TD139, A Novel Inhaled Galectin-3 Inhibitor for The Treatment of Idiopathic Pulmonary Fibrosis (IPF). Results from The First in (IPF) Patients Study.

N. Hirani (University of Edinburgh, UK)
L. Nicol (University of Edinburgh, UK)
A.C. MacKinnon (University of Edinburgh, UK)
P. Ford (Galecto Biotech AB, Copenhagen, Denmark)
H. Schambye (Galecto Biotech AB, Copenhagen, Denmark)
Pedersen (Galecto Biotech AB, Copenhagen, Denmark)
U. Nilsson (Galecto Biotech AB, Copenhagen, Denmark)
H. Leffler (Galecto Biotech AB, Copenhagen, Denmark)
T. Thomas (Simbec Research, Merthyr Tydfil, UK)
O. Knott (Simbec Research, Merthyr Tydfil, UK)
M. Gibbons (Royal Devon & Exeter Foundation NHS Trust, UK)
J. Simpson (Newcastle University, Newcastle upon Tyne, UK)
T. Maher (Royal Brompton Hospital - London, UK)

RATIONALE: TD139 is a novel, inhaled, dry powdered, anti-Galectin 3 small molecule drug being developed for the treatment of IPF.

METHODS: This study is a randomized, double-blind, multicenter, placebo-controlled, phase IIa study to assess the safety, tolerability, PK (pharmacokinetics) and PD (pharmacodynamics) of TD139 in 24 IPF patients. Three dose cohorts of 8 subjects are being evaluated using a 5:3 ratio (active:placebo). TD139 is delivered to the lungs of IPF patients using the Plastiape inhaler device at the following 3 doses: 0.3mg, 3mg, and 10mg. IPF patients undergo bronchoalveolar lavage (BAL) prior to daily dosing for 14 days, after which a further BAL is performed. TD139 drug concentration is measured in the BAL cell pellets and plasma.

RESULTS: Administration of TD139 is extremely well tolerated at all 3 doses. Currently, there are no significant drug related side effects. TD139 is rapidly absorbed, with mean Tmax values ranging from 2 to 5hrs. $t^{1}/_{2}$ is 7hrs. The drug concentration of TD139 in BAL cell pellets is very high (c. 500 fold vs. systemic exposure). Early results indicate suppression of Galectin-3 (Gal-3) may be readily achievable, confirmed using measurements of cell surface Gal-3 by FACS analysis in alveolar macrophages (AM's) obtained from the BAL.

CONCLUSION: Results from this first-in-IPF patients study indicate that TD139 is both safe and well tolerated in man. In addition, suppression of Gal-3 seems corroborated by FACS analysis in AM's from the same IPF patients. Should final results be favorable, a phase IIb study is planned in IPF patients.