European Commission Approves Expanded Use Of Mimpara® (Cinacalcet) For The Treatment Of Secondary Hyperparathyroidism In Children With End-Stage Renal Disease On Dialysis

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THOUSAND OAKS, Calif., Aug. 31, 2017 /PRNewswire/ -- Amgen (NASDAQ:AMGN) today announced that the European Commission (EC) has granted Marketing Authorization of a pediatric formulation (granules in capsule for opening) of Mimpara® (cinacalcet) for the treatment of secondary hyperparathyroidism (HPT) in children aged three years and older with end-stage renal disease (ESRD) on maintenance dialysis therapy in whom secondary HPT is not adequately controlled with standard of care therapy.

"Secondary HPT is a serious and complex condition, and there are currently limited treatment options available for pediatric patients living with this disease," said Sean E. Harper, M.D., executive vice president of Research and Development at Amgen. "We are pleased with today's approval and the opportunity to provide patients and health care providers with an important therapy."

The EC approved Mimpara based on studies Amgen began in 2007 to assess the use of Mimpara in pediatric patients with secondary HPT, who have very few treatment options.

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
Secondary hyperparathyroidism (HPT) is a chronic and serious condition which affects many of the approximately two million people throughout the world who are receiving dialysis.[1,2] It occurs in both adults and children. Approximately 88 percent of chronic kidney disease (CKD) patients on hemodialysis will develop secondary HPT.[3] Secondary HPT 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 phosphate from the bone.[4,5] Secondary HPT is often initially silent and asymptomatic. As a result, secondary HPT is frequently underdiagnosed and undertreated.[6]

About Mimpara® (cinacalcet)
Mimpara® (cinacalcet) was originally approved in the EU in 2004 and is the first oral calcimimetic agent approved by the EC for the treatment of secondary HPT in patients with ESRD on maintenance dialysis therapy. The therapy is also approved in the EU for the reduction of hypercalcemia in adult patients with parathyroid carcinoma and 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
- Hypocalcaemia

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. Cases of QT prolongation and ventricular arrhythmia have been reported in patients treated with cinacalcet. 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 in adults. Once the maintenance dose has been established, serum calcium should be measured approximately monthly.

For pediatric patients, closely monitor serum calcium levels and patient compliance during treatment with Mimpara. Do not initiate cinacalcet or increase the dose if non-compliance is suspected. Prior to initiating cinacalcet and during treatment, consider the risks and benefits of treatment and the ability of the patient to comply with the recommendations to monitor and manage the risk of hypocalcaemia. Inform pediatric patients and/or their caregivers about the symptoms of hypocalcaemia and about the importance of adherence to instructions about serum calcium monitoring, and posology and method of administration. Serum calcium should be measured within 1 week after initiation or dose adjustment of Mimpara and weekly once the maintenance dose has been established in pediatric patients.

Seizures: Cases of seizures have been reported in patients treated with Mimpara. The threshold for seizures is lowered by significant reductions in serum calcium levels. Therefore, serum calcium levels should be closely monitored in patients receiving Mimpara, particularly in patients with a history of a seizure disorder.

Hypotension and/or worsening heart failure: 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.

Co-administration with other medicinal products: Administer Mimpara with caution in patients receiving any other medicinal products known to lower serum calcium. Closely monitor serum calcium. Patients receiving Mimpara should not be given etelcalcetide. Concurrent administration may result in

severe hypocalcaemia.

General: Adynamic bone disease may develop if PTH levels are chronically suppressed below approximately 1.5 times the upper limit of normal with the iPTH assay. If PTH levels decrease below the recommended target range in patients treated with Mimpara, the dose of Mimpara and/or vitamin D sterols should be reduced or therapy discontinued.

Testosterone levels: Testosterone levels are often below the normal range in patients with end-stage renal disease. The clinical significance of these reductions in serum testosterone is unknown.

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.

Lactose: Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.
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 ema.europa.eu

About Sensipar® (cinacalcet) in the U.S.
Sensipar is the first oral calcimimetic agent approved by the FDA for the treatment of secondary HPT in adult patients with CKD on dialysis. Sensipar is not indicated for use in adult patients with CKD who are not on dialysis because of an increased risk of hypocalcemia. The therapy is also approved in the U.S. for treatment of hypercalcemia in adult 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, but who are unable to undergo parathyroidectomy. Sensipar binds to the calcium-sensing receptor, resulting in a drop in parathyroid hormone (PTH) levels by inhibiting PTH synthesis and secretion. The reduction in PTH is associated with a concomitant decrease in serum calcium levels. Sensipar is not indicated for use in pediatric patients (patients less than 18 years of age).

Sensipar Important Safety Information in the U.S.
Contraindication: Sensipar® (cinacalcet) treatment initiation is contraindicated if serum calcium is less than the lower limit of the normal range (8.4 mg/dL).

Hypocalcemia: Sensipar® lowers serum calcium and can lead to hypocalcemia. Life threatening events and fatal outcomes associated with hypocalcemia have been reported in patients treated with Sensipar®, including pediatric patients. The safety and effectiveness of Sensipar® have not been established in pediatric patients.

Decreases in serum calcium can prolong the QT interval, potentially resulting in ventricular arrhythmia. Cases of QT prolongation and ventricular arrhythmia have been reported in patients treated with Sensipar®. Patients with conditions that predispose to QT interval prolongation and ventricular arrhythmia may be at increased risk for QT interval prolongation and ventricular arrhythmias if they develop hypocalcemia due to Sensipar®. Closely monitor corrected serum calcium and QT interval in patients at risk receiving Sensipar®.

Significant reductions in calcium may lower the threshold for seizures. Monitor serum calcium levels in patients with seizure disorders on Sensipar®.

Concurrent administration of Sensipar® with calcium-lowering drugs including other calcimimetics could result in severe hypocalcemia. Parsabiv™ (etelcalcetide) and Sensipar® should not be given together. Closely monitor serum calcium in patients receiving Sensipar® and concomitant therapies known to lower serum calcium levels.

Patients with secondary HPT: Serum calcium and serum phosphorus should be measured within 1 week and PTH should be measured 1 to 4 weeks after initiation or dose adjustment of Sensipar®. Once the maintenance dose has been established, serum calcium and serum phosphorus should be measured approximately monthly, and PTH every 1 to 3 months.

Patients with primary HPT or parathyroid carcinoma: Serum calcium should be measured within 1 week after initiation or dose adjustment of Sensipar®. Once maintenance dose levels have been established, serum calcium should be measured every 2 months.

Upper Gastrointestinal Bleeding: Cases of gastrointestinal (GI) bleeding, mostly upper GI bleeding, have occurred in patients using calcimimetics, including Sensipar®, from postmarketing and clinical trial sources. The exact cause of GI bleeding in these patients is unknown.

Patients with risk factors for upper GI bleeding, such as known gastritis, esophagitis, ulcers or severe vomiting, may be at increased risk for GI bleeding with Sensipar®. Monitor patients for worsening of common Sensipar® GI adverse reactions and for signs and symptoms of GI bleeding and ulcerations during Sensipar® therapy.

Hypotension, Worsening Heart Failure and/or Arrhythmias: In Sensipar® postmarketing use, isolated, idiosyncratic cases of hypotension, worsening heart failure, and/or arrhythmia were reported in patients with impaired cardiac function. The causal relationship to Sensipar® therapy could not be completely excluded and may be mediated by reductions in serum calcium levels.

Adynamic Bone: Adynamic bone disease may develop if intact parathyroid hormone (iPTH) levels are suppressed below 100 pg/mL.

Adverse Reactions: In clinical trials of patients with secondary HPT comparing Sensipar® to placebo, the most commonly reported side effects were nausea (31 percent vs. 19 percent), vomiting (27 percent vs. 15 percent), and diarrhea (21 percent vs. 20 percent). In clinical trials of patients with primary HPT and parathyroid carcinoma treated with Sensipar®, the most commonly reported side effects were nausea (63 percent), vomiting (46 percent), and paresthesia (20 percent).

Please see Sensipar® **Full Prescribing Information**.

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 current reports on 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. 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. Discovery or identification of new product candidates cannot be guaranteed and movement from concept to product is uncertain; consequently, there can be no guarantee that any particular product candidate will be successful and become a commercial product. Further, some raw materials, medical devices and component parts for our products are supplied by sole third-party suppliers. Certain of our distributors, customers and payers have substantial purchasing leverage in their dealings with us. 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.

The scientific information discussed in this news release relating to new indications is preliminary and investigative and is not part of the labeling approved by the U.S. Food and Drug Administration for the product. The product is not approved in the U.S. for the investigational use(s) discussed in this news release, and no conclusions can or should be drawn regarding the safety or effectiveness of the product for these uses.

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