

Pfizer Announces Publication of New Analysis Showing Long-Term Therapy with VYNDAQEL (tafamidis) Slowed Progression of Rare Neurodegenerative Disease

Monday, August 08, 2016 - 04:00am

“This analysis, which is based on the longest prospective evaluation to date of any medication being studied for TTR-FAP, provides health care professionals with important insights into the management of patients with this disease.”

Pfizer Inc. (NYSE:PFE) announced the publication of a new post-hoc analysis of data from three studies of VYNDAQEL in patients with mild transthyretin familial amyloid polyneuropathy (TTR-FAP). The analysis, which included patients with the Val30Met mutation treated over varying periods of up to 5.5 years, showed that treatment with VYNDAQEL initiated during the early stage of the disease resulted in minimal neurological disease progression and in preservation of body weight, which often declines as the disease progresses. VYNDAQEL was well tolerated with no new safety signals observed. The new findings were published online in [*Amyloid: The Journal of Protein Folding Disorders*](#).¹

“These findings underscore the long-term benefits of early intervention with VYNDAQEL for symptomatic patients with TTR-FAP,” said Dr. Kevin W. Williams, Chief Medical Officer, Rare Disease, Pfizer Innovative Health. “This analysis, which is based on the longest prospective evaluation to date of any medication being studied for TTR-FAP, provides health care professionals with important insights into the management of patients with this disease.”

TTR-FAP is a rare, genetic, progressive, and irreversible neurodegenerative disease that significantly impairs quality of life and is estimated to affect about 10,000 people worldwide.² When left untreated, people with TTR-FAP die within 10 years of symptom onset, on average.^{3,4} The disease is caused by a mutation in the gene for the protein transthyretin (TTR), resulting in production of unstable TTR proteins that can accumulate as amyloid deposits in nerves and other organs, interfering with normal function.^{5,6} VYNDAQEL is a medicine designed to specifically stabilize TTR, preventing or slowing the formation of abnormal TTR proteins and subsequent amyloid deposits.⁷

*Mild neurological impairment was defined as Neuropathy Impairment Score for Lower Limbs (NIS-LL) total score of 10 or less. NIS-LL, a standard measure of disease progression in TTR-FAP, ranges from 0 (normal) to 88 (absence of any lower limb activity).

Results From Long-Term VYNDAQEL Analysis

The new findings reported in *Amyloid* are based on data from three sequential studies: an 18-month randomized, double-blind, placebo-controlled Phase 3 pivotal trial of 125 TTR-FAP patients; its 12-month open-label

extension; and a second, ongoing, long-term open-label extension study. This descriptive analysis examined a subset of 71 of the randomized patients whose neurological impairment was defined as mild* just prior to starting treatment with VYND AQEL, either at study start (for those randomized to VYND AQEL) or upon entry into the first open-label extension (for those randomized to placebo). In the 31 patients observed at

5.5 years, the evaluation showed that treatment with VYND AQEL resulted in minimal neurologic disease progression: a mean change from baseline of 5.3 NIS-LL points. This translates to an annual rate of 1.0 point increase in NIS-LL. The lack of a direct control group is a limitation of this study.¹

TTR-FAP is typically accompanied by gastrointestinal issues that can lead to malnutrition and unintentional weight loss, resulting in a decline in modified body mass index (mBMI), a clinical indicator of disease progression and treatment response.⁸ The published analysis showed that mBMI was preserved during long-term VYND AQEL treatment, with less than one percent decrease at 5.5 years from baseline.¹

No new safety issues or side effects of VYND AQEL were identified in the long-term evaluation of these 71 patients. The most common (occurring in 10 percent or more of patients) treatment-emergent adverse events were urinary tract infections (28.2 percent); cold (nasopharyngitis, 25.4 percent); influenza (23.9 percent); diarrhea (22.5 percent); headache and pain in an extremity (both 19.7 percent); back pain (16.9 percent); upper respiratory tract infection (15.5 percent); depression and thermal burn (both 14.1 percent); upper abdominal pain, anxiety, death of cells on the surface of the cornea (punctate keratitis), sore throat (pharyngitis), and decreased tear breakup time (an indicator of “dry eye”) (all 12.7 percent); and constipation, nausea, and vomiting (each at 11.3 percent).¹

Burden of TTR-FAP

Patients with TTR-FAP experience a considerable burden of illness early in the course of disease and this burden increases with disease progression. They typically require assistance with walking 5 to 6 years after initial symptoms. As TTR-FAP symptoms progress, patients require a considerable amount of assistance, are unable to care for themselves, and may become bedridden or require hospitalization.^{9,10}

About VYND AQEL

VYND AQEL is a novel specific TTR stabilizer indicated in the European Union for the treatment of TTR-FAP in adult patients with early-stage symptomatic polyneuropathy to delay peripheral neurologic impairment. Since its EU approval in 2011, VYND AQEL has also been approved in Japan, Mexico, Argentina, Israel, and South Korea. VYND AQEL is not approved in the United States.¹¹

Important Safety Information

- VYND AQEL is contraindicated in patients who had previous hypersensitivity to the active substance or to any excipients of VYND AQEL.
- In the clinical program, the safety and tolerability profile of VYND AQEL was studied in 127 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
 - VYND AQEL is generally well tolerated in patients with TTR-FAP. Patients in the clinical studies were evaluated for a total of 30 months.⁸
- There are no data available regarding use of VYND AQEL post-liver transplantation; therefore, VYND AQEL 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.

About Pfizer and Rare Diseases

Rare diseases are among the most serious of all illnesses and impact 350 million patients worldwide, often children. Although there are over 7,000 known rare diseases, only five percent have an approved medication. For rare disease patients and their loved ones, better treatment options cannot come soon enough. At Pfizer, we share their urgency and passionately dedicate our resources, expertise and global reach to bring them the transformative medicines they need. The Pfizer focus on rare diseases builds on more than two decades of experience, a pipeline of more than 20 compounds and a global portfolio of more than 20 medicines approved worldwide that treat rare diseases in the areas of hematology, neuroscience, inherited metabolic disorders, and pulmonology. Pfizer Rare Disease is inspired by patients, born from science and powered by the passion of the hundreds of colleagues in Pfizer who dedicate their work to helping patients with rare diseases.

As a leader in the TTR-FAP community, Pfizer Inc. has been at the forefront of educational initiatives to raise awareness of this rare disease among health care professionals and to facilitate dialogue between patients, their families, and their physicians. These efforts have contributed to a global increase in diagnosis rates and treatment.¹¹

Pfizer Inc.: 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, Pfizer has worked to make a difference for all who rely on us. To learn more, please visit us at www.pfizer.com. In addition, to learn more, follow us on Twitter at @Pfizer and @Pfizer_News, LinkedIn, and like us on Facebook at Facebook.com/Pfizer.

DISCLOSURE NOTICE: The information contained in this release is as of August 8, 2016. 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 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

application may be filed in any other jurisdictions for tafamidis; whether and when the FDA or regulatory authorities in any other jurisdictions where applications for tafamidis may be pending 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, 2015 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.

References

- ¹ Waddington Cruz M, Amass L, Keohane D, Schwartz J, Li H, Gundapaneni B. Early intervention with tafamidis provides long term (5.5 year) delay of neurologic progression in transthyretin familial amyloid polyneuropathy. *Amyloid* 2016. doi:10.1080/13506129.2016.1207163.
- ² Plante-Bordeneuve V. Update in the diagnosis and management of transthyretin familial amyloid polyneuropathy. *J Neurol*. 2014;261:1227-1233. doi:10.1007/s00415-014-7373-0.
- ³ Plante-Bordeneuve V, Ferreira A, Lalu T, et al. Diagnostic pitfalls in sporadic transthyretin familial amyloid polyneuropathy (TTR-FAP). *Neurology*. 2007;69:693-698.
- ⁴ Coelho T, Maia LM, Martins da Silva A, et al. Long-term effects of tafamidis for the treatment of transthyretin familial amyloid polyneuropathy. *J Neurol*. 2013. doi: 10.1007/s00415-013-7051-7.
- ⁵ Benson MD, Kincaid JC. The molecular biology and clinical features of amyloid neuropathy. *Muscle Nerve*. 2007;36:411-423.
- ⁶ Hou X, Aguilar M-I, Small DH. Transthyretin and familial amyloidotic polyneuropathy: recent progress in understanding the molecular mechanism of neurodegeneration. *FEBS J*. 2007;274:1637-1650.
- ⁷ Coelho, T, Merlini G, Bulawa CE, et al. Mechanism of action and clinical application of tafamidis in hereditary transthyretin amyloidosis. *Neurol Ther*. 2016;5:1. doi:10.1007/s40120-016-0040-x.
- ⁸ Suhr OB, Conceição IM, Karayal ON, Mandel FS, Huertas PE, Ericzon BG. Post hoc analysis of nutritional status in patients with transthyretin familial amyloid polyneuropathy: impact of tafamidis. *Neurol Ther*. doi: 10.1007/s40120-014-0023-8.
- ⁹ Suhr OB, Svendsen IH, Andersson R, Danielsson A, Holmgren G, Ranløv PJ. Hereditary transthyretin amyloidosis from a Scandinavian perspective. *J Intern Med*. 2003;254(3):225-235.
- ¹⁰ Jonsèn E, Athlin E, Suhr O. Familial amyloidotic patients' experience of the disease and of liver transplantation. *J Adv Nurs*. 1998;27:52-58.
- ¹¹ Data on file. Pfizer Inc, New York, NY.
- ¹² Vyndaqel (tafamidis). Annex I: Summary of Product Characteristics. European Medicines Agency. November 16, 2011.

Media Steven Danehy, 212-733-1538 Steven.Danahy@pfizer.com or Investors Chuck Triano, 212-733-3901
Charles.E.Triano@pfizer.com