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Genkyotex's Lead Product Candidate, GKT831, Halts the Tumor Promoting Effect of Cancer Associated Fibroblasts in New Preclinical Study

Study Published in International Journal of Cancer

Genkyotex (Euronext Paris & Brussels: FR00011790542 – GKTX), a biopharmaceutical company and the leader in NOX therapies, announced today that data in a preclinical model showed that GKT831, the Company's NOX1 and NOX4 inhibitor, efficiently targeted cancer associated fibroblasts (CAFs) in prostate cancer and abrogated the pro-tumorigenic influence of the tumor micro-environment. The results of this study, which was conducted by Dr. Natalie Sampson and colleagues at the Medical University of Innsbruck, were published in the International Journal of Cancer (https://doi.org/10.1002/ijc.31316).

CAFs are an essential component of the tumor-associated stromal microenvironment, which is a major driver of prostate cancer progression and independent predictor of disease prognosis.

CAFs are largely driven by cancer-derived cytokines, such as transforming growth factor-β (TGFβ1), which fuels cancer cell proliferation and migration. The results of this study showed that stromal areas with clusters of intense NOX4 staining were localized adjacent to tumor foci with abundant TGFβ1 expression. *In vitro*, GKT831 significantly reduced TGFβ1-induced expression of CAF markers at both the mRNA and protein levels.

Additionally, GKT831 halted the proliferation and migration of prostate cancer cells. Collectively, these data demonstrated that GKT831 efficiently disrupts the TGFβ1-NOX4 signaling axis underlying reciprocal epithelial-stromal cell crosstalk, fibroblast activation and stromal-driven tumor cell promoting properties.

"These studies highlight the central role of NOX4 in driving CAF activation in prostate cancer. Importantly, the results demonstrate that GKT831 abrogates the tumor promoting properties of CAFs, further supporting our focus on the therapeutic potential of NOX inhibitors in oncology. These new data follow previous preclinical results published mid-2017, showing that GKT831 can efficiently target CAFs and delay tumor growth in head and neck cancer," said Philippe Wiesel, M.D., Executive Vice President and Chief Medical Officer of Genkyotex.

The role of NOX4 in CAFs activation shares many similarities with its role in the activation of myofibroblasts, a key characteristic of fibrogenesis in many fibrotic diseases. GKT831 has also demonstrated potent anti-fibrotic activity in multiple preclinical models of liver, lung, skin, and renal fibrosis. Genkyotex is currently assessing the safety and efficacy of GKT831 in patients with

respectively primary biliary cholangitis and diabetic kidney disease, two progressive fibrotic disorders, in two ongoing different Phase 2 trials.

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 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 up to $57 million in future revenues for Genkyotex, before royalties on sales.

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

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