Nplate® (romiplostim) Now Approved For Earlier Use In Adults With Immune Thrombocytopenia

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32% of Patients Achieved Treatment-Free Remission for at Least Six Months in a Single-Arm Trial
93% of Patients Achieved a Platelet Response

THOUSAND OAKS, Calif., Oct. 18, 2019 /PRNewswire/ -- Amgen (NASDAQ:AMGN) today announced that the U.S. Food and Drug Administration (FDA) approved Amgen's Supplemental Biologics License Application (sBLA) for Nplate® (romiplostim) to include new data in its U.S. prescribing information showing sustained platelet responses in adults with immune thrombocytopenia (ITP), a rare, serious autoimmune disease characterized by low platelet counts. The updated indication expands treatment with Nplate to newly diagnosed and persistent adult ITP patients who have had an insufficient response to corticosteroids, immunoglobulins or splenectomy. In December of last year, the FDA approved another sBLA for Nplate in the treatment of pediatric patients with ITP.

"These new data are the first of their kind to prospectively examine treatment-free remission as an outcome for patients with ITP. Thirty-two percent of patients who received Nplate soon after an insufficient response to the first course of steroids maintained platelet response for at least six months without Nplate or any other ITP therapy," said David M. Reese, M.D., executive vice president of Research and Development at Amgen. "This approval will provide patients the opportunity to receive Nplate earlier in the course of their disease, potentially reducing their need for prolonged steroid use. We are excited to make Nplate available to more patients with this rare blood disorder."

The sBLA was based on an open-label, single-arm Phase 2 trial of adults with ITP diagnosed ≤ 6 months prior who had an insufficient response to first-line treatment, including corticosteroids (N=75). The median time from ITP diagnosis to study enrollment was 2.2 months. On the primary endpoint, the median number of months with platelet response (≥ 50 x 10^9/L) was 11 months during the 12-month treatment period (95% CI: 10, 11), with a median time to first platelet response of 2.1 weeks (95% CI: 1.1, 3.0). Additionally, 93% (70) of patients achieved one or more platelet responses during the 12-month treatment period. On the secondary endpoint, 32% (24) of patients achieved remission for at least six months, defined by maintaining a platelet count ≥ 50 x 10^9/L in the absence of Nplate and any medication for ITP (concomitant or rescue).

"Among adults with immune thrombocytopenia, there is a need for treatment options that can get patients to sustained remission," said Caroline Kruse, president and chief executive officer, Platelet Disorder Support Association. "The addition of this new data will help physicians and patients communicate and weigh the benefits and risks of treatment to find an appropriate treatment choice."

The safety profile of Nplate was similar across patients, regardless of ITP duration. The following adverse reactions (at least 5% incidence and at least 5% more frequent with Nplate compared with placebo or standard of care) occurred in Nplate patients with ITP duration up to 12 months: bronchitis, sinusitis, vomiting, arthralgia, myalgia, headache, dizziness, diarrhea, upper respiratory tract infection, cough, nausea and oropharyngeal pain. The adverse reaction of thrombocytosis occurred with an incidence of 2% in adults with ITP duration up to 12 months.

About the Phase 2 Study
The Phase 2 study was a single-arm, open-label study designed to assess the safety and efficacy of Nplate in adult patients who had an insufficient response (platelet count ≤ 30 x 10^9/L) to first line therapy (N=75). The median time from ITP diagnosis to study enrollment was 2.2 months. Prior ITP treatments included corticosteroids, immunoglobulins and anti-D immunoglobulins. Rescue therapies were permitted. Patients received single weekly SC injections of Nplate over a 12-month treatment period, with individual dose adjustments to maintain platelet counts (50 x 10^9/L to 200 x 10^9/L).

About Immune Thrombocytopenia (ITP)
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 incidence of ITP is 6.1 per 100,000 adults annually.[2] Nearly 20,000 people are newly diagnosed with ITP each year in the U.S.[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 ITP.[3]

In the U.S:

- Nplate is approved for the treatment of thrombocytopenia in adult patients with ITP who have had an insufficient response to corticosteroids, immunoglobulins, or splenectomy.
- Nplate is approved for the treatment of thrombocytopenia in pediatric patients 1 year of age and older with ITP for at least 6 months who have had an insufficient response to corticosteroids, immunoglobulins, or splenectomy.

In the European Union (EU):

- 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 69 countries, including Canada and Australia.

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

IMPORTANT SAFETY INFORMATION

Risk of Progression of Myelodysplastic Syndromes to Acute Myelogenous Leukemia

- In Nplate® (romiplostim) clinical trials of 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 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. Adverse drug reactions in adults with a ≥ 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%).
- The safety profile of Nplate was similar across patients, regardless of ITP duration. The following adverse reactions (at least 5% incidence and at least 5% more frequent with Nplate compared with placebo or standard of care) occurred in Nplate patients with ITP duration up to 12 months: bronchitis, sinusitis, vomiting, arthralgia, myalgia, headache, dizziness, diarrhea, upper respiratory tract infection, cough, nausea and oropharyngeal pain. The adverse reaction of thrombocytosis occurred with an incidence of 2% in adults with ITP duration up to 12 months.

Pediatric ITP

- The most common adverse reactions experienced by ≥ 5% of patients receiving Nplate with ≥ 5% higher incidence 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%).
- 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%).

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.

INDICATIONS

Nplate® is a thrombopoietin receptor agonist indicated for the treatment of thrombocytopenia in adult patients with immune thrombocytopenia (ITP) who have had an insufficient response to corticosteroids, immunoglobulins, or splenectomy. Nplate® is indicated for the treatment of thrombocytopenia in pediatric patients 1 year of age and older with ITP for at least 6 months who have had an insufficient response to corticosteroids, immunoglobulins, or splenectomy.

Nplate® is not indicated for the treatment of thrombocytopenia due to myelodysplastic syndrome (MDS) or any cause of thrombocytopenia other than ITP. Nplate® should be used only in patients with ITP whose degree of thrombocytopenia and clinical condition increase the risk for bleeding. Nplate® should not be used in an attempt to normalize platelet counts.

Please see full Prescribing Information and Medication Guide.

About Amgen Oncology

Amgen is searching for and finding answers to incredibly complex questions that will advance care and improve lives for cancer patients and their families. Our research drives us to understand the disease in the context of the patient's life – not just their cancer journey – so they can take control of

their lives.

For the last four decades, we have been dedicated to discovering the firsts that matter in oncology and to finding ways to reduce the burden of cancer. Building on our heritage, Amgen continues to advance the largest pipeline in the Company's history, moving with great speed to advance those innovations for the patients who need them.

At Amgen, we are driven by our commitment to transform the lives of cancer patients and keep them at the center of everything we do.

For more information, follow us on www.twitter.com/amgenoncology.

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 any statements on the outcome, benefits and synergies of the acquisition of Otezla® (apremilast), including anticipated Otezla sales growth and the timing of non-GAAP EPS accretion, as well as 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. We rely on collaborations with third parties for the development of some of our product candidates and for the commercialization and sales of some of our commercial products. 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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3. Nplate® (romiplostim) prescribing information, Amgen.

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