US FDA Accepts Regulatory Submissions for Review of Tafamidis to Treat Transthyretin Amyloid Cardiomyopathy

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—FDA grants a Priority Review based on Phase 3 ATTR-ACT study findings in ATTR-CM—

Pfizer Inc. (NYSE: PFE) announced today that the US Food and Drug Administration (FDA) accepted for filing the company's New Drug Applications (NDAs) for tafamidis for the treatment of transthyretin amyloid cardiomyopathy (ATTR-CM). Pfizer has submitted two NDAs based on two forms of tafamidis: meglumine salt and free acid. Tafamidis is the only product to complete a Phase 3 trial evaluating its efficacy, safety, and tolerability in patients with ATTR-CM, a rare, fatal, and underdiagnosed condition.1,2

The tafamidis meglumine form (20 mg capsule) has been granted Priority Review. The FDA grants Priority Review to medicines that may offer significant advances in treatment or may provide a treatment where no adequate therapy exists. The target Prescription Drug User Fee Act (PDUFA) action date for a decision by the FDA is in July 2019.

The tafamidis free acid form (61 mg capsule) will be under Standard Review. This form is bioequivalent to the 80 mg tafamidis meglumine dose, which was administered as four 20 mg capsules in the pivotal trial; it was developed for patient convenience to enable a single capsule for daily administration. The target PDUFA action date for a decision by the FDA is in November 2019.

"The diagnosis of ATTR-CM is often delayed, primarily because disease awareness is low and patients often present with symptoms similar to more common causes of heart failure. In fact, we believe less than one percent of patients living with this disease are

currently diagnosed," said Brenda Cooperstone MD, Senior Vice President and Chief Development Officer, Rare Disease, Pfizer Global Product Development. "The FDA's filing acceptance is an encouraging step toward our goal of further raising awareness and providing a treatment option for ATTR-CM patients who are in desperate need of an approved pharmacologic therapy. We look forward to working with the FDA to bring the first treatment for this deadly disease to patients."

The submission is based on findings from the pivotal Phase 3 Transthyretin Amyloid Cardiomyopathy (ATTR-ACT) study, which evaluated the efficacy, safety, and tolerability of tafamidis meglumine compared to placebo for the treatment of patients with ATTR-CM. In the primary analysis of the study, tafamidis met the primary endpoint, demonstrating 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). Tafamidis was well tolerated, with an observed safety profile comparable to placebo.3 The 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. Results from additional sub-group analyses were presented during the Late Breaking Clinical Trials session at the Heart Failure Society of America 22nd Annual Scientific Meeting in Nashville, TN, in September 2018. For more information on the ATTR-ACT trial, go to www.clinicaltrials.gov.

About Tafamidis3

Tafamidis is an oral, investigational product being evaluated as a potential treatment for ATTR-CM. Tafamidis is a small molecule that selectively binds at specific sites on the transthyretin tetramer to prevent destabilization of the transthyretin transport protein and formation of amyloid that causes ATTR-CM. Tafamidis is not approved for any use in the United States.

Tafamidis was granted Orphan Drug Designation for ATTR-CM in both the EU and US in 2012 and in Japan in 2018. In June 2017 and May 2018, respectively, the FDA granted tafamidis Fast Track and Breakthrough Therapy designations for ATTR-CM. In November 2018, the FDA granted Priority Review designation for the NDA for tafamidis meglumine. Additionally, in March 2018, the Ministry of Labor Health and Welfare in Japan granted SAKIGAKE designation to tafamidis for this indication. Following the SAKIGAKE designation, a regulatory marketing application for tafamidis for ATTR-CM was submitted to the Pharmaceuticals and Medical Devices Agency (PMDA) in November 2018.

About the ATTR-ACT Study[3]

ATTR-ACT is a Phase 3 international, multicenter, double-blind, placebo-controlled, randomized, 3-arm clinical study in 441 patients with ATTR-CM that investigated the efficacy, safety, and tolerability of an oral daily dose of 20 mg or 80 mg tafamidis meglumine compared to placebo. The study included both patients with the hereditary form of the disease, and those with wild-type form, which is not hereditary and may occur as people age. The primary analysis of the study, which compared a pooled tafamidis (80 mg and 20 mg) treatment group to placebo, was the hierarchical combination of all-cause mortality and frequency of cardiovascular-related hospitalizations over a 30-month period in patients with transthyretin amyloid cardiomyopathy.

About ATTR-CM

ATTR-CM is a rare and progressive disease caused by destabilization of a transport protein called transthyretin, which is composed of four identical subunits (a tetramer). In ATTR-CM, heart failure occurs when unstable tetramers dissociate, resulting in misfolded proteins that aggregate into amyloid fibrils and deposit predominantly in the heart.[1,2]

Pfizer Rare Disease

Rare disease includes some of the most serious of all illnesses and impacts millions of patients worldwide,[4] 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.[3]

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 January 14, 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 for tafamidis for the treatment of transthyretin amyloid 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 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; the risk that clinical trial data are subject to differing interpretations, and, even when we view data as sufficient to support the safety and/or effectiveness of a product candidate, regulatory authorities may not share our views and may require additional data or may deny approval altogether; 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 FDA and the PMDA may approve the pending applications for tafamidis for the Potential Indication and whether and when regulatory authorities in any such other jurisdictions where applications for

tafamidis may be pending (including the application pending with the FDA for the potential treatment of transthyretin familial amyloid polyneuropathy, for which the company received a complete response letter in 2012) or filed for the Potential Indication or any other potential indications for tafamidis 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, and, if approved, whether tafamidis will be commercially successful; decisions by regulatory authorities regarding labeling and 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, 2017 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 Maurer MS, Elliott P, Merlini G, et. al. Design and rationale of the phase 3 ATTR-ACT clinical trial (tafamidis in transthyretin cardiomyopathy clinical trial). Circ Heart Fail. 2017;10:1-7. 2 Rapezzi C, Quarta CC, Riva L, et al. Transthyretin-related amyloidoses and the heart: a clinical overview. Nat Rev Cardiol. 2010;7:398-408. 3 Data on file. Pfizer Inc. New York, NY. 4 Pfizer Inc. Rare disease. http://www.pfizer.com/health-and-wellness/health-topics/rare-diseases/areas-of-focus. Accessed January 11, 2019.

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