

## **Clinical development of idebenone (CATENA<sup>®</sup>) for the treatment of Duchenne Muscular Dystrophy – A summary of Phase II study results and design of a Phase III clinical study**

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**Background:** Respiratory and cardiac complications cause early morbidity and mortality in patients with Duchenne muscular dystrophy (DMD). Use of glucocorticoids slows decline in respiratory function, but long-term use is hampered by side effects. Idebenone (CATENA<sup>®</sup>) supports mitochondrial respiratory chain function and reduces oxidative stress, pathways that are involved in DMD pathogenesis. Long-term blinded controlled preclinical *in vivo* studies in the homologous *mdx* mouse indicate that idebenone is cardioprotective and improves exercise performance in murine dystrophin-deficiency.

**Summary of Phase II clinical study (DELPHI):** This 12-month study has evaluated the efficacy and tolerability of treatment with idebenone compared to placebo in children with DMD. 21 DMD patients (8-16 y) with cardiac dysfunction were enrolled in the double-blind randomized placebo-controlled trial. Thirteen patients received idebenone at a dose of 450 mg/d for 52 weeks, 8 patients received placebo. All subjects completed the study. Frequency and type of adverse events was comparable in both groups, indicating good safety and tolerability of idebenone. The primary endpoint was change in peak systolic radial strain of the left ventricular inferolateral wall, the region of the heart affected early and most severely in DMD. Patients on idebenone improved during the study period to a significantly greater extent than placebo. In addition, idebenone treatment was associated with improvement in peak expiratory flow and peak flow % predicted whilst patients on placebo deteriorated in these respiratory parameters. This study provided the first indication of clinical efficacy with idebenone on early functional cardiac and respiratory parameters in DMD.

**Design of a Phase III clinical study (DELOS):** The study has a randomized, double-blind, placebo-controlled design with ~25 participating centers in Europe, USA and Canada. 240 ambulatory and non-ambulatory patients, aged 10-18 years will be enrolled and will receive either 900 mg/d idebenone (CATENA<sup>®</sup>, 150 mg film-coated tablets) or placebo for 12 months. The DELOS study is designed to demonstrate improvement in a clinically meaningful early parameter of respiratory function in DMD.