

## Summit Therapeutics plc

('Summit', or 'the Company')

### SUMMIT ANNOUNCES NEW ANALYSIS SHOWING EZUTROMID SIGNIFICANTLY REDUCED MUSCLE INFLAMMATION IN PHASE 2 CLINICAL TRIAL IN DMD

- **MRS-T2 Data Provide Evidence of Early Impact of Ezutromid on Downstream Muscle Health**
- **Data Build on Positive Biopsy Findings that Showed Significant Decrease in Muscle Damage**

**Oxford, UK, 26 February 2018** – Summit Therapeutics plc (NASDAQ:SMMT, AIM:SUMM) announces further positive findings from PhaseOut DMD, a Phase 2 open-label, multi-centre clinical trial of the utrophin modulator ezutromid in Duchenne muscular dystrophy ('DMD'). Further analysis of the 24-week interim dataset showed a statistically significant decrease in muscle inflammation as measured by magnetic resonance spectroscopy transverse relaxation time T2 ('MRS-T2').

*"MRS-T2 is an objective technique used to monitor DMD disease progression as it allows for the precise quantification of changes in muscle breakdown and inflammation. MRS-T2 values typically increase over time in DMD," commented Dr H Lee Sweeney, Director of the Myology Institute at the University of Florida and Co-Director of Imaging DMD. "The decrease in MRS-T2 seen in PhaseOut DMD is encouraging and suggests ezutromid is having a positive effect on muscle health. These data could be an early indication that these patients are experiencing a decrease in disease severity and highlight ezutromid's potential as a disease modifying treatment. I look forward to seeing further findings from PhaseOut DMD."*

The reduction in MRS-T2 measured in PhaseOut DMD is consistent with the expected activity of ezutromid to stabilise muscle fibre membranes and thereby reduce muscle fibre damage and inflammation. A statistically significant and meaningful reduction in muscle fibre damage was observed in previously reported 24-week findings from patient biopsies in PhaseOut DMD.

Published research has shown reductions in MRS-T2 in DMD patients treated with steroids.<sup>[1]</sup> All patients in PhaseOut DMD have been on stable steroid regimens and therefore the MRS-T2 reductions observed are in addition to any anti-inflammatory effect provided by steroids.

The new MRS data showed a statistically significant decrease from baseline in the T2-relaxation time in the soleus (calf muscle) in patients (n=38) treated with ezutromid. The mean decrease was -0.861 milliseconds from baseline to 24 weeks (31.850 milliseconds to 30.989 milliseconds, 95% CI, -1.440, -0.281). The soleus is one of the most reliable leg muscles for monitoring disease progression via T2 relaxation time in DMD with increases shown to correlate to loss of functional ability.<sup>[1,2]</sup> Published natural history data show that T2 relaxation times increase with disease progression due to the relentless cycle of muscle damage and repair leading to inflammation.<sup>[1,2]</sup> A mean decrease of -0.470 milliseconds in MRS-T2 was also observed in the vastus lateralis (thigh muscle) in ezutromid-treated patients (n=37) from baseline to 24 weeks (32.265 milliseconds to 31.795 milliseconds, 95% CI, -1.158, 0.218).

*"The 24-week interim analysis has shown encouraging signs of ezutromid activity in PhaseOut DMD. These MRS-T2 findings show a positive impact on downstream muscle health," added Dr David Roblin, Chief Medical Officer and President of R&D at Summit. "This, combined with the evidence that ezutromid can modulate production of utrophin protein and significantly reduce muscle damage, is further evidence of the potential of ezutromid as a disease modifying approach for the treatment of all genetic forms of DMD."*

[1] Arpan et al., *Neurology*, 2014, 83: 974-980.

[2] Willcocks et al., *Neuromuscul Disord*. 2014, 25(5): 393-401.

#### 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 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 is a multi-centre trial that enrolled 40 patients in the US and UK, aged from their fifth to their tenth birthdays. PhaseOut DMD is 48 weeks in length after which patients have the option of enrolling into an extension phase and continuing to be dosed with ezutromid. 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. 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. Positive interim 24-week data were reported in January 2018 that showed a significant and meaningful reduction in muscle damage as measured by a decrease in levels of the biomarker developmental myosin as measured by muscle biopsy. PhaseOut DMD is going. Top-line 48-week results are expected to be reported in the third quarter of 2018.

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

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