ATTR-ACT: Transthyretin Amyloid Cardiomyopathy Tafamidis Study
A Phase 3 Clinical Study in Transthyretin Cardiomyopathy (TTR-CM)

What is TTR-CM?
Transthyretin cardiomyopathy (TTR-CM) is a rare, progressive and universally fatal disease. There are no approved treatments for this disease and it is believed to be vastly underdiagnosed.

TTR-CM is caused by destabilization of a transport protein called "transthyretin", which is composed of 4 identical sub units (a "tetramer"). In TTR-CM, heart failure occurs when unstable tetramers dissociate resulting in misfolded proteins that aggregate into amyloid fibrils and deposit in the heart.

What is tafamidis?
Tafamidis meglumine is an investigational medicine for TTR-CM, and is not approved in the United States.

Tafamidis is a selective stabilizer of TTR in the form of an oral capsule. Tafamidis binds to specific sites on the TTR tetramer to prevent tetramer dissociation and formation of the misfolded proteins, thus inhibiting amyloid formation.

What is the design of the ATTR-ACT study?
In December 2013, Pfizer initiated a phase 3 double-blind, randomized, placebo-controlled study of tafamidis in up to 400 patients with TTR-CM, which is the first phase 3 clinical study initiated in TTR-CM.

The study includes two active doses of tafamidis (20mg and 80 mg) versus placebo over 30 months. Approximately 50 percent more patients are on active medicine than on placebo.

The primary outcome measure of the study is a combination of all-cause mortality and frequency of cardiovascular-related hospitalization. The secondary outcome measures include the 6-minute walk test (6MWT), the Kansas City Cardiomyopathy Questionnaire Overall Score (KCCQ-OS), and TTR stabilization at Month 1.

The study completed enrollment in August 2015. All patients who complete the study will have the opportunity to receive tafamidis treatment in a long-term extension study.

Overview: ATTR-ACT Phase 3 Study
- Phase 3 double-blind, randomized, placebo-controlled study of tafamidis in up to 400 patients worldwide with TTR-CM
- ATTR-ACT is the first phase 3 clinical study initiated in TTR-CM.
- Investigating the efficacy, safety and tolerability of a daily oral dose of 20mg or 80mg tafamidis in comparison to placebo
- 30-month treatment duration
- 54 sites worldwide participating in the trial
- All patients who complete the study will have the opportunity to receive tafamidis treatment in a long-term extension study.
- The study completed enrollment in August 2015.
- Additional information about the study is available at www.clinicaltrials.gov (direct link: http://1.usa.gov/18kkIwv).
- The clinicaltrials.gov identifier is NCT01994889.
How many clinical trial sites are part of the study, and where are the sites located?

There are 54 sites worldwide participating in the trial. The study regions include North America, South America, the EU and Japan. For additional information about the study, visit www.clinicaltrials.gov (direct link: http://1.usa.gov/18kkIwv). The clinicaltrials.gov identifier is NCT01994889.3

Which doses are being studied?

The study is investigating the efficacy, safety and tolerability of a daily oral dose of 20mg or 80mg tafamidis.

What are the inclusion criteria for the ATTR-ACT study?

Selected inclusion criteria for the study are:

- Medical history of Heart Failure (HF) with at least 1 prior hospitalization for HF or clinical evidence of HF (without hospitalization).3
- Evidence of cardiac involvement by echocardiography with an end-diastolic interventricular septal wall thickness greater than 12 mm.3
- Presence of amyloid deposits in biopsy tissue and presence of a variant TTR genotype and/or TTR precursor protein identification by mass spectrometry.3

What are the exclusion criteria for the ATTR-ACT study?

Selected exclusion criteria for the study are:

- A New York Heart Association (NYHA) classification of stage IV heart failure.3
- Presence of primary (light chain) or secondary (AA) amyloidosis.3
- Prior liver or heart transplantation.3

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3 Pfizer data on file, New York, NY.
4 Rapezzi C, Quarta CC, Riva L, et al. Transthyretin-related amyloidoses and the heart: a clinical overview. Nat Rev Cardiol 2010;7:398–408