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Genkyotex Announces Investigator-Initiated Phase 2 Clinical Trial to be Conducted with GKT831 in Patients with Idiopathic Pulmonary Fibrosis

Trial to be fully funded via a grant from the United States National Institutes of Health to a consortium of leading academic institutions

Genkyotex (Euronext Paris & Brussels: FR00011790542 – GKTX), a biopharmaceutical company and the leader in NOX therapies, announced today that the United States National Institutes of Health (NIH) has awarded an $8.9 million grant[1] to Professor Victor Thannickal at the University of Alabama at Birmingham (UAB) to fund a multi-year research program evaluating the role of NOX enzymes in idiopathic pulmonary fibrosis (IPF), a chronic lung disease that results in fibrosis of the lungs. The core component of the program will be to conduct a 24-week Phase 2 trial of the Company's lead product candidate, GKT831, in patients with IPF.

The academic consortium also includes Dr. Steven Duncan at UAB, Dr. Gerard Criner at Temple University, Dr. Hyun Kim at the University of Minnesota, Dr. Kevin Flaherty at the University of Michigan, and Dr. Joseph Lasky at Tulane University. Professor Thannickal and his colleagues previously published a seminal study in *Nature Medicine* identifying NOX4 as a key driver of lung fibrosis[2]. In a subsequent publication in *Science Translational Medicine*, the researchers demonstrated that pharmacological inhibition of NOX1/4 with GKT831 achieved marked anti-fibrotic effects and prolonged survival in a stringent model of lung fibrosis in aged mice[3]. Separately, NOX1 has been shown to drive vascular remodeling, a critical factor contributing to disease progression in IPF, in several preclinical models of lung disease[4,5]. In these preclinical models, GKT831 was shown to efficiently reduce vascular remodeling and secondary right heart disease.

The investigator-initiated Phase 2 trial will be a placebo-controlled, double-blind, randomized, parallel group study to evaluate the safety and efficacy of oral GKT831 in patients with IPF receiving standard of care therapies. A total of 60 patients will be allocated to a 24-week treatment with oral GKT831 or matching placebo. The primary endpoint of the study will be the change in plasma levels, at the end of the 24-week treatment period, of o,o'-dityrosine, which is an oxidized covalent modification of protein

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[2] Hecker L et al. NADPH Oxidase-4 Mediates Myofibroblast Activation and Fibrogenic Responses to Lung Injury. Nat Med. 2009 September; 15(9): 1077–1081. doi:10.1038/nm.2005

[3] Hecker L et al. Reversal of persistent fibrosis in aging by targeting Nox4-Nrf2 redox imbalance. Sci Transl Med. 2014 Apr 9;6(231):231ra47

[4] Barman S *et al*. Nox4 Is Expressed In Pulmonary Artery Adventitia And Contributes To Hypertensive Vascular Remodeling. Arterioscler Thromb Vasc Biol. 2014 August ; 34(8): 1704–1715. doi:10.1161/ATVBAHA.114.303848

[5] Green DE *et al*. The nox4 inhibitor, gkt137831, attenuates hypoxia-induced pulmonary vascular cell proliferation. Am J Respir Cell Mol Biol. 2012; 47:718–726. [PubMed: 22904198]

tyrosine residues that has been shown to be a marker of pulmonary oxidative stress and is markedly elevated in patients with interstitial lung disease[6]. Key secondary endpoints include changes in 6-minute walk distance, forced vital capacity and high-resolution CT. The patient enrollment is expected to begin during the first half of 2019.

"We are pleased to advance our research on NOX enzymes to the clinical stage," said Professor Thannickal. *"Importantly, NOX1/4 inhibition may have profound disease modifying effects by addressing the fibrotic and vascular remodeling, which drives disease progression. Based on the preclinical data generated to date, we believe GKT831 has the potential to be an effective treatment in IPF. GKT831 has previously shown marked anti-fibrotic activity in preclinical models, and we now look forward to further evaluating this promising candidate in a Phase 2 clinical trial."*

"We are very excited about this planned investigator-initiated Phase 2 trial, which expands the clinical evaluation of GKT831 into an additional fibrotic disorder," said Dr. Philippe Wiesel, Chief Medical Officer of Genkyotex. *"There is a critical need for effective therapies that can safely delay or reverse disease progression in IPF patients and, based on its profile, we believe that GKT831 could become an important treatment option in this indication. We are thankful to the consortium for supporting and conducting this strategic research program."*

GKT831 is currently being evaluated in two separate Phase 2 clinical trials in patients with respectively liver and kidney fibrosis.

About Genkyotex

Genkyotex is the leading biopharmaceutical company in NOX therapies, listed on the Euronext Paris and Euronext Brussels markets. A leader in NOX therapies, its unique therapeutic approach is based on a selective inhibition of NOX enzymes that amplify multiple disease processes such as fibrosis, inflammation, pain processing, cancer development, and neurodegeneration.

Genkyotex's platform enables the identification of orally available small-molecules that selectively inhibit specific NOX enzymes. Genkyotex is developing a pipeline of first-in-class product candidates targeting one or multiple NOX enzymes. The lead product candidate, GKT831, a NOX1 and NOX4 inhibitor is evaluated in a phase II clinical trial in primary biliary cholangitis (PBC, a fibrotic orphan disease) and in an investigator-initiated Phase II clinical trial in Type 1 Diabetes and Kidney Disease (DKD). This product candidate may also be active in other fibrotic indications. Its second product candidate, GKT771, is a NOX1 inhibitor targeting multiple pathways in angiogenesis, pain processing, and inflammation, currently undergoing preclinical testing.

Genkyotex also has a versatile platform well-suited to the development of various immunotherapies (Vaxiclase). A partnership covering the use of Vaxiclase as an antigen per se (GTL003) has been established with Serum Institute of India Private Ltd (Serum Institute), the world's largest producer of vaccine doses, for the development by Serum Institute of cellular multivalent combination vaccines against a variety of infectious diseases. This partnership could generate approximately €150 million in future revenues for Genkyotex, before royalties on sales.

***For further information, please go to** www.genkyotex.com.*

[6] Thannickal V *et al.* Oxidative Modifications of Protein Tyrosyl Residues Are Increased in Plasma of Human Subjects with Interstitial Lung Disease. Am J Respir Crit Care Med. 2016 Apr 15; 193(8): 861–868. PMID: 26575972

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