Summit Therapeutics Presents Ri-CoDIFy Trial Results for Microbiome-Sparing Ridinilazole at IDWeek 2022

- *Ridinilazole resulted in a 53% relative risk reduction in recurrence of* C. difficile *infection compared to treatment with vancomycin*
- *Ridinilazole preserved the gut microbiome compared to vancomycin: both in composition and diversity of the microbiome community*
- *Ri-CoDIFy represents the largest and most comprehensive CDI assessment of the gut microbiome to date from over 600 CDI patients*
- *Ridinilazole's features are consistent with the principles of good antibiotic stewardship*

Menlo Park, California, October 20, 2022 – Summit Therapeutics Inc. (NASDAQ: SMMT) ("Summit," "we," or the "Company") and its product candidate, ridinilazole, today had an oral podium presentation at IDWeek 2022. IDWeek is the joint annual meeting of the Infectious Diseases Society of America (IDSA), the Society for Healthcare Epidemiology of America (SHEA), the HIV Medicine Association (HIVMA), the Pediatric Infectious Diseases Society (PIDS), and the Society of Infectious Diseases Pharmacists (SIDP).

The oral presentation, entitled "Ri-CoDIFy - A Phase 3, Randomized, Double-Blind Study to Evaluate the Efficacy and Safety of Ridinilazole Compared with Vancomycin for the Treatment of *Clostridioides difficile* Infection," delivered by Dr. Pablo C. Okhuysen, M.D., Professor, Department of Infectious Diseases at MD Anderson Cancer Center, detailed the scientific data from the Ri-CoDIFy trial for our investigational, first-in-class antibiotic, ridinilazole, for the treatment of *Clostridioides difficile* infection ("*C. diff.* infection," or "CDI"). There were 759 patients enrolled, with the mITT population comprising 745 patients; 323 were over the age of 65, 400 were hospitalized at the beginning of treatment, and 112 were previously diagnosed with COVID-19.

- Ridinilazole achieved a numerically higher sustained clinical response rate (73.0% vs 70.7%) than vancomycin, but did not achieve the pre-specified superiority endpoint
- Ridinilazole resulted in a 53% relative risk reduction in recurrence rates of *C. diff.* infection vs. vancomycin
    - Recurrence of *C. diff.* infection is a major concern for patients with the disease; recurrence rates for infection in the United States are estimated to be approximately 20%-25% in patients after the initial treatment and with increased probabilities of recurrence after each subsequent episode [i, ii]
    - Ridinilazole resulted in an 8.1% recurrence rate of CDI vs. 17.3% for patients treated with vancomycin
- Ridinilazole consistently resulted in decreased rates of recurrence compared to vancomycin in each of the prespecified subgroup analyses performed
    - Patients with 10+ daily unformed bowel movements prior to treatment receiving ridinilazole experienced a disease recurrence rate of 5.8% as compared to 28.0% for vancomycin
    - Patients, aged 65 or over experienced a 9.3% recurrence rate when treated with ridinilazole vs. 22.2% with vancomycin
    - Patients with a prior COVID-19 diagnosis experienced recurrence 5.5% of the time when treated with ridinilazole vs. 24.6% when administered vancomycin
    - Immunocompromised patients recurred 13.6% with ridinilazole vs. 26.3% with vancomycin
- Ri-CoDIFy is the largest and most comprehensive CDI assessment of the gut microbiome comprising over 600 CDI patients globally across different regions to date
- Patients treated with ridinilazole experienced a minimal impact on gut microbiome diversity compared to those patients treated with vancomycin

- Ridinilazole preserved the levels of protective secondary bile acids at the end of the treatment period, an important component of the microbiome, while vancomycin resulted in a substantial decrease in secondary bile acids
- Higher levels of secondary bile acids at the end of the treatment window are associated with earlier recovery of gut microbiome health and associated with a lower rate of recurrence of CDI

- Ridinilazole did not increase the gut resistome as evidenced by the relative lack of abundance of antibacterial resistance genes; exposure to vancomycin resulted in an expansion of the gut resistome
  - Increases in the gut resistome are associated with an increased risk of resistance to antibiotics that a patient may be using or may use in the future
- Ridinilazole was well tolerated with a low rate of treatment discontinuation for adverse events in the Phase 3 study

"While both ridinilazole and vancomycin target *Clostridioides difficile*, the lower recurrence rates in those CDI patients treated with ridinilazole compared to that of vancomycin highlight the differing effects of the two drugs on the gut microbiome," stated Dr. Pablo C. Okhuysen, the presenter of this data at IDWeek 2022. "Ridinilazole spared the gut microbiome and did not select for an increase in antimicrobial resistance at the end of treatment. Conversely, vancomycin decreased the microbiota diversity and selected for an increase of antimicrobial resistance to commonly-used antibiotics. The clinical and molecular results presented continue to validate the need to develop new antibiotics, that like ridinilazole, can selectively treat CDI (or for that matter, any infectious agent) while at the same time preserve microbiome diversity and not promote the emergence of antibiotic resistance. These features are consistent with the hallmark principles of antimicrobial stewardship and should be the focus of future anti-infective drug development."

"We believe that this study may be indicative as to the need to change the way in which anti-infective agents are developed and assessed going forward, including the need for monitoring the impact of treatments on the gut microbiome," added Robert W. Duggan, Chairman and Chief Executive Officer of Summit. "A diverse microbiome is critical to human health and protecting it must be a focus going forward. As we saw in the Ri-CoDIFy study, the health of the microbiome was associated with a lower rate of recurrence of CDI. I am very proud of the work of Team Summit in this significant breakthrough to the infectious disease space and beyond. As we have referenced several times and further illustrated by Drs. Giovanni, Schneider, Calder, and Fauci in the *Journal of Infectious Diseases*,[iii] the microbiome not only impacts infectious diseases, but can impact immune-mediated diseases and potentially beyond: maintaining a healthy, diverse microbiome is critical to maximizing patient safety and optimizing overall human health."

A poster, entitled "A US-Based National Surveillance Study for the Susceptibility and Epidemiology of *Clostridioides difficile* Associated Diarrheal Isolates with Special Reference to Ridinilazole: 2020-2021" is also available throughout IDWeek 2022.

Ridinilazole is not currently approved for use by any regulatory authority.

The presentation and poster are now available within the "Scientific Literature & Publications" section of our website: https://www.summittxinc.com/publications/.

Summit Therapeutics' Mission Statement
To build a viable, long-lasting health care organization that assumes full responsibility for designing, developing, trial execution and enrollment, regulatory submission and approval, and successful commercialization of patient, physician, caregiver, and societal-friendly medicinal therapy intended to: improve quality of life, increase potential duration of life, and resolve serious medical healthcare needs. To identify and control promising product candidates based on exceptional scientific development and administrational

expertise, develop our products in a rapid, cost-efficient manner, and to engage commercialization and/or development partners when appropriate.

We accomplish this by building a team of world class professional scientists and business administrators that apply their experience and knowledge to this mission. Team Summit exists to pose, strategize, and execute a path forward in medicinal therapeutic health care that places Summit in a well-deserved, top market share, leadership position. Team Summit assumes full responsibility for stimulating continuous expansion of knowledge, ability, capability, and well-being for all involved stakeholders and highly-valued shareholders.

About Summit Therapeutics
Summit was founded in 2003 and our shares are listed on the Nasdaq Global Market (symbol 'SMMT'). We are headquartered in Menlo Park, California, and we have additional offices in Oxford, UK and Cambridge, UK. For more information, please visit https://www.summittxinc.com and follow us on Twitter @summitplc.

Contact Summit Investor Relations:
Dave Gancarz
Head of Stakeholder Relations & Corporate Strategy
david.gancarz@summitplc.com

General Inquiries:
investors@summitplc.com

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, potential acquisitions 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 results of our evaluation of the underlying data in connection with the topline results of our Phase III Ri-CoDIFy study evaluating ridinilazole, the outcome of discussions with regulatory authorities, including the Food and Drug Administration, the uncertainties inherent in the initiation of future clinical trials, availability and timing of data from ongoing and future clinical trials, the results of such trials, and their success, and 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, whether business development opportunities to expand the Company's pipeline of drug candidates, including without limitation, through potential acquisitions of, and/or collaborations with, other entities occur, expectations for regulatory approvals, laws and regulations affecting government contracts and funding awards, availability of funding sufficient for the Company's foreseeable and unforeseeable operating expenses and capital expenditure requirements and other factors discussed in the "Risk Factors" section of filings that the Company makes with the Securities and Exchange Commission. Any change to our ongoing trials could cause delays, affect our future expenses, and add uncertainty to our commercialization efforts, as well as to affect the likelihood of the successful completion of clinical development of ridinilazole. 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 instance of *C. difficile* Infection.[ii]

Clostridia – a class of bacteria that exist within a healthy gut microbiome that likely plays a largely crucial role in microbiome homeostasis by interacting with the other resident microbe populations and providing specific and essential functions to the overall microbiome. While most groups of Clostridia have a commensal, or co-existing, relationship with the rest of the gut microbiome, some Clostridia can be pathogenic, when larger concentrations of the bacteria exist, such as *Clostridioides difficile* bacteria.[iv]

***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.[v]

***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.[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 the gut microbiome's role in keeping a person healthy and free of certain conditions or diseases.[ii, vi]

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.[vii]

Microbiome - a community of microorganisms (such as bacteria, fungi, and viruses) that live in or on humans; the collection of microbial genomes that contribute to the broader genetic portrait, or metagenome, of a human.[viii]

Vancomycin – an antibiotic that is used to treat CDI

[i] Song JH, Kim YS. Recurrent Clostridium difficile Infection: Risk Factors, Treatment, and Prevention. *Gut Liver* Vol 13(1):16-24, 2019.

[ii] 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.

[iii] Giovanni, Schneider, Calder, and Fauci. Refocusing Human Microbiota Research in Infectious and Immune-Mediated Diseases: Advancing to the Next Stage. The Journal of Infectious Diseases, Vol. 224, Issue 1: 5-8, Jul 2021.

[iv] Lopetuso, L.R., *et al.* Commensal Clostridia: leading players in the maintenance of gut homeostasis. *Gut Pathog* 5, 23, 2013.

[v] United States Centers for Disease Control and Prevention. https://www.cdc.gov/cdiff/what-is.html. Accessed October 2022.

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

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

[viii] Britannica Medical Dictionary. https://www.britannica.com/science/microbiome. Accessed March 2022.