



Affymax and Takeda Announce FDA Approval of OMONTYS® (Peginesatide) Injection for the Treatment of Anemia Due to Chronic Kidney Disease (CKD) in Adult Patients on Dialysis

Only Once-Monthly ESA Treatment For Dialysis Patients To Be Made Available In The United States

PALO ALTO, Calif. & OSAKA, Japan--(BUSINESS WIRE)-- Affymax, Inc. (Nasdaq:AFFY) and Takeda Pharmaceutical Company Limited (TSE:4502), today announced that the U.S. Food and Drug Administration (FDA) approved OMONTYS® (peginesatide) Injection for the treatment of anemia due to chronic kidney disease (CKD) in adult patients on dialysis. OMONTYS is the only once-monthly erythropoiesis-stimulating agent (ESA) for anemia to be made available to the dialysis patient population in the United States.

The FDA's decision was based on a New Drug Application (NDA), which included results from two randomized, controlled, open-label, Phase 3 studies (EMERALD 1 and 2) that demonstrated the safety and efficacy of OMONTYS dosed once monthly, compared to epoetin dosed between one-to-three times per week (according to product labels), in maintaining hemoglobin (Hb) levels in anemic CKD patients on dialysis. In these studies, the most commonly reported adverse reactions were shortness of breath, diarrhea, nausea, cough and arteriovenous fistula site complication. The EMERALD studies were part of the largest clinical program to support the NDA of an ESA in the treatment of anemia in CKD. Enrolling 2,606 patients, including approximately 1,600 dialysis patients, the OMONTYS Phase 3 program was also the first to prospectively compare, in a head-to-head manner, the cardiovascular safety of different ESAs. Cardiovascular safety was evaluated based on a composite cardiovascular safety endpoint adjudicated by a blinded and independent committee. See below for Important Safety Information about OMONTYS, including Boxed Warnings as well as limitations of use.

In the approval action letter, the FDA outlined post-marketing requirements: an observational study and a randomized controlled trial to be completed with final reports submitted in 2018 and 2019, respectively. The objectives of the studies are to evaluate cardiovascular safety and assess safety of long-term use in adult patients on dialysis, in particular in the incident patient population. In addition, the post-marketing commitment includes the initiation of pediatric studies with target dates for completion between 2016 and 2027. Letters will be sent to nephrology healthcare providers as part of a Risk Evaluation and Mitigation Strategy (REMS) to inform them that OMONTYS is not indicated in patients with CKD not on dialysis. In two trials of OMONTYS, patients with CKD not on dialysis experienced increased specific cardiovascular events.

"The approval of OMONTYS now provides a therapeutic alternative to treat anemia of CKD in adult patients on dialysis, one of the most common complications affecting this patient population," said John Orwin, chief executive officer, Affymax. "For over two decades, doctors have relied primarily on one erythropoietin-based treatment in the dialysis setting. With OMONTYS, doctors and patients will have access to a once-monthly alternative for the treatment of anemia in adult CKD patients on dialysis."

"The FDA's approval of OMONTYS signifies an important milestone for the partnership between Takeda and Affymax as we fulfill our goal of providing an important new treatment option for the hundreds of thousands of CKD patients on dialysis who live with anemia," said Azmi Nabulsi, M.D., president, Takeda Global Research & Development Center, Inc. "OMONTYS is an example of our commitment to making treatment options available that accommodate the needs of evolving healthcare markets, such as the renal community."

Anemia (a condition in which blood has a lower than normal number of red blood cells) is a common complication in dialysis patients because their kidneys no longer produce enough erythropoietin, the hormone that stimulates red blood cell production in the body. According to the Centers for Medicaid and Medicare Services (CMS), nearly 95 percent of dialysis patients in the United States are being treated for anemia with ESAs. Until the approval of OMONTYS, ESAs were recombinant (genetically engineered) versions of endogenous erythropoietin (erythropoietin that is made in the patient's body) that are injected up to three times a week. OMONTYS is a synthetic, pegylated, peptide-based ESA that is dosed once monthly.

"For dialysis patients, anemia is another aspect of their challenging condition that must be addressed," said Brigitte Schiller, M.D., chief medical officer, Satellite Healthcare, Inc. "As a nephrologist who oversees the care of adult CKD patients on dialysis, I am glad to now have another option for the treatment of anemia."

Affymax Teleconference and Webcast

Affymax will host a teleconference and webcast at 11:45 a.m. Pacific Time; 2:45 p.m. Eastern Time today, Tuesday, March 27 to

further discuss the FDA approval of OMONTYS. Interested parties can listen to the live teleconference by dialing (866) 393-1565 from the U.S. or +1(973) 409-9608 for international callers. Individuals may access the live audio webcast by visiting www.affymax.com and going to the Investors section. A replay of the webcast will be available on the Company's website for 30 days following the live event.

About OMONTYS

OMONTYS[®] (peginesatide) Injection is a synthetic, pegylated, peptide-based ESA. It is the only ESA that is peptide-based and its building blocks (amino acids) are arranged in a different order than erythropoietin (i.e., it has no sequence homology to endogenous erythropoietin). OMONTYS was discovered by Affymax and will be co-commercialized in the United States by Affymax and Takeda. In February 2012, Takeda and its wholly-owned subsidiary, Takeda Global Research & Development Centre (Europe) Ltd., announced the acceptance of a Marketing Authorization Application for peginesatide by the European Medicines Agency. The application is currently under review by that agency.

The objective of the OMONTYS Phase 3 dialysis studies (EMERALD 1 and 2) was to evaluate the safety and efficacy of OMONTYS, dosed once monthly, compared to epoetin alfa or beta, dosed one-to-three times per week (according to the product labels), in maintaining Hb levels. The primary efficacy endpoint of these two studies was a mean change in Hb between baseline and evaluation period (between weeks 29 through 36) following entry into the study.

In the EMERALD studies, CKD patients on dialysis who were stable on epoetin were randomized to receive OMONTYS either once monthly or to continue treatment with epoetin.

For more information about OMONTYS, visit www.omontys.com.

About Anemia Due to CKD in Adult Patients on Dialysis

Anemia is a complication of CKD that is associated with cardiovascular illness and mortality. As of 2009, the United States Renal Data System noted there were nearly 400,000 people in the United States who were on dialysis.

INDICATION AND LIMITATIONS OF USE

OMONTYS[®] (peginesatide) Injection is indicated for the treatment of anemia due to chronic kidney disease (CKD) in adult patients on dialysis.

OMONTYS is not indicated and is not recommended for use in patients with CKD not on dialysis, in patients receiving treatment for cancer and whose anemia is not due to CKD, or as a substitute for red blood cell (RBC) transfusions in patients who require immediate correction of anemia. OMONTYS has not been shown to improve symptoms, physical functioning, or health-related quality of life.

IMPORTANT SAFETY INFORMATION

WARNING: ESAs INCREASE THE RISK OF DEATH, MYOCARDIAL INFARCTION, STROKE, VENOUS THROMBOEMBOLISM, THROMBOSIS OF VASCULAR ACCESS AND TUMOR PROGRESSION OR RECURRENCE.

Chronic Kidney Disease:

- **In controlled trials, patients experienced greater risks for death, serious adverse cardiovascular reactions, and stroke when administered erythropoiesis-stimulating agents (ESAs) to target a hemoglobin level of greater than 11 g/dL.**
- **No trial has identified a hemoglobin target level, ESA dose, or dosing strategy that does not increase these risks.**
- **Use the lowest OMONTYS dose sufficient to reduce the need for red blood cell (RBC) transfusions.**

Contraindications

OMONTYS is contraindicated in patients with uncontrolled hypertension.

Warnings and Precautions

Increased mortality, myocardial infarction, stroke, and thromboembolism:

- Using ESAs to target a hemoglobin level of greater than 11 g/dL increases the risk of serious adverse cardiovascular reactions and has not been shown to provide additional benefit. Use caution in patients with coexistent cardiovascular disease and stroke. Patients with CKD and an insufficient hemoglobin response to ESA therapy may be at even greater risk for cardiovascular reactions and mortality than other patients. A rate of hemoglobin rise of > 1 g/dL over 2 weeks may contribute to these risks
- In controlled clinical trials of ESAs in patients with cancer, increased risk for death and serious adverse cardiovascular reactions was observed. These adverse reactions included myocardial infarction and stroke
- In controlled clinical trials of ESAs, ESAs increased the risk of death in patients undergoing coronary artery bypass graft surgery (CABG) and deep venous thrombosis (DVT) in patients undergoing orthopedic procedures
- In 2 trials of OMONTYS, patients with CKD not on dialysis experienced increased specific cardiovascular events

Increased mortality and/or increased risk of tumor progression or recurrence in patients with cancer: The safety and efficacy of OMONTYS have not been established for use in patients with anemia due to cancer chemotherapy. OMONTYS is not indicated in patients with cancer receiving chemotherapy.

Hypertension: OMONTYS is contraindicated in patients with uncontrolled hypertension. Appropriately control hypertension prior to initiation of and during treatment with OMONTYS. Reduce or withhold OMONTYS if blood pressure becomes difficult to control. Advise patients of the importance of compliance with antihypertensive therapy and dietary restrictions.

Lack or loss of response to OMONTYS: For lack or loss of hemoglobin response to OMONTYS, initiate a search for causative factors. If typical causes of lack or loss of hemoglobin response are excluded, evaluate for antibodies to peginesatide.

Dialysis management: Patients receiving OMONTYS may require increased anticoagulation with heparin to prevent clotting of the extracorporeal circuit during hemodialysis.

Laboratory monitoring: Evaluate transferrin saturation and serum ferritin prior to and during OMONTYS treatment. Administer supplemental iron therapy when serum ferritin is less than 100 mcg/L or when serum transferrin saturation is less than 20%.

Adverse reactions

The most common adverse reactions in clinical studies in patients with CKD on dialysis treated with OMONTYS were dyspnea, diarrhea, nausea, cough, and arteriovenous fistula site complication.

Please click [here](#) for Full Prescribing Information, including Boxed WARNINGS, or visit www.omontys.com.

About Affymax, Inc.

Affymax, Inc. is a biopharmaceutical company committed to developing novel drugs to improve the treatment of serious and often life-threatening conditions. For additional information, please visit www.affymax.com.

This release contains forward-looking statements, including statements regarding the potential advantages of OMONTYS, the continuation and success of Affymax's collaboration with Takeda, the timing and scope of the OMONTYS post-marketing studies and Risk Evaluation and Mitigation Strategy (REMs) and the commercialization of OMONTYS. Affymax's actual results may differ materially from those indicated in these forward-looking statements due to risks and uncertainties, including risks relating to regulatory requirements, including post-marketing studies and REMs, in particular the FDA's interpretation and review of the data in the New Drug Application (NDA) including issues related to the subgroup analyses in non-dialysis, study design, the continued safety and efficacy of OMONTYS in clinical development, the timing of patient accrual in ongoing and planned clinical studies, research and development efforts, industry and competitive environment, additional studies that may be required by the FDA or other regulatory authorities, financing requirements and our ability to access capital and other matters that are described in Affymax's Annual Report on Form 10-K filed with the Securities and Exchange Commission. Investors are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date of this release. Affymax undertakes no obligation to update any forward-looking statement in this press release.

About Takeda Pharmaceutical Company Limited

Located in Osaka, Japan, Takeda is a research-based global company with its main focus on pharmaceuticals. As the largest pharmaceutical company in Japan and one of the global leaders of the industry, Takeda is committed to strive towards better health for patients worldwide through leading innovation in medicine. Additional information about Takeda is available through its corporate website, www.takeda.com.

About Takeda Pharmaceuticals U.S.A., Inc. and Takeda Global Research & Development Center, Inc.

Based in Deerfield, Ill., Takeda Pharmaceuticals U.S.A., Inc. and Takeda Global Research & Development Center, Inc. are subsidiaries of Takeda Pharmaceutical Company Limited, the largest pharmaceutical company in Japan. The respective companies currently market oral diabetes, insomnia, rheumatology, gastroenterology and cardiovascular disease treatments and seek to bring innovative products to patients through a pipeline that includes compounds in development for diabetes, gastroenterology, neurology and other conditions. To learn more about these Takeda companies, visit www.tpna.com.

This press release contains forward-looking statements. Forward-looking statements include statements regarding Takeda's plans, outlook, strategies, results for the future, and other statements that are not descriptions of historical facts. Forward-looking statements may be identified by the use of forward-looking words such as "may," "believe," "will," "expect," "project," "estimate," "should," "anticipate," "plan," "assume," "continue," "seek," "pro forma," "potential," "target," "forecast," "guidance," "outlook" or "intend" or other similar words or expressions of the negative thereof. Forward-looking statements are based on estimates and assumptions made by management that are believed to be reasonable, though they are inherently uncertain and difficult to predict. Investors are cautioned not to unduly rely on such forward-looking statements.

Forward-looking statements involve risks and uncertainties that could cause actual results or experience to differ materially from that expressed or implied by the forward-looking statements. Some of these risks and uncertainties include, but are not limited to, (1) the economic circumstances surrounding Takeda's business, including general economic conditions in Japan, the United States and worldwide; (2) competitive pressures and developments; (3) applicable laws and regulations; (4) the success or failure of product development programs; (5) actions of regulatory authorities and the timing thereof; (6) changes in exchange rates; (7) claims or concerns regarding the safety or efficacy of marketed products or product candidates in development; and (8) integration activities with acquired companies.

The forward-looking statements contained in this press release speak only as of the date of this press release, and Takeda undertakes no obligation to revise or update any forward-looking statements to reflect new information, future events or circumstances after the date of the forward-looking statement. If Takeda does update or correct one or more of these statements, investors and others should not conclude that Takeda will make additional updates or corrections.

Photos/Multimedia Gallery Available: <http://www.businesswire.com/cgi-bin/mmg.cgi?eid=50219545&lang=en>

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