# Pfizer’s VYNDAQEL®/VYNDAMAX® Reduced the Risk of All-Cause Mortality by 41% Among Patients with Transthyretin Amyloid Cardiomyopathy, Five-Year Follow-Up Data Demonstrate

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-- Post-hoc, interim analysis published in Circulation: Heart Failure evaluated patients who received continuous treatment with VYNDAQEL/VYNDAMAX compared to those who first received placebo in ATTR-ACT --

NEW YORK--(BUSINESS WIRE)-- Pfizer Inc. (NYSE: PFE) announced today the publication of a post-hoc, interim analysis showing that treatment with VYNDAQEL® (tafamidis meglumine) / VYNDAMAX® (tafamidis) provided a clinically significant survival benefit at five years for patients with transthyretin amyloid cardiomyopathy (ATTR-CM). This analysis from the Phase 3 Transthyretin Amyloid Cardiomyopathy Clinical Trial (ATTR-ACT) and its long-term extension (LTE) study was published in Circulation: Heart Failure.

In ATTR-ACT, patients were randomized to receive VYNDAQEL 80 mg, 20 mg or placebo, and upon study completion at 30 months could enroll in the LTE study. In the LTE study, patients who had been treated with VYNDAQEL 80 mg continued this therapy, then transitioned to the bioequivalent single-capsule VYNDAMAX. Patients treated with placebo in ATTR-ACT were randomized to receive either VYNDAQEL 80 mg or 20 mg in the LTE

study and were subsequently transitioned to VYNDAMAX. VYNDAMAX 61 mg is bioequivalent to VYNDAQEL 80 mg but is not interchangeable on a per-mg basis.

“The results from this analysis build upon the positive primary results from the pivotal trial, ATTR-ACT, and reinforce that VYNDAQEL and VYNDAMAX have the potential to significantly extend survival for patients with ATTR-CM,” said Brenda Cooperstone, M.D., Chief Development Officer, Rare Disease, Pfizer Global Product Development. “VYNDAQEL and VYNDAMAX represent a breakthrough for these patients who have no other approved medicines and the ATTR-ACT and the LTE study demonstrate that earlier treatment is crucial for patients with ATTR-CM.”

In ATTR-ACT, treatment with VYNDAQEL demonstrated a 30% reduction in mortality at 30 months compared to placebo. With a median follow up of nearly five years, the analysis published in Circulation: Heart Failure showed a clinically significant 41% reduction in the risk of all-cause mortality among patients who received continuous VYNDAQEL/VYNDAMAX treatment (median follow up 58.5 months) compared to patients who first received placebo in ATTR-ACT before transitioning to VYNDAQEL/VYNDAMAX in the LTE (median follow up 57.1 months; HR: 0.59; 95% CI: 0.44–0.79; P<0.001). Median survival was 67 months (95% CI: 47.0–N/E) in the continuous treatment arm compared to 35.8 months (95% CI: 29.7–41.1) in the placebo to treatment arm. The preliminary five-year survival rate was 53.2% in the continuous treatment arm versus 32.4% in the placebo to treatment arm.

“The survival benefit seen in the primary analysis is further supported by these long-term results, emphasizing the importance of early diagnosis and treatment with VYNDAQEL/VYNDAMAX for patients living with ATTR-CM,” said Perry Elliott, M.D., Professor of Cardiovascular Medicine, Director of the Institute for Cardiovascular Science, University College London and lead author of the analysis. “While there has been progress in the diagnosis of ATTR-CM due to increased awareness and improvements in diagnostic approaches, the condition is still overlooked, preventing patients from benefiting from disease modifying treatment.”

Reduction in mortality was consistent across all sub-groups, including wild-type and hereditary ATTR-CM with a 39% reduction in the risk of all-cause mortality in patients with wild-type ATTR-CM (HR: 0.61; 95% CI: 0.43–0.87; P=0.006), and a 43% reduction in patients with hereditary ATTR-CM (HR: 0.57; 95% CI: 0.33–0.99; P=0.05) in patients receiving continuous VYNDAQEL/VYNDAMAX treatment, compared with the placebo to treatment arm. In addition, the analysis demonstrated a 44% reduction in the risk of all-cause mortality in patients with baseline NYHA class I or II (HR: 0.56; 95% CI: 0.38–0.82;

P=0.003), and a 35% reduction in patients with baseline NYHA class III (HR: 0.65; 95% CI: 0.41–1.01; P=0.06) in the continuous treatment arm compared with the placebo to treatment arm. In ATTR-ACT, VYNDAQEL had a safety profile comparable to placebo. No new safety concerns were identified throughout the LTE study and adverse events remained similar to placebo.

VYNDAQEL and VYNDAMAX are indicated for the treatment of the cardiomyopathy of wild-type or hereditary transthyretin-mediated amyloidosis in adults to reduce cardiovascular mortality and cardiovascular-related hospitalization. They are the first and only medicines approved for the treatment of wild-type and hereditary ATTR-CM, which is underrecognized and underdiagnosed in patients with heart failure. This rare, progressive and life-threatening disease is caused by unstable transthyretin proteins that misfold and aggregate into amyloid fibrils that can build up in the heart and other parts of the body. The buildup of transthyretin amyloid in the heart causes the heart muscle to stiffen over time, eventually leading to heart failure. Once diagnosed, the median life expectancy in untreated patients with ATTR-CM is approximately two to 3.5 years.

About ATTR-ACT and the Long-Term Extension The Phase 3 study, ATTR-ACT, is the first and only completed global, double-blind, randomized, placebo-controlled clinical trial to investigate a pharmacologic therapy for the treatment of ATTR-CM in both hereditary and wild-type ATTR-CM. The primary analysis of the study, which compared a pooled VYNDAQEL (80 mg and 20 mg) treatment group to placebo, demonstrated a significant reduction in the hierarchical combination of all-cause mortality and frequency of cardiovascular-related hospitalizations compared to placebo over a 30-month period in patients with wild-type or hereditary ATTR-CM (p=0.0006), the study’s primary endpoint. 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.

Patients who completed ATTR-ACT were eligible to enroll in the long-term extension (LTE) study for up to 60 months. The LTE is an open-label study that was initially designed to obtain additional safety data for VYNDAQEL 20 mg or 80 mg in subjects diagnosed with ATTR-CM, and to continue to provide patients originally enrolled in ATTR-ACT with VYNDAQEL until local availability. The LTE protocol was amended to transition patients treated with VYNDAQEL 20 mg or 80 mg to single-capsule VYNDAMAX 61 mg. A single VYNDAMAX 61 mg capsule is bioequivalent to VYNDAQEL 80 mg (four 20 mg capsules) and is not interchangeable on a per-mg basis.

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. A single VYNDAMAX 61 mg capsule is bioequivalent to VYNDAQEL 80 mg (four 20 mg capsules) and is not interchangeable on a per-mg basis.

Tafamidis is approved for the treatment of ATTR-CM over 55 countries including the US, EU, Brazil, UAE and Canada, among others. VYNDAMAX 61 mg and VYNDAQEL 80 mg are the only U.S. Food and Drug Administration approved doses for the treatment of ATTR-CM.

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 over 40 countries, including Japan, countries in Europe, Brazil, Mexico, Argentina, Israel, Russia, and South Korea. VYNDAQEL and VYNDAMAX are not approved for ATTR-PN in the US.

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.

About 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 rare hematologic, neurologic, cardiac 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.

About Pfizer: 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 170 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 20, 2021. 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 meglumine) and VYNDAMAX (tafamidis), 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, uncertainties regarding the commercial success of VYNDAQEL/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 or VYNDAMAX; whether and when regulatory authorities in any other jurisdictions where applications for VYNDAQEL or VYNDAMAX may be pending or filed for the treatment of wild-type or hereditary transthyretin amyloidosis in adult patients with cardiomyopathy (ATTR-CM) or any other potential indications for VYNDAQEL or VYNDAMAX 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 or 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 or VYNDAMAX; the impact of COVID-19 on our business, operations and financial results; 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, 2020 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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