FDA Approves Gamifant® (emapalumab-lzsg), the First and Only Treatment Indicated for Primary Hemophagocytic Lymphohistiocytosis (HLH)

− Primary HLH is an ultra-rare syndrome of hyper-inflammation that usually occurs within the first year of life and can rapidly become lethal unless diagnosed and treated –

− To date, primary HLH required immediate induction therapy with steroids and chemotherapy to control hyper-inflammation, followed by hematopoietic stem cell transplant, but mortality remained high –

− FDA approval of Gamifant marks first significant improvement in primary HLH induction therapy in 24 years –

WALTHAM, Mass., November 20 — Sobi, an international biopharmaceutical company dedicated to rare diseases, and Novimmune SA, a Swiss biotech company, today announced that the U.S. Food and Drug Administration (FDA) has approved Gamifant® (emapalumab-lzsg), an interferon gamma (IFNγ) blocking antibody for the treatment of pediatric (newborn and older) and adult patients with primary hemophagocytic lymphohistiocytosis (HLH) with refractory, recurrent or progressive disease or intolerance to conventional HLH therapy. Primary HLH is an ultra-rare syndrome of hyper-inflammation with high morbidity and mortality and for which there was previously no approved drug. Gamifant represents a major advance in the treatment of these patients through a targeted mode of action.

The FDA approval of Gamifant was based on results from a global, multicenter, open-label, single-arm pivotal Phase 2/3 clinical study (NCT01818492), which enrolled 34 primary HLH patients. The efficacy of Gamifant was evaluated in the cohort of 27 patients with refractory, recurrent or progressive disease during conventional HLH therapy or who were intolerant to conventional HLH therapy, meaning that they had not responded, not achieved a satisfactory response, not maintained a satisfactory response, or not been able to tolerate conventional therapy. Gamifant was administered concomitantly with dexamethasone, which could be tapered during the study. The primary endpoint was achieved, with 63% of patients (p=0.013) demonstrating an overall response at the end of treatment, defined as achievement of either a complete or partial response, or HLH improvement. In addition, 70% of patients proceeded to hematopoietic stem cell transplant (HSCT). Of the 27 refractory patients treated in the study, 82% had a genetically confirmed primary HLH diagnosis. The most common adverse reactions reported during the study were infections (56%), hypertension (41%), infusion-related reactions (27%), and fever (24%).

Results from the pivotal study will be presented at forthcoming international meetings.

“Today’s landmark approval of Gamifant will allow Sobi to bring the first and only FDA-approved treatment for primary HLH to a rare disease community that has faced high mortality without much improvement in care for the past 24 years,” said Rami Levin, President of Sobi in North America.

"HLH is a disorder of immune regulation in which many cytokines are deranged, but interferon gamma appears to play a critical role. While we have long understood the pivotal role of this cytokine in HLH, until emapalumab's approval we did not have a medicine that could specifically hit this target," said Michael Jordan, M.D., a physician-scientist in the division of Bone Marrow Transplantation and Immune Deficiency at Cincinnati Children's Hospital Medical Center HLH Center of Excellence, and Primary Investigator in the emapalumab clinical trial. "Emapalumab represents an entirely new approach to treating primary HLH and helping these very sick patients reach hematopoietic stem cell transplant."

Jeff Toughill, President of the Histiocytosis Association, said, “I applaud the FDA approval of Gamifant for the treatment of primary hemophagocytic lymphohistiocytosis. We are excited that this drug will be available to patients diagnosed with this rare, life-threatening disease, and we are optimistic that this approval will help to increase awareness and improve diagnosis, ultimately giving more patients a chance.”

“Gamifant is the first drug specifically targeted to neutralize IFNγ. Based on the clinical validation of this new target, additional clinical studies are ongoing or being planned with emapalumab in diseases for which IFNγ is considered pathogenic. We would like to extend our heartfelt thanks to the patients, families and the healthcare providers who participated in the emapalumab clinical study in primary HLH and whose efforts helped make today’s approval possible. We would also like to thank the FDA for their continuous support during emapalumab development,” says Cristina de Min, Chief Medical Officer at Novimmune.

Gamifant is expected to be available for administration in treatment centers across the U.S. in the first quarter of 2019. Sobi is committed to helping people access the medicines they are prescribed and will be offering support services for people prescribed Gamifant. More information on Sobi’s patient support programs may be accessed by calling 1-833-597-6530.

Gamifant was developed and submitted for approval to the FDA by Novimmune SA. Sobi acquired the global rights to Gamifant from Novimmune SA through an exclusive licensing agreement announced in July 2018 and closed in August 2018. In the U.S., Gamifant was reviewed under Priority Review and received Orphan Drug Designation,

Breakthrough Therapy Designation and Rare Pediatric Disease Designation from the FDA.

About Primary Hemophagocytic Lymphohistiocytosis (HLH)
Primary hemophagocytic lymphohistiocytosis (HLH) is an ultra-rare, rapidly-progressive, often-fatal syndrome of hyper-inflammation in which massive overexpression of interferon gamma (IFNγ) is thought to drive immune system hyperactivation, ultimately leading to organ failures. It is estimated that fewer than 100 cases of primary HLH are diagnosed each year in the U.S. Diagnosis is challenging due to the variability in signs and symptoms, which may include fevers, swelling of the liver and spleen, severe low red and white blood cell counts, bleeding disorders, infections, neurological symptoms, organ dysfunction and organ failure. Primary HLH usually begins to show symptoms within the first year of life and can rapidly become lethal if left untreated, with median survival of less than two months. The immediate goal of treatment is to quickly bring the hyperinflammatory emergency under control and to prepare for hematopoietic stem cell transplant, which is the only cure. The current conventional induction therapies used prior to transplant include steroids and chemotherapy, which are not specifically approved to treat HLH.

About Gamifant® (emapalumab-lzsg)
Gamifant (emapalumab-lzsg) is a monoclonal antibody (mAB) that binds to and neutralizes interferon gamma (IFNγ), which nonclinical data suggest plays a pivotal role in HLH. Gamifant is indicated for the treatment of adult and pediatric (newborn and older) patients with primary hemophagocytic lymphohistiocytosis (HLH) with refractory, recurrent or progressive disease or intolerance with conventional HLH therapy. Gamifant is the first and only medicine approved for primary HLH, an ultra-rare syndrome of hyper-inflammation that usually occurs within the first year of life and can rapidly become fatal unless diagnosed and treated. Gamifant is indicated to be administered in combination with the steroid therapy dexamethasone, through intravenous (IV) infusion over one hour twice per week until hematopoietic stem cell transplant (HSCT). Visit www.gamifant.com for more information, including full Prescribing Information.

IMPORTANT SAFETY INFORMATION
Indication and Usage
Gamifant® (emapalumab-lszg) is an interferon gamma (IFNγ)-blocking antibody indicated for the treatment of adult and pediatric (newborn and older) patients with primary hemophagocytic lymphohistiocytosis (HLH) with refractory, recurrent, or progressive disease or intolerance with conventional HLH therapy.
Important Safety Information
Before initiating Gamifant, patients should be evaluated for infection, including latent tuberculosis (TB). Prophylaxis for TB should be administered to patients who are at risk for TB or known to have positive purified protein derivative (PPD) test result or positive IFNγ release assay.

During Gamifant treatment, patients should be monitored for TB, adenovirus, Epstein-Barr virus (EBV), and cytomegalovirus (CMV) every 2 weeks and as clinically indicated. Patients should be administered prophylaxis for herpes zoster, *Pneumocystis jirovecii*, and fungal infections prior to Gamifant administration.
Do not administer live or live attenuated vaccines to patients receiving Gamifant and for at least 4 weeks after the last dose of Gamifant. The safety of immunization with live vaccines during or following Gamifant therapy has not been studied.

Infusion-Related Reactions

Infusion-related reactions, including drug eruption, pyrexia, rash, erythema, and hyperhidrosis, were reported with Gamifant treatment in 27% of patients. In one-third of these patients, the infusion-related reaction occurred during the first infusion.

Adverse Reactions

In the pivotal trial, the most commonly reported adverse reactions (≥10%) for Gamifant included infection (56%), hypertension (41%), infusion-related reactions (27%), pyrexia (24%), hypokalemia (15%), constipation (15%), rash (12%), abdominal pain (12%), CMV infection (12%), diarrhea (12%), lymphocytosis (12%), cough (12%), irritability (12%), tachycardia (12%), and tachypnea (12%).
Additional selected adverse reactions (all grades) that were reported in less than 10% of patients treated with Gamifant included vomiting, acute kidney injury, asthenia, bradycardia, dyspnea, gastro-intestinal hemorrhage, epistaxis, and peripheral edema.
Visit www.gamifant.com for more information, including full Prescribing Information.

About Sobi in North America

As the North American affiliate of international biopharmaceutical company Sobi™, our team is committed to Sobi's vision of providing access to innovative treatments that make a significant difference in the lives of individuals with rare diseases. Our product portfolio includes multiple approved treatments, focused on inflammation/immunology and genetics/metabolism. With North American headquarters in the Boston area, Canadian headquarters in the Toronto area, and field sales, medical and market access representatives spanning North America, our growing team has a proven track record of commercial excellence. More information is available at www.sobi-northamerica.com.
For more information about Sobi, visit www.sobi.com.

About Novimmune

Novimmune SA is a privately held, Swiss biopharmaceutical company focused on discovering and developing antibody-based drugs targeted for the treatment of inflammatory diseases, immune-related disorders and cancer. Founded in 1998 by the renowned immunologist Professor Bernard Mach, Novimmune has more than 150 employees and operates in two sites in Geneva and Basel (Switzerland). Since its foundation, Novimmune has built a significant R&D pipeline of drug candidates, of which emapalumab is the most advanced. The development program of Gamifant was supported by a FP7 grant from the European Commission (FIGHT HLH). Novimmune has also developed a bispecific antibody generation platform designed to streamline the

identification, production and characterization of fully-human bispecific antibodies. More information is available at www.novimmune.com.

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