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Genkyotex Announces FDA Approval of Phase 2 Investigator-Initiated Trial with GKT831 in IPF

- ***Study expands potential clinical indications for lead compound***
- ***Trial fully funded via a grant from the United States National Institutes of Health***

Genkyotex (Euronext Paris & Brussels: **FR0013399474 – GKTX)** a biopharmaceutical company and the leader in NOX therapies, announced today that the United States Food and Drug Administration (FDA) has approved the Investigational New Drug (IND) application allowing the initiation of a Phase 2 trial of the Company's lead product candidate, GKT831, in patients with idiopathic pulmonary fibrosis (IPF).

This will be the third Phase 2 clinical trial of GKT831 in a fibrotic disease, adding lung fibrosis to liver fibrosis and kidney fibrosis as potential clinical indications for this compound. GKT831 recently demonstrated clinical evidence of anti-fibrotic and anti-inflammatory activity in patients with primary biliary cholangitis (PBC), a fibrotic liver disease.

The Company had previously announced that the United States National Institutes of Health (NIH) 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 IPF, a chronic lung disease that results in fibrosis of the lungs. The investigator-initiated 24-week Phase 2 trial of GKT831 in patients with IPF is the core component of the program.

"This is an important step forward in translating seminal preclinical discoveries to patients with fibrotic lung disease," said Professor Thannickal. *"NOX1/4 inhibition may have profound disease modifying effects on the fibrotic and vascular remodeling, which drives disease progression in IPF. 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 now in patients with liver fibrosis, and we look forward to further evaluating this promising candidate in IPF patients."*

"We congratulate Professor Victor Thannickal and his colleagues for obtaining FDA approval for this important trial," said Dr. Philippe Wiesel, Chief Medical Officer of Genkyotex. *"The clear efficacy, excellent safety, and quality of life improvement achieved by GKT831 in our recently reported PBC trial suggest that GKT831 may provide important therapeutic benefits in patients with IPF."*

[1] Research reported in this publication was supported by the National Heart, Lung, And Blood Institute of the National Institutes of Health under Award Number P01HL114470. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

About the Phase 2 clinical trial of GKT831 in 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. GKT831 will be dosed at 400mg twice a day, the dose which achieved statistically significant improvements in multiple efficacy endpoints and demonstrated an excellent safety profile in the recently completed Phase 2 trial in patients with primary biliary cholangitis (PBC), a fibrotic liver disease. The primary endpoint of the IPF trial 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 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 imaging.

About Genkyotex

Genkyotex is the leading biopharmaceutical company in NOX therapies, listed on the Euronext Paris and Euronext Brussels markets. Its unique platform enables the identification of orally available small-molecules which selectively inhibit specific NOX enzymes that amplify multiple disease processes such as fibrosis, inflammation, pain processing, cancer development, and neurodegeneration.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 has shown evidence of anti-fibrotic activity in a Phase II clinical trial in primary biliary cholangitis (PBC, a fibrotic orphan disease) and Genkyotex is planning to initiate a Phase III clinical trial in PBC following its positive Phase II results. GKT831 is also being evaluated in an investigator-initiated Phase II clinical trial in Type 1 Diabetes and Kidney Disease (DKD). A grant from the United States National Institutes of Health (NIH) of $8.9 million was awarded 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 Phase 2 trial with the GKT831 in patients with IPF. This product candidate may also be active in other fibrotic indications.

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.

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

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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]

[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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