Precision Antibiotic Ridinilazole, Compared to Vancomycin, on the Gut Resistome in a Phase II Study
    - Interactive Session S149 - 3e. Resistance detection / prediction approaches
    - Monday, July 12, 2021 (16:00 to 17:00 CEST; 10:00am to 11:00am EDT)
- Metagenomic Analysis of the Differential Impact of Ridinilazole and Vancomycin on the Gut Microbiota in a Phase II Study
    - Review Session S15: Methods for improving diagnostics and strain typing-Category: 4. Diagnostics
    - Monday, July 12, 2021 (14:15 to 15:15 CEST; 8:15am to 9:15am EDT)
- Identification of the Mechanism of Action for Ridinilazole, a Phase III Antibiotic for Treatment of *Clostridioides difficile*
    - Session S163-5a. Mechanism of action new compounds, preclinical data, & pharmacology of antibacterial agents
    - Available throughout the ECCMID Conference

Each poster is available within the "Scientific Literature & Publications" section of our website: https://www.summittxinc.com/publications/.

About Summit Therapeutics
The overriding objective of Summit Therapeutics is to create value for patients, hospital caregivers, and community-based healthcare providers, as well as healthcare payers around the world. We seek to create value by developing drugs with high therapeutic efficacy - curing the cause of the patient's condition with minimal or zero disease recurrence or antimicrobial resistance, for the longest extent possible - and minimizing the trauma caused to the patient and healthcare ecosystem by minimizing serious side effects, disease recurrence, and inaccessibility to our treatments as a result of financial or other barriers. Summit Therapeutics, empowered by its Discuva Platform, the Company's innovative antibiotic discovery engine, supported by BARDA and CARB-X funding, intends to be the leader in patient-friendly and paradigm-shifting treatments for infectious diseases and other significant unmet medical needs while being an ally to physicians. Our new mechanism pipeline product candidates are designed with the goal to become the patient-friendly, new-era standard of care, by working in harmony with the human microbiome to treat prospective patients suffering from infectious disease, initially focusing on *Clostridioides difficile* infections (CDI). Currently, Summit's lead product candidate, ridinilazole, is engaged in two pivotal global Phase III trials, Ri-CoDIFy 1 & 2, each enrolling approximately 680 patients vs. the standard of care (vancomycin) for the treatment and reduction of recurrence of *C. difficile* infections, in addition to an adolescent trial, Ri-CoDIFy 3. Commercialization of ridinilazole for the treatment and the reduction of recurrence of CDI is subject to regulatory approvals. SMT-738, the second candidate within Summit's portfolio, is currently in the IND-enabling phase for the treatment of multidrug resistant infections, specifically those caused by carbapenem-resistant Enterobacteriaceae (CRE).

For more information, please visit https://www.summittxinc.com and follow us on Twitter @summitplc. For more information on the Company's Discuva Platform, please visit https://www.summittxinc.com/our-science/discuva-platform.

About *C. difficile* Infection
Clostridioides difficile, or *C. difficile,* infection (CDI) is a bacterial infection of the colon that produces toxins causing inflammation of the colon and severe watery diarrhea, painful abdominal cramping, nausea, fever, and dehydration. CDI can also result in more serious disease complications, including bowel perforation, sepsis, and death. CDI is a contagious infectious disease that represents a serious healthcare issue in hospitals, long-term care homes, and the wider community. Summit estimates that there are approximately 500,000 cases of CDI each year across the United States with acute care costs exceeding $5.4 billion in the US based on a meta-analysis published in the *Journal of Global Health*, June 2019.

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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, the therapeutic potential of the Company's product candidates, the potential commercialization of the Company's product candidates, the timing of initiation, completion and availability of data from clinical trials, the potential submission of applications for marketing approvals, the impact of the COVID-19 pandemic on the Company's operations and clinical trials 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 uncertainties inherent in the initiation of future clinical trials, availability and timing of data from ongoing and future clinical trials and the results of such trials, global public health crises, including the coronavirus COVID-19 outbreak, 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, 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. 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.

Appendix: Glossary of Critical Terms Contained Herein

Antibiotic resistance genes – Genes known to be involved in bacterial resistance; such genes may include for example beta-lactamases which can inactivate various beta-lactam antibiotics.

Bile acids – a collection of steroid-based gut metabolites, the balance of the amount of and types of bile acids in the gut microbiome are believed to play an important role in the development of or prevention of an initial and potential recurrent infection of *Clostridioides difficile.*[i]

***Clostridioides difficile* (*C. difficile* or *C. diff.*)** – a germ (bacterium) that can cause severe diarrhea and colitis (an inflammation of the colon). *C. difficile* can live naturally in the intestines (gut) of humans and not cause any problem. Sometimes changes in the gut microbiome lead the bacteria to grow and produce toxins from which illness can develop.[ii]

***C. diff.* Infection (CDI)** – a bacterial infection of the colon that produces toxins causing inflammation of the colon and severe watery diarrhea, very painful and persistent abdominal cramping, nausea, fever, and dehydration. CDI can also result in more serious disease complications, including bowel perforation (a tear in the gastrointestinal tract), sepsis, and death. Most cases of *C. diff.* infection occur while a person is taking antibiotics or not long after a person has finished taking antibiotics. CDI is an insidious and debilitating disease that necessitates patient isolation because of its contagious nature, making it able to be passed from one person to another either in a hospital or long-term care facility setting or in the community.[iii]

Enterobacteriaceae – a large family of different types of bacteria (germs) that commonly cause infections both in healthcare settings, such as hospitals and long-term care facilities, and in communities. Examples of germs in the Enterobacteriaceae family include *Escherichia coli* (commonly known as *E. coli*) and *Klebsiella pneumoniae*. Enterobacteriaceae are frequent carriers of resistance genes to many of the currently available antibiotics used to treat bacterial infections. Because they are bacteria, Enterobacteriaceae can be passed from person to person.[iv]

Gastrointestinal tract – a series of hollow organs joined in a long, twisting tube from the mouth to the anus. These organs also include the esophagus, stomach, small intestine, and large intestine.[v]

Gut microbiome – within the human gastrointestinal tract, the gut microbiome is a collection of microbiota, consisting of trillions of microorganisms that inhabit the gut. The gut microbiota is considered an important partner to human cell systems, interacting extensively with other organs in the body to influence a wide range of functions from digestion to immunity. The balance of the different types of cells and microorganisms within the microbiome is considered to be important in the microbiome's ability to properly play its role within the human body. Disruption in the balance of microorganisms within the gut microbiome (known as dysbiosis) is believed to impact its role in keeping a person healthy and free of certain conditions or diseases.[vi] [vii]

Gut microbiota – the trillions of microorganisms, including symbiotic and pathogenic microorganisms, that inhabit the gut. Examples of these microorganisms include bacteria, fungi, viruses, protists, and archaea.

Gut resistome – within the human gastrointestinal tract, the diversity and dynamics of the antibiotic resistance genes that are harbored by the gut microbiota. Examples of the gut resistome include genes associated with resistance to carbapenem antibiotics.[viii]

Shotgun metagenomic analysis – shotgun metagenomic sequencing sequences all genomic DNA present in a sample. This allows a more accurate taxonomic annotation of the microbiota compared to other techniques such as 16S rRNA amplicon sequencing as well as antibiotic resistance gene profiling and metabolic function profiling.

Vancomycin – an antibiotic first discovered in the 1950's that is used to treat CDI when taken by mouth.

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[i] Qian, X, *et. al.* Ridinilazole, a narrow spectrum antibiotic for treatment of *Clostridioides difficile* infection, enhances preservation of microbiota-dependent bile acids. *Am J Physiol Gasterintest Liver Physiol* 319: G227-G237, 2020.

[ii] Virginia Department of Health. https://www.vdh.virginia.gov/epidemiology/epidemiology-fact-sheets/clostridiodes-difficile/. Accessed February 2021.

[iii] United States Centers for Disease Control and Prevention. https://www.cdc.gov/cdiff/what-is.html. Accessed February 2021.

[iv] United States Centers for Disease Control and Prevention. https://www.cdc.gov/hai/organisms/ESBL.html. Accessed February 2021.

[v] US National Institute of Health, National Institute of Diabetes and Digestive and Kidney Diseases. https://www.niddk.nih.gov/health-information/digestive-diseases/digestive-system-how-it-works. Accessed February 2021.

[vi] Cani PD. Human gut microbiome: hopes, threats and promises. British Medical Journal (BMJ) *Gut* 67**:**1716-1725, 2018.

[vii] Qian, X, *et. al.* Ridinilazole, a narrow spectrum antibiotic for treatment of *Clostridioides difficile* infection, enhances preservation of microbiota-dependent bile acids. *Am J Physiol Gasterintest Liver Physiol* 319: G227-G237, 2020.

[viii] van Schaik, W. The human gut resistome. *Philos Trans R Soc Lond B Biol Sci.* 370(1670):20140087, 2015.