

## Summit Therapeutics plc

('Summit', or 'the Company')

### **EZUTROMID SIGNIFICANTLY REDUCED MUSCLE DAMAGE IN DMD PATIENTS IN 24-WEEK INTERIM DATA FROM SUMMIT'S PhaseOut DMD CLINICAL TRIAL**

- **Increase in Utrophin Protein Expression Observed**
- **Summit Accelerating Preparations for Pivotal Clinical Trial**
- **Ezutromid is a Potential Disease-Modifying Treatment for the Entire DMD Patient Population**
- **Conference Call Scheduled for 1:00pm GMT / 8:00am EST**

**Oxford, UK, 25 January 2018** – Summit Therapeutics plc (NASDAQ:SMMT, AIM:SUMM), the drug discovery and development company advancing therapies for rare diseases and infectious diseases, today announces positive 24-week interim results from the open-label Phase 2 proof of concept clinical trial, PhaseOut DMD. PhaseOut DMD is evaluating the utrophin modulator ezutromid in patients with Duchenne muscular dystrophy ('DMD'). The focus of the planned interim analysis was on biopsy measures that show:

- Treatment with ezutromid resulted in a statistically significant and meaningful reduction in muscle damage as measured by a 23% decrease in mean developmental myosin in muscle biopsies at 24 weeks compared to baseline (11.37% to 8.76%, 95% CI, -4.33, -0.90). Developmental myosin is a biomarker of muscle damage and is found in repairing fibres.
- A total of 14 of 22 patients showed a decrease in developmental myosin, with five of those showing a greater than 40% reduction.
- Increase in mean utrophin protein intensity levels of 7% in biopsies at 24 weeks compared to baseline (0.370 to 0.396, 95% CI, -0.005, 0.058).

The combination of reduced muscle fibre damage and increased levels of utrophin provides the first evidence of ezutromid target engagement and proof of mechanism.

*"The significant reduction in muscle damage coupled with the increase in utrophin expression seen in PhaseOut DMD trial patients at 24 weeks is very encouraging as it suggests ezutromid may slow the relentless cycle of muscle fibre degeneration and regeneration that is a hallmark of DMD," said Professor Francesco Muntoni, Director of the Dubowitz Neuromuscular Centre, at the UCL Institute of Child Health and Great Ormond Street Hospital for Children, London, UK, and Principal Investigator in PhaseOut DMD. "These favourable interim results are certainly a step forward in the development of utrophin modulation as a treatment approach for this fatal disease in all patients with DMD."*

*"The benefits of continual production of utrophin protein to protect against the progression of DMD have been well established in preclinical studies," added Professor Dame Kay E. Davies FRS, Dr Lee's Professor of Anatomy of the University of Oxford and Co-Founder of Summit. "These data provide the first evidence of utrophin modulation working in patients. If further findings build on this evidence they could establish ezutromid as a universal, disease-modifying treatment and bring hope to all patients and families living with DMD."*

DMD is caused by genetic faults that prevent muscle cells from making dystrophin, a protein that maintains the structure and healthy functioning of muscles. The absence of dystrophin, as seen in patients with DMD, leads to a catastrophic cycle of muscle damage and repair. Utrophin protein performs a similar role to dystrophin in developing and repairing muscle fibres. As a muscle fibre matures, utrophin is switched off and replaced by dystrophin in the case of healthy individuals. During the early stages of natural muscle repair, utrophin and developmental myosin are expressed concurrently, and are then slowly switched off. Ezutromid aims to maintain utrophin expression in patients with DMD so it can substitute for the lack of dystrophin and break this cycle.

*“Achieving this significant reduction in muscle damage after only 24 weeks of ezutromid treatment is a landmark moment for our utrophin modulation programme,” commented Mr Glyn Edwards, Chief Executive Officer of Summit. “These promising interim data enhance our belief that longer-term treatment with ezutromid could achieve meaningful functional benefits for patients living with DMD. We now look forward to announcing the top-line data from the full 48-week trial in the third quarter of this year and in parallel accelerating preparations for the advancement of ezutromid into a pivotal clinical trial in patients.”*

Additional findings from the PhaseOut DMD 24-week interim results:

- All patients achieved plasma levels of ezutromid sufficient to modulate utrophin.
- Pharmacological responses were observed in patients treated with either the F3 or F6 formulations. There were no observed relationships between drug exposure and responses in pharmacology or safety measures at this stage.
- In an additional biopsy measure, average muscle fibre diameter decreased from 42.1µm at baseline to 40.3µm at 24-weeks.
- Changes in muscle pathology can be monitored using magnetic resonance spectroscopy (‘MRS’) to evaluate the amount of fat in muscles, which increases over time in DMD. The mean fat fraction in the vastus lateralis (thigh) was 14.7% at baseline and 18.5% at 24 weeks (n=37). Longer term dosing of patients is expected to be required to detect changes in MRS parameters, which is the 48-week primary endpoint.
- Functional tests, which naturally decline over time in DMD, were included as exploratory measures. The mean six-minute walk distance was 404m at baseline and 395m at 24 weeks (n=39). Mean North Star Ambulatory Assessment score was 25.0 at baseline and 24.4 at 24 weeks (n=39). The North Star Ambulatory Assessment is a multi-point test of motor function with a maximum score of 34.
- All patients retained ambulation after 24 weeks of treatment.
- Ezutromid has been well tolerated to date.

The muscle biopsies were analysed using fully automated techniques that can assess whole cross-sections of biopsies containing several thousand individual fibres. These techniques were developed by Summit in collaboration with Flagship Biosciences Inc. Following strict handling and processing protocols, all biopsies contributed to the overall dataset with 22 matched pairs of baseline/week 24 biopsies assessed in the developmental myosin and fibre diameter assay and 18 matched pairs of baseline/week 24 biopsies assessed in the utrophin assay.

PhaseOut DMD is ongoing. Top-line results are expected to be reported in the third quarter of 2018. After 48 weeks of treatment, all patients have the option of enrolling into an extension phase, which is gathering long-term MRS, functional and safety data on ezutromid; to date 18 of 19 eligible patients have enrolled into the extension phase. Summit plans to conduct a randomised, placebo controlled trial that could potentially support the accelerated and conditional approval of ezutromid in the US and EU respectively.

Additional details of the 24-week interim data are expected to be presented at medical and scientific conferences.

#### **About PhaseOut DMD**

PhaseOut DMD aims to provide proof of concept for ezutromid and utrophin modulation by measuring utrophin protein and muscle fibre regeneration in muscle biopsies, as well as muscle fat infiltration. The primary endpoint of the open-label trial is the change from baseline in magnetic resonance spectroscopy parameters related to fat infiltration and inflammation of the leg muscles. Biopsy measures evaluating utrophin and muscle damage are included as secondary endpoints. Exploratory endpoints include the six-minute walk distance, the North Star Ambulatory Assessment and patient reported outcomes. PhaseOut DMD enrolled 40 patients in the US and UK, aged from their fifth to their tenth birthdays. PhaseOut DMD is 48 weeks in length. Under the protocol, 30 patients receive 2,500mg of the F3 formulation of ezutromid twice a day and ten patients receive 1,000mg of the F6 formulation of ezutromid twice a day. All patients had a bicep muscle biopsy taken at baseline with 24 patients scheduled to have their second biopsy after 24 weeks of dosing, and the remaining 16 patients

scheduled to have their second biopsy after 48 weeks of dosing. The number of patients on each formulation assigned to each biopsy group is proportionally consistent. Two patients withdrew from the trial prior to their second biopsy for reasons unrelated to ezutromid; one patient was on a 24-week second biopsy schedule and the other was on a 48-week second biopsy schedule.

### Conference Call Details

Summit will host a conference call and webcast to review the data today at 1:00pm GMT / 8:00am EST. To participate in the conference call, please dial +44 (0)330 336 9411 (UK and international participants) or +1 323-794-2551 (US local number) and use the conference confirmation code 2238624. Investors may also access a live audio webcast of the call via the investors section of the Company's website [www.summitplc.com](http://www.summitplc.com). A replay of the webcast will be available shortly after the completion of the call.

### About Utrophin Modulation in DMD

DMD is a progressive muscle wasting disease that affects around 50,000 boys and young men in the developed world. The disease is caused by different genetic faults in the gene that encodes dystrophin, a protein that is essential for the healthy function of all muscles. There is currently no cure for DMD and life expectancy is into the late twenties. Utrophin protein is functionally and structurally similar to dystrophin. In preclinical studies, the continued expression of utrophin had meaningful, positive effect on muscle performance. Summit believes that utrophin modulation has the potential to slow down or even stop the progression of DMD, regardless of the underlying dystrophin gene mutation. Summit also believes that utrophin modulation could potentially be complementary to other therapeutic approaches for DMD. The Company's lead utrophin modulator, ezutromid, is an orally administered, small molecule. DMD is an orphan disease, and the US Food and Drug Administration ('FDA') and the European Medicines Agency have granted orphan drug status to ezutromid. Orphan drugs receive a number of benefits including additional regulatory support and a period of market exclusivity following approval. In addition, ezutromid has been granted Fast Track designation and Rare Pediatric Disease designation by the FDA.

### About Summit Therapeutics

Summit is a biopharmaceutical company focused on the discovery, development and commercialisation of novel medicines for indications for which there are no existing or only inadequate therapies. Summit is conducting clinical programs focused on the genetic disease Duchenne muscular dystrophy and the infectious disease *C. difficile* infection. Further information is available at [www.summitplc.com](http://www.summitplc.com) and Summit can be followed on Twitter (@summitplc).

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**Forward-looking Statements**

Any statements in this press release about Summit's future expectations, plans and prospects, including but not limited to, statements about the clinical and preclinical development of Summit's product candidates, the therapeutic potential of Summit's product candidates, the timing of initiation, completion and availability of data from clinical trials, the potential submission of applications for regulatory approvals, the sufficiency of Summit's cash resources, 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, 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, availability of funding sufficient for Summit's foreseeable and unforeseeable operating expenses and capital expenditure requirements and other factors discussed in the "Risk Factors" section of filings that Summit makes with the Securities and Exchange Commission including Summit's Annual Report on Form 20-F for the fiscal year ended January 31, 2017. 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 Summit's views only as of the date of this release and should not be relied upon as representing Summit's views as of any subsequent date. Summit specifically disclaims any obligation to update any forward-looking statements included in this press release.

This announcement contains inside information for the purposes of Article 7 of EU Regulation 596/2014 (MAR).

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