Pfizer Receives Positive CHMP Opinion for VYNDAQEL® for Use in Patients with Transthyretin Amyloid Cardiomyopathy, a Rare and Fatal Disease

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—If approved by the European Commission (EC), VYNDAQEL® will be the first pharmacologic therapy in the EU for patients with transthyretin amyloid cardiomyopathy—

NEW YORK--(BUSINESS WIRE)--Pfizer Inc. (NYSE: PFE) announced today that the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) has adopted a positive opinion recommending the approval of VYNDAQEL® (tafamidis), a once-daily 61 mg oral capsule, for the treatment of wild-type or hereditary transthyretin amyloidosis in adult patients with cardiomyopathy (ATTR-CM).

“The CHMP positive opinion of VYNDAQEL for ATTR-CM reflects our steadfast commitment to improving outcomes for patients living with this rare and fatal disease,” said Brenda Cooperstone, MD, Senior Vice President and Chief Development Officer, Rare Disease, Pfizer Global Product Development. “In ATTR-ACT, VYNDAQEL reduced mortality and the frequency of cardiovascular-related hospitalizations in patients with wild-type or hereditary forms of the disease. If approved, VYNDAQEL would represent a real breakthrough for patients.”

ATTR-CM is a rare, life-threatening disease characterized by the buildup of abnormal deposits of misfolded protein called amyloid in the heart and is defined by restrictive

cardiomyopathy and progressive heart failure.1,2,3 On average, patients live only 2 to 3.5 years following diagnosis.4

“For those living with ATTR-CM, a progressive and fatal rare disease, there are currently no available pharmacologic treatments for patients,” said Jean-Christophe Fidalgo, President of the Amyloidosis Alliance. “The Amyloidosis Alliance applauds the CHMP opinion, and we hope the EC will swiftly approve VYNDAQEL for ATTR-CM so patients can receive timely access to this medicine.”

In 2011, a different form of VYNDAQEL, tafamidis meglumine 20 mg capsule, was approved in the EU for transthyretin amyloidosis in adult patients with stage 1 symptomatic polyneuropathy (ATTR-PN) to delay peripheral neurologic impairment. For ATTR-CM, the tafamidis 61 mg capsule corresponds to an 80 mg tafamidis meglumine dose (4x 20mg capsules) and was developed for patient convenience to enable a single capsule for daily administration.

The European line extension application was based on the Phase 3 ATTR-ACT study, the first and only completed global, double-blind, randomised, placebo-controlled clinical trial to investigate a pharmacologic therapy for the treatment of ATTR-CM.5 In the primary analysis of the study, VYNDAQEL (tafamidis meglumine) demonstrated a significant reduction in the hierarchical combination of all-cause mortality and frequency of cardiovascular-related hospitalisations compared to placebo over a 30-month period in patients with wild-type or hereditary ATTR-CM ($p=0.0006$).5 Additionally, individual components of the primary analysis demonstrated a relative reduction in the risk of all-cause mortality and frequency of cardiovascular-related hospitalization of 30% ($p=0.026$) and 32% ($p<0.0001$), respectively, with VYNDAQEL versus placebo.5 The application is also based on findings from an evaluation of the free acid form of tafamidis 61 mg.6 The ATTR-ACT primary results were presented in a Hot Line session at the ESC Congress 2018 in Munich, Germany, and simultaneously published online in the *New England Journal of Medicine (NEJM)* in August 2018.

The CHMP’s opinion will now be reviewed by the EC and a final decision is expected in the coming months.

About ATTR Amyloidosis

ATTR amyloidosis is rare, progressive disease characterized by the abnormal buildup of amyloid deposits composed of misfolded transthyretin protein in the body’s organs and tissues. ATTR amyloidosis can impact numerous organs and tissues in the body, including the peripheral nervous system, and organs such as the heart, kidneys, gastrointestinal

tract, and eyes. ATTR-CM and ATTR-PN are two presentations of the disease.

ATTR-CM affects the heart and leads to restrictive cardiomyopathy and progressive heart failure. There are two sub-types of ATTR-CM: hereditary, which is caused by a mutation in the transthyretin gene and can occur in people as early as their 50s and 60s; or the wild-type form which is associated with aging, and is thought to be more common, usually affecting men after age 60.7,8 Often ATTR-CM is diagnosed only after symptoms have become severe. Once diagnosed, the median life expectancy in patients with ATTR-CM, dependent on sub-type, is approximately two to 3.5 years.4

ATTR-PN results from a genetic mutation of the transthyretin gene, amyloid fibrils form in the peripheral and autonomic nerves. ATTR-PN typically occurs during active adult years with onset as early as the 30s in some patients, followed by disease progression that may reach the terminal stage in approximately 10 years on average from disease onset.

About VYNDAQEL® (tafamidis 61 mg) and VYNDAQEL® (tafamidis meglumine 20 mg) 1,6

VYNDAQEL (tafamidis 61 mg) and VYNDAQEL (tafamidis meglumine 20 mg) are oral transthyretin stabilizers that selectively bind to transthyretin, stabilizing the tetramer of the transthyretin transport protein and slowing the formation of amyloid that causes ATTR-CM.

The tafamidis 61 mg capsule corresponds to an 80 mg tafamidis meglumine dose (4x 20mg capsules) and was developed for patient convenience to enable a single capsule for daily administration. VYNDAQEL 61 mg and VYNDAQEL 20 mg are not substitutable on a per milligram basis.

Tafamidis was granted Orphan Drug Designation for ATTR-CM in both the EU and US in 2012 and in Japan in 2018. Tafamidis was approved in Japan under SAKIGAKE designation for the treatment of ATTR-CM in March 2019, in the United States in May 2019, and in the United Arab Emirates in November 2019.

VYNDAQEL (20 mg) was first approved in 2011 in the EU for the treatment of transthyretin amyloid polyneuropathy (ATTR-PN), in adult patients with stage 1 symptomatic polyneuropathy to delay peripheral neurologic impairment. Currently, it is approved for ATTR-PN in 45 countries, including Japan, countries in Europe, Brazil, Mexico, Argentina, Israel, Russia, and South Korea.

VYNDAQEL has not received marketing authorisation for patients with ATTR-CM in the EU.

VYNDAQEL® (tafamidis meglumine) and VYNDAMAX™ (tafamidis) From the U.S. Important Safety Information

Adverse Reactions

In studies in patients with ATTR-CM the frequency of adverse events in patients treated with VYNDAQEL was similar to placebo.

Specific Populations

Pregnancy: Based on findings from animal studies, VYNDAQEL and VYNDAMAX may cause fetal harm when administered to a pregnant woman.

Lactation: There are no available data on the presence of tafamidis in human milk, the effect on the breastfed infant, or the effect on milk production. Tafamidis is present in rat milk. When a drug is present in animal milk, it is likely the drug will be present in human milk. Breastfeeding is not recommended during treatment with VYNDAQEL and VYNDAMAX.

The full prescribing information for VYNDAQEL and VYNDAMAX can be found here

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.

Pfizer Inc.: Breakthroughs that change patients' lives

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, including innovative medicines and vaccines. 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 December 13, 2019. 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 a potential indication in the EU for Vyndaqel for the treatment of wild-type or hereditary transthyretin amyloidosis in adult patients with cardiomyopathy (the "Potential Indication") and Pfizer's rare disease portfolio, including their 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, the uncertainties inherent in research and development, including the ability to meet anticipated clinical endpoints, commencement and/or completion dates for our clinical trials, regulatory submission dates, regulatory approval dates and/or launch dates, as well as the possibility of unfavorable new clinical data and further analyses of existing clinical data; the risk that clinical trial data are subject to differing interpretations and assessments by regulatory authorities; whether regulatory authorities will be satisfied with the design of and results from our clinical studies; whether and when any new or supplemental drug applications may be filed in any other jurisdictions for tafamidis for the Potential Indication; whether and when the EMA may approve the pending application for tafamidis for the Potential Indication and whether and when regulatory authorities in any such other jurisdictions where applications for tafamidis may be pending or filed for the Potential Indication or any other potential indications for tafamidis may approve any

such applications, which will depend on myriad factors, including making a determination as to whether the product's benefits outweigh its known risks and determination of the product's efficacy and, if approved, whether tafamidis will be commercially successful; decisions by regulatory authorities impacting labeling, manufacturing processes, safety and/or other matters that could affect the availability or commercial potential of tafamidis, including for the Potential Indication; 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, 2018 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 Rapezzi C, Lorenzini M, Longhi S, et al. Cardiac amyloidosis: the great pretender. *Heart Fail Rev*. 2015;20(2):117-124.

2 Ando Y, Coelho T, Berk JL, et al. Guideline of transthyretin-related hereditary amyloidosis for clinicians. *Orph J of Rare Diseases*. 2013;8:31.

3 Rapezzi C, Quarta CC, Riva L, et al. Transthyretin related amyloidoses and the heart: a clinical overview. *Nat Rev Cardiol.* 2010;7:398-408.

4 Castano A, Drachman BM, Judge J, et al. Natural history and therapy of TTR-cardiac amyloidosis: emerging disease-modifying therapies from organ transplantation to stabilizer and silencer drugs. Heart Fail Rev. 2015; 20(2): 163–178. doi:10.1007/s10741-014-9462-7.

5 Maurer MS, Schwartz JH, Gundapaneni B, et al. Tafamidis treatment for patients with transthyretin amyloid cardiomyopathy. N Engl J Med. 2018;379(11):1007-1016.

6 Data on file. Pfizer Inc. New York, NY.

7 Connors LH, Sam F, Skinner M, et al. Heart failure due to age-related cardiac amyloid disease associated with wild-type transthyretin: a prospective, observational cohort study. *Circulation*. 2016;133(3):282-290.

8 Swiecicki PL, Zhen DB, Mauermann ML, et al. Hereditary ATTR amyloidosis: a single-institution experience with 266 patients. *Amyloid*. 2015;22(2):123-131.

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