



**Summit Therapeutics plc**  
(‘Summit’ or the ‘Company’)

## **Summit Presented *In Vivo* Proof of Concept Data for Targeted Enterobacteriaceae Antibiotics at ASM/ESCMID Conference**

- **New Mechanism Antibiotic has Potential to Overcome Known Resistance Mechanisms**

**Oxford, UK, and Cambridge, MA, US, 5 September 2019** – Summit Therapeutics plc (NASDAQ: SMMT, AIM: SUMM) presented *in vivo* proof of concept data for its targeted Enterobacteriaceae antibiotics in animal models of sepsis, pneumonia and urinary tract infection (‘UTI’). Efficacy data of Summit’s DDS-04 series of antibiotics was comparable to marketed antibiotics in all three disease models. These data were presented in a poster session at the ASM/ESCMID Conference on Drug Development to Meet the Challenge of Antimicrobial Resistance held in Boston, MA, September 3-6, 2019. The findings build on previously reported *in vitro* studies that showed this new antibiotic class had high potency and specificity for multiple resistant and non-resistant Enterobacteriaceae strains.

*“Currently marketed broad-spectrum antibiotics for Enterobacteriaceae infections are failing patients at an increasingly alarming rate due to rising antibiotic resistance,” said Dr David Roblin, President of R&D of Summit. “Our DDS-04 series works via a new mechanism which has the potential to successfully cure patients by overcoming all known bacterial resistance mechanisms. The data presented at ASM/ESCMID show the promise of our DDS-04 series in combatting Enterobacteriaceae infections that we estimate cause more than one million infections annually in the US alone.”*

Increasing resistance has rendered many marketed antibiotics ineffective against Enterobacteriaceae. Two Enterobacteriaceae resistance trends seen in the clinic are on the US Centers for Disease Control and Prevention’s list of urgent and serious bacterial threats. Against the backdrop of increasing resistance to current antibiotics, there is a clear need for the development of a new class of antibiotics that could overcome all known resistance liabilities.

**Dr Roblin added,** *“We designed our DDS-04 series of new class antibiotics with the aim of treating infections at all sites where resistance is a clinical issue. That way, we have the chance to make the greatest positive impact on patients. We are extremely excited by the initial proof of concept data our DDS-04 series has shown across sepsis, pneumonia and UTI, and the prospect of moving this series forward.”*

The DDS-04 series is undergoing lead optimisation.

Details from the poster presentation:

### *Sepsis Model*

- Non-neutropenic mouse model (CD-1 mice) infected with *E. coli*
- Mice dosed intravenously with DDS-04 series representative three times once every three hours, starting one hour post-infection
- Tigecycline used as reference, dosed 40mg/kg, two times, once at each of one and six hours post-infection
- After nine hours, bacterial burden was below the limit of detection in the blood, kidneys, liver, lungs and spleen for both the DDS-04 compound and tigecycline

### *Pneumonia Model*

- CD-1 mice infected with *K. pneumoniae*
- Mice dosed intravenously with DDS-04 series representative three times, once every eight hours, starting two hours post-infection
- Tigecycline used as reference, dosed 40mg/kg, three times daily every eight hours subcutaneously
- After 26 hours, a 4.5 log<sub>10</sub> reduction in bacterial burden was observed in the lungs for the DDS-04 compound and a similar reduction was observed with tigecycline



#### *UTI Model*

- C3H/HeN female mice were infected with *E. coli*
- Mice dosed intravenously with DDS-04 series representative three times daily every eight hours over three days
- Ciprofloxacin used as reference, dosed 10mg/kg, three times daily every eight hours over three days
- On day four, a significant reduction in bacterial burden was observed in the urine, bladder and kidneys for both the DDS-04 compound and ciprofloxacin

#### **About DDS-04**

The DDS-04 series comprises targeted-spectrum compounds that act *via* a novel bacterial target, LoICDE. With its new mechanism of action, the DDS-04 series was rapidly bactericidal and highly potent across globally diverse Enterobacteriaceae strains in research studies, which included multi-drug resistant isolates. Importantly, the DDS-04 series has also shown a low propensity for resistance development and did not show cross-resistance with existing classes of antibiotics, suggesting the DDS-04 series has the potential to overcome known resistance mechanisms. This profile makes the DDS-04 series attractive for further development for the treatment of Enterobacteriaceae infections.

#### **About Enterobacteriaceae**

Enterobacteriaceae are a family of Gram-negative bacteria responsible for severe and often deadly infections. They account for a significant fraction of cases across conditions, including bloodstream infections, hospital-acquired pneumonias and complicated urinary tract infections. Summit estimates there are more than 1 million infections in the US annually caused by Enterobacteriaceae across these three settings. Increasing resistance of Enterobacteriaceae has rendered many marketed antibiotics ineffective against these bacteria. Two of the most alarming antibiotic resistance trends are extended-spectrum beta-lactamase (ESBL)-producing Enterobacteriaceae and carbapenem-resistant Enterobacteriaceae (CRE). ESBL is an enzyme that allows bacteria to become resistant to a wide variety of penicillin and cephalosporin antibiotics. CRE are resistant to nearly all existing antibiotics, including carbapenems which are considered the antibiotics of last resort.

#### **About Summit Therapeutics**

Summit Therapeutics is a leader in antibiotic innovation. Our new mechanism antibiotics are designed to become the new standards of care for the benefit of patients and create value for payors and healthcare providers. We are currently developing new mechanism antibiotics for infections caused by *C. difficile*, *N. gonorrhoeae* and ESKAPE pathogens and are using our proprietary Discuva Platform to expand our pipeline. For more information, visit [www.summitplc.com](http://www.summitplc.com) and follow us on Twitter @summitplc.

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