SANOFI DIABETES

Sanofi Announces Results of ORIGIN, the World's Longest and Largest Randomised Clinical Trial in Insulin in Pre- and Early Diabetes

Dublin, Ireland (15 June 2012) – Sanofi presented results from the landmark ORIGIN trial (Outcome Reduction with Initial Glargine Intervention) at the American Diabetes Association 72nd Scientific sessions. The key findings showed that, compared to standard care, Lantus® (insulin glargine [rDNA] injection) had no statistically significant positive or negative impact on cardiovascular (CV) outcomes versus standard care during the study period and that there was no association between insulin glargine use and increased risk of any cancer. Furthermore, the study findings, which are also published online in the *New England Journal of Medicine* (NEJM) [1], showed that insulin glargine delayed progression from pre-diabetes to Type 2 diabetes (T2DM).

ORIGIN was a six-year randomised clinical trial designed to assess the effects of treatment with insulin glargine versus standard care on CV outcomes. The study involved over 12,500 participants worldwide with pre-diabetes or early Type 2 diabetes mellitus and high CV risk, with 6,264 participants randomised to receive insulin glargine titrated to achieve fasting normoglycaemia. There were two coprimary composite cardiovascular outcomes. The first was death from cardiovascular causes, nonfatal myocardial infarction, or nonfatal stroke, and the second was a composite of any of these events, a revascularisation procedure (cardiac, carotid, or peripheral), or hospitalisation for heart failure. Other adjudicated outcomes were a composite microvascular outcome, incident cases of diabetes in participants without baseline diabetes, all-cause mortality, and new or recurrent cancers.

Professor Seamus Sreenan, Consultant in Endocrinology & Diabetes, Connolly Hospital Dublin and Ireland Principle Investigator ORIGIN, said "ORIGIN is an impressive study delivered by an international collaborative addressing a clinically important question. It was demonstrated, in these high risk CV patients, that the use of insulin glargine confirmed no additional benefit in terms of CV outcomes. But it demonstrated that insulin glargine was a highly effective agent in achieving and maintaining HbA1c."

He continued, "An additional important outcome of this study is that it provides conclusive evidence in the context of this long duration clinical trial that there was no increase in cancer associated with insulin glargine."

The study demonstrated that achieving fasting normoglycaemia did not affect CV outcomes in these participants with early dysglycaemia during the study period (first co-primary endpoint: Hazard Ratio [HR]: 1.02; 95% confidence interval [CI], 0.94 to 1.11: p = 0.63, NS; and second co-primary endpoint: HR: 1.04; 95% CI, 0.97 to 1.11: p = 0.27, NS).

Insulin glargine maintained targeted long-term glycaemic control (median fasting plasma glucose 5.2 mmol/L and HbA_{1c} 6.2% from baseline 6.4%), which was sustained over the 6.2 years of follow-up.

There was no association between insulin glargine and increased incidence of any cancer (HR: 1.00; 95% CI, 0.88 to 1.13: p = 0.97, NS). Neither analysis of death from cancer, nor analysis of cancer at specific sites, suggested an increased risk for the users of insulin glargine.

Results showed that insulin glargine delayed progression from pre-diabetes (impaired fasting glucose/IFG or impaired glucose tolerance/IGT) to T2DM by 28% (25% progressed with insulin glargine vs. 31% with standard care; HR: 0.72; 95% CI, 0.58 to 0.91: p = 0.006). Other secondary outcomes included a composite microvascular outcome (metrics of kidney or eye disease; (HR: 0.97; 95% CI, 0.90 to 1.05: p= 0.43), and all-cause mortality (HR: 0.98; 95% CI, 0.90 to 1.08: p= 0.70).

Mike Baxter, Consultant in Diabetes and Endocrinology and consultant to Sanofi commented, "The results have shown that glargine treatment is a highly effective intervention for patients with established and early diabetes, which can achieve normoglycaemia without the need to escalate therapy, or use multiple tablets, for at least six years. The inference that there is a beneficial effect of glargine on the progression of diabetes may be clinically important."

Hypoglycaemic events were infrequent. In the insulin glargine arm, the rate of severe symptomatic hypoglycaemia was 0.01 episodes per patient-year of exposure versus 0.003 episodes per patient-year for standard care. Rates for overall symptomatic hypoglycaemia with insulin glargine were 16.7 patients with events per 100 patient-years of exposure versus 5.2 patients with events per 100 patient-years for standard care. In addition, weight gain was modest for participants in the insulin glargine arm, at an average of 3.5 pounds over the duration of the study.

ORIGIN investigated the use of insulin glargine in a population in which insulins are not typically used,[2] providing new data on the potential benefits and risks of initiation of insulin glargine therapy earlier in the course of diabetes (average disease duration since diagnosis at entry in trial: 5.5 years). Of the patients on insulin glargine, 58% were free of any symptomatic hypoglycaemic episode for the entire duration of the study.

"Our commitment to funding this vitally important long-term trial exemplifies our aim to help identify new ways of treating and understanding diabetes," commented Pierre Chancel, Senior Vice President, Global Diabetes, Sanofi. "I am pleased to announce that Sanofi will extend the observations of ORIGIN by an additional two years."

The extension of the observations of ORIGIN will be called ORIGINALE (Outcome Reduction with an Initial Glargine Intervention and Legacy Effect).

Notes to editors

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About ORIGIN

ORIGIN (Outcome Reduction with Initial Glargine Intervention) is a unique, six-year landmark cardiovascular (CV) outcomes trial, evaluating Lantus® (insulin glargine) versus standard care in over 12,500 individuals who are at high CV risk with pre-diabetes or early type 2 diabetes mellitus. Spanning 40 countries worldwide, it is the world's longest and largest randomized clinical trial of its type in this population, and the first to formally evaluate the effects of insulin on CV outcomes. The trial used a 2x2 factorial design to determine whether using insulin glargine to target fasting normoglycaemia (FPG ≤ 95mg/dL / 5.3 mmol/L), and separately omega-3 polyunsaturated fatty

acids (PUFA), could reduce cardiovascular morbidity and/or mortality[3]. Participants assigned to standard care were treated on the basis of the investigator's best judgment and local guidelines, including lifestyle measures, dietary modifications, metformin, sulfonylureas and other oral anti-diabetic agents.

For the insulin glargine arm of the study, there are two co-primary endpoints:

- First co-primary endpoint: occurrence of CV death, nonfatal MI or nonfatal stroke
- Second co-primary endpoint: occurrence of CV death, nonfatal MI, nonfatal stroke, revascularisation or hospitalisation for heart failure.

For the insulin glargine arm of the study, secondary outcomes include:

- All-cause mortality
- A composite endpoint of microvascular events (including either kidney or eye disease)
- Progression to type 2 diabetes in participants with IFG or IGT at baseline

About Lantus®

Lantus is an insulin analogue for the treatment of adults, adolescents and children of six years or above with diabetes mellitus, where treatment with insulin is required. It is not indicated for the treatment or prevention of CV outcomes, nor to prevent the progression of IFG/IGT to diabetes.

About Diabetes

Diabetes is a long-term disease that occurs either when the pancreas does not produce enough insulin (the hormone that regulates blood glucose concentrations), or when the body cannot effectively use the insulin it produces, or both. This results in raised blood glucose concentrations (hyperglycemia). Over time, uncontrolled hyperglycemia leads to the macrovascular and microvascular complications of diabetes[4]. Macrovascular complications, which affect the large blood vessels, include heart attack, stroke and peripheral vascular disease. Microvascular complications affect the small blood vessels of the eyes (retinopathy), kidney (nephropathy) and nerves (neuropathy). The incidence of T2DM is growing at an alarming rate, with over 340 million people worldwide living with the condition today[5].

About Sanofi Diabetes

Sanofi strives to help people manage the complex challenge of diabetes by delivering innovative, integrated and personalized solutions. Driven by valuable insights that come from listening to and engaging with people living with diabetes, the Company is forming partnerships to offer diagnostics, therapies, services, and devices including innovative blood glucose monitoring systems. Sanofi markets both injectable and oral medications for people with Type 1 or Type 2 diabetes. Investigational compounds in the pipeline include an injectable GLP-1 agonist being studied as a single agent, in combination with basal insulin, and/or in combination with oral antidiabetic agents.

To view the Sanofi ADA electronic press packet, please go to www.epresspack2.net/Sanofi-at-ADA/

About Sanofi

Sanofi, a global and diversified healthcare leader, discovers, develops and distributes therapeutic solutions focused on patients' needs. Sanofi has core strengths in the field of healthcare with seven growth platforms: diabetes solutions, human vaccines, innovative drugs, consumer healthcare, emerging markets, animal health and the new Genzyme. Sanofi is listed in Paris (EURONEXT: SAN) and in New York (NYSE: SNY).

References

1. The ORIGIN Trial investigators, Basal Insulin and Cardiovascular and Other Outcomes in Dysclycaemia. *New England Journal of Medicine*. In press.
2. Lantus® is indicated for treatment of diabetes mellitus when insulin is required.
3. ORIGIN Trial Investigators, Gerstein H, Yusuf S, *et al*. Rationale, design, and baseline characteristics for a large international trial of cardiovascular disease prevention in people with dysglycaemia: the ORIGIN Trial (Outcome Reduction with an Initial Glargine Intervention). *Am Heart J* 2008;**155**(1):26–32.
4. UK Prospective Diabetes Study (UKPDS) Group, Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33), Lancet 1998;352(9131):837-853
5. World Health Organisation diabetes fact sheet, August 2011

Glossary of terms

Dysglycaemia: an imbalance in the sugar metabolism/energy production mechanisms of the body

Hypoglycaemia: an abnormally diminished content of glucose in the blood resulting in low blood sugar

Normoglycaemia: the presence of a normal concentration of glucose in the blood

HbA1c: *Glycated hemoglobin (haemoglobin A1c, HbA_{1c}, A1C, or Hb_{1c}; sometimes also HbA1c) is a form of haemoglobin that is measured primarily to identify the average plasma glucose concentration over prolonged periods of time.*

Sanofi Forward Looking Statements

This press release contains forward-looking statements as defined in the Private Securities Litigation Reform Act of 1995, as amended. Forward-looking statements are statements that are not historical facts. These statements include projections and estimates and their underlying assumptions, statements regarding plans, objectives, intentions and expectations with respect to future financial results, events, operations, services, product development and potential, and statements regarding future performance. Forward-looking statements are generally identified by the words "expects", "anticipates", "believes", "intends", "estimates", "plans" and similar expressions. Although Sanofi's management believes that the expectations reflected in such forward-looking statements are reasonable, investors are cautioned that forward-looking information and statements are subject to various risks and uncertainties, many of which are difficult to predict and generally beyond the control of Sanofi, that could cause actual results and developments to differ materially from those expressed in, or implied or projected by, the forward-looking information and statements. These risks and uncertainties include among other things, the uncertainties inherent in research and development, future clinical data and analysis, including post marketing, decisions by regulatory authorities, such as the FDA or the EMA, regarding whether and when to approve any drug, device or biological application that may be filed for any such product candidates as well as their decisions regarding labeling and other matters that could affect the availability or commercial potential of such products candidates, the absence of guarantee that the products candidates if approved will be commercially successful, the future approval and commercial success of therapeutic alternatives, the Group's ability to benefit from external growth opportunities as well as those discussed or identified in the public filings with the SEC and the AMF made by Sanofi, including those listed under "Risk Factors" and "Cautionary Statement Regarding Forward-Looking Statements" in Sanofi's annual report on Form 20-F for the year ended December 31, 2011. Other

than as required by applicable law, Sanofi does not undertake any obligation to update or revise any forward-looking information or statements.