# Multaq® First-line Option in New 2010 ESC Guidelines for the Management of Atrial Fibrillation

**Paris, France – August 29, 2010–** Sanofi aventis (EURONEXT: SAN and NYSE: SNY) announced today that the European Society of Cardiology (ESC) 2010 new Guidelines for the Management of Atrial Fibrillation (AF) have been released and recommend that Multaq® (dronedarone) should be used for maintenance of sinus rhythm as a first-line treatment option in all patients with paroxysmal and persistent AF *(class of recommendation I, level of evidence A)* other than those with CHF NYHA class III/IV or unstable CHF NYHA class II *(class of recommendation III, level of evidence B)*.

Multaq® was granted a Class I recommendation, a designation assigned in the guidelines when "there is evidence and/or general agreement that a given procedure/therapy is beneficial, useful, and effective." The Task Force for the Management of Atrial Fibrillation of the ESC recognised the extensive clinical development of Multaq®, giving it their highest ranking A for level of evidence. Moreover, the guidelines recommend that Multaq® may also be used to achieve rate control in non-permanent AF except for patients with NYHA class III – IV or unstable heart failure *(class of recommendation IIa, level of evidence B).* [1]

Importantly the new guidelines include, for the first time, a statement on the importance of reducing hospitalisation as a key therapeutic goal in the management of AF. They also state that Multaq® should be considered in order to reduce cardiovascular hospitalisation in patients with non-permanent AF and cardiovascular risk factors *(Class of recommendation IIa, level of evidence B)* as well as in patients with AF and stable heart failure (NYHA Class I, II) *(Class of recommendation IIa, level of evidence C).* [1]

The guidelines do not recommend use of Multaq® in patients with NYHA class III and IV or with recently unstable (decompensation within the prior month) NYHA class II heart failure. [1]

*"Sanofi-aventis is pleased with this first-line recommendation for Multaq® in the AF guidelines which recognises the extensive clinical development for the product as well as the innovative outcome of reducing cardiovascular hospitalisation as demonstrated in the ATHENA trial,"* said Marc Cluzel, M.D., PhD, Executive Vice President, Research and Development, sanofi-aventis. *"Multaq® provides symptom control and for the first time for an anti-arrhythmic drug, a long term benefit by reducing the risk of distressing and repeat cardiovascular hospitalisations. AF Hospitalisations represent a significant human and economic burden for patients, healthcare practitioners and payers as recently reported."* [2]



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## More about the Guidelines

ESC Clinical Practice Guidelines are scientifically recognised worldwide as providing practicing physicians with the best possible recommendations on diagnosis, treatment and management of specific topics in cardiology medicine. Guidelines are created and edited under the umbrella of the ESC Board and the Committee for Practice Guidelines (CPG), who form a Task Force of appropriate experts from the ESC Associations, Working Groups, Councils, and National Societies, and from other bodies when required. They are the result of consensus amongst the Task Force appointed to prepare them, and they are peer-reviewed in a thorough and rigorous process that ensures accuracy, best-practice and relevance. Guidelines are available in a variety of printed and electronic media and in multiple formats including full documents, pocket guides and summaries. [1]

## About Atrial Fibrillation

The incidence of atrial fibrillation is growing worldwide in relation to aging populations. It is emerging as a public health concern, affects about 4.5 million people in Europe and represents one-third of hospitalizations for arrhythmia in the European Union.[3] Atrial fibrillation leads to potential life-threatening complications. AF increases the risk of stroke up to five-fold [4], worsens the prognosis of patients with cardiovascular risk factors [5], and doubles the risk of mortality [6] with significant burden on patients, health care providers and payers. Seventy percent of AF management costs are driven by hospital care and interventional procedures in the European Union.[7]

## About AF Hospitalisation

AF is associated with high rates of hospitalisation.[3] There are a variety of reasons for AF hospitalisation, including palpitations, initiation of antiarrhythmic therapy, procedures, complications of co-morbid conditions, as well as readmissions related to these causes. There is evidence that the rate of AF-related hospitalisations and associated cost is increasing over time, mainly because of the aging population.[3] In the U.S., hospitalisations for AF were almost three times higher in 2000 compared to two decades earlier.[8] In France, one study found that 31.3 percent of AF patients were hospitalised over a one-year period.[9]

AF is a chronic, progressive disease and cost increases with each recurrence, mainly driven by hospitalisation. The proportion of expenditure for AF treatment attributable to hospitalisation ranges from 44 – 73 percent. [7,10,11,12,13] The total cost burden across five EU countries was approximated at more than 6 billion Euros.[9,12] In the UK, National Health Service spending for AF hospital admissions increased 2.2-fold between 1995 and 2000.[11]

## About Multaq®

Multaq®, discovered and developed by sanofi-aventis, has been studied in a clinical development program, including seven international, multicenter, randomized clinical trials involving more than 7000 patients with almost 4000 patients receiving Multaq®. The landmark ATHENA trial was the largest anti-arrhythmic drug trial conducted in patients with AF/AFL, involving 4,628 patients with a follow-up of 30 months. In this trial, Multaq®, on top of standard cardiovascular therapy, significantly reduced cardiovascular hospitalization or death by 24 percent ($p<0.001$) when compared to placebo, meeting the study's primary endpoint. This result was entirely attributable to a reduction in cardiovascular hospitalization.

Multaq® has a fixed dose regimen of twice daily 400 mg tablets to be taken with morning and evening meals. Treatment with Multaq® does not require a loading dose and can be initiated in an outpatient setting. Most common adverse reactions are diarrhea, nausea, vomiting, abdominal pain, asthenia (weakness) and skin rash.

The European Commission granted marketing authorization for Multaq® in November 2009. Multaq® is indicated in the EU in adult clinically stable patients with a history of, or current non-permanent atrial fibrillation (AF) to prevent recurrence of AF or to lower ventricular rate. The use of Multaq® in unstable patients with NYHA class III and IV heart failure is contraindicated. Because of limited experience in stable patients with recent (1 to 3 months) NYHA class III heart failure or with Left Ventricular Ejection Fraction (LVEF) <35%, the use of Multaq® is not recommended in these patients.[14]

In the U.S., Multaq® is 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 (i.e., age >70, hypertension, diabetes, prior cerebrovascular accident, left atrial diameter ≥50 mm or left ventricular ejection fraction [LVEF] <40%), who are in sinus rhythm or who will be cardioverted.[15] Multaq® 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.

Multaq® is currently available in 20 countries including the U.S., Canada, Switzerland, Mexico, Taiwan, South Korea, Germany, Denmark, Ireland, Norway, Finland, Austria, Cyprus, Malta, Estonia, Sweden, Israel, Peru, Mexico, Hong Kong the UK and is being launched in most European countries in 2010.

For more information about AF and Multaq®: www.dronedarone-atrial-fibrillation-pressoffice.com

## 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.

## *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-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 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 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-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, 2009. 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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