



## **Update on Phase 3 Tadalafil Trial**

*We are writing to share disappointing news about our Phase 3 study of tadalafil in approximately 330 patients with Duchenne muscular dystrophy (DMD). We recently completed analysis of the initial data from the placebo controlled, double-blind period of the trial, and unfortunately did not see any evidence of efficacy for tadalafil to slow the decline in 6 Minute Walk Distance (6MWD) compared with placebo through 48 weeks. The study also included other secondary assessments of motor function, including the North Star Ambulatory Assessment and timed function tests (10 meter walk/run, rise from floor, and 4-stair climb), and there was no evidence of efficacy observed in these endpoints either. There also was no evidence of efficacy in subgroup analyses of the primary 6MWD endpoint in boys with differing disease severities at baseline. The complete efficacy and safety data from the trial will be reviewed over the coming weeks.*

*Because the trial provided no evidence that once-daily tadalafil treatment has a meaningful effect to slow disease progression compared with placebo, the open-label extension (OLE) phase of the study will be stopped. This decision was made in consultation with experts in DMD research on the trial Steering Committee, who agreed that stopping the OLE is in the best interest of all the patients in the study and their families. All investigators were informed of this decision late last week and provided with guidance on discontinuing the patients from the study.*

*Based on initial results, the overall adverse events were consistent with the known tadalafil safety profile and the DMD disease state. In a sub study of 27 boys who had a cardiac MRI, the average increase in left heart ventricle volumes was larger in the tadalafil groups relative to placebo. Other markers of heart function such as ejection fraction on echocardiogram were similar to placebo. Further analyses are ongoing with cardiology experts in the DMD community to understand the clinical interpretation and relevance of these findings.*

*We will be working closely with the patient advocacy community in the coming months to arrange a webinar to communicate the full results and to provide an opportunity for families to ask questions. We also will be submitting the study results for presentation at scientific and patient advocacy group meetings, and will submit a paper for publication of the full study results in a scientific peer-review journal.*

*We would like to sincerely thank all the families who participated in the study for their time and commitment. Obviously these are not the outcomes we had hoped for; however, they provide a definitive answer to an important and urgent question that was prompted by compelling pre-clinical and clinical data. We hope that the new data from this trial, which includes functional measures, quality of life, laboratory findings, measures of cardiac function, and muscle imaging data, can also be used to further advance the understanding of DMD and inform the design of future clinical trials.*