

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

**SUMMIT PRESENTS NEW POSITIVE PRECLINICAL EFFICACY DATA ON ITS SELECTIVE C DIFFICILE ANTIBIOTIC SMT19969 AT ICAAC 2014**

**Oxford, UK, 8 September 2014** – Summit (AIM: SUMM), the drug discovery and development company advancing therapies for Duchenne Muscular Dystrophy and *C. difficile* infection (‘CDI’), reports new positive preclinical efficacy data on SMT19969, a novel and selective antibiotic for the treatment of CDI, at the 54th Interscience Conference on Antimicrobial Agents and Chemotherapy (‘ICAAC 2014’) held in Washington DC, USA from September 5-9 2014.

The data being presented is from a series of preclinical *in vivo* and *in vitro* efficacy studies whose results show that SMT19969 continues to display superiority over vancomycin, the current standard of care for the treatment of CDI. In comparison to vancomycin, SMT19969 provided increased survival rates and prevention of recurrent disease *in vivo*, displayed superior *C. difficile* killing, and reduced toxin B production.

Infectious diseases expert and hospital epidemiologist with a specialist interest in *C. difficile* disease, **Dale Gerding MD, Professor of Medicine at Loyola University Stritch School of Medicine** commented, “*C. difficile* infection is associated with high levels of recurrent disease and, to reduce this, it is imperative that antibiotics which minimise impact on the natural bacterial flora of the gut are used. The gut flora and its protective role are typically disrupted in CDI patients. Antibiotics that have a targeted spectrum of activity, such as SMT19969, could allow restoration of the protective flora to happen sooner and so reduce disease recurrence. The results on SMT19969 are encouraging and it warrants further evaluation in patient clinical trials.”

**Glyn Edwards, Chief Executive Officer of Summit** added, “These results further illustrate that SMT19969 has potential to be a new and differentiated antibiotic for the treatment of initial CDI infection and for the prevention of recurrent disease, the key clinical issue. It is an exciting time in the development of SMT19969 with patients now being enrolled into a Phase 2 proof of concept trial as we work towards establishing the potential of this highly selective antibiotic for the treatment of CDI.”

The results were detailed in five poster presentations given by Summit and its collaborators that include Dr Joseph Blondeau (Royal University Hospital and the University of Saskatchewan, Canada), Professor Kevin Garey (University of Houston College of Pharmacy, Houston, US) and Professor Nigel Minton (School of Life Sciences, University of Nottingham, UK). The details of the presentations were as follows:

***In vivo* Efficacy of SMT19969, Vancomycin and Fidaxomicin in a Hamster Model of CDAD**

*J. Teague, P. Thommes, E. Burgess, G. Daws, L. J. Payne, R. Vickers, P. Warn (Poster F-243)*

A study conducted in an *in vivo* disease model of CDI reported that SMT19969 provided 100% survival during dosing and acute infection and significant protection from recurrent disease with survival rates of 90-100%. Vancomycin, the current standard of care, was associated with significant disease recurrence with only 0-10% survival rates. Fidaxomicin was comparable to SMT19969 against 027 but was less effective against strain 012 in protecting against recurrent disease.

***In vitro* Pharmacodynamics of SMT19969, Vancomycin and Fidaxomicin Against *Clostridium difficile***

*D. Corbett, S. Birchall, A. Wise, L.J. Payne, R.J. Vickers, P.A. Warn (Poster F-240)*

This study reported that SMT19969 was bactericidal with the killing of *C. difficile* highly consistent across all the strains tested. SMT19969 also showed a prolonged post antibiotic effect with no recovery of bacterial growth seen at higher drug concentrations.

**The effect of SMT19969, Fidaxomicin and Vancomycin on sporulation in *Clostridium difficile***

Michelle L. Kelly, Richard Vickers, Klaus Winzer, Nigel P. Minton, and Sarah A. Kuehne (Poster F-241)

This *in vitro* study reported that SMT19969 significantly reduced spore count against all strains of *C. difficile* tested. SMT19969 was also associated with a delay or inhibition of spore outgrowth. The reduction in sporulation may have a positive benefit on rates of recurrent disease.

**Mutant Prevention Concentration of SMT19969 against Clinical Isolates of *Clostridium difficile***

J.M. Blondeau, S.D. Shebelski, R. Vickers (Poster F-245)

The first report of SMT19969 mutant prevention concentration (MPC) testing against *C. difficile* clinical isolates. The results indicate that SMT19969 has a low resistance development profile and this was favourable when compared with metronidazole, the most commonly prescribed agent for treatment of CDI.

**Sub-MIC effect of SMT19969 vs. comparators on *Clostridium difficile* toxin A and B concentrations and cell cytotoxicity**

M Khaleduzzaman, M.J. Alam, and K.W. Garey (Poster F-244)

*C. difficile* typically produces two main toxins with the primary virulence factor being toxin B. The results from this *in vitro* study showed that exposure of *C. difficile* to SMT19969 significantly decreased toxin B concentrations with associated decreased cellular toxicity observed. Superiority to vancomycin and metronidazole was demonstrated.

Copies of the presentations will be available from the 'Programmes' section of Summit's website, [www.summitplc.com](http://www.summitplc.com).

The development of SMT19969 is being substantially supported through to completion of the on-going Phase 2 clinical trial in North America, by a Translational Award from the Wellcome Trust.

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**Notes to Editors**

**About *C. difficile* Infection**

*C. difficile* infection is a serious healthcare threat in hospitals, long-term care homes and increasingly the wider community. It is a serious illness caused by infection of the colon by the bacteria *C. difficile*, which produces toxins that cause inflammation, severe diarrhoea and in the most serious cases can be fatal. Patients typically develop CDI following the use of broad-spectrum antibiotics that disrupt the natural balance of the gastrointestinal (gut) flora allowing *C. difficile* to flourish. Existing CDI antibiotics cause further damage to the gut flora and are associated with high rates of recurrent disease. This is the key clinical issue as repeat episodes are typically more severe and associated with an increase in mortality rates and healthcare costs. Recent years have seen a significant increase in CDI resulting a high economic burden with the annual cost of care in the US alone estimated at over \$4.8 billion.

**About SMT19969**

SMT19969 is a novel, oral small molecule antibiotic that is being developed specifically for the treatment of CDI. Results from non-clinical efficacy studies show that SMT19969 combines potent bactericidal activity against *C. difficile* with high levels of antibacterial selectivity. A Phase 1 trial conducted in healthy volunteers showed SMT19969 to be safe and well tolerated at all doses tested. In addition, a significant reduction in total clostridia but not in other bacterial groups was reported which demonstrated that SMT19969 was highly sparing of gut flora. The Phase 2 proof of concept CoDIFy trial is currently being conducted in North America.

**About the Wellcome Trust**

The Wellcome Trust is the second-highest-spending global charitable foundation, dedicated to achieving extraordinary improvements in human and animal health. We support bright minds in biomedical research and the medical humanities, including public engagement, education and the application of research to improve health. We are independent of both political and commercial interests.

### About Summit

Summit is a drug discovery and development company targeting two high-value areas of unmet medical: the muscle wasting disease Duchenne Muscular Dystrophy and *C. difficile* infection. Summit is listed on the AIM market of the London Stock Exchange and trades under the ticker symbol SUMM. Further information is available at [www.summitplc.com](http://www.summitplc.com) and follow Summit on Twitter ([@summitplc](https://twitter.com/summitplc)).

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### Forward Looking Statements

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