

## Results of a Phase III Trial on Elitek® Presented at ASH Annual Meeting

### **- The study Showed that Elitek® (rasburicase) Significantly Reduced Plasma Uric Acid Levels versus Allopurinol in Adults with Hematologic Cancers at Risk for Tumor Lysis Syndrome -**

**Paris, France - December 7, 2008** - Sanofi-aventis announced today the results of a randomized phase III study presented at the 50th Annual Meeting of the American Society of Hematology. The study in adult patients with hematological malignancies at high or potential risk for tumor lysis syndrome (TLS) demonstrated that Elitek® (rasburicase) significantly reduced plasma uric acid (PUA) levels compared to allopurinol alone (p=0.0012).

The study also compared a sequential intake of the two agents (Elitek® for three days followed by allopurinol for three days, with one day overlap) versus allopurinol alone, which showed a reduction in plasma uric acid levels for the sequential intake versus allopurinol alone (p=0.06). The study did not show any unexpected side-effects related to the different compounds and there were no differences in terms of safety between the 3 arms of the study.

Tumor lysis syndrome is a potentially life-threatening metabolic complication that can result either spontaneously or following treatment of certain types of rapid-growing cancers, particularly leukemia or lymphoma. The syndrome develops when a particularly large volume of cells associated with fast growing tumors are destroyed, releasing cellular by-products into the blood system such as uric acid, faster than can be eliminated. Elevated levels of plasma uric acid can cause hyperuricemia, a serious condition that can lead to renal failure if not controlled.

*"In this investigational study, Elitek® controlled plasma uric acid in a larger percentage of patients and in a shorter period of time than allopurinol, the current US standard treatment in adults,"* said principal investigator Dr. Jorge Cortes, Professor of Medicine and Deputy Chair, Department of Leukemia at The University of Texas, MD Anderson Cancer Center, in Houston, Texas.

These study results will form the basis for a supplemental new drug application submission to the U.S. Food and Drug Administration.

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### **Background on Study**

Patients eligible to enter the study were at least 18 years old with Eastern Cooperative Oncology Group (ECOG) performance 0-3, a life expectancy of greater than three months and at either high or potential risk for TLS defined as hyperuricemia from the cancer at baseline (plasma uric acid >7.5 mg/dL), very aggressive lymphoma/leukemia as defined by the Revised European-American Lymphoma (REAL) criteria, acute myeloid leukemia (AML), chronic myeloid leukemia (CML) in blast crisis, or high grade myelodysplastic syndrome (MDS) with >10% bone marrow involvement. Potential risk for TLS was defined as diagnosis of aggressive lymphoma/leukemia based on REAL



classification plus one or more of the following criteria: LDH>2xULN (IU/l), Stage III-IV disease or Stage I-III disease with at least one lymph node/tumor >5 cm.

Patients received Elitek® at a dosage of 0.20 mg/kg/day for five days (n=92), Elitek® at the same dosage for three days plus allopurinol (300 mg/day) starting on the third day and continuing for another two days (n=92), or allopurinol (300 mg/day) for five days (n=91).

The primary objective of the multi-center, open-label, randomized, parallel group comparative study was to compare the adequacy of control of PUA concentration and the safety profile in three treatment arms. Secondary objectives of the study were to evaluate among the three treatment arms the AUC (area under the curve) of plasma uric acid from baseline through 48 hours after the last planned anti-hyperuricemic treatment, the time to plasma uric acid control, safety (including immunogenicity) and pharmacokinetics.

Among the three treatment arms, 87% of patients treated with Elitek® obtained or maintained a normal plasma uric acid levels (PUA) of < 7.5 mg/dl at days 3-7 compared to 66% receiving allopurinol alone (p=0.001) and 78% with Elitek®/allopurinol (p=0.06). Among patients at high risk for tumor lysis syndrome, the normalization or the maintenance of a normal PUA was obtained in 89% with Elitek vs. 68% with allopurinol and 79% with the Elitek®/allopurinol sequential intake (p=0.0012). The PUA response rate among patients with baseline hyperuricemia defined as plasma uric acid >7.5mg/dL, was 90% with Elitek versus 53% with allopurinol and 77% with Elitek/allopurinol (p=0.0151). The time to control PUA in hyperuricemic patients was 4.1 hours among patients treated with Elitek® (n=18 [95% CI=4.0 to 4.5]), 4.1 hours with the Elitek®/allopurinol sequential intake (n=12 [95% CI=3.9 to 4.5) and 27.0 hours in the allopurinol alone arm (n=17 [95% CI=4.0 to 49.0]).

In both Elitek® groups, there was a 2% incidence of Grade 3/4 related events and <5% hypersensitivity or immuno-allergic reactions, 1% of which were Grade 3 or higher. The most common serious adverse reactions regardless of the relationship to study drug were neutropenic sepsis (5.4%/1.1%/3.3%), neutropenic infection (5.4%/4.3%/8.0%), and febrile neutropenia (4.3%/3.3%/5.5%), pulmonary hemorrhage (1.1%/3.3%/0.0%), and respiratory failure (2.2%/3.3%/1.1%) in the Elitek® arm, Elitek®/allopurinol arm and allopurinol arm, respectively. Elitek® treatment-related events were considered rarely serious, and <1% led to discontinuation of treatment. Investigators reported that there were no major differences in safety or tolerability between the three treatment arms, and that most adverse events were related to chemotherapy and/or the underlying disease.

#### **About Elitek® /Fasturtec®**

Elitek®/Fasturtec® is a recombinant enzyme.

In the US, Elitek® is indicated for the initial management of plasma uric acid levels in paediatric patients with leukaemia, lymphoma, and solid tumor malignancies who are receiving anti-cancer therapy expected to result in tumor lysis and subsequent elevation of plasma uric acid.

In Europe, Elitek® is commercialized as Fasturtec® and indicated in treatment and prophylaxis of acute hyperuricemia, in order to prevent acute renal failure, in patients with haematological malignancy with a high tumour burden and at risk of a rapid tumour lysis or shrinkage at initiation of chemotherapy. This indication is available for adult and paediatric patients in Europe and for paediatric patients in the US.

#### **About sanofi-aventis**

Sanofi-aventis, a leading global pharmaceutical company, discovers, develops and distributes therapeutic solutions to improve the lives of everyone. Sanofi-aventis is listed in Paris (EURONEXT: SAN) and in New York (NYSE: SNY). For more information, please visit: [www.sanofi-aventis.com](http://www.sanofi-aventis.com).

### **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 product development, product potential projections and estimates and their underlying assumptions, statements regarding plans, objectives, intentions and expectations with respect to future events, operations, products and services, 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-aventis’ 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-aventis, 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 EMEA, 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 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 as well as those discussed or identified in the public filings with the SEC and the AMF made by sanofi-aventis, including those listed under “Risk Factors” and “Cautionary Statement Regarding Forward-Looking Statements” in sanofi-aventis’ annual report on Form 20-F for the year ended December 31, 2007. Other than as required by applicable law, sanofi-aventis does not undertake any obligation to update or revise any forward-looking information or statements.*