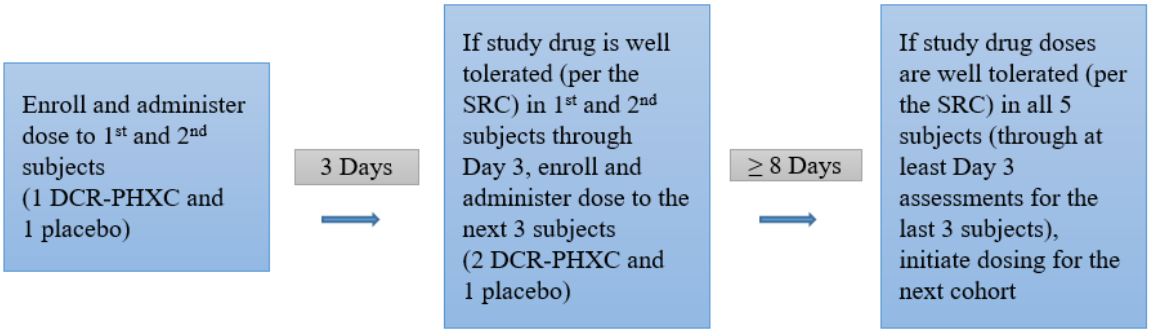
Figure S1: PHYOX1-Group A study design schematic



All participants in Group A were enrolled at a single site in the UK. Participants were randomized by a centrally administered interactive web response system into 5 sequential cohorts (0.3 mg/kg, 1.5 mg/kg, 3.0 mg/kg, 6.0 mg/kg, 12.0 mg/kg), with 5 participants (3 nedosiran, 2 placebo) in each cohort. The dispensing pharmacist was unblinded to the treatment assignment. All participants, investigators, and study personnel were blinded to the treatment assignment throughout the safety assessment period. Participants received a single subcutaneous dose of DCR-PHXC (nedosiran) or placebo on Day 1. The first 2 participants in each cohort (the 'sentinel pair') received study intervention on the same day (1 nedosiran, 1 placebo). After a 3-day observation period, if deemed safe and tolerated (with no medically important AEs) by the safety review committee (SRC), the remaining participants in the cohort were to be randomized (2 nedosiran: 1 placebo) and receive study intervention. Escalation to the next dose cohort only occurred after the SRC had reviewed available safety data and made a determination that it was acceptable to continue.