FDA Approves Nplate® (Romiplostim) For Use In Pediatric Patients With Immune Thrombocytopenia

December 14, 2018

Application Granted Priority Review Designation
Approval Based on Results That Demonstrated Nplate Successfully Increased and Sustained Platelet Counts in Children Affected by Rare Blood Disorder

THOUSAND OAKS, Calif., Dec. 14, 2018 /PRNewswire/ -- Amgen (NASDAQ:AMGN) today announced that the U.S. Food and Drug Administration (FDA) has approved the supplemental Biologics License Application (sBLA) for Nplate® (romiplostim) for the treatment of pediatric patients one year of age and older with immune thrombocytopenia (ITP) for at least six months who have had an insufficient response to corticosteroids, immunoglobulins or splenectomy.

"Today's approval underscores our long-standing commitment to making a positive impact on the lives of patients with rare and difficult-to-treat hematological disorders," said David M. Reese, M.D., executive vice president of Research and Development at Amgen. "In the 10 years since the FDA approved Nplate as the first platelet booster for adult patients with chronic ITP, it has made a difference in the lives of thousands of adults, and we're proud to bring this treatment option to children who need it most."

The approval was based on two placebo-controlled studies – Phase 3 and Phase 1/2 – evaluating the safety and efficacy of Nplate in pediatric patients. In the Phase 3 study, published in *The Lancet*, rates of overall platelet response were increased with the Nplate group (71 percent) compared with placebo (20 percent), $p<0.05$. Additionally, durable platelet response occurred more frequently with Nplate (52 percent) compared with placebo (10 percent), $p<0.05$. In the two placebo-controlled trials, adverse reactions with an incidence of ≥ 25 percent in the Nplate arm were contusion, upper respiratory tract infection and oropharyngeal pain.

"Children with ITP are at risk for serious bleeding events and spontaneous bruising due to low platelet counts, which can be worrying for these young patients and their parents. Currently, these patients have a limited number of treatment options, especially for those with refractory disease," said Michael D. Tarantino, M.D., president of the Bleeding and Clotting Disorders Institute and professor of Pediatrics and Medicine, University of Illinois College of Medicine-Peoria, Peoria, Ill. "Today's approval of Nplate offers new hope to the pediatric ITP community as it provides children with a new treatment option that may help to maintain safe platelet counts."

ITP is a rare, serious autoimmune disease characterized by low platelet counts in the blood (a condition known as thrombocytopenia) and impaired platelet production.[1] In the U.S., the estimated prevalence of ITP in children is 5.3 per 100,000 children annually.[1] The treatment goal for children with ITP is to achieve and maintain a platelet count that reduces the risk of bleeding.[2]

About Nplate® (romiplostim)
Nplate is a thrombopoietin (TPO) receptor agonist that mimics the body's natural TPO and is designed to increase platelet counts in patients with chronic immune thrombocytopenia (ITP).[3] In the U.S. and European Union, Nplate is approved for the treatment of chronic ITP in adults and in children age one year and older with ITP for at least six months, who have had an insufficient response to other medicines or had surgery to remove the spleen.

Nplate is also approved in 67 countries, including Canada, Australia and Japan.

For more information about Nplate, please visit www.Nplate.com.

Important U.S. Nplate® Safety Information

Risk of Progression of Myelodysplastic Syndromes to Acute Myelogenous Leukemia

- In Nplate® clinical trials of adult patients with myelodysplastic syndromes (MDS) and severe thrombocytopenia, progression from MDS to acute myelogenous leukemia (AML) has been observed.
- Nplate® is not indicated for the treatment of thrombocytopenia due to MDS or any cause of thrombocytopenia other than chronic ITP.

Thrombotic/Thromboembolic Complications

- Thrombotic/thromboembolic complications may result from increases in platelet counts with Nplate® use. Portal vein thrombosis has been reported in patients with chronic liver disease receiving Nplate®.
- To minimize the risk for thrombotic/thromboembolic complications, do not use Nplate® in an attempt to normalize platelet counts. Follow the dose adjustment guidelines to achieve and maintain a platelet count of ≥ 50 x 10^9/L.

Loss of Response to Nplate®

- Hyporesponsiveness or failure to maintain a platelet response with Nplate® should prompt a search for causative factors, including neutralizing antibodies to Nplate®.
- To detect antibody formation, submit blood samples to Amgen (1-800-772-6436). Amgen will assay these samples for antibodies to Nplate® and thrombopoietin (TPO).

- Discontinue Nplate® if the platelet count does not increase to a level sufficient to avoid clinically important bleeding after 4 weeks at the highest weekly dose of 10 mcg/kg.

Adverse Reactions

Adult ITP

- In the placebo-controlled trials of adult ITP patients, headache was the most commonly reported adverse drug reaction, occurring in 35% of patients receiving Nplate® and 32% of patients receiving placebo. Headaches were usually of mild or moderate severity.
- Most common adverse reactions in adults (≥ 5% higher patient incidence in Nplate® versus placebo) were Arthralgia (26%, 20%), Dizziness (17%, 0%), Insomnia (16%, 7%), Myalgia (14%, 2%), Pain in Extremity (13%, 5%), Abdominal Pain (11%, 0%), Shoulder Pain (8%, 0%), Dyspepsia (7%, 0%), and Paresthesia (6%, 0%).

Pediatric ITP

- In pediatric patients of age ≥ 1 year receiving romiplostim for ITP, adverse reactions with an incidence of ≥ 25% in the two randomized trials were: contusion (41%), upper respiratory tract infection (31%), and oropharyngeal pain (25%).
- Most common adverse reactions (≥ 5% incidence and ≥ 5% more frequent in the romiplostim arm) across the two placebo-controlled trials were contusion (41%), upper respiratory tract infection (31%), oropharyngeal pain (25%), pyrexia (24%), diarrhea (20%), rash (15%), and upper abdominal pain (14%).

Nplate® administration may increase the risk for development or progression of reticulin fiber formation within the bone marrow. This formation may improve upon discontinuation of Nplate®. In a clinical trial, one patient with ITP and hemolytic anemia developed marrow fibrosis with collagen during Nplate® therapy.

Women who become pregnant during Nplate® treatment are encouraged to enroll in Amgen's Pregnancy Surveillance Program. Patients or their physicians should call 1-800-77-AMGEN (1-800-772-6436) to enroll.

Please see full U.S. Prescribing Information and Medication Guide at www.Nplate.com.

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. 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, including our devices, 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. 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, including in Puerto Rico, 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. 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. A breakdown, cyberattack or information security breach could compromise the confidentiality, integrity and availability of our systems and our data. 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. We may not be able to access the capital and credit markets on terms that are favorable to us, or at all.

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2. Children's National Health System. Pediatric Idiopathic Thrombocytopenia Purpura (ITP). https://childrensnational.org/choose-childrens/conditions-and-treatments/blood-marrow/idiopathic-thrombocytopenia-purpura-itp. Accessed Nov. 2, 2018
3. Nplate® (romiplostim) prescribing information, Amgen.

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