European Commission Approves Parsabiv™ (etelcalcetide) For The Treatment Of Secondary Hyperparathyroidism In Adults On Hemodialysis

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First Treatment Advance for Secondary Hyperparathyroidism in More Than a Decade and First Intravenous Calcimimetic to Help Healthcare Providers Lower Key Lab Values

THOUSAND OAKS, Calif., Nov. 11, 2016 /PRNewswire/ -- Amgen (NASDAQ:AMGN) today announced that the European Commission (EC) has granted marketing authorization for Parsabiv™ (etelcalcetide) for the treatment of secondary hyperparathyroidism (sHPT) in adult patients with chronic kidney disease (CKD) on hemodialysis. Parsabiv is the first calcimimetic agent that can be administered intravenously by a healthcare provider three times a week at the end of a hemodialysis session.

"Keeping relevant lab values in recommended target ranges is an important part of managing sHPT, a chronic and complex disease with an already complicated medication regimen for many patients," said John Cunningham, M.D., professor of nephrology at University College London Medical School. "Treatment failures are quite common and Parsabiv provides a new tool that should give physicians more confidence that patients are getting the medication they need to treat their sHPT."

The EC approved Parsabiv based on three Phase 3 studies, all of which met their primary endpoints, including two pooled placebo-controlled trials in more than 1,000 patients, and a head-to-head study with cinacalcet. Additionally, etelcalcetide was superior to cinacalcet for the secondary endpoints of proportion of patients achieving greater than 30 percent and greater than 50 percent reduction in mean parathyroid hormone (PTH) during the Efficacy Assessment Phase (EAP) compared with baseline.

"Treatment adherence can be a challenge with any oral medicine," said Sean E. Harper, M.D., executive vice president of Research and Development at Amgen. "If poorly controlled, sHPT may progress and can have significant clinical consequences. With Parsabiv, we can put the delivery of the therapy in the hands of the healthcare provider and help ensure that these patients receive this important treatment as part of their dialysis session three times a week."

Approval from the EC grants a centralized marketing authorization with unified labeling in the 28 countries that are members of the EU. Norway, Iceland and Liechtenstein, as members of the European Economic Area (EEA), will take corresponding decisions on the basis of the decision of the EC.

About Secondary Hyperparathyroidism (sHPT)

sHPT is a chronic and serious condition which affects many of the approximately two million people throughout the world who are receiving dialysis.[1,2] In Europe, the prevalence of sHPT within dialysis populations ranges from 30 to 49 percent.[3] Approximately 88 percent of dialysis patients and 79 percent of patients on hemodialysis will develop sHPT.[4] sHPT refers to the excessive secretion of parathyroid hormone (PTH) by the parathyroid glands in response to decreased renal function and impaired mineral metabolism.[1] The elevated levels of PTH can lead to an increase in the release of calcium and phosphorus from the bones.[5] sHPT is often initially silent and asymptomatic.[1] As a result, sHPT is frequently underdiagnosed and undertreated.[1,6]

About Parsabiv™ (etelcalcetide)

Parsabiv is a novel calcimimetic agent indicated for the treatment of secondary hyperparathyroidism (sHPT) in adult patients with chronic kidney disease (CKD) on hemodialysis therapy. A calcimimetic is a drug that mimics the action of calcium by activating the calcium-sensing receptors on the parathyroid gland. Parsabiv binds to and activates the calcium-sensing receptor on the parathyroid gland, thereby decreasing PTH levels.

Important Safety Information

Contraindications: Hypersensitivity to the active substance or to any of the excipients. Parsabiv should not be initiated if corrected serum calcium is less than the lower limit of the normal range.

Special Warnings and Precautions:

Hypocalcaemia: Since etelcalcetide lowers serum calcium, patients should be advised to seek medical attention if they experience symptoms of hypocalcaemia and should be monitored for the occurrence of hypocalcaemia. Serum calcium levels should be measured prior to initiating treatment, within 1 week of initiation or dose adjustment of Parsabiv and every 4 weeks during treatment. Potential manifestations of hypocalcaemia include paraesthesias, myalgias, muscle spasm and seizures. Decreases in serum calcium can prolong the QT interval, potentially resulting in ventricular arrhythmia. The threshold for seizures may be lowered by significant reductions in serum calcium levels.

Worsening heart failure: Decreased myocardial performance, hypotension, and congestive heart failure may be associated with significant reductions in serum calcium levels.

Co-administration with other medicinal products

Administer Parsabiv with caution in patients receiving any other medicinal products known to lower serum calcium. Patients receiving Parsabiv should not be given cinacalcet. Concurrent administration may result in severe hypocalcaemia.

Interactions: No interaction studies have been performed. There is no known risk of pharmacokinetic interaction with Parsabiv.

Fertility, Pregnancy and Lactation: There are no or limited amount of data from the use of Parsabiv in pregnant women. Animal studies do not

indicate direct or indirect harmful effects with respect to reproductive toxicity. As a precautionary measure, it is preferable to avoid the use of Parsabiv during pregnancy. A risk to breastfed newborns/infants cannot be excluded. A decision must be made whether to discontinue breast-feeding or discontinue/abstain from Parsabiv therapy taking into account the benefit of breast-feeding for the child and the benefit of therapy for the woman. No data are available on the effect of etelcalcetide on human fertility. Animal studies do not indicate direct or indirect harmful effects with respect to fertility.

Undesirable Effects: The following common (≥10%) adverse reactions have been reported in pivotal, controlled clinical studies: decreases in serum calcium, diarrhoea, nausea, vomiting, and muscle spasms.

Pharmaceutical Precautions: Store in a refrigerator (2 degrees C – 8 degrees C). Once removed from the refrigerator, Parsabiv must be used within 7 days if stored in the original carton.

About Mimpara® (cinacalcet)

Mimpara® (cinacalcet) is the first oral calcimimetic agent approved by the European Medicines Agency for the treatment of sHPT in patients with CKD on dialysis. The therapy is also approved in the EU for the treatment of hypercalcemia in patients with parathyroid carcinoma and hypercalcemia in adult patients with primary HPT for whom parathyroidectomy would be indicated on the basis of serum calcium levels (as defined by relevant treatment guidelines), but in whom parathyroidectomy is not clinically appropriate or is contraindicated. Mimpara binds to the calcium-sensing receptor, resulting in a drop in PTH levels by inhibiting PTH synthesis and secretion. In addition, the reductions in PTH lower serum calcium and phosphorus levels.

Important Safety Information

Contraindications: Hypersensitivity to the active substance or to any of the excipients

Special Warnings and Precautions:

Serum Calcium:

Mimpara treatment should not be initiated in patients with a serum calcium below the lower limit of the normal range. Life threatening events and fatal outcomes associated with hypocalcaemia have been reported in adult and paediatric patients treated with Mimpara. Manifestations of hypocalcaemia may include paraesthesias, myalgias, cramping, tetany and convulsions. Decreases in serum calcium can also prolong the QT interval, potentially resulting in ventricular arrhythmia secondary to hypocalcaemia. The threshold for seizures is lowered by significant reductions in serum calcium levels. Patients should be monitored carefully for the occurrence of hypocalcaemia. Serum calcium should be measured within 1 week after initiation or dose adjustment of Mimpara. Once the maintenance dose has been established, serum calcium should be measured approximately monthly.

Hypotension and/or worsening heart failure: In post-marketing safety surveillance, isolated, idiosyncratic cases of hypotension and/or worsening heart failure have been reported in patients with impaired cardiac function, in which a causal relationship to cinacalcet could not be completely excluded and may be mediated by reductions in serum calcium levels.

Hepatic impairment:

Due to the potential for 2 to 4 fold higher plasma levels of cinacalcet in patients with moderate to severe hepatic impairment, Mimpara should be used with caution in these patients and treatment should be closely monitored

In the treatment of secondary hyperparathyroidism the most commonly reported adverse reactions in clinical trials were nausea and vomiting.

To see the full Mimpara Safety Information, visit http://www.ema.europa.eu

About Amgen

Amgen is committed to unlocking the potential of biology for patients suffering from serious illnesses by discovering, developing, manufacturing and delivering innovative human therapeutics. This approach begins by using tools like advanced human genetics to unravel the complexities of disease and understand the fundamentals of human biology.

Amgen focuses on areas of high unmet medical need and leverages its expertise to strive for solutions that improve health outcomes and dramatically improve people's lives. A biotechnology pioneer since 1980, Amgen has grown to be one of the world's leading independent biotechnology companies, has reached millions of patients around the world and is developing a pipeline of medicines with breakaway potential.

For more information, visit www.amgen.com and follow us on www.twitter.com/amgen.

Forward-Looking Statements

This news release contains forward-looking statements that are based on the current expectations and beliefs of Amgen. All statements, other than statements of historical fact, are statements that could be deemed forward-looking statements, including estimates of revenues, operating margins, capital expenditures, cash, other financial metrics, expected legal, arbitration, political, regulatory or clinical results or practices, customer and prescriber patterns or practices, reimbursement activities and outcomes and other such estimates and results. Forward-looking statements involve significant risks and uncertainties, including those discussed below and more fully described in the Securities and Exchange Commission reports filed by Amgen, including our most recent annual report on Form 10-K and any subsequent periodic reports on Form 10-Q and Form 8-K. Unless otherwise noted, Amgen is providing this information as of the date of this news release and does not undertake any obligation to update any forward-looking statements contained in this document as a result of new information, future events or otherwise.

No forward-looking statement can be guaranteed and actual results may differ materially from those we project. Discovery or identification of new product candidates or development of new indications for existing products cannot be guaranteed and movement from concept to product is uncertain; consequently, there can be no guarantee that any particular product candidate or development of a new indication for an existing product will be successful and become a commercial product. Further, preclinical results do not guarantee safe and effective performance of product candidates in humans. The complexity of the human body cannot be perfectly, or sometimes, even adequately modeled by computer or cell culture systems or animal models. The length of time that it takes for us to complete clinical trials and obtain regulatory approval for product marketing has in the past

varied and we expect similar variability in the future. Even when clinical trials are successful, regulatory authorities may question the sufficiency for approval of the trial endpoints we have selected. We develop product candidates internally and through licensing collaborations, partnerships and joint ventures. Product candidates that are derived from relationships may be subject to disputes between the parties or may prove to be not as effective or as safe as we may have believed at the time of entering into such relationship. Also, we or others could identify safety, side effects or manufacturing problems with our products after they are on the market.

Our results may be affected by our ability to successfully market both new and existing products domestically and internationally, clinical and regulatory developments involving current and future products, sales growth of recently launched products, competition from other products including biosimilars, difficulties or delays in manufacturing our products and global economic conditions. In addition, sales of our products are affected by pricing pressure, political and public scrutiny and reimbursement policies imposed by third-party payers, including governments, private insurance plans and managed care providers and may be affected by regulatory, clinical and guideline developments and domestic and international trends toward managed care and healthcare cost containment. Furthermore, our research, testing, pricing, marketing and other operations are subject to extensive regulation by domestic and foreign government regulatory authorities. We or others could identify safety, side effects or manufacturing problems with our products after they are on the market. Our business may be impacted by government investigations, litigation and product liability claims. In addition, our business may be impacted by the adoption of new tax legislation or exposure to additional tax liabilities. If we fail to meet the compliance obligations in the corporate integrity agreement between us and the U.S. government, we could become subject to significant sanctions. Further, while we routinely obtain patents for our products and technology, the protection offered by our patents and patent applications may be challenged, invalidated or circumvented by our competitors, or we may fail to prevail in present and future intellectual property litigation. We perform a substantial amount of our commercial manufacturing activities at a few key facilities and also depend on third parties for a portion of our manufacturing activities, and limits on supply may constrain sales of certain of our current products and product candidate development. In addition, we compete with other companies with respect to many of our marketed products as well as for the discovery and development of new products. Further, some raw materials, medical devices and component parts for our products are supplied by sole third-party suppliers. The discovery of significant problems with a product similar to one of our products that implicate an entire class of products could have a material adverse effect on sales of the affected products and on our business and results of operations. Our efforts to acquire other companies or products and to integrate the operations of companies we have acquired may not be successful. We may not be able to access the capital and credit markets on terms that are favorable to us, or at all. We are increasingly dependent on information technology systems, infrastructure and data security. Our stock price is volatile and may be affected by a number of events. Our business performance could affect or limit the ability of our Board of Directors to declare a dividend or our ability to pay a dividend or repurchase our common stock.

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