Archamps (France), November 5, 2018 at 07:00 am CET

Genkyotex Meets Both Primary and Secondary Interim Efficacy Endpoints in Phase 2 Trial of GKT831 in Primary Biliary Cholangitis

- ***After only 6 weeks of treatment, gamma glutamyl transpeptidase (GGT) levels were reduced by 23% in the 400mg BID group (p<0.01)***
- ***In patients with higher baseline GGT, reduction in GGT levels was even greater with 29% (p<0.01)***
- ***Alkaline phosphatase (ALP) levels were reduced by 17% in the 400mg BID group (p<0.001)***
- ***Genkyotex to hold a conference call and webcast today at 3:00 pm CET / 09:00 am EDT***

Genkyotex (Euronext Paris & Brussels: FR00011790542 – GKTX) announced today that its lead product candidate GKT831, a NOX1/4 inhibitor, met both the primary and secondary interim efficacy endpoints with high statistical significance after only 6 weeks of treatment. The data establish GKT831 as an attractive therapeutic option in a broad PBC population and support its development in multiple fibrotic diseases including NASH and IPF.

GKT831 achieved even greater GGT reductions (29%, p<0.01 vs placebo) in patients with higher baseline GGT (≥ 2.5 XULN, n=68), suggesting that it may also benefit patients with more advanced disease, the patient population with the highest medical need and limited therapeutic options.

In addition, the progressive reductions from baseline to week 2 and to week 6 suggest that further improvements can be achieved with continued treatment. Specifically, the 400mg twice daily dose (BID) achieved a 15% reduction in GGT at week 2 and a 23% reduction at week 6. ALP reductions were 12% at week 2 and 17% at week 6.

The interim analysis was conducted in 92 patients after 6 weeks of treatment. Final study results after 24 weeks of treatment in 111 PBC patients are expected in Spring 2019. The final results will also include additional endpoints assessing quality of life (fatigue and pruritus), fibrosis and cholestasis.

Elias Papatheodorou, Chief Executive Officer of Genkyotex, commented: *"The clinical data further establish GKT831 as a novel anti-fibrotic candidate and confirm the therapeutic value of NOX inhibition for patients. NOX inhibitors are an emerging therapeutic class able to address many human diseases with unmet medical need. Following these interim results we are investigating options in non-alcoholic steatohepatitis (NASH) and primary sclerosing cholangitis (PSC).*"

Philippe Wiesel, Chief Medical Officer of Genkyotex, commented: "*The significant effect on the primary endpoint GGT, a marker of inflammatory and cholestatic liver injury, provides clinical confirmation of GKT831's mechanism of action. We are very impressed by the highly significant effect on ALP, which indicates cholangiocyte protection. Importantly, ALP is a key endpoint used globally for regulatory approval. We are looking forward to the launch of the NIH funded IPF Phase 2 trial scheduled in H1 2019, the continuation of the JDRF funded DKD Phase 2 trial, and of course, seeing the final data of the PBC Phase 2 trial at week 24 in Spring 2019."*

About the PBC phase 2 trial of GKT831

The 24-week placebo-controlled study is being conducted in 62 centers (US, Canada, Belgium, Germany, Greece, Italy, Spain, UK and Israel). The trial enrolled PBC patients with inadequate response to ursodeoxycholic acid (UDCA). This is a difficult to treat patient population likely to progress to cirrhosis and eventually liver transplant or death. To be eligible for the trial, patients were required to have elevated alkaline phosphatase (ALP; >1.5XULN) and elevated gamma glutamyl transpeptidase (GGT; >1.5 XULN).

The primary efficacy endpoint is change in GGT at week 24. Key secondary endpoints include additional markers of liver and bile duct injury, markers of inflammation, non-invasive markers of liver fibrosis including liver stiffness assessed by transient elastography, the Enhanced Liver Fibrosis (ELF) score, and circulating collagen fragments including proC3. In addition, indicators of quality of life including pruritus and fatigue will be assessed. Markers of bile acid metabolism and immune activation will be also investigated.

A total of 111 patients have been allocated according to a 1:1:1 randomization ratio to three groups: UDCA plus placebo, UDCA plus GKT831 400mg once a day (OD) and UDCA plus 400mg twice a day (BID). This trial is one of the largest phase 2 PBC trials conducted to date.

For additional information about the trial design and eligibility criteria, please refer to the ClinicalTrial.gov website: NCT03226067.

About the interim analysis and baseline patient characteristics

The interim efficacy analysis was conducted when 92 patients completed 6 weeks of treatment. At baseline, mean ALP levels were respectively 304, 282, and 350 IU/L in the placebo, 400mg GKT831 OD, and 400mg GKT831 BID groups. Mean baseline GGT levels were respectively 224, 215, and 237 IU/L in the placebo, 400mg GKT831 OD, and 400mg GKT831 BID groups.

Changes in the primary efficacy endpoint GGT, a marker of liver and bile duct injury, were: -7% in the placebo, -12% in the 400mg OD, and -23%, in the 400mg BID groups ($p<0.01$ for the 400mg BID group vs placebo).

Changes in the key secondary efficacy endpoint ALP, a marker of bile duct injury, were: -2%, in the placebo, -8%, 400mg OD and -17% 400mg BID groups ($p<0.001$ for the 400mg BID group vs placebo). In PBC, a reduction in ALP of at least 15% is considered a meaningful biochemical response. Reduction of 15% in ALP was achieved in 53% of patients in the 400mg BID group compared to 16% in the placebo and 26% GKT831 400mg OD groups.

Markers of liver injury and inflammation were assessed. Although enrolled patients had relatively low levels of liver transaminases and high sensitivity C-reactive protein, dose dependent reductions were observed.

Baseline Patient characteristics and absolute changes in GGT & ALP

Baseline patient characteristics	Placebo	GKT831 400mg OD	GKT831 400mg BID
N	31	31	30
Age (years)	56 (10)	56 (10)	55 (9)
Females (%)	97	84	93
GGT (IU/L)	224 (212)	215 (154)	237 (193)
ALP (IU/L)	304 (151)	282 (89)	350 (177)
ALT (IU/L)	44 (18)	44 (22)	55 (34)
AST (IU/L)	44 (19)	43 (20)	50 (33)
Total bilirubin (µmol/L)	10.2 (4.1)	11.0 (4.6)	10.8 (4.7)
hsCRP (mg/L)	5.0 (4.9)	5.8 (5.7)	4.7 (5.1)
Absolute and percent changes in GGT & ALP at week 6			
GGT percent changes (%)	-7 (18)	-12 (23)	-23 (23)
GGT absolute changes (IU/L)	-16 (63)	-19 (81)	-57 (69)
ALP percent changes (%)	-2 (16)	-8 (13)	-17 (13)
ALP absolute changes (IU/L)	-17 (64)	-25 (43)	-62 (64)

Values expressed as mean (SD). Baseline: Day 1.

About clinical safety and pharmacokinetic (PK) analysis

To date, GKT831 has been well tolerated in PBC patients. On October 25 2018, the 3rd Safety Monitoring Board assessed safety data collected in 110 patients allocated to GKT831 400mg OD, GKT831mg BID, or placebo. From the patients reviewed, 87 patients had completed 6 weeks of treatment, 69 subjects had reached week 12 and of these 41 had completed the full 24-week treatment. The SMB provided a positive recommendation. A single serious adverse event (SAE), a case of grade 1 urinary tract infection, has been reported to date. Study drug was not interrupted and the SAE was deemed unrelated to study drug. Importantly, to date there has been no patient drop out due to pruritus.

An initial PK analysis was conducted. Plasma levels of GKT831 and its main active metabolite GKT138184 were measured after 2, 12, and 18 weeks of dosing. Available drug levels at the time of the interim analysis were analyzed. As anticipated, patients receiving 400mg BID had higher through (pre-dose) levels compared to patients receiving 400mg OD. Overall, these results indicate that drug exposure levels were consistent with expectations and with the two dosing levels included in the trial. These results will inform dose selection for future clinical trials of GKT831 in multiple fibrotic disorders.

Conference call details

Genkyotex will host a conference call today, Monday, November 5 2018 at 03:00 pm CET / 09:00 am EDT to discuss these results.

To access the conference call, please dial the following numbers:

France: +33 (0)1 72 72 74 03
Belgium: +32 24 03 58 16
Switzerland: +41 445 831 805
United Kingdom: +44 207 194 37 59
United States: +1 (646) 722 49 16

Pin: 79 25 79 31#

The presentation commented by the management team will be available on the link below:

Genkyotex conference call

A replay of the conference call will be available for 90 days after the session with the following logins:

France: +33 (0)1 70 71 01 60
Belgium: +32 24 03 72 61
Switzerland: +41 225 804 208
UK: +44 203 364 51 47
US: +1 (646) 722 49 69

Access code: 41 88 03 324 #

About Primary Biliary Cholangitis

PBC is an orphan chronic autoimmune disease resulting in the progressive destruction of bile ducts. Decreased bile flow and build up of toxic bile acids results in further bile duct damage and liver injury. Over time, patients develop progressive liver fibrosis, cirrhosis, liver failure and are at higher risk of developing liver cancer. PBC affects primarily women and has a major impact of quality of life by causing fatigue and itching.

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). 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.

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.*

GKTX
LISTED
EURONEXT

ELIGIBLE
PEA
PME

Disclaimer

This press release may contain forward-looking statements by the company with respect to its objectives. Such statements are based upon the current beliefs, estimates and expectations of Genkyotex's management and are subject to risks and uncertainties such as the company's ability to implement its chosen strategy, customer market trends, changes in technologies and in the company's competitive environment, changes in regulations, clinical or industrial risks and all risks linked to the company's growth. These factors as well as other risks and uncertainties may prevent the company from achieving the objectives outlined in the press release and actual results may differ from those set forth in the forward-looking statements, due to various factors. Without being exhaustive, such factors include uncertainties involved in the development of Genkyotex's products, which may not succeed, or in the delivery of Genkyotex's products marketing authorizations by the relevant regulatory authorities and, in general, any factor that could affects Genkyotex's capacity to commercialize the products it develops. No guarantee is given on forward-looking statements which are subject to a number of risks, notably those described in the registration document (document de reference) registered by the French Markets Authority (the AMF) on 27 April 2018 under number R.18-037, and those linked to changes in economic conditions, the financial markets, or the markets on which Genkyotex is present. Genkyotex products are currently used for clinical trials only and are not otherwise available for distribution or sale.

INVESTORS	MEDIA	US
NewCap Dušan Orešanský, Tristan Roquet Montégon and Emmanuel Huynh +33 1 44 71 94 92 genkyotex@newcap.eu	**NewCap** Nicolas Merigeau, Arthur Rouillé +33 1 44 71 00 15 genkyotex@newcap.eu	**LifeSci Advisors, LLC** Brian Ritchie +1-212-915-2578 britchie@lifesciadvisors.com