Sanofi Receives FDA Approval of Thymoglobulin® for the Prevention of Acute Kidney Transplant Rejection

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New U.S. indication approved for Thymoglobulin [anti-thymocyte globulin (rabbit)]; first since 1998

Sanofi today announced that the U.S. Food and Drug Administration (FDA) approved Thymoglobulin® [anti-thymocyte globulin (rabbit)], for use in conjunction with concomitant immunosuppression in the prophylaxis, or prevention, of acute rejection in patients receiving a kidney transplant.

Kidney disease is the ninth leading cause of death in the US; 468,000 patients are currently on dialysis for kidney failure, including an estimated 100,000 who are waiting for a kidney transplant. Kidney transplantation offers patients with end-stage renal disease longer survival and better quality of life compared to dialysis. With kidney transplantation, however, there is a risk of acute rejection, which can lead to graft complications and potential loss of the transplanted kidney.

"Thymoglobulin has been a well-established medication used in kidney transplantation for nearly 20 years, and this FDA approval is an important milestone for the transplant community," said Daniel Brennan, MD, Professor of Medicine, Director of Transplant Nephrology, Barnes-Jewish Hospital of Washington University School of Medicine in St. Louis. "Transplant rejection can be particularly discouraging for patients. The use of Thymoglobulin beginning just prior to transplantation may be an important step to ensuring a successful kidney implantation."

"Sanofi has been connected and committed to the kidney transplant community for decades. This FDA approval of Thymoglobulin for prophylactic use underscores our continued commitment to patients and their caregivers who will be receiving a potentially life-saving kidney transplant," said David Meeker, MD, Executive Vice President and Head, Sanofi Genzyme. “We remain focused on developing treatments for patients in need of new medications for life-threatening and limiting illnesses, including patients receiving a kidney transplant."

The FDA approval was based on two randomized multicenter studies comparing Thymoglobulin to interleukin-2 receptor antagonists (IL2RA: basiliximab or daclizumab) in deceased donor kidney transplant recipients. The first study in kidney transplant patients (n=278) at increased risk of acute rejection or delayed graft function showed a significantly lower incidence of the treatment failure as measured by a composite endpoint (biopsy-proven acute rejection, graft loss, death or lost to follow-up) within 12 months following transplantation in the Thymoglobulin group compared to patients in the basiliximab group (25 percent versus 38 percent; p=0.02).

The second study was an investigator-sponsored study in kidney transplant patients (n=230) at high immunological risk of rejection. Patients received either Thymoglobulin or daclizumab and also showed a lower incidence of treatment failure as measured by the composite endpoint (biopsy-proven acute rejection, graft loss, death or lost to follow-up) within 12 months following transplantation in the Thymoglobulin group compared to patients in the basiliximab group (25 percent versus 38 percent; p=0.02).

The pooled analysis of both studies (n=508) showed a composite endpoint rate within 12 months post transplantation of 25.1 percent in the Thymoglobulin group compared with 36.0 percent in the IL2RA group. The estimated between-treatment group difference (Thymoglobulin to daclizumab) was -9% (95% CI, -19.9% to 3.6%) demonstrating non-inferiority of Thymoglobulin compared with daclizumab.

The most frequent adverse reactions seen in these clinical trials (more than 25% of patients receiving Thymoglobulin) include: leukopenia, hyperkalemia, urinary tract infection and pyrexia.

Thymoglobulin was originally approved by US regulatory authorities in 1998 for the treatment of renal transplant acute rejection. Thymoglobulin is marketed by Sanofi Genzyme, the specialty care global business unit of Sanofi.

IMPORTANT SAFETY INFORMATION

WARNING: IMMUNOSUPPRESSION. Thymoglobulin should only be used by physicians experienced in immunosuppressive therapy in transplantation.
• **Contraindications.** Thymoglobulin is contraindicated in patients with a history of allergy or anaphylaxis to rabbit proteins or to any product excipients, or who have active acute or chronic infections which contraindicate any additional immunosuppression.

• **Management of Immunosuppression.** To prevent over-immunosuppression, physicians may wish to decrease the dose of the maintenance immunosuppression regimen during the period of Thymoglobulin use. Dosing for Thymoglobulin is different from dosing for other ATG products, because protein composition and concentrations vary depending on the source of ATG. White blood cell (WBC) and platelet counts should be monitored. Monitoring the lymphocyte count may help assess the degree of T-cell depletion.

• **Immune Mediated Reactions.** Serious immune-mediated reactions, including anaphylaxis or severe cytokine release syndrome (CRS), have been reported with the use of Thymoglobulin. Fatal anaphylaxis has been reported. If an anaphylactic reaction occurs, the infusion should be terminated immediately.

• **Infusion-Associated Reactions.** Cases consistent with cytokine release syndrome (CRS) have been reported with rapid infusion rates. CRS is attributed to the release of cytokines by activated monocytes and lymphocytes. Severe acute CRS can cause serious cardiorespiratory events and/or death. Close compliance with the recommended dosage and infusion time may reduce the incidence and severity of infusion-associated reactions (IARs). Slowing the infusion rate may minimize many of these IARs. Reactions at the infusion site may include pain, swelling, and redness of the skin.

• **Hematologic Effects.** Low counts of platelets and white blood cells (including low counts of lymphocytes and neutrophils) have been identified and are reversible following dose adjustments. Total white blood cell and platelet counts should be monitored.

• **Infection and Malignancy.** Infections, reactivation of infection, febrile neutropenia, sepsis, malignancies including lymphoproliferative disorders (LPD) and other lymphomas as well as solid tumors have been reported after Thymoglobulin administration in combination with multiple immunosuppressive agents. These infections can be fatal.

• **Immunization.** The safety of immunization with attenuated live vaccines following Thymoglobulin therapy has not been studied; therefore, immunization with attenuated live vaccines is not recommended for patients who have recently received Thymoglobulin.

• **Thymoglobulin should be used under strict medical supervision in a hospital setting, and patients should be carefully monitored during the infusion.**

• **Overdosage.** Thymoglobulin overdose may result in leukopenia (including lymphopenia and neutropenia) and/or thrombocytopenia, which can be managed with dose reduction.

• **During post-marketing surveillance, arthralgia/myalgia, lymphadenopathy, proteinuria, and decreased oxygen saturation tend to occur 5 to 15 days after Thymoglobulin infusion and are consistent with serum sickness.** Symptoms are manageable with corticosteroid treatment.

• **Adverse Reactions.** The most common adverse reactions and laboratory abnormalities (incidence >5% higher than comparator) are urinary tract infection, abdominal pain, hypertension, nausea, shortness of breath, fever, headache, anxiety, chills, increased potassium levels in the blood, and low counts of platelets and white blood cells.

Please CLICK HERE for full Prescribing Information including Boxed WARNING.

**INDICATION**

Thymoglobulin® (anti-thymocyte globulin (rabbit)) is indicated for the prophylaxis and treatment of acute rejection in patients receiving a kidney transplant. Thymoglobulin is to be used in conjunction with concomitant immunosuppression.

**About Sanofi**

Sanofi, a global healthcare leader, discovers, develops and distributes therapeutic solutions focused on patients’ needs. Sanofi is organized into five global business units: Diabetes and Cardiovascular, General Medicines and Emerging Markets, Sanofi Genzyme, Sanofi Pasteur and Consumer Healthcare. Sanofi is listed in Paris (EURONEXT: SAN) and in New York (NYSE: SNY).

Sanofi Genzyme focuses on developing specialty treatments for debilitating diseases that are often difficult to diagnose and treat, providing hope to patients and their families.

**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 labelling and other matters that could affect the availability or commercial potential of such product candidates, the absence of guarantee that the product candidates if approved will be commercially successful, the future approval and commercial success of therapeutic alternatives, Sanofi's ability to benefit from external growth opportunities and/or obtain regulatory clearances, risks associated with intellectual property and any related pending or future litigation and the ultimate outcome of such litigation, trends in exchange rates and prevailing interest rates, volatile economic conditions, the impact of cost containment initiatives and subsequent charges thereonto, the average number of shares outstanding 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, 2016. Other than as required by applicable law, Sanofi does not undertake any obligation to
update or revise any forward-looking information or statements.