

## **FDA Approves Multaq<sup>®</sup> for Patients with Atrial Fibrillation or Atrial Flutter**

**- Multaq<sup>®</sup> approved to reduce the risk of cardiovascular hospitalization in patients with atrial fibrillation or atrial flutter -**

**- U.S commercial launch planned for the summer of 2009 -**

**Paris, France – July 2, 2009** – Sanofi-aventis (EURONEXT: SAN and NYSE: SNY) announced today that the U.S. Food and Drug Administration (FDA) has approved Multaq<sup>®</sup> (dronedarone) 400 mg Tablets. Patients with atrial fibrillation (AF) or atrial flutter (AFL) soon will have a new treatment option to help improve current management of their disease. Multaq<sup>®</sup> is the first drug approved in the United States that has shown a clinical benefit to reduce cardiovascular hospitalization in patients with AF/AFL.

Multaq<sup>®</sup> is an anti-arrhythmic indicated to reduce the risk of cardiovascular hospitalization in patients with paroxysmal or persistent atrial fibrillation (AF) or atrial flutter (AFL), with a recent episode of AF/AFL and associated cardiovascular risk factors, who are in sinus rhythm or who will be cardioverted. Associated cardiovascular risk factors include age over 70 years, hypertension, diabetes, prior cerebrovascular accident, left atrial diameter  $\geq 50$  mm or left ventricular ejection fraction [LVEF]  $< 40\%$ . The FDA approval is based on five international, multi-center, randomized clinical trials involving nearly 6,300 patients.

*“The FDA approval of Multaq<sup>®</sup> is an important milestone in the management of atrial fibrillation or atrial flutter that demonstrates the commitment of sanofi-aventis to provide patients and physicians with important new medicines in therapeutic areas with significant healthcare needs,”* said Christopher A. Viehbacher, Chief Executive Officer of sanofi-aventis. *“Sanofi-aventis is proud of its ability to bring innovative therapies to market and contribute to reducing the public health burden of atrial fibrillation.”*

The landmark ATHENA trial evaluated the efficacy and safety of Multaq<sup>®</sup> in patients with AF/AFL or a recent history of these conditions (71% of these patients had no heart failure, 29% were in NYHA class I-III with stable heart failure). This trial showed that Multaq<sup>®</sup> (dronedarone) 400 mg BID, in addition to standard therapy, reduced the combined endpoint of cardiovascular hospitalization or death from any cause by 24% ( $p < 0.001$ ) when compared to placebo, meeting the study's primary endpoint.

This reduction was generally consistent across study subgroups based on baseline characteristics or medications. Patients taking Multaq<sup>®</sup> had higher rates of diarrhea, nausea, bradycardia, QT-interval prolongation and cutaneous rash than patients taking placebo.

Initiation of Multaq<sup>®</sup> treatment is contraindicated in patients with severe heart failure (NYHA class IV) or NYHA Class II – III heart failure with a recent decompensation requiring hospitalization or referral to a specialized heart failure clinic. This unstable population corresponds to the population of the ANDROMEDA trial in which patients receiving dronedarone had a greater than 2-fold increase in mortality compared to placebo.

The ATHENA and ANDROMEDA trials provided two sets of data supporting the assessment of the product's benefit risk ratio in two significantly different patient populations.

To ensure the use of Multaq® in the appropriate patient population, sanofi-aventis U.S. LLC also announced the launch of mPACT™ – Multaq® Partnership for Appropriate Care and Treatment – the Risk Evaluation and Mitigation Strategy (REMS) developed by sanofi-aventis U.S. LLC. The mPACT™ Partnership was developed to assist healthcare professionals (HCPs) with the identification of appropriate patients and to ensure the safe use of Multaq® while minimizing risk. The risk mitigation program consists of a Communication Plan for HCPs, a medication guide for patients and post-marketing surveillance.

*“We are pleased that the FDA has granted approval of Multaq® for patients in a therapeutic area that has seen few new treatment options in the last twenty years,”* said Marc Cluzel, MD, Senior Vice President, Research and Development, sanofi-aventis. *“Sanofi-aventis’ commitment to research and development in this area is rewarded today, and we hope it will benefit many patients suffering from this disease.”*

The incidence of atrial fibrillation is growing worldwide in relation to aging populations. It is emerging as a public health concern and affects about 2.5 million people in the United States and 4.5 million people in the European Union. Atrial fibrillation is a potentially life-threatening condition, with significant burden on patients, health care providers and payers.

*“It is exciting that Multaq® will now be available as a treatment option for patients with paroxysmal or persistent atrial fibrillation or atrial flutter,”* said Stuart Connolly, M.D., Professor of Medicine & Director, Division of Cardiology, McMaster University, Hamilton, Canada, and co-principal investigator in the ATHENA study. *“Based on clinical studies, Multaq® reduces the risk of cardiovascular hospitalizations in patients with atrial fibrillation / atrial flutter, this outcome could change the way we approach the management of the disease.”*

Multaq® is to be given twice daily as a 400 mg tablet and should be taken as one tablet with the morning and evening meals. Treatment with Multaq® can be initiated in an outpatient setting. Most common adverse reactions are diarrhea, nausea, vomiting, abdominal pain, asthenia (weakness) and cutaneous rash.

A registration dossier of Multaq® is also under regulatory review by the European Medicines Agency (EMA).

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### **About dronedarone (Multaq®)**

Multaq®, discovered and developed by sanofi-aventis, is one of the major therapeutic innovations in patients with atrial fibrillation in the last twenty years.

The efficacy and safety of Multaq® 400 mg twice daily was evaluated in five controlled studies, ATHENA, ANDROMEDA, EURIDIS, ADONIS, and DAFNE, involving nearly 6,300 patients including more than 3200 patients who received Multaq®.

The ATHENA trial, which involved 4,628 patients with AF or AFL and more than 2,300 patients receiving Multaq® on top of standard therapy, demonstrated a 24% reduction in time to first CV hospitalization or all-cause mortality (P<0.001) compared with placebo meeting the primary endpoint.

The ANDROMEDA study, was terminated prematurely after enrolment of 627 of 1000 planned patients with congestive heart failure, in relation to excess mortality due to worsening heart failure in the dronedarone group [n=25 versus 12 (placebo), p=0.027].

The patient population enrolled in the ANDROMEDA and ATHENA studies was significantly different. The patients enrolled in ANDROMEDA had relatively severe heart failure and had been hospitalized, or referred to a specialty heart failure clinic for worsening symptoms. Patients were predominantly NYHA II and III (New York Heart Association classification) and only 25% had a history of AF/AFL at

randomization. In contrast, in ATHENA, all patients had a history of AF/AFL, and 71% of patients had no heart failure, 25% were NYHA class I or II, and only 4% were class III.

The ANDROMEDA and ATHENA trials were published in the New England Journal of Medicine (NEJM) respectively in 2008 and 2009.

### Important Safety Information

Multaq<sup>®</sup> is contraindicated in patients with NYHA Class IV heart failure or NYHA Class II-III heart failure with a recent decompensation requiring hospitalization or referral to a specialized heart failure clinic. In a placebo-controlled study in patients with severe heart failure requiring recent hospitalization or referral to a specialized heart failure clinic for worsening symptoms (the ANDROMEDA study), patients given dronedarone had a greater than two-fold increase in mortality. Such patients should not be given dronedarone.

Multaq<sup>®</sup> is also contraindicated in second- or third-degree atrioventricular (AV) block or sick sinus syndrome (except when used in conjunction with a functioning pacemaker), bradycardia <50 bpm, QTc Bazett interval ≥500 ms and severe hepatic impairment.

Multaq<sup>®</sup> should not be given to patients who are or may become pregnant (Category X) or nursing.

Multaq<sup>®</sup> should not be coadministered with strong CYP 3A inhibitors or medicinal products that prolong the QT interval.

In patients with new or worsening heart failure, the suspension or discontinuation of Multaq<sup>®</sup> should be considered.

Serum creatinine levels increase by about 0.1mg/dL following Multaq<sup>®</sup> treatment initiation. The elevation has a rapid onset, reaches a plateau after 7 days and is reversible after discontinuation.

Hypokalemia and hypomagnesemia may occur with concomitant administration of potassium-depleting diuretics. Potassium levels should be maintained in the normal range pre and during administration.

**For full prescribing information, please visit <http://products.sanofi-aventis.us/Multaq/Multaq.pdf>**

### About Atrial Fibrillation/Atrial Flutter

Atrial fibrillation is the leading cause of hospitalization for arrhythmia in the U.S. and represents one-third of hospitalizations for arrhythmia in Europe. Hospitalization associated with AF has increased dramatically (two-to-three fold) in recent years in the U.S. Atrial fibrillation is a complex disease that increases the risk of stroke up to five-fold, worsens the prognosis of patients with cardiovascular risk factors, and doubles the risk of mortality. Atrial flutter, another type of arrhythmia generating in the atrium, occurs less frequently, and may evolve into atrial fibrillation.

### 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).

### 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, 2008. 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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## **FOR MORE INFORMATIONS PLEASE VISIT:**

**Multimedia News Release:** <http://www.prnewswire.com/mnr/multag/37750/>

**Dronedarone press office:** <http://www.dronedarone-atrial-fibrillation-pressoffice.com>