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GFT505 POTENTIATES INSULIN ACTION IN HUMANS

NEW CLINICAL DATA SHOW THAT GFT505 IMPROVES THE INSULIN-MEDIATED RESPONSE PRODUCED AFTER A MEAL, CONFIRMING THE ANTI-DIABETIC POTENTIAL OF GFT505.

Lille (France), Cambridge (Massachusetts, United States), September 9, 2010 – GENFIT (Alternext: ALGFT; ISIN: FR0004163111), a biopharmaceutical company at the forefront of drug discovery and development, focusing on the early diagnosis and preventive treatment of cardiometabolic and associated disorders, today announces clinical results giving new insights into the mechanism of action of GFT505 in humans. The clinical trial (GFT505-109-6) demonstrates that GFT505 significantly improves insulin action on the adipose tissues following a meal test. This strong increase in the insulin sensitivity of peripheral tissues is pivotal in the mechanism of action of GFT505 and confirms its anti-diabetic potential.

During a meal, the hypoglycemic hormone insulin is rapidly secreted by the pancreas in response to food intake. Secreted insulin then blocks fat mobilization in adipose tissues (by inhibition of lipolysis) and reduces the circulating level of free fatty acids. This action limits free fatty acid uptake by other tissues, in particular the liver and skeletal muscle, and favors the use of glucose by the skeletal muscles.

The GFT505-109-6 study conducted in healthy volunteers demonstrates that after only 14 days of treatment at 100 mg/d, GFT505 potentiates the effect of a meal test on plasma free fatty acids. At the end of the treatment period, the fasting free fatty acid plasma concentration was significantly lowered in the GFT505 group (-14±6%, $p=0.012$ vs baseline), while it remained unchanged in the placebo group (-1.6%, $p=0.655$ vs baseline). More importantly, the meal-induced decline in plasma free fatty acids (area under the curve between 0-6 hours after meal) was significantly potentiated in subjects treated with GFT505 (+22%, $p<0.001$ vs baseline) but not in placebo-treated subjects (+4%, $p=0.852$ vs baseline). Inter-group comparison confirmed the potentiating effect of GFT505 treatment ($p<0.05$ vs placebo group).

These effects of GFT505 on the response to the meal test likely result from an increase in the modifying action of insulin on lipolysis in adipose tissues. Indeed, in both groups, the peaks of plasma insulin and c-peptide were not modified by the treatment and were comparable.

In addition, after 14 days of treatment, significant decreases in fasting plasma triglycerides (-25%, $p<0.001$ vs baseline), total cholesterol (-7%, $p=0.006$ vs baseline) and LDL-Cholesterol (-12%, $p=0.006$ vs baseline) were observed in the GFT505-treated group but not in the placebo group. The GFT505-induced decrease in plasma triglycerides persisted throughout the duration of the meal test, such that plasma exposure between 0-6 hours after the meal test significantly declined by 20% ($p<0.001$ vs baseline)

Pr. Bart Staels, President of the Scientific Advisory Board, commented "The effect of GFT505 on the free fatty acid response to a meal test not only gives additional proof of efficacy but also supports the originality of this new PPARα/δ dual agonist compared to pure PPARα agonists. From a mechanistic point of view, the effect on the free fatty acid response may result from an increased sensitivity of the adipose tissues to insulin secreted during the meal. Of course, other studies should be done to confirm the mechanism of action of GFT505, but these new data strongly suggest an insulin-sensitizing effect in man and support the anti-diabetic potential of GFT505."

About the GFT505-109-6 clinical trial:
The GFT505-109-6 study was a randomized, double-blind, placebo-controlled trial in healthy volunteers. The objective was to compare the responses to a meal test, before and after oral administrations of GFT505 (100 mg/d) or placebo in two parallel groups (20 patients under GFT505 vs 10 patients under placebo). The meal test (approx 680 kCal) was performed in the morning after 12-hour fasting. Responses to meal tests were evaluated by measuring variations in plasma free fatty acids, triglycerides, glucose, insulin, c-peptide and active GLP-1, every 30 minutes, from 0 to 6 hours post-meal.

About the treatment of prediabetes and diabetes:
The worldwide epidemic of obesity forecasts a parallel increase in the prevalence of type 2 diabetes and associated complications. According to the WHO, this "epidemic disease" could affect up to 300 million people by 2025 whereas they were only 30 million in 1985. Thus, the prevention and treatment of micro and macro-vascular diseases associated with prediabetes and diabetes are considered as worldwide public health issues by both academic societies (IAS, ADA, EASD) and health organizations (WHO, FDA, EMEA). The prediabetic and diabetic patients suffer from overlapping disorders (high blood pressure, dyslipidemia, insulin resistance, inflammation...) which increase the risk of developing type 2 diabetes as well as related micro and macro-vascular diseases: myocardial infarction, stroke, retinopathy, kidney disease, diabetic foot or arteritis… The weaknesses of diagnostic tools and current treatments do not totally cover this global medical need. At present, even treated patients remain at high risk of developing vascular diseases. In particular, beyond improvement of glucose metabolism, atherogenic dyslipidemia (characterized by low plasma concentration of good cholesterol (HDL-C) and high level of triglycerides), the pro-inflammatory and oxidative states are promising therapeutic targets for the medical management of pre-diabetic and diabetic populations.

About GENFIT:

GENFIT is a biopharmaceutical company focused on the Discovery and Development of drug candidates in therapeutic fields linked to cardiometabolic disorders (prediabetes/diabetes, atherosclerosis, dyslipidemia, inflammatory diseases…). GENFIT uses a multi-pronged approach based on early diagnosis, preventive solutions, and therapeutic treatments and advances therapeutic research programs, either independently or in partnership with leading pharmaceutical companies (SANOFI-AVENTIS, SERVIER, …), to address these major public health concerns and their unmet medical needs.
GENFIT's research programs have resulted in the creation of a rich and diversified pipeline of drug candidates at different stages of development, including GENFIT's lead proprietary compound, GFT505, that is currently in Phase II.
With facilities in Lille, France, and Cambridge, MA (USA), the Company has approximately 100 employees. GENFIT is a public company listed on the Alternext trading market by Euronext™ Paris (Alternext: ALGFT; ISIN: FR0004163111). www.genfit.com

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