Further clinical studies are planned to determine a consistently effective dose.

Methods:

The (now completed) trial evaluated the systemic delivery of AVI-4658 once following systemic administration. Preliminary, laboratory data from the remaining cohorts bode well for safe, long-term administration of AVI-4658. In patients dosed with total exposures of up to 10,813 mg of AVI-4658, no drug infusion related adverse events have been observed. Adverse events tended to be mild or moderate, unrelated to treatment and resolved readily.

All 19 DMD patients who enrolled have now completed the initial 12 week dosing phase and have also now completed the observation follow up period. Dosing escalation is shown in Figure 1. In patients dosed with total exposures of up to 10,813 mg of AVI-4658, no drug infusion related adverse events have been observed. Adverse events tended to be mild or moderate, unrelated to treatment and resolved readily (Table 2). Serious Adverse Events (SAEs) were reported, both unrelated to the drug; 1 post-operative nausea and vomiting; 1 ankle fracture; Both in 14 week follow-up. Subject 202 had treatment discontinued after 7 doses when his cardiomyopathy was noted to deteriorate, but he remained under observation and was stabilized on ACE1 and β blockade. Results of immunohistochemical analysis of muscle biopsies taken 2 weeks after last dose were compared with samples taken pre-treatment (and normal control) and are presented in Figures 2 and 3.

Conclusions (tolerability, exon skipping and dystrophin expression): AVI-4658 well tolerated by IV administration

No adverse safety signal
- Max Single dose of 900mg
- All 48 doses to 4 patients at 10mg/kg and all 48 doses to 4 patients at 20mg/kg well tolerated
- Max Cumulative dose of 10,813mg
- 220 infusions administered without any infusion associated reactions

Exon skipping, RNA and dystrophin expression confirms "proof of concept"

Further clinical studies are planned to determine a consistently effective dose.