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Revolade® Approved in EU as First in Class Therapy for Children Aged 1 Year and Above with Chronic ITP

- Revolade is marketed as Promacta® in the United States
- EU approval of Revolade expands treatment options for pediatric patients aged 1 year and above with chronic ITP who have not responded to other therapies
- Two formulations approved: once-daily tablet and oral suspension formulation designed for younger children who may not be able to swallow tablets
- For about one in four children with ITP, a disorder of low blood platelet count and potential bleeding, the condition becomes chronic[1,2]

SAN DIEGO-- **Ligand Pharmaceuticals Incorporated (NASDAQ: LGND)** announces that the European Commission (EC) has approved Revolade® (eltrombopag), a Novartis product, for the treatment of pediatric (aged 1 year and above) chronic immune (idiopathic) thrombocytopenic purpura (ITP) patients who are refractory to other treatments (e.g. corticosteroids, immunoglobulins). The approval includes the use of tablets as well as a new oral suspension formulation of Revolade, which is designed for younger children who may not be able to swallow tablets. Revolade was approved by the EC in 2010 for use in adults with the same condition.

ITP is a rare blood disorder that affects about five in 100,000 children each year and is characterized by a low platelet count[2,3]. Because people with ITP have a low number of platelets, they may bruise easily and experience bleeding that is hard to stop[2]. Chronic ITP, defined as ongoing disease more than 12 months after diagnosis[4], occurs in 13–36% of children with ITP[1]. A small number of pediatric patients with chronic ITP may be at risk of significant bleeding[5].

The approval is based on data from two double-blind, randomized, placebo-controlled trials, including the largest Phase III clinical trial in this patient population. In these studies, patients in the treatment and placebo arms were permitted to use some stable maintenance ITP therapies, per local treatment practices. Treatment with Revolade significantly increased and sustained platelet counts among pediatric patients with chronic ITP who were refractory to or had relapsed after prior chronic ITP therapies, and some patients taking concomitant ITP medications were able to reduce or discontinue their use of these medications, primarily corticosteroids.

The EC approval applies to all 28 European Union member states, plus Iceland, Norway and Liechtenstein.

Revolade is a once-daily oral thrombopoietin (TPO) receptor agonist that works by inducing stimulation and differentiation of megakaryocytes (large cells, found especially in bone marrow) from bone marrow stem cells to increase platelet production[6]. In August 2015, the U.S. Food and Drug Administration (FDA) approved a new oral suspension formulation, which expanded use of eltrombopag to include children 1 year of age and older with chronic ITP who have had an insufficient response to corticosteroids, immunoglobulins or splenectomy.

About the PETIT and PETIT2 Clinical Trials

PETIT is a Phase II, multi-center, three-part study to investigate the efficacy, safety and tolerability of Revolade in pediatric patients (ages 1 to 17 years) with previously treated chronic ITP. The trial included patients living with ITP for six months or longer who had a platelet count <30 Gi/L. Part one was an open label, dose finding study; part two was double-blind and placebo-controlled, and part three was an open-label extension. Patients in the study were permitted to use some stable maintenance ITP therapies, per local treatment practices. The primary efficacy outcome, which was percentage of participants who achieved a platelet count >=50 Gi/L without rescue therapy at least once between weeks one and six, was met by 62% and 32% of patients in the Revolade arm and the control arm, respectively (p=0.011). The secondary efficacy endpoint analyses demonstrated clinically meaningful benefit in terms of decreased need for rescue treatment (13% of patients on Revolade compared to 50% of patients in the control arm). Patients received Revolade for a total of six months during the trial[6,7].

PETIT2 is a Phase III, multi-center, two-part study to investigate the efficacy, safety and tolerability of Revolade in pediatric patients (ages 1 to 17 years) with previously treated chronic ITP. The trial included patients living with chronic ITP for 12 months or longer who also had a platelet count <30 Gi/L. Part one was randomized, double-blind and placebo-controlled and part two was an open-label extension. Patients in the study were permitted to use some stable maintenance ITP therapies, per local treatment practices. The primary efficacy outcome, which was percentage of participants who achieved a platelet count >=50 Gi/L without rescue therapy for at least six out of eight weeks between weeks five and 12 of part one of the study, was met by 40% of patients treated with Revolade and 3% of patients in the control arm (p<0.001). This result was consistent across the age cohorts. The secondary efficacy endpoint analyses demonstrated clinically meaningful benefit in terms of decreased need for rescue treatment (19% of patients on Revolade compared to 24% of patients in the control arm) during the randomized, double-blind period. Patients were permitted to reduce or discontinue baseline ITP therapy only during the open-label phase of the trial. In the open label eltrombopag-only period, 15 of 87 patients were taking concomitant ITP medications at baseline. Of these 15 patients, eight (53%) had a sustained reduction or permanent discontinuation of at least one baseline ITP medication (seven patients permanently discontinued and one patient had sustained reduction for >=18 weeks). Patients received Revolade for a total of nine months during the trial[6,8].

In both studies, safety was consistent with the known safety profile of Revolade in chronic ITP in adults and the population under study. No new safety signals were detected. The most common adverse reactions in pediatric chronic ITP patients 1 year and older (greater than or equal to 10% and greater than placebo) were upper respiratory tract infection and nasopharyngitis[6,7,8].

About Chronic ITP

ITP is a blood disorder characterized by blood that does not clot as it should due to a low number of platelets. People who have ITP often have purple bruises or tiny red or purple dots on the skin. They also may have nosebleeds, bleeding from the gums during dental work, or other bleeding that's hard to stop. In most cases, an autoimmune response is thought to cause ITP in which a person's immune system attacks and destroys its own platelets[2].

The two types of ITP are acute (temporary or short-term) and chronic (long-lasting). Acute ITP mainly occurs in children, often after a viral infection, and generally lasts less than six months. The platelet count returns to normal within six to 12 months and treatment may not be needed[2]. Chronic ITP, defined as ongoing disease more than 12 months after diagnosis[4], occurs in 13–36% of children with ITP[1]. A small number of pediatric patients with chronic ITP may be at risk of significant bleeding[5].

The goal of treatment in chronic ITP for children is to maintain a safe platelet count that reduces the risk of bleeding[2]. The most commonly available and used therapies—corticosteroids and intravenous immunoglobulin (IVIG)—are associated with side effects that are often difficult to tolerate in a pediatric setting[5,9,10].

About Revolade® (eltrombopag)

Revolade is approved in more than 100 countries worldwide for the treatment of thrombocytopenia in adult patients with chronic immune (idiopathic) thrombocytopenic purpura (ITP) who have had an inadequate response or are intolerant to other treatments. Eltrombopag (marketed as Promacta® in the USA), is approved by the US Food and Drug Administration for once-daily use in pediatric patients 1 year and older with chronic ITP who have had an insufficient response to corticosteroids, immunoglobulins or splenectomy. Revolade is also approved in over 45 countries worldwide for the treatment of thrombocytopenia (low blood platelet counts) in patients with chronic hepatitis C to allow them to initiate and maintain interferon-based therapy. In September 2015, the European Commission approved Revolade for the treatment of adults with severe aplastic anemia (SAA) who were either refractory to prior immunosuppressive therapy or heavily pretreated and are unsuitable for hematopoietic stem cell transplant.

Revolade Important Safety Information

Revolade may cause serious side effects, such as liver problems, high platelet counts and a higher chance for blood clots, bleeding after stopping treatment, and bone marrow problems.

Revolade may damage the liver and cause serious, even life threatening, illness. Blood tests to check the liver are needed before taking Revolade and during treatment. When certain antiviral treatments are given together with Revolade for the treatment of thrombocytopenia due to hepatitis C virus (HCV) infections, some liver problems can get worse.

A doctor will order the blood tests and any other tests required. In some cases Revolade treatment may need to be stopped. Patients should tell a doctor right away if they have any of these signs and symptoms of liver problems: yellowing of the skin or the whites of the

eyes (jaundice), unusual darkening of the urine, unusual tiredness, right upper stomach area pain.

Patients have a higher chance of getting a blood clot if their platelet count is too high during treatment with Revolade, but blood clots can occur with normal or even low platelet counts. Patients who have cirrhosis of the liver are at risk of a blood clot in a blood vessel that feeds the liver. Patients may have severe complications from some forms of blood clots, such as clots that travel to the lungs or that cause heart attacks or strokes. A doctor will check the patient's blood platelet counts, and change the dose or stop Revolade if platelet counts get too high. Patients should tell their doctor right away if they have signs and symptoms of a blood clot in the leg, such as swelling or pain/tenderness of one leg.

When patients with chronic ITP stop taking Revolade, their blood platelet count will drop back down to what it was before they started taking Revolade. These effects are most likely to happen within 4 weeks after patients stop taking Revolade. The lower platelet counts may increase risk of bleeding. A doctor will check platelet counts for at least 4 weeks after patients stop taking Revolade. Patients should tell their doctor or pharmacist if they have any bruising or bleeding after they stop taking Revolade.

Patients being treated for the disease may have problems with their bone marrow. Medicines like Revolade could make this problem worse. Signs of bone marrow changes may show up as abnormal results in blood tests. A doctor may also carry out tests to directly check the bone marrow during treatment with Revolade.

The most common side effects of Revolade when used to treat adult patients with chronic ITP include headache, anemia, decreased appetite, insomnia, cough, nausea, diarrhea, alopecia, pruritus, myalgia, pyrexia, fatigue, influenza-like illness, asthenia, chills and peripheral edema.

The most common side effects of Revolade when used to treat pediatric patients with chronic ITP include upper respiratory tract infection, nasopharyngitis, cough, diarrhea, pyrexia, rhinitis, abdominal pain, oropharyngeal pain, toothache, rash, increased AST and rhinorrhea.

The most common side effects of Revolade when used to treat patients with chronic HCV and antiviral agents include headache, anemia, decreased appetite, insomnia, cough, nausea, diarrhea, alopecia, pruritus, myalgia, pyrexia, fatigue, influenza-like illness, asthenia, chills and peripheral edema.

The most common side effects of Revolade when used to treat patients with severe aplastic anemia (SAA) include headache, dizziness, insomnia, cough, dyspnea, oropharyngeal pain, rhinorrhea, nausea, diarrhea, abdominal pain, transaminases increased, ecchymosis, arthralgia, muscle spasms, pain in extremity, fatigue, febrile neutropenia, and pyrexia. Common side effects that may show up in blood tests include increase in some liver enzymes and laboratory tests that may show abnormal changes to the cells in the bone marrow.

Please see full EU Summary of Product Characteristics for Revolade (eltrombopag).

About Ligand Pharmaceuticals

Ligand is a biopharmaceutical company focused on developing or acquiring technologies that help pharmaceutical companies discover and develop medicines. Our business model creates value for stockholders by providing a diversified portfolio of biotech and pharmaceutical product revenue streams that are supported by an efficient and low corporate cost structure. Our goal is to offer investors an opportunity to participate in the promise of the biotech industry in a profitable, diversified and lower-risk business than a typical biotech company. Our business model is based on doing what we do best: drug discovery, early-stage drug development, product reformulation and partnering. We partner with other pharmaceutical companies to leverage what they do best (late-stage development, regulatory management and commercialization) to ultimately generate our revenue. Ligand's Captisol® platform technology is a patent-protected, chemically modified cyclodextrin with a structure designed to optimize the solubility and stability of drugs. OmniAb® is a patent-protected transgenic animal platform used in the discovery of fully human mono-and bispecific therapeutic antibodies. Ligand has established multiple alliances, licenses and other business relationships with the world's leading pharmaceutical companies including Novartis, Amgen, Merck, Pfizer, Celgene, Gilead, Janssen, Baxter International and Eli Lilly.

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Forward-Looking Statements

This news release contains forward-looking statements by Ligand that involve risks and uncertainties and reflect Ligand's judgment as of the date of this release. These include statements regarding the size of the patient population for ITP, Ligand's potential revenue under its license agreement with Novartis and Ligand's corporate cost structure. Actual events or results may differ from our expectations. For example, there can be no assurances that Novartis will successfully develop or market Revolade in the EU. The failure to meet expectations with respect to any of the foregoing matters may reduce Ligand's stock price. Additional information concerning these and other important risk factors affecting Ligand (including Ligand's current reliance on revenues based on sales of Promacta® and Kyprolis®, and various risks to which Ligand's Captisol® cyclodextrin operations are subject) can be found in Ligand's prior press releases available at www.ligand.com as well as in Ligand's public periodic filings with the Securities and Exchange Commission, available at www.sec.gov. Ligand disclaims any intent or obligation to update these forward-looking statements beyond the date of this press release, except as required by law. This caution is made under the safe harbor provisions of the Private Securities Litigation Reform Act of 1995.

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