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# U.S. FDA Approves VYNDAQEL® and VYNDAMAX™ for Use in Patients with Transthyretin Amyloid Cardiomyopathy, a Rare and Fatal Disease

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— First and only medicines approved for patients with either wild-type or hereditary transthyretin amyloid cardiomyopathy —

NEW YORK--(BUSINESS WIRE)--Pfizer Inc. (NYSE:PFE) announced today that the U.S. Food and Drug Administration (FDA) has approved both VYNDAQEL® (tafamidis meglumine) and VYNDAMAX™ (tafamidis) for the treatment of the cardiomyopathy of wild-type or hereditary transthyretin-mediated amyloidosis (ATTR-CM) in adults to reduce cardiovascular mortality and cardiovascular-related hospitalization. VYNDAQEL and VYNDAMAX are two oral formulations of the first-in-class transthyretin stabilizer tafamidis, and the first and only medicines approved by the FDA to treat ATTR-CM.

Transthyretin amyloid cardiomyopathy 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. Previously, there were no medicines approved to treat ATTR-CM; the only available options included symptom management, and, in rare cases, heart (or heart and liver) transplant. It is estimated that the prevalence of ATTR-CM is approximately 100,000 people in the U.S. and only one to two percent of those patients are diagnosed today.

“The approvals of VYNDAQEL and VYNDAMAX are a testament to the significant research and development investment in our innovative cardiovascular outcomes trial, ATTR-ACT. We are proud to bring these medicines to ATTR-CM patients who are in dire need of treatment,” said Brenda Cooperstone, MD, Senior Vice President and Chief Development Officer, Rare Disease, Pfizer Global Product Development. “VYNDAQEL and VYNDAMAX reduce cardiovascular mortality and the frequency of cardiovascular-related hospital stays in patients with wild-type or hereditary forms of this rare disease, giving them a chance for more time with their loved ones.”

“Pfizer's purpose is to deliver breakthrough medicines that change patients' lives. The approvals of VYNDAQEL and VYNDAMAX deliver on this promise for patients with ATTR-CM,” said Paul Levesque, Global President, Rare Disease. “This milestone is a gamechanger for patients, who until today had no approved medicines for this rare, debilitating and fatal disease. We will continue to focus efforts on working with the physician community to increase awareness and ultimately detection and diagnosis of this disease.”

The recommended dosage is either VYNDAQEL 80 mg orally once-daily, taken as four 20 mg capsules, or VYNDAMAX 61 mg orally once-daily, taken as a single capsule. VYNDAMAX was developed for patient convenience; VYNDAQEL and VYNDAMAX are not substitutable on a per milligram basis.

“ATTR-CM is not only fatal, but also significantly underdiagnosed, with some patients cycling through multiple doctors and a myriad of tests over a period of years while the disease progresses,” said Isabelle Lousada, Founder and CEO, Amyloidosis Research Consortium. “ATTR-CM is a rare disease for which more education and awareness is needed. The approval of these medicines represents an important advance for patients; however, it is equally important that we work as a community to recognize the critical importance of early diagnosis.”

The FDA approval was based on data from the pivotal Phase 3 Transthyretin Amyloidosis Cardiomyopathy Clinical Trial (ATTR-ACT), the first global, double-blind, randomized, placebo-controlled clinical study to investigate a pharmacological therapy for the treatment of this disease. In ATTR-ACT, VYNDAQEL significantly reduced the hierarchical combination of all-cause mortality and frequency of cardiovascular-related hospitalizations compared to placebo over a 30-month period ($p=0.0006$). 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. Approximately 80% of total deaths were cardiovascular-related in both treatment groups. VYNDAQEL also had significant and consistent treatment effects compared to placebo on functional capacity and health status first observed at six months and continuing through 30 months. Specifically, VYNDAQEL reduced the decline in performance on the six-minute walk test ($p<0.0001$) and reduced the decline in health status as measured by the Kansas City Cardiomyopathy Questionnaire – Overall Summary score ($p<0.0001$). VYNDAQEL was well tolerated in this study, with an observed safety profile comparable to placebo. The frequency of adverse events in patients treated with VYNDAQEL was similar to placebo, and similar proportions of VYNDAQEL-treated patients and placebo-treated patients discontinued the study drug because of an adverse event.

Pfizer is committed to helping eligible ATTR-CM patients who have been prescribed VYNDAQEL or VYNDAMAX gain appropriate access. Pfizer supports patients by helping them understand their insurance coverage requirements and can connect eligible patients with financial assistance resources which may be available including the Pfizer Patient Assistance Program.*

**About ATTR-CM**
Transthyretin amyloid cardiomyopathy (ATTR-CM) is a rare and fatal condition that is caused by destabilization of a transport protein called transthyretin, which is composed of four identical sub units (a tetramer). When unstable transthyretin tetramers dissociate, they result in misfolded proteins that aggregate into amyloid fibrils and deposit in the heart, causing the heart muscle to become stiff, eventually resulting in heart failure. There are two sub-types of ATTR-CM: hereditary, also known as variant, which is caused by a mutation in the transthyretin gene and can occur in people as early as their 50s and 60s; or with no mutation and associated with aging, known as the wild-type form, which is thought to be more common and usually affects men after age 60. 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.

**About VYNDAQEL (tafamidis meglumine) and VYNDAMAX (tafamidis)**
VYNDAQEL (tafamidis meglumine) and VYNDAMAX (tafamidis) 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.

VYNDAMAX 61 mg is a once-daily oral capsule developed for patient convenience. VYNDAQEL and VYNDAMAX are not substitutable on a per milligram basis.

VYNDAQEL was granted Orphan Drug Designation for ATTR-CM in both the EU and U.S. in 2012 and in Japan in 2018. In June 2017 and May 2018, respectively, the FDA granted VYNDAQEL Fast Track and

Breakthrough Therapy designations for ATTR-CM. In November 2018, the FDA granted Priority Review for the new drug application (NDA) for VYNDAQEL.

In March 2019, the Ministry of Labor Health and Welfare in Japan approved VYNDAQEL, under SAKIGAKE designation, for patients with wild-type and variant forms of ATTR-CM. Regulatory submissions for the use of VYNDAQEL in patients with ATTR-CM have been submitted to the European Medicines Agency (EMA) and are under review.

VYNDAQEL was first approved in 2011 in the EU for the treatment of transthyretin amyloid polyneuropathy (ATTR-PN), in adult patients with early-stage symptomatic polyneuropathy to delay peripheral neurologic impairment. ATTR-PN is a neurodegenerative form of amyloidosis that leads to sensory loss, pain and weakness in the lower limbs and impairment of the autonomic nervous system, Currently, it is approved for ATTR-PN in 40 countries, including Japan, countries in Europe, Brazil, Mexico, Argentina, Israel, Russia, and South Korea. VYNDAQEL and VYNDAMAX are not approved for the treatment of ATTR-PN in the U.S.

**VYNDAQEL (tafamidis meglumine) and VYNDAMAX (tafamidis) 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.

**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 May 6, 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 Pfizer's rare disease portfolio, VYNDAQEL (tafamidis meglumine) and VYNDAMAX (tafamidis) and approvals in the U.S. for the treatment of adults with ATTR-CM, 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, uncertainties regarding the commercial success of VYNDAQEL and VYNDAMAX; 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 VYNDAQEL and VYNDAMAX; whether and when the pending applications with the EMA and whether and when regulatory authorities in any other jurisdictions where applications for VYNDAQEL and VYNDAMAX may be pending or filed 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 VYNDAQEL and VYNDAMAX 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 VYNDAQEL and VYNDAMAX; 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.*

*Free medicines from Pfizer are provided through the Pfizer Patient Assistance Foundation™. The Pfizer Patient Assistance Foundation is a separate legal entity from Pfizer Inc. with distinct legal restrictions.

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