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## **Santhera Announces Start of US Phase III Clinical Trial with SNT-MC17 in Friedreich's Ataxia and Provides Details on Study Design**

**Initiation of a six month study with 51 FRDA patients and ICARS as primary endpoint expected shortly. Fast-track designation granted by FDA.**

**Liestal, Switzerland, September 28, 2007 – Santhera Pharmaceuticals (SWX:SANN), a Swiss specialty pharmaceutical company focused on neuromuscular diseases, announced today that it has reached an agreement with the US Food and Drug Administration (FDA) under the Special Protocol Assessment (SPA) procedure relating to the Phase III clinical trial to evaluate SNT-MC17 (INN: idebenone) for the treatment of Friedreich's Ataxia (FRDA). The protocol incorporates advice provided by the FDA on the design of the study, its endpoints, statistical analysis and conduct. The FDA granted a fast track designation to Santhera's compound in FRDA.**

The positive clinical results from a recently reported study conducted in collaboration with the US National Institutes of Health (NIH) formed the basis for the design of the phase III trial. The trial with SNT-MC17, named IONIA (Idebenone effects On Neurological ICARS Assessments), is a double-blind, randomized, placebo-controlled study of six months duration investigating the efficacy of two doses of SNT-MC17 compared to placebo. The primary endpoint of IONIA will be a neurological endpoint, measured by the International Cooperative Ataxia Rating Scale (ICARS), comparing the change in the ICARS for each of the treatment groups with placebo over the 24 week study period. The study will also investigate additional neurological endpoints as well as activities of daily living parameters and cardiac measures.

Based on the efficacy data obtained in the NIH study, particularly for the neurological outcome measures, Santhera's first dose group in the IONIA trial will be 450 mg/day for patients below 45 kg body weight and a corresponding dose of 900 mg/day for patients above 45 kg body weight. The second dose group will be 1350 mg/day for patients below 45 kg of body weight and 2250 mg/day for patients above 45 kg. Using Santhera's 150 mg tablet, the daily dose of SNT-MC17 will be divided into three equal doses to be taken with a meal.

The IONIA study will recruit a minimum of 51 ambulatory FRDA patients between the ages of 8 and 17 years and will be conducted at two clinical centers in the US – the Children's Hospital of Philadelphia and the School of Medicine of the University of California, Los Angeles. Patient recruitment is expected to start soon. Santhera has committed to an open label extension study of

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12 months duration offering FRDA patients who have enrolled and completed the IONIA trial, the continuation of treatment with SNT-MC17 at the 1350/2250 mg/day dose level. The purpose of this extension study is to generate additional safety and tolerability data on SNT-MC17 in longer use.

In response to FDA's advice under the SPA, Santhera has, to the extent possible, incorporated the Agency's recommendations into the design of the protocol for this pivotal clinical trial. Discussion points with the FDA have been the size of the study and the safety data base regarding the high dose at the time of filing for a new drug application (NDA). Santhera acknowledges both aspects as they are resulting primarily from the orphan nature of the disease.

Furthermore, the FDA granted a fast-track designation for the compound in FRDA that allows a rolling submission of the NDA enabling the Agency to review the product's NDA with a higher priority in a potentially shorter review time. The compound earlier received orphan drug designation for the indication FRDA in the US, allowing for a market exclusivity of 7 years after marketing approval.

Klaus Schollmeier, Santhera's CEO commenting on today's announcement said: "I am pleased that we could finalize the protocol for the pivotal trial in the US. With the offering of an extension study and FDA's fast-track designation granted, we now believe that we can successfully complete the development of SNT-MC17 for FRDA in the US during the course of 2009. SNT-MC17 has a good chance to become the first pharmaceutical product approved in the US for this devastating disease."

"We are excited that Santhera is announcing today the commencement of the first Phase III clinical trial in FRDA in the US", said Ronald J. Bartek, President of the Friedreich Ataxia Research Alliance (FARA). "SNT-MC17/idebenone has shown clinical promise in previous trials and FARA is committed to actively support Santhera in the timely enrollment of patients for this pivotal trial, as every day counts in advancing this effort to achieve treatment for FRDA."

Santhera has applied for marketing authorization of SNT-MC17 for the treatment of FRDA in the EU and will submit shortly the marketing application in Canada. Market approval in both territories is expected for the second half of 2008. The Company has partnered the marketing rights for SNT-MC17 in FRDA in the EU and Switzerland to Takeda and intends to market the product in the US and Canada via its own specialty sales force.

### **About Friedreich's Ataxia (FRDA)**

Friedreich's Ataxia (FRDA) is a rare but severe genetic neuromuscular disorder that results in the degeneration of an individual's nerve and muscle tissue. This disorder causes loss of muscle control, uncoordinated movements, muscle wasting and thickening of heart walls which frequently leads to a shortened life span. FRDA affects both Caucasian males and females equally and it is estimated that about 20,000 patients suffer from the disease in both North America and Europe. Average life expectancy for FRDA patients is limited to approximately 35 to 50 years.

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The disorder results from a genetic defect in the gene encoding for *frataxin*. Reduced levels of this protein ultimately result in impaired energy production in mitochondria, the cells' energy production centers, and elevated oxidative stress. Tissues that have the highest need for energy, in particular nerve and cardiac tissues, are primarily affected by *frataxin* deficiency resulting in pathological changes in heart muscle anatomy and function and loss of nerve cells. SNT-MC17 is believed to improve the balance and flow of electrons within the mitochondria, therefore increasing the energy production within nerve and muscle cells of FRDA patients, protecting these cells from cell death. A number of clinical trials have provided strong evidence that SNT-MC17 may offer an effective treatment option for FRDA associated heart wall thickening (cardiomyopathy). In addition, data from the collaborative NIH clinical trial suggest positive effects on neurological function.

### Background on International Cooperative Ataxia Rating Scale (ICARS)

ICARS consists of a one-hundred-point semi-quantitative scale based upon 19 simple neurological testing maneuvers compartmentalized into postural and stance, limb ataxia, speech, and oculomotor components and has been previously applied to this patient population in clinical studies.

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### About Santhera

Santhera Pharmaceuticals (SWX: SANN) is a Swiss specialty pharmaceutical company focused on the discovery, development and marketing of small-molecule pharmaceutical products for the treatment of severe neuromuscular diseases. Santhera's vision is to become a leading specialty pharmaceutical company offering therapies for a number of indications in this area of high unmet medical need which includes many orphan indications with no current therapy.

Santhera currently has five clinical-stage development programs, three of which are investigating its lead compound, SNT-MC17 (INN: idebenone), for the treatment of Friedreich's Ataxia (FRDA), Duchenne Muscular Dystrophy (DMD) and Leber's Hereditary Optic Neuropathy (LHON). Another clinical program is investigating JP-1730 (INN: fipamezole) for the treatment of Dyskinesia in Parkinson's Disease (DPD) in cooperation with Juvantia, the compound's owner. The fifth program comprises SNT-317 (INN: omigapil) in Congenital Muscular Dystrophies (CMD), a compound in-licensed from Novartis. The most advanced program, SNT-MC17 in FRDA, is currently under review for marketing approval in the EU and will be submitted shortly in Canada. The compound is also in Phase III clinical development for FRDA in the US while the while the other clinical programs are in Phase II. For further information, please visit [www.santhera.com](http://www.santhera.com).

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**Conference call**

At **16.00 CET / 15.00 UKT / 10:00 EST today September 28, 2007**, Santhera will host a conference call. People interested in participating may join the teleconference facility using the following dial-in in **Switzerland +41 52 267 07 31 (no PIN code needed)**. The conference call will be recorded for playback and is available one hour after the conference call ends and for 10 days under +41 52 267 07 00 (reference 548258#).

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