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Title: Safety profile and pharmacokinetics of SB010, an inhaled GATA-3-specific DNAzyme, in phase I clinical trials in healthy and asthmatic subjects

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Body: SB010 (a solution of the human GATA-3-specific DNAzyme hgd40) has been developed as a treatment for Th2-driven asthma. DNAzymes are single-stranded catalytic DNA molecules that bind and cleave target mRNAs. Aim of these trials was to investigate safety, tolerability and pharmacokinetics of orally inhaled SB010 in healthy subjects and asthmatic patients. We performed 3 Phase I trials: single and multiple applications in healthy subjects (trials 1, 2) and single application in stable allergic asthma patients with airway hyperresponsiveness (trial 3). All trials were performed as randomized, double-blind, placebo-controlled, parallel group (per dose level) dose-escalation trials in male subjects. SB010 was applied as nebulized solution in 6 dose levels (0.4 – 40 mg trial 1) or in 3 dose levels (5 – 20 mg trials 2+3). Adverse events (AE), vital signs, clinical chemistry, hematology, urinalysis, ECG, pulmonary function testing and overall tolerability were assessed in 108 subjects. Plasma concentrations were analyzed using a hybridization ELISA. AEs were of minor clinical relevance and fully reversible during the trials. Maximum plasma concentrations of hgd40 were detected within the highest dose groups: 1 hour after single and multiple administration in healthy subjects (29.2±20.6 ng/mL, 10.0±14.5 ng/mL); 0.75 h after single application in asthmatic patients (14.0±16.6 ng/mL), hgd40 was no longer detectable 12 h after administration. Overall, inhaled SB010 was well tolerated after single or multiple inhalation in healthy subjects or single inhalation in patients. Based on these results SB010 is currently evaluated in Phase IIa clinical trials.