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## **IDRAPARINUX SHOWS ENCOURAGING RESULTS IN THE PREVENTION OF THROMBOEMBOLIC EVENTS IN PATIENTS WITH ATRIAL FIBRILLATION**

**Paris, France, July 11, 2007** - Sanofi-aventis announced today that a weekly subcutaneous administration of idraparinux was as effective as warfarin, a Vitamin K Antagonist (VKA), in reducing stroke and non Central Nervous System (CNS) systemic embolic events in patients with atrial fibrillation (AF), a population at risk of thromboembolic events (TE). The results of the AMADEUS study were presented at the XXI<sup>st</sup> ISTH Congress (International Society on Thrombosis and Haemostasis) in Geneva.

The AMADEUS trial, which enrolled a total of 4,576 patients with atrial fibrillation, met its primary endpoint. The event rate of the composite endpoint of any strokes (ischemic, hemorrhagic, and undefined) and non-CNS systemic embolism was 0.9% with idraparinux and 1.3% with warfarin ( $p= 0.007$ ), meeting the criteria for non-inferiority.

The incidence of clinically relevant bleeding, the primary safety outcome, was significantly higher in the idraparinux group than in the comparator group (19.7% vs. 11.3%,  $p<0.0001$ ), although, overall no difference was observed in the all causes mortality between the two treatment groups. Bleeding appeared over time and was more pronounced in patients with impaired renal function and in the elderly. These observations indicate the need to consider a dose reduction of idraparinux depending on these characteristics in patients with AF. This will be addressed in the new BOREALIS-AF study that will compare the new neutralizable form of idraparinux (biotinylated idraparinux) to VKA in patients with atrial fibrillation and in which the dose will be adjusted depending on age and renal function after 7 weeks of treatment.

Despite the early termination of the study due to the imbalance of bleeding events and low event rates, the trial succeeded in demonstrating the efficacy of idraparinux and met the criteria for non inferiority.

*“With once a week idraparinux treatment we could have a convenient alternative to the cumbersome VKA treatment for patients suffering from atrial fibrillation recurrent complications.”* said Professor Harry Büller, from the University of Amsterdam’s Academic Medical Center Department of Vascular Medicine and principal investigator of the AMADEUS study. *“Nevertheless, the improvement of the safety profile while preserving efficacy should be addressed in the new BOREALIS-AF study with the once a week treatment with reversible biotinylated idraparinux, (a big step forward, well suited for a long acting agent) and dose adjustment according to patients characteristics.”* he added.

### **About atrial fibrillation**

Atrial fibrillation (AF) is the most common cardiac arrhythmia (abnormal heart rhythm) with rapid and irregular heart beat, leading to potential serious embolic consequences. AF leads to formation of thrombus (clots) in the auricle (upper chamber of the heart) which can dislodge into the circulation and obstruct arteries in the central nervous system (CNS), causing stroke, or outside the CNS, causing non-CNS systemic embolism (SE).

The most serious clinical complication of AF is thromboembolism, which can present as a stroke or other systemic embolic event. About 15% of all strokes are directly attributable to AF. About two thirds of strokes in patients with AF are due to embolism of clots originating from the heart (cardioembolic stroke).

AF affects over 1% of the population and currently affects around 6 million people in Europe and the USA.

### **About AMADEUS study**

The phase III AMADEUS study was a randomised, open label trial designed to compare the efficacy and safety of once-a-week idraparinux versus oral VKA treatment for the long-term prevention of thromboembolic events (stroke and non-central nervous system systemic embolism) in patients with AF and at least one additional risk factor for stroke. The predefined risk factors were previous ischemic stroke, transient ischemic attack or SE, hypertension requiring drug treatment, left ventricular dysfunction, age >75 years, age between 65-75 years plus diabetes mellitus, or age between 65-75 years plus symptomatic coronary heart disease.

4,576 patients (2,283 in the idraparinux group and 2,293 in the VKA group) have been randomized between September 2003 and July 2005.

Patients with AF who were eligible for VKA treatment were randomized to receive either subcutaneous idraparinux 2.5 mg once a week or VKA therapy adjusted to achieve the target international normalized ratio (INR) of 2.5 (range 2 to 3). The study was powered to show non-inferior efficacy of idraparinux, compared with standard vitamin K antagonist (VKA) treatment in patients with AF who require prolonged oral anticoagulation. The primary efficacy endpoint was the composite of all strokes (ischemic, hemorrhagic and undefined) and non-CNS SE within the planned treatment period. The principal safety endpoint was the occurrence of major bleeding or clinically relevant non-major bleeding. The other safety outcome was all cause mortality.

### **About BOREALIS-AF study**

BOREALIS-AF is a multicenter, randomized, double-blind, assessor-blind, non-inferiority study comparing the efficacy and safety of once-a-week subcutaneous biotinylated idraparinux with adjusted-dose warfarin in the prevention of stroke and systemic thromboembolic events in patients with atrial fibrillation.

Treatment will be administered for a period of 6 months to 2 years. All patients will start with biotinylated idraparinux 3 mg (equivalent to base idraparinux 2.5 mg) once-a-week for 7 weeks, and then the dose will be reduced depending on age and renal function.

### **About idraparinux**

Idraparinux sodium is a novel long-acting synthetic highly potent synthetic and specific indirect inhibitor of coagulation factor Xa, injectable subcutaneously. Its long-duration of action makes it suitable for weekly administration.



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### **About biotinylated idraparinux**

Biotinylated idraparinux is structurally similar to idraparinux sodium with the addition of a biotin segment. It has the same anticoagulant activity as idraparinux sodium in vivo and the same pharmacological activity (PK/PD). The biotin arm is a “hook” with a strong and specific affinity for avidin (neutralizing agent) to allow immediate “fishing” and then rapid elimination and neutralization of the anticoagulant activity if needed (in case of unplanned surgery for instance).

### **About sanofi-aventis**

Sanofi-aventis is one of the world leaders in the pharmaceutical industry, ranking number one in Europe. Backed by a world-class R&D organization, sanofi-aventis is developing leading positions in seven major therapeutic areas: cardiovascular, thrombosis, oncology, metabolic diseases, central nervous system, internal medicine and vaccines. Sanofi-aventis is listed in Paris (EURONEXT: SAN) and in New York (NYSE: SNY).

### **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 financial 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 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, 2006. Other than as required by applicable law, sanofi-aventis does not undertake any obligation to update or revise any forward-looking information or statements.*

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