

Revolade® Recommended by CHMP for EU Approval to Treat Patients with Severe Aplastic Anemia, a Serious Blood Disorder

- *Revolade is marketed as Promacta® in the USA*
- *If approved, Revolade would be the first treatment option in its class in the EU for certain patients with SAA*
- *Approximately 40% of SAA patients unresponsive to initial immunosuppressive therapy (IST) die from infection or bleeding within five years of diagnosis¹*
- *No approved therapies exist for patients with SAA who have not responded to IST or are ineligible for hematopoietic stem cell transplantation²*

SAN DIEGO-- **Ligand Pharmaceuticals Incorporated (NASDAQ: LGND)** announces the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) adopted a positive opinion for Revolade® (eltrombopag), a Novartis product, for the treatment of adult patients with acquired severe aplastic anemia (SAA) who were either refractory to prior immunosuppressive therapy (IST) or heavily pretreated and are unsuitable for hematopoietic stem cell transplantation.

SAA is a blood disorder where the bone marrow fails to make enough red blood cells, white blood cells and platelets³. Two out of every one million people in Europe and North America are diagnosed with aplastic anemia per year, a portion of which are severe cases^{4,5}. The exact cause of the disease is still unknown, but most cases of SAA are believed to be triggered by an autoimmune reaction where the body attacks blood-forming stem cells located in the bone marrow^{3,6}. As a result, patients with SAA are at risk for life-threatening infections or bleeding⁶.

Treatment of SAA is focused on increasing a patient's blood cell count. The current standard of care includes IST or hematopoietic stem cell transplantation⁶. Of patients treated with IST, one-quarter to one-third will not respond and 30-40% of responders will relapse, causing symptoms to return⁶. Approximately 40% of SAA patients who don't respond to initial IST die from infection or bleeding within five years of their diagnosis¹.

The CHMP positive opinion is based on the results of a pivotal open-label Phase 2 study (ELT112523) and two supporting Phase 2 studies (ELT116826 and ELT116643) conducted by the National Heart, Lung and Blood Institute (NHLBI) at the National Institutes of Health (NIH). The pivotal study demonstrated a hematologic response (40%) in SAA patients treated with Revolade who had an insufficient response to IST. The most common adverse reactions (≥20%) in the pivotal single-arm study of 43 patients were nausea (33%), fatigue

(28%), cough (23%), diarrhea (21%), and headache (21%)⁷.

The European Commission will review the CHMP recommendation and is expected to deliver its final decision within three months. The decision will be applicable to all 28 EU member states plus Iceland, Norway and Liechtenstein. In August of 2014, eltrombopag (marketed as Promacta® in the USA), was approved by the US Food and Drug Administration for once-daily use in patients with SAA who have had an insufficient response to IST. Eltrombopag is also approved for SAA in Canada.

About the NIH Study

In the single-arm, single-center, open-label Phase 2 study (NCT00922883), eltrombopag was evaluated in 43 patients with SAA who have had an insufficient response to at least one prior IST and who had a platelet count $\leq 30 \times 10^9/L$ ⁸. At baseline, the median platelet count was $20 \times 10^9/L$, hemoglobin was 8.4 g/dL, absolute neutrophil count (ANC) was $0.58 \times 10^9/L$, and absolute reticulocyte count was $24.3 \times 10^9/L$ ⁸. The treated population had a median age of 45 years (range 17 to 77 years) and 56% were male. The majority of patients (84%) received at least two prior immunosuppressive therapies⁸.

Eltrombopag was administered at an initial dose of 50 mg once daily for two weeks and increased over two-week periods up to a maximum dose of 150 mg once daily⁸. The primary endpoint was hematologic response, which was initially assessed after 12 weeks of treatment with eltrombopag⁸. Treatment was discontinued after 16 weeks if no hematologic response was observed. Additional efficacy assessments included median duration of response in months⁸.

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, and in over 50 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. Eltrombopag (marketed as Promacta® in the USA), is approved by the US Food and Drug Administration for once-daily use in patients with SAA who have had an insufficient response to IST and was also recently approved for the treatment of children six years and older with chronic ITP who have had an insufficient response to corticosteroids, immunoglobulins or splenectomy.

Important Safety Information for Revolade® (eltrombopag)

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 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 patients with chronic ITP include nausea, diarrhea, increase of liver enzymes, dry mouth, vomiting, unusual hair loss or thinning, rash, back pain, muscle pain, sore throat and discomfort when swallowing, urinary tract infection.

The most common side effects of Revolade when used to treat patients with chronic HCV and antiviral agents include fever, feeling very tired, chills, headache, cough, nausea, diarrhea, unusual hair loss or thinning, muscle pain, itching, feeling weak, difficulty sleeping, loss of appetite, flu-like symptoms, and swelling of the hands, ankles or feet.

The most common side effects of Revolade when used to treat patients with severe aplastic anemia (SAA) include cough, headache, shortness of breath, pain in the nose and throat, runny nose, abdominal pain, diarrhea, bruising, joint pain, muscle spasms, pain in extremities, dizziness, feeling very tired, fever, inability to sleep (insomnia). 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 with a business model focused on developing or acquiring royalty generating assets and coupling them with a lean corporate cost structure.

Ligand's goal is to produce a bottom line that supports a sustainably profitable business. By diversifying the portfolio of assets across numerous technology types, therapeutic areas, drug targets and industry partners, we offer investors an opportunity to invest in the increasingly complicated and unpredictable pharmaceutical industry. In comparison to its peers, we believe Ligand has assembled one of the largest and most diversified asset portfolios in the industry with the potential to generate revenue in the future. These therapies seek to address the unmet medical needs of patients for a broad spectrum of diseases including diabetes, hepatitis, muscle wasting, Alzheimer's disease, dyslipidemia, anemia, asthma and osteoporosis. Ligand's Captisol[®] platform technology is a patent-protected, chemically modified cyclodextrin with a structure designed to optimize the solubility and stability of drugs. Ligand has established multiple alliances with the world's leading pharmaceutical companies including; Novartis, Amgen, Merck, Pfizer, 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 forward-looking statements include statements regarding the content, scope and timing of the decision regarding Revolade by the European Commission, prevalence rates and the size of patient populations of SAA, the effects of treatment and side effects of Revolade, potential new indications or labeling for Revolade, and potential future revenues from Revolade and Promacta. 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.

References

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