



# Tafamidis, An Oral, Investigational Compound For The Treatment Of Transthyretin Familial Amyloid Polyneuropathy (TTR-FAP) Sustained A Slowing Of Disease Progression Over 30 Months

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Data Presented in an Oral Session at the 63rd Annual Meeting of the American Academy of Neurology

"TTR-FAP is a devastating disease with limited therapy options, representing a significant unmet medical need. Life expectancy for untreated patients is only 10 years, on average, from the onset of symptoms,"

(BUSINESS WIRE)--Pfizer Inc. (NYSE: PFE) announced today data from an open-label extension study (Fx-006) of the pivotal Phase II/III (Fx-005) trial. This extension study evaluated the long-term clinical outcomes of tafamidis, a novel, oral, investigational compound being studied as a treatment for patients with Transthyretin Familial Amyloid Polyneuropathy (TTR-FAP). TTR-FAP is a rare and fatal neurodegenerative disease affecting approximately 8,000 patients worldwide. These data showed that slowing of disease progression was sustained over 30 months. The data was presented in an oral session at the 63rd Annual Meeting of the American Academy of Neurology.

"TTR-FAP is a devastating disease with limited therapy options, representing a significant unmet medical need. Life expectancy for untreated patients is only 10 years, on average, from the onset of symptoms," said Dr. Teresa Coelho, Hospital Santo Antonio in Porto, Portugal, a principal investigator in the study. "We are encouraged by the consistency of

the results and preservation of neurologic function across all endpoints, as well as the long-term maintenance effect over 30 months.”

#### Design and Results of 12-Month Extension Study (Fx-006):

Following the completion of the pivotal Phase II/III clinical trial (Fx-005), an open-label, 12-month extension study (Fx-006) was conducted to evaluate long-term safety and efficacy, in which patients who completed the 18-month pivotal study were eligible to enroll. In this analysis, earlier treatment with tafamidis resulted in better outcomes. Patients treated with tafamidis for 30 months had less neurologic deterioration than patients who began tafamidis 18 months later (i.e. placebo-tafamidis group), showing a 55.9 percent preservation of function as measured by the Neuropathy Impairment Score-Lower Limb (NIS-LL), or a mean change from baseline of 3.0 for those treated for 30 months versus 6.8 for those initiating treatment 18 months later ( $p=0.04$ ). In addition, patients treated with tafamidis over 30 months showed preservation in large (66 percent preservation or 1.6 versus 4.7 for those treated 18 months later,  $p=0.007$ ) and small nerve fiber function (45.5 percent or 1.2 versus 2.2 for those treated 18 months later,  $p=ns$ ). Despite having more severe disease (i.e. those patients initiating treatment 18 months later), initiation of tafamidis in patients previously on placebo resulted in slowing of disease progression. A total of 86 patients were enrolled in this extension study. No new safety concerns as compared to the pivotal study were observed over 30 months and no patients discontinued due to adverse events.

#### Design and Results of 18-month Pivotal Phase II/III Study (Fx-005):

The pivotal 18-month Phase II/III international, multicenter, randomized, double-blind, placebo-controlled clinical trial (Fx-005), designed to evaluate the safety and efficacy of tafamidis when administered orally as a once-daily dose of 20 mg to patients with TTR-FAP compared with placebo, was initiated in early 2007. A total of 128 patients were enrolled and randomized to treatment (65 to tafamidis and 63 to placebo). Primary end points in the study were Neuropathy Impairment Score-Lower Limb (NIS-LL) and quality of life as measured by the Norfolk QOL-Diabetic Neuropathy (DN). While the data showed that the 18-month study (Fx-005) missed its co-primary endpoints (analysis in the Intent-to-Treat (ITT) population), it did meet statistical significance in a predefined secondary analysis (Efficacy Evaluable (EE) population), which was designed to adjust for the impact of patient attrition due to liver transplantation. As liver transplant is a currently available treatment option for TTR-FAP1, a significant portion (70 percent) of the patients in this study also remained on liver transplant waiting lists within their respective countries. The adverse drug reactions reported included diarrhea, upper abdominal pain, urinary tract

infection, and vaginal infection.

## About TTR-FAP

Protein misfolding followed by amyloid formation is the cause of several neurodegenerative diseases.<sup>2</sup> In TTR-FAP, the destabilization of TTR resulting from a genetic mutation leads to the formation of misfolded proteins and subsequent amyloid fibrils in the peripheral and autonomic nerves, as well as other organs (GI tract, kidneys, and heart).<sup>3,4</sup> Patients with TTR-FAP experience significantly diminished quality of life due to symptoms including polyneuropathy characterized by sensory loss, pain, and weakness in the lower limbs; as well as severe impairment of the autonomic nervous system commonly manifesting as dyshidrosis, erectile dysfunction, alternating diarrhea and constipation, unintentional weight loss, orthostatic hypotension, urinary incontinence, urinary retention, and delayed gastric emptying.<sup>5,6,7</sup> TTR-FAP typically occurs during active, adult years with onset commonly in the 30s.<sup>8</sup> When untreated, TTR-FAP reaches the terminal stage in 10 years, on average, from the onset of symptoms.

## About Pfizer's Specialty Care Business

Pfizer's Specialty Care Business Unit is the world's largest specialty pharmaceuticals business, with a commitment to the eradication, remission, and relief of serious diseases. Pfizer's Specialty Care Business is committed to bringing together the best scientific minds to challenge the most feared diseases of our time.

Pfizer Inc.: Working together for a healthier world™

At Pfizer, we apply science and our global resources to improve health and well-being at every stage of life. We strive to set the standard for quality, safety, and value in the discovery, development, and manufacturing of medicines for people and animals. Our diversified global health care portfolio includes human and animal biologic and small molecule medicines and vaccines, as well as nutritional products and many of the world's best-known consumer products. Every day, Pfizer colleagues work across developed and emerging markets to advance wellness, prevention, treatments, and cures that challenge the most feared diseases of our time. Consistent with our responsibility as the world's leading biopharmaceutical company, we also collaborate with health care providers, governments, and local communities to support and expand access to reliable, affordable health care around the world. For more than 150 years, Pfizer has worked to make a difference for all who rely on us. To learn more about our commitments, please visit us at [www.pfizer.com](http://www.pfizer.com).

DISCLOSURE NOTICE: The information contained in this release is as of April 12, 2011. Pfizer assumes no obligation to update forward-looking statements contained in this release as the result of new information or future events or developments.

This release contains forward-looking information that involves substantial risks and uncertainties about a product candidate, tafamidis, including its potential benefits. Such risks and uncertainties include, among other things, the uncertainties inherent in research and development; whether and when the Company will resubmit a new drug application for tafamidis with the FDA, and whether and when the FDA will accept any such resubmission based on additional information that is available without further clinical studies; decisions by regulatory authorities regarding whether and when to approve any drug applications that may be filed for tafamidis as well as their decisions regarding labeling and other matters that could affect its availability or commercial potential; and competitive developments.

A further description of risks and uncertainties can be found in Pfizer's Annual Report on Form 10-K for the fiscal year ended December 31, 2010 and in its reports on Form 10-Q and Form 8-K.

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1 Benson2007/p 420/col 1/para 3/lines 1-4; p 420/col 2/para 1/lines 3-10, Benson2007/p 420/col 2/pars 2/lines 1-2

2 Soto2003/p49/col1/para1/lines8-10

3 Hou2007/1639/1/2/1-2; Hou2007/1639/2/1/1-4; Benson2007/416/2/2/3-11

4 Dattilo2009/1/1/1-3, Ando2005/1058/2/1/1-2; Andos2005/1058/2/1/11-12; Enson2007/411/2/2/1-5

5 Sekijima2009/2/3/1-8

6 Hou2007/2/2/7-12; Benson2007/414/2/2/18-22

7 Hou2007/1637/2/1/1-2; Jonsen1998/53/1/2/4-6

8 Hou2007/p 1637/col 2/para 1/lines 1-2; Plante-Bordeneuve/p 693/para 1/line 1

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