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## Beyond the Horizon: HELIOS Clinical Trials in ATTR Cardiomyopathy

### Announcer:

Welcome to ReachMD. This activity, titled “Beyond the Horizon: HELIOS Clinical Trials in ATTR Cardiomyopathy” is provided by Medtelligence.

### Dr. Fontana:

The HELIOS clinical trials are a groundbreaking phase 3 program. They are evaluating the safety and efficacy of the RNA interference therapeutic vutrisiran in patients with hereditary and wild-type ATTR amyloidosis. So building upon a successful phase 1 study demonstrating vutrisiran’s safety profile and ability to reduce serum TTR levels, HELIOS is composed of 2 pivotal trials, HELIOS-A and HELIOS-B. And today, I am highlighting the cardiac exploratory analysis of HELIOS-A and the design of the HELIOS-B.

This is ReachMD, and I am Dr. Marianna Fontana.

Vutrisiran is an RNA interference therapeutic in development for the treatment of patients with ATTR cardiomyopathy. It’s already licensed for the treatment of patients with ATTR polyneuropathy, but in development for patients with ATTR cardiomyopathy. So what vutrisiran does, is that inhibits the production of disease-causing transthyretin protein by the liver, leading to a significant and durable reduction in the level of TTR in the blood. So vutrisiran is administered subcutaneously under the skin and utilizes one of Alnylam’s delivery platform known as Enhanced Stabilization Chemistry-GalNAc-conjugate delivery platform. And vutrisiran is administered every 3 months.

HELIOS-A was a phase 3 global, open-label study comparing the efficacy and safety of vutrisiran with an external placebo group from the APOLLO study. Patients were randomized 3:1 to subcutaneous vutrisiran 25 mg every 3 months, or intravenous patisiran 0.3 mg/kg every 3 weeks for 18 months. And the study objective was to assess the effect of vutrisiran to reduce TTR production in patients with hereditary transthyretin amyloidosis with polyneuropathy. And vutrisiran significantly improved multiple disease-relevant outcomes for ATTR-variant amyloidosis versus external placebo with an acceptable safety profile.

But also, when we looked at the cardiac subpopulation, so a prespecified analysis within the HELIOS-A study, there was a clear evidence of improvement across multiple parameters, which included blood biomarkers like NT-proBNP. So there was a significant improvement in the vutrisiran arm as compared to the external placebo, and also across a wide range of deformation and nondeformation-based parameters assessed by echocardiography. So there was a very encouraging signal that vutrisiran was not only effective on the polyneuropathy of these patients, but also on the cardiomyopathic phenotype.

So HELIOS-B is a global phase 3, randomized, double-blind, placebo-controlled study to evaluate the efficacy and safety of vutrisiran in adult patients with ATTR amyloidosis with cardiomyopathy, and these included both patients with hereditary ATTR amyloidosis and wild-type ATTR amyloidosis. The enrollment of the study is complete, and patients were randomized on a 1:1 basis to receive either 25 mg of vutrisiran or placebo administered as a sub-cut injection every 3 months for up to 36 months. The primary endpoint of the study will be to assess the efficacy of vutrisiran versus placebo on the composite endpoint of all-cause mortality and recurrent cardiovascular events. So cardiovascular hospitalization and urgent heart failure visits.

A wide range of secondary endpoints will also be analyzed, and these will include a 6-minute walking test to assess the functional capacity, quality of life as assessed by the KCCQ, a wide range of deformation and nondeformation-based parameters on the echocardiography, blood biomarkers like NT-proBNP and troponin, and also, we will analyze a kind of new endpoint which is emerging as an important endpoint that has been extensively assessing the heart failure community of heart failure patients, which is outpatient diuretic intensification.

So outpatient diuretic intensification represents an important event in the lives of our patients because it's in response of heart failure worsening.

HELIOS-B results will have a tremendous impact on patients with ATTR cardiomyopathy. At present, we've got 1 single drug which is approved for treatment of patients with the ATTR cardiomyopathy which is tafamidis. And also in the next few months, it's likely that a secondary drug, acoramidis, within the class, again, of stabilizer, will be approved. But vutrisiran will be the first gene silencer in patients with ATTR cardiomyopathy. So it will represent the single compound in a second class which uses a completely different mechanism of actions compared to the only drug that we have available until this age. So it will represent a milestone change in the treatment landscape of patients with this condition.

That's all the time we have today, so I want to thank the audience for listening and keeping up with the changing landscape of ATTR cardiomyopathy.

**Announcer:**

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