Archamps (France), July 25, 2019 at 07:00AM CEST

GENKYOTEX ANNOUNCES POSITIVE POST-HOC ANALYSIS OF PBC PHASE 2 TRIAL AND REPORTS CASH POSITION AT JUNE 30, 2019

- ***Setanaxib (GKT831) achieved statistical significance (p=0.02) for primary endpoint with the 400mg BID versus placebo, after correction of non-normal distribution (outliers) in 400mg OD***
- ***In advanced patients, setanaxib 400mg BID achieved significant reductions in GGT (-32%) and ALP (-24%)***
- ***Cash and cash equivalents of €4.5 million as of June 30, 2019, providing cash runway to April 2020***

Genkyotex (Euronext Paris & Brussels: FR0013399474 – GKTX), a biopharmaceutical company and the leader in NOX therapies, announced today positive post-hoc analysis of PBC phase 2 trial.

As previously reported, setanaxib achieved clinically meaningful reductions in liver stiffness, statistically significant reduction in gamma glutamyl transpeptidase (GGT) (p<0.002) and alkaline phosphatase (ALP) (p<0.001) over the 24-week treatment period, but did not achieve statistical significance in the reduction of GGT at week 24, the predefined primary efficacy endpoint. This result was unexpected, as setanaxib had achieved statistical significance in GGT reduction (p<0.01) and ALP reduction (p<0.001) at week 6 interim analysis. Therefore, Genkyotex performed a post-hoc analysis to identify the reasons for the loss of statistical significance at week 24, and to further explore the therapeutic benefits achieved with setanaxib.

The analysis identified a non-normal distribution of GGT values in the 400mg OD dose at week 24, as the cause for the loss of statistical significance at week 24. Statistical significance of p=0.02 is achieved for the primary endpoint for 400mg BID at week 24 when correcting for the non-normal distribution in the 400mg OD group. This correction is achieved with a standard statistical correction method (log-transformation) to minimize the impact of such non-normal data distribution.

As previously reported, setanaxib 400mg BID achieved an important reduction (-22%) in liver stiffness in patients with advanced disease (≥9.6 kPa at baseline). New analysis shows that in these patients setanaxib also achieves clinically meaningful reductions in GGT (-32%) and ALP (-24%) at week 24. These new data indicate that setanaxib could become an important new therapeutic option for the difficult to treat patient populations with advanced liver fibrosis in PBC and other liver diseases, including advanced NASH. Following these positive results, the PBC phase 3 trial is being planned.

In addition, Genkyotex announced in July that:

- the World Health Organization (WHO) recognized NOX inhibitors as a new therapeutic class while approving the new stem "naxib". The WHO recommended setanaxib as the international non-proprietary name (INN, or generic name) for GKT831.
- the United States Food and Drug Administration (FDA) approved in July 2019 the Investigational New Drug (IND) application allowing the initiation of the Phase 2 trial with setanaxib in patients with IPF in the coming months.

Elias Papatheodorou, CEO of Genkyotex, commented: "The full analysis of the data confirms that setanaxib could become an important therapeutic solution in multiple fibrotic indications including NASH. Setanaxib's effect on liver stiffness and quality of life, along with the excellent safety of the product, positions setanaxib as a unique product candidate in the liver fibrosis landscape. As the leader in NOX therapeutics, we are particularly excited with the WHO's decision to formally recognize NOX inhibitors as a novel therapeutic class."

Research highlights

Genkyotex continues to explore the therapeutic value of NOX inhibition in additional therapeutic areas, including oncology. The Company expects to secure non-dilutive grant financing to support its ongoing collaborations with academic partners. During the second quarter of 2019, the Company announced the following important publications:

- The manuscript "Activated Hepatic Stellate Cells and Portal Fibroblasts contribute to cholestatic liver fibrosis in MDR2 knockout mice" was published in May 2019 in the *Journal of Hepatology*. The regression of liver fibrosis observed in this model of cholestatic liver disease is consistent with the reduction in liver stiffness achieved in Phase 2 with setanaxib after just 24 weeks of treatment in PBC patients.
- The Company also announced the publication of preclinical studies in *Clinics and Research in Hepatology and Gastroenterology* showing that its anti-fibrotic drug candidate setanaxib, prevents multiple complications of portal hypertension.
- The manuscript "Inhibition of host NOX1 blocks tumor growth and enhances checkpoint inhibitor–based immunotherapy » was published in July in the *journal Life Science Alliance*. These preclinical results show that NOX1 inhibition represents a novel therapeutic strategy to treat colorectal cancer, particularly in combination with checkpoint inhibition.

Financial highlights

On June 30, 2019, Genkyotex' cash and cash equivalents totaled €4.5 million vs. €7.3 million on March 31, 2019. The Company's cash burn was primarily driven by investments in the ongoing phase 2 trial in PBC. Genkyotex expects its current resources to support anticipated operations until April 2020.

Upcoming financial meeting and publication

- September 19, 2019. 2019 half-year results
- October 24, 2019. Business & cash position update 3rd quarter 2019

Conference call details

Genkyotex will hold a conference call on July 25, 2019 at 2pm CEST and will discuss the *post-hoc* analysis of its Phase 2 trial with setanaxib in PBC and more generally its activities.

Participants numbers for the call:

- US : +1 212 999 6659
- France : +33 (0) 1 7037 7166
- UK (Standard International Access) : +44 (0) 20 3003 2666

Please provide the following password to the operator : Genkyotex

Webcast link : https://channel.royalcast.com/webcast/genkyotexen/20190725_1/

A replay of the conference call will be available for 1 year after the session at the same url : https://channel.royalcast.com/webcast/genkyotexen/20190725_1/

To ensure that the conference call starts on time, please dial in 5-10 minutes before the scheduled start time.

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, setanaxib (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. setanaxib 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 setanaxib 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 or investors@genkyotex.com*

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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 26 April 2019 under number R.19-014, 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.

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APENDIX

Reminder of the Phase 2 clinical trial in Primary Biliary Cholangitis (PBC) final results and other news reported in May and July 2019:

- Setanaxib 400mg BID achieved statistically significant reductions in GGT and ALP over the 24-week treatment period (p<0.002 and p<0.001, respectively).
- The lack of statistical significance for change in GGT at week 24, the predefined primary efficacy endpoint, was due to the non-normal distribution of GGT data in the 400mg OD group. When applying a standard statistical adjustment method (log transformation), statistical significance for the primary endpoint was met (p=0.02) for the 400mg BID group.
- As expected, there was a strong correlation (p<0.0001) between changes in GGT and ALP, indicating that setanaxib induced consistent reductions in markers of bile duct injury.
- After just 24 weeks of treatment, setanaxib 400mg BID achieved a clinically meaningful, 22% reduction in liver stiffness in PBC patients with advanced disease (defined as baseline liver stiffness ≥9.6 kPa), compared to a 4% increase for placebo (p=0.038). Liver stiffness values ≥9.6 kPa are estimated to correspond to a histologic fibrosis score of F3 or higher.
    - Setanaxib is the first compound to achieve a rapid and clinically meaningful reduction in liver stiffness, a non-invasive marker of liver fibrosis and prognostic marker in PBC patients. Therefore, setanaxib is uniquely positioned to contribute its anti-fibrotic effects to generic anticholestatic therapies.
- Furthermore, patients with advanced disease also achieved marked reductions in GGT (-32%) and ALP (-24%) in the GKT831 400mg BID group. This new data indicates that setanaxib is particularly effective in advanced patients who have the highest unmet medical need.
- Patients with advanced disease are at risk of accelerated progression to cirrhosis and reduced survival. Therefore, the marked reductions in liver stiffness and bile duct injury achieved with setanaxib in these patients are particularly important.
- Patients with even moderately elevated liver stiffness ≥7.3 kPa (estimated to have a fibrosis score of F2 or higher) also achieved marked reductions in ALP (19%).
- Setanaxib 400mg BID significantly improved multiple quality of life (QoL) metrics important to PBC patients, including fatigue (p=0.027 vs placebo). Setanaxib is the first compound to achieve significant improvement in QoL for PBC patients.
- Setanaxib had an excellent safety profile at all doses, with no safety signal identified over the 24-week treatment period

This study was a 24-week, double-blind, placebo-controlled study evaluating the safety and efficacy of setanaxib in patients with PBC and inadequate response to ursodeoxycholic acid (UDCA). A total of 111 PBC patients were enrolled, versus the original target of 102 patients, and allocated to three treatment arms: UDCA plus placebo, UDCA plus setanaxib at 400mg once a day, and UDCA plus setanaxib at 400mg twice a day.

Investigator-initiated Phase 2 trial in patients with idiopathic pulmonary fibrosis (IPF):

The United States Food and Drug Administration (FDA) approved in July 2019 the Investigational New Drug (IND) application allowing the initiation of the Phase 2 trial with setanaxib in patients with IPF in the coming months.

The United States National Institutes of Health (NIH) awarded in 2018 an $8.9 million grant to Professor Victor Thannickal at the University of Alabama at Birmingham to fund a multi-year research program evaluating the role of NOX enzymes in IPF, a chronic disease that results in progressive fibrosis of the lungs. The core component of the program is a 24-week Phase 2 trial of setanaxib in patients with IPF.

This placebo-controlled, double-blind, randomized, parallel group study will evaluate the safety and efficacy of oral setanaxib in patients with IPF receiving standard of care therapies. A total of 60 patients will be allocated to a 24-week treatment regimen of either oral setanaxib at 400mg BID or matching placebo.

The primary efficacy endpoint will be the change in plasma levels of o,o'-dityrosine, a mechanistic biomarker of protein oxidation, at the end of the 24-week treatment period compared to baseline. Key secondary endpoints include changes in 6-minute walk distance, forced vital capacity and high-resolution CT.

Investigator-initiated Phase 2 trial in type 1 diabetes and kidney disease (DKD):

This placebo-controlled, double-blind, randomized, parallel study is evaluating the effect of oral setanaxib on the urine albumin-to-creatinine ratio (UACR) in patients with type 1 diabetes and persistent albuminuria, despite treatment with optimal standard of care. First patients completed the full 48 weeks treatment period and the study continues to enroll patients.

A total of 142 patients are planned to be enrolled at approximately 15 investigational centers in Australia. This trial is being led by world-renowned diabetes experts, Professor Mark Cooper, Head of Department of Diabetes at Monash University, and Professor Jonathan Shaw, Deputy Director (Clinical and Population Health) at the Baker Heart and Diabetes Institute in Melbourne, Australia.

The Phase 2 trial is fully funded by the Juvenile Diabetes Research Foundation Australia and the Baker Institute.