Amyloid Publishes Long-Term Data Analysis from Pfizer Suggesting Tafamidis Delays Progression of TTR-FAP, a Rare Disease

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Analysis Provides Longest Evaluation of Any Medication for Hereditary Transthyretin Amyloid Polyneuropathy (TTR-FAP), a Neurodegenerative Disease

Pfizer Inc. (NYSE:PFE) announced the publication of a new interim analysis of long-term data from four studies indicating that treatment with tafamidis is associated with delay in disease progression in patients with hereditary transthyretin amyloid polyneuropathy (TTR-FAP) and was well tolerated, with no unexpected side effects. The publication, " Long-term safety and efficacy of tafamidis for the treatment of hereditary transthyretin amyloid polyneuropathy: results up to 6 years," is available online in the journal Amyloid: The Journal of Protein Folding Disorders.1 The analysis included patients with the most common TTR-FAP mutation, Val30Met, who either initiated treatment with tafamidis at the beginning of the pivotal study or who started treatment 18 months later during an open-label extension, as well as non-Val30Met patients who completed 12 months of treatment and then continued in the same open-label extension. Tafamidis, marketed under the trade name VYNDAQEL, is approved in 40 countries for the treatment of TTR-FAP in adult patients with early-stage symptomatic polyneuropathy to delay peripheral neurologic impairment. Tafamidis is not approved in the United States.

TTR-FAP is a rare, genetic, progressive, irreversible, and fatal neurodegenerative disease. It significantly impairs quality of life and is estimated to affect at least 10,000 people worldwide,2 although the prevalence may be much higher.3 People with TTR-FAP experience a considerable burden of illness that increases with disease progression; when left untreated, people with TTR-FAP die within 10 years of symptom onset, on

average.4,5 The disease is caused by a mutation in the gene for the protein transthyretin (TTR), resulting in production of unstable TTR that can accumulate as amyloid deposits in nerves and other organs, interfering with normal function.6,7 Tafamidis is a medicine designed to specifically stabilize TTR, preventing or slowing the formation of abnormal TTR and subsequent amyloid deposits.8

“This is a life-long disease, so these findings are important because they suggest that tafamidis not only provided a sustained disease-modifying effect, it also was generally well tolerated over the long term,” said Fabio Barroso, MD, lead author and neurologist at the Raul Carrea Institute for Neurological Research, FLENI, in Buenos Aires, Argentina. “These results offer hope for people with TTR-FAP, many of whom have witnessed family members and loved ones suffer from this relentless, progressive, and fatal disease.”

This analysis is part of a broader clinical development program that includes 22 studies involving tafamidis. Pfizer is also the sole sponsor of the Transthyretin Amyloidosis Outcomes Survey (THAOS) (www.thaos.net), an international registry and the largest real-world database focused on TTR amyloidosis. Additionally, the company has been at the forefront of educational initiatives to raise awareness of TTR amyloidosis among healthcare professionals and to facilitate dialogue between patients, their families, and their physicians.

“The analysis is the longest prospective evaluation to date of any medicine being studied for TTR-FAP and builds on previous studies suggesting tafamidis provides benefit when given early in the disease and is associated with delay in disease progression over the long term,” said Dr. Kevin W. Williams, Chief Medical Officer, Rare Disease, Pfizer Innovative Health. “Evaluating potential therapies for the treatment of rare diseases that have limited to no treatment options, such as TTR-FAP, is critical, and Pfizer Rare Disease is pleased that these findings help us to better understand the long-term safety and efficacy in patients with this debilitating illness.”

Long-Term Tafamidis Analysis

The findings reported in Amyloid are from an analysis of an ongoing, long-term, open-label extension study of tafamidis in 93 patients with TTR-FAP who had participated in previous studies with the medication.1 Of these 93 patients, 75 had the Val30Met mutation and 18 had the non-Val30Met mutation. Different TTR mutations can be associated with differences in disease symptoms and severity.

In the Val30Met group, 38 patients had started taking tafamidis on day one in a previous 18-month randomized, double-blind, placebo-controlled Phase 3 pivotal trial and, after

completing the trial, continued on the medication in a 12-month open-label extension study.5, 9 The other 37 patients had taken the placebo in the 18-month trial, then switched to tafamidis upon entry in the 12-month extension. After completing the 12-month extension study, both groups entered the ongoing, long-term study.

The analysis suggests that, by month 66, patients who started tafamidis at the start of the 18-month pivotal trial had numerically less disease progression than patients who started on placebo, based on the degree of worsening in three standard measures: a test called the Neuropathy Impairment Score for Lower Limbs (NIS-LL), a subscale of the NIS-LL that assesses muscle weakness, and a measure of total quality of life (TQOL). This group was also less likely than the group that started on placebo to progress to the next ambulatory stage – for example, from no assistance required to needing a cane to using a wheelchair.

The analysis also suggested the rates of worsening in NIS-LL, NIS-LL muscle weakness, and TQOL over time were less for the patients who started on tafamidis versus placebo on entry to the pivotal trial; moreover, after the placebo, in patients switched to tafamidis during the open-label extension, the rates slowed and were comparable to those seen in patients who had been started on the medication from the beginning of the study.

In the patients with non-Val30Met mutations, who had previously completed a separate, 12-month, open-label study, some worsening of NIS-LL and other measures were observed.10 The lack of a control or comparator group of non-Val30Met patients made interpretation of the findings in those patients difficult and is a limitation of this new analysis.1

Among all 93 patients in the analysis, tafamidis was generally well-tolerated, with no unexpected safety issues identified. The most common adverse events (occurring in 10 percent or more of patients) were urinary tract infections (16.1 percent); fall (12.9 percent), thermal burn (11.8 percent), influenza (10.8 percent), headache (9.7 percent), and upper respiratory tract infection (9.7 percent). The most common serious adverse events (occurring in 2 percent or more of patients) were cardiac failure and chest pain (both 3.2 percent); and sepsis, urinary tract infection, and transient ischemic attack (all 2.2 percent). Eight patients died during the study or after completion or discontinuation; none of the deaths were treatment related.1

About Tafamidis

Tafamidis, marketed under the trade name VYNDAQEL, was first approved in 2011 in the European Union (EU) for the treatment of TTR-FAP in adult patients with early-stage

symptomatic polyneuropathy to delay peripheral neurologic impairment. Currently, VYNDAQEL is approved in 40 countries, including countries in Europe, Japan, Brazil, Mexico, Argentina, Israel, Russia, and South Korea. Pfizer received a complete response letter from the US Food and Drug Administration (FDA) on its application to approve tafamidis for TTR-FAP in 2012; tafamidis is not approved in the United States.11

As a leader in TTR amyloidosis, Pfizer Rare Disease continues to partner with the FDA regarding a potential path to approval of tafamidis for TTR-FAP, as the company hopes to achieve the objective of providing TTR-FAP patients living in the United States with the same treatment option as those patients living in many other parts of the world.

Important Safety Information

VYNDAQEL is contraindicated in patients who had previous hypersensitivity to the active substance or to any excipients of VYNDAQEL. In the clinical program, the safety and tolerability profile of VYNDAQEL was studied in 128 patients. In the pivotal study, adverse events (AEs) in both treatment groups were generally mild or moderate in severity. The adverse drug reactions reported in the pivotal study are diarrhea, upper abdominal pain, urinary tract infection, and vaginal infection.12 There are no data available regarding use of VYNDAQEL post-liver transplantation; therefore, VYNDAQEL should be discontinued in patients who undergo liver transplantation. There are no data on the use of VYNDAQEL in pregnant or nursing women. VYNDAQEL is not recommended for use during pregnancy, in women who are breast feeding or in women of childbearing age not using contraception. Women of childbearing potential should use appropriate contraception when taking VYNDAQEL and continue to use appropriate contraception for 1-month after stopping treatment with VYNDAQEL. Children and adolescents do not have the symptoms of TTR Amyloid Polyneuropathy. VYNDAQEL is therefore not used for children and adolescents.

Pfizer Rare Disease

Rare disease includes some of the most serious of all illnesses and impacts millions of patients worldwide, representing an opportunity to apply our knowledge and expertise to help make a significant impact on addressing unmet medical needs. The Pfizer focus on rare disease builds on more than two decades of experience, a dedicated research unit focusing on rare disease, and a global portfolio of multiple medicines within a number of disease areas of focus, including hematology, neuroscience, and inherited metabolic disorders.

Pfizer Rare Disease combines pioneering science and deep understanding of how diseases work with insights from innovative strategic collaborations with academic

researchers, patients, and other companies to deliver transformative treatments and solutions. We innovate every day, leveraging our global footprint to accelerate the development and delivery of groundbreaking medicines and the hope of cures.

Click here to learn more about our Rare Disease portfolio and how we empower patients, engage communities in our clinical development programs, and support programs that heighten disease awareness and meet the needs of patient families.

Working together for a healthier world®

At Pfizer, we apply science and our global resources to bring therapies to people that extend and significantly improve their lives. We strive to set the standard for quality, safety and value in the discovery, development and manufacture of health care products. Our global portfolio includes medicines and vaccines as well as many of the world's best-known consumer health care 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 one of the world's premier innovative biopharmaceutical companies, we 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, we have worked to make a difference for all who rely on us. We routinely post information that may be important to investors on our website at www.pfizer.com. In addition, to learn more, please visit us on www.pfizer.com and follow us on Twitter at @Pfizer and @Pfizer_News, LinkedIn, YouTube and like us on Facebook at Facebook.com/Pfizer.

DISCLOSURE NOTICE: The information contained in this release is as of August 31, 2017. 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 about VYNDAQEL (tafamidis), including its potential benefits, that involves substantial risks and uncertainties that could cause actual results to differ materially from those expressed or implied by such statements. Risks and uncertainties include, among other things, uncertainties regarding the commercial success of tafamidis; the uncertainties inherent in research and development, including, without limitation, the ability to meet anticipated clinical trial commencement and completion dates and regulatory submission dates, as well as the possibility of unfavorable clinical trial results, including unfavorable new clinical data and additional analyses of existing clinical data; whether and when any new or supplemental

drug applications may be filed in any other jurisdictions for tafamidis; whether and when regulatory authorities in any such jurisdictions where applications for tafamidis may be pending (including the application pending with the FDA for the treatment of TTR-FAP, for which the company received a complete response letter in 2012) or filed may approve any such applications, which will depend on the assessment by such regulatory authority of the benefit-risk profile suggested by the totality of the efficacy and safety information submitted; decisions by regulatory authorities regarding labeling and other matters that could affect the availability or commercial potential of tafamidis; 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, 2016 and in its subsequent reports on Form 10-Q, including in the sections thereof captioned "Risk Factors" and "Forward-Looking Information and Factors That May Affect Future Results", as well as in its subsequent reports on Form 8-K, all of which are filed with the U.S. Securities and Exchange Commission and available at www.sec.gov and www.pfizer.com.

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