# Nplate® (Romiplostim) Study In The Lancet Shows Significant Increase In Durable Platelet Response Among Children With Immune Thrombocytopenia

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**Nplate Reduced Rates of Bleeding by More Than 30 Percent in Children Affected by Blood Disorder**

THOUSAND OAKS, Calif., April 19, 2016 /PRNewswire/ -- Amgen (NASDAQ:AMGN) today announced that *The Lancet* published results from a Phase 3 randomized, double-blind, placebo-controlled study of Nplate® (romiplostim) in children with symptomatic immune thrombocytopenia (ITP). The study showed that 52 percent of Nplate patients achieved a durable platelet response, compared with 10 percent of placebo-treated patients (*p*=0.002, odds ratio 9.1, 95 percent CI: 1.9, 43.2).

"Children with ITP are at risk for serious bleeding events due to low platelet counts, which can be very frightening for these children and their parents," said Michael D. Tarantino, M.D., The Bleeding and Clotting Disorders Institute, professor of Pediatrics and Medicine, University of Illinois College of Medicine-Peoria, Peoria, Illinois. "The results of this study suggest that romiplostim could reduce the frequency and severity of bleeding events for children suffering from symptomatic ITP, thus providing them with another potential treatment option."

The study met the primary endpoint of durable platelet response and showed that children who were treated with Nplate had increased rates of overall platelet response, and patients who responded to Nplate maintained consistently elevated platelet counts. These findings demonstrate that Nplate may be a potential treatment option for children with symptomatic ITP of more than six months duration. The most frequently reported adverse events (AEs) included contusion, epistaxis, headache and upper respiratory tract infections. The overall safety profile observed in the Nplate arm was similar to the known safety profile of Nplate.

"Nplate helps bone marrow produce more platelets, which in turn helps prevent bruising and bleeding which is important for children faced with this condition. These data are important in understanding how Nplate may play a role in helping children manage this disease," said Sean E. Harper, M.D., executive vice president of Research and Development at Amgen. "We will work with regulatory authorities towards an approval for Nplate for pediatric patients."

The treatment goal for children with ITP is to promote a platelet count that maintains appropriate control of bleeding,[1] improve symptoms and increase the number of platelets.[2]

ITP is a rare, serious autoimmune disease characterized by low platelet counts in the blood (a condition known as thrombocytopenia) and impaired platelet production.[2,3] In the United States (U.S.), an average estimate of the incidence in children is 5 cases in 1,000 each year.[4]

**About the Phase 3 Study**
This Phase 3 double-blind study randomized 62 children who have had ITP for more than six months to weekly Nplate or placebo (2:1) for 24 weeks. Durable platelet response, the primary endpoint of the study, was defined as achieving weekly platelet responses (increased platelets) without rescue medication in at least six of the final eight weeks.

Secondary endpoints of the study included the evaluation of overall platelet response, the total number of weekly platelet responses, the use of ITP rescue medications, composite bleeding episodes and the overall safety of Nplate. Exploratory endpoints included the evaluation of bleeding incidence and changes in patient reported outcomes. Rescue medication was defined as any medication intended to increase platelet counts or prevent bleeding, and any increase in dose, frequency or additional therapy was categorized as rescue medication. Patients entering the study were permitted to use the same standard-of-care therapy, dose and schedule from when screening platelet counts were measured.

By the final eight weeks of the study, noncutaneous bleeding had decreased with Nplate, and rates of durable platelet response were 52 percent compared to 10 percent with placebo (*p*=0.002, odds ratio 9.1, 95 percent CI: 1.9, 43.2). Rates of overall platelet response with Nplate were 71 percent (30/42) compared with 20 percent with placebo (*p*=0.0002, odds ratio 9.0, 95 percent CI: 2.5, 32.3), and rates of any platelet response were 81 percent (34/42) with Nplate compared to 55 percent (11/20) with placebo (*p*=0.0313).

The overall safety profile on the pediatric subjects who received Nplate in this study was similar to the known safety profile of Nplate. The most frequently reported AEs included contusion, epistaxis, headache and upper respiratory tract infections. Oropharyngeal pain occurred more frequently with Nplate [26.2 percent (11/42) vs. 5.3 percent (1/19) in placebo-treated patients]; of the 11 patients treated with Nplate with oropharyngeal pain, streptococcal pharyngitis (n=2), allergic rhinitis (n=2), gastroesophageal reflux (n=1) and serum sickness from IVIg (n=1) were also reported. No oropharyngeal pain AEs were serious or considered treatment-related. No patients died and none withdrew due to AEs.

Serious adverse events (SAEs) were seen in 23.8 percent of Nplate patients and 5.3 percent of placebo patients. SAEs seen in the Nplate arm included epistaxis, contusion and headache (n=2 each), bronchiolitis, nausea, petechiae, epilepsy, fever, thrombocytosis, urinary tract infection and vomiting (n=1 each). One subject with treatment-related SAEs experienced headache and thrombocytosis, which did not recur when romiplostim was restarted. There were no thrombotic events reported in the study.

**About Nplate® (romiplostim)**
Nplate is a thrombopoietin receptor agonist indicated for the treatment of low blood platelet counts in adults with chronic immune thrombocytopenia (ITP), who had an insufficient response to other medicines or surgery. Nplate mimics the body's natural thrombopoietin and is designed to increase platelet counts in patients with chronic ITP.[5]

Nplate is the first FDA-approved treatment specifically for adult chronic ITP. It is also being investigated for potential use in children ages 12 months to 18 years old with chemotherapy-induced thrombocytopenia.

In the U.S., Nplate is indicated for the treatment of thrombocytopenia in patients with chronic ITP 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 chronic 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.

In the European Union (EU), Nplate is indicated for the treatment of adult chronic ITP patients who are refractory to other treatments (e.g., corticosteroids, immunoglobulins).

Nplate was named as a recipient of the U.S. Prix Galien 2009 "Best Biotechnology Product" award and also received the 2009 Scrip Awards for "Best New Drug." Nplate has also been honored with numerous awards throughout the EU, including a 2010 Prix Galien in France in the category of "Drugs for Rare Diseases," and the 2011 Prix Galien in Germany in the category of "Specialist Care." In September 2010, Nplate was awarded the 2010 International Prix Galien Award, an award granted every two years which recognizes the "Best of the Best" selected from previous national Prix Galien award recipients.

Nplate is also approved in Canada, Australia, Russia, Mexico, Switzerland, Lichtenstein, Japan, Argentina, Israel, South Korea, Hong Kong, Chile, Serbia, Kazakhstan, Malaysia, Singapore, Colombia, Kuwait, Taiwan, South Africa, Brazil, Guatemala, Morocco, Ecuador, Macau, Egypt, Lebanon, Peru and Venezuela. Nplate has received orphan designation for chronic ITP in the U.S. (2003), the EU (2005), Switzerland (2005), Japan (2006), Mexico and South Korea (2010).

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

**Important U.S. Safety Information Regarding Nplate (romiplostim)**

**Risk of Progression of Myelodysplastic Syndromes to Acute Myelogenous Leukemia**

- In Nplate 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 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 109/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.

**Laboratory Monitoring**

- Obtain CBCs, including platelet counts, weekly during the dose adjustment phase of Nplate therapy and then monthly following establishment of a stable Nplate dose.
- Obtain CBCs, including platelet counts, weekly for at least two weeks following discontinuation of Nplate.

**Adverse Reactions**

- In the placebo-controlled trials, 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 (≥ 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%).
- 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.

Please see full Prescribing Information for Nplate at www.Nplate.com.

**Important EU Nplate Safety Information**
The EU Summary of Product Characteristics for Nplate lists the following Special Warnings and Precautions: reoccurrence of thrombocytopenia and bleeding after cessation of treatment, increased bone marrow reticulin, thrombotic/thromboembolic complications, progression of existing MDS (in patients with MDS), medication errors, loss of response to Nplate, and effects on red and white blood cells.

The most common adverse reactions observed include hypersensitivity reactions (including cases of rash, urticarial and angioedema) and headache.

As with all therapeutic proteins, there is a potential for immunogenicity.

**About Amgen's Commitment to Oncology**
Amgen Oncology is committed to helping patients take on some of the toughest cancers, such as those that have been resistant to drugs, those that progress rapidly through the body and those where limited treatment options exist. Amgen's supportive care treatments help patients combat certain side effects of strong chemotherapy, and our targeted medicines and immunotherapies focus on more than a dozen different malignancies, ranging from blood cancers to solid tumors. With decades of experience providing therapies for cancer patients, Amgen continues to grow its portfolio of innovative and biosimilar oncology medicines.

**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 biologics manufacturing 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 Inc. and are subject to a number of risks, uncertainties and assumptions that could cause actual results to differ materially from those described. All statements, other than statements of historical fact, are statements that could be deemed forward-looking statements. Forward-looking statements involve significant risks and uncertainties, including those discussed below and more fully described in the Securities and Exchange Commission (SEC) reports filed by Amgen Inc., including Amgen Inc.'s 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 expressly disclaims any duty to update information contained in this news release.

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. Even when clinical trials are successful, regulatory authorities may question the sufficiency for approval of the trial endpoints we have selected. In addition, 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. 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 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. We perform a substantial amount of our manufacturing activities at a few key manufacturing 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, sales of our products are affected by the 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. Government and others' regulations and reimbursement policies as well as political and public scrutiny may affect the development, usage and pricing of our 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. We believe that some of our newer products, product candidates or new indications for existing products, may face competition when and as they are approved and marketed. Our products may compete against products that have lower prices, established reimbursement, superior performance, are easier to administer, or that are otherwise competitive with our products. We expect to face increasing competition from biosimilars. In addition, while we routinely obtain patents for products and technology, the protection of our products offered by patents and patent applications may be challenged, invalidated or circumvented by competitors and there can be no guarantee of our ability to obtain or maintain patent protection for our products or product candidates or to prevail in intellectual property litigation. We cannot guarantee that we will be able to produce commercially successful products or maintain the commercial success of our existing products. Our stock price may be volatile and may be affected by actual or perceived market opportunity, competitive position, and success or failure of our products or product candidates. Further, 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 Amgen, or at all. 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 common stock.

The scientific information discussed in this news release related to new indications for Amgen's products is preliminary and investigative and is not part of the labeling approved by the U.S. Food and Drug Administration for the products. The products are not approved 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 products for these uses.

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**References:**


1. US National Institutes of Health. Immune Thrombocytopenia. http://www.nhlbi.nih.gov/book/export/html/4917. Accessed Feb. 4, 2016.
2. http://patient.info/health/immune-thrombocytopenia-leaflet. Accessed Mar 16, 2016
3. Cines DB et al. Immune thrombocytopenic purpura. *N Engl J Med*. 2002; 346:995-1008.
4. Platelet Disorder Support Association. About ITP. http://www.pdsa.org/about-itp.html. Accessed Feb. 4, 2016.
5. Fogarty PF et al. The epidemiology of immune thrombocytopenic purpura. *Curr Opin Hematol*. 2007;14(5):515-519.




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