A RANDOMIZED, DOUBLE-BLIND, PLACEBO CONTROLLED TRIAL OF REPEATED NEBULISATION OF NON-VIRAL CFTR GENE THERAPY IN PATIENTS WITH CYSTIC FIBROSIS

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In support of a translation programme of gene therapy for CF, the UK CF Gene Therapy Consortium has conducted a large preclinical programme and six Phase 1/2a clinical studies. These have cumulatively defined a) the optimum vector (Lipid 67A), b) plasmid configuration (Elongation Factor Ia promoter, human CMV enhancer, codon optimised and CpG depleted), c) nebuliser (Trudell AeroEclipse II), d) dosing interval (monthly), e) patient subgroup (50%<FEV1<90%) and f) primary (percentage change in predicted FEV1) and secondary outcomes. We recently completed a Phase 2b double-blind, placebo-controlled trial comparing the above formulation with 0.9% saline, nebulised at twelve monthly intervals in a 1:1 randomisation. Two small subgroups underwent either additional nasal administration or bronchoscopic evaluation to allow assessment of molecular surrogates (2:1 randomisation Active:Placebo). The Per Protocol group (predefined as receiving ≥9 doses) consisted of 116 patients (52 Placebo and 64 Active). Data on both safety and efficacy will be available before Oct 7, 2015.

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