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Title: Safety profile and pharmacokinetics of an inhaled GATA-3-specific DNAzyme in a first-in man study in healthy subjects

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Body: SB010 (a nebulization solution of the human GATA-3-specific DNAzyme hgd40) has been developed and preclinically characterized as an intended treatment of Th2-driven asthma. DNAzymes are single-stranded catalytic DNA molecules that specifically bind and cleave target mRNA sequences. Aim of the present study was to investigate safety, tolerability and pharmacokinetics of orally inhaled single ascending doses of SB010 in a First-in-Man Phase I clinical trial. The study was performed as a randomized, double-blind, placebo controlled, parallel group (per dose level) dose-escalation study in 46 adult healthy male Caucasian subjects (18-45 years). SB010 was applied as nebulized solution via a controlled breathing system (AKITA2 APIXNEB®) in 6 dose levels ranging from 0.4 – 40 mg. Adverse events, vital signs, clinical chemistry, hematology, urinalysis, ECG, pulmonary function testing, body temperature, and overall tolerability were assessed. Plasma concentrations were analyzed using a hgd40-specific hybridization ELISA system. All doses were well tolerated, no serious or severe adverse events and no dose limiting effects were observed. Occasional adverse events (such as headache or cough) were of minor clinical relevance and were fully reversible during the study period. Maximum plasma concentrations of hgd40 were detected within the highest dose group at one hour after administration (29.2

pg/mL ± 20.6) and hgd40 was no longer detectable at time point 12 hours after administration. Overall, inhaled SB010 turned out to be well tolerated after single inhalative exposure in healthy male subjects and is now under evaluation in subsequent clinical studies.