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FDA Grants Orphan Drug Exclusivity to EVOMELA™ (melphalan) for Injection, Indicated for Multiple Myeloma

HENDERSON, Nev.--(BUSINESS WIRE)-- Spectrum Pharmaceuticals (NasdaqGS: SPPI), a biotechnology company with fully integrated commercial and drug development operations with a primary focus in Hematology and Oncology, announced today that the U.S. Food and Drug Administration (FDA) Office of Orphan Products Development (OOPD) has granted 7 years of Orphan Drug Exclusivity for EVOMELA for use as a high-dose conditioning treatment prior to hematopoietic progenitor (stem) cell transplantation in patients with multiple myeloma. EVOMELA has also been recently listed in the Orange Book, including two composition of matter patents that do not expire until March 2029.

"We are pleased to receive FDA Orphan Drug Exclusivity for EVOMELA, another important regulatory milestone for Spectrum," said Rajesh C. Shrotriya, MD, Chairman and Chief Executive Officer of Spectrum Pharmaceuticals. "EVOMELA is reconstituted with normal saline and does not contain propylene glycol. EVOMELA's formulation is based on Captisol® technology and is stable at room temperature for 1 hour following reconstitution and for an additional 4 hours after further dilution. We believe EVOMELA has the potential to become an important therapy for multiple myeloma patients undergoing high-dose conditioning treatment prior to hematopoietic stem cell transplantation and fits very well with our existing Hematology/Oncology infrastructure. Revenues from our niche products like EVOMELA help us develop our late-stage drugs that target blockbuster markets."

The FDA Orphan Drug Designation program provides a special status to drugs and biologics intended to treat, diagnose or prevent so-called orphan diseases and disorders that affect fewer than 200,000 people in the U.S. Orphan Drug Designation provides the sponsor certain benefits and incentives, including a period of marketing exclusivity if regulatory approval is ultimately received for the designated indication, potential tax credits for certain activities, eligibility for orphan drug grants, and the waiver of certain administrative fees.

Spectrum Pharmaceuticals gained global development and commercialization rights to EVOMELA from Ligand Pharmaceuticals Incorporated (NASDAQ: LGND) in March 2013. Spectrum assumed responsibility for completing the pivotal Phase 2 clinical trial, and was responsible for filing the NDA. Under the license agreement, Ligand received a license fee, and NDA approval milestone, and is eligible to receive further potential milestones and royalties in connection with commercialization.

About Multiple Myeloma

Multiple Myeloma is a systemic malignancy of plasma cells that accumulate in the bone marrow, usually associated with monoclonal antibody secretion, and results in bone marrow failure and bone destruction. It is the second most common hematologic disease with nearly 30,000 new cases projected in the US in 2016 and over 11,000 deaths annually (American Cancer Society Stats, 2016). The rate of autologous stem cell transplantation (ASCT) for patients with MM is growing by approximately 3.3% annually.

Melphalan is the most commonly used IV agent for high-dose conditioning for patients undergoing ASCT for MM. The current IV melphalan market is approximately $100 million annually, with predominant use in ASCT; EVOMELA is the only intravenous melphalan product that is approved for use in the high-dose conditioning indication.

About EVOMELA™

EVOMELA was approved by FDA based on its bioequivalence to the standard melphalan formulation (Alkeran) in a Phase 2 clinical study (Aljitawi et al, Bone Marrow Transplant, 2014) via the 505(b)(2) regulatory pathway. EVOMELA has been granted Orphan Drug Designation by the FDA for its use as a high-dose conditioning regimen for patients with MM undergoing ASCT.

EVOMELA's melphalan formulation does not contain propylene glycol. The use of the Captisol® technology to reformulate also contributes to the 4-hour admixture stability of EVOMELA at room temperature. This is in addition to the 1 hour stability of reconstituted EVOMELA drug product at room temperature and 24 hour stability at refrigerated temperature (5°C).

Please see the Important Safety Information below and the full prescribing information, including BOXED WARNINGS, for EVOMELA at www.evomela.com.

Important Safety Information

WARNING: SEVERE BONE MARROW SUPPRESSION, HYPERSENSITIVITY, and LEUKEMOGENICITY

- **Severe bone marrow suppression with resulting infection or bleeding may occur. Controlled trials comparing intravenous (IV) melphalan to oral melphalan have shown more myelosuppression with the IV formulation. Monitor hematologic laboratory parameters.**
- **Hypersensitivity reactions, including anaphylaxis, have occurred in approximately 2% of patients who received the IV formulation of melphalan. Discontinue treatment with EVOMELA for serious hypersensitivity reactions.**
- **Melphalan produces chromosomal aberrations *in vitro* and *in vivo*. EVOMELA should be considered potentially leukemogenic in humans.**

Contraindications

- History of serious allergic reaction to melphalan.

Warnings and Precautions

- Nausea, vomiting, diarrhea or oral mucositis may occur. Provide supportive care using antiemetic and antidiarrheal medications as needed.
- Hepatic disorders ranging from abnormal liver function tests to clinical manifestations such as hepatitis and jaundice have been reported after treatment with melphalan. Hepatic veno-occlusive disease has also been reported. Monitor liver chemistries.
- EVOMELA can cause fetal harm when administered to a pregnant woman. Advise females of reproductive potential to avoid pregnancy during and after treatment with EVOMELA. If this drug is used during pregnancy or if the patient becomes pregnant while taking this drug, advise the patient of potential risk to the fetus.
- Melphalan-based chemotherapy regimens have been reported to cause suppression of ovarian function in premenopausal women, resulting in persistent amenorrhea in approximately 9% of patients. Reversible or irreversible testicular suppression has also been reported.

Adverse Reactions

- The most common adverse reactions observed in at least 50% of patients with multiple myeloma treated with EVOMELA were neutrophil count decreased (100%), white blood cell count decreased (100%), lymphocyte count decreased (98%), platelet count decreased (98%), diarrhea (93%), nausea (90%), fatigue (77%), hypokalemia (74%), anemia (66%), and vomiting (64%).
- In a single-arm clinical study, twelve (20%) patients with multiple myeloma who received EVOMELA conditioning for ASCT experienced a treatment emergent serious adverse reaction. The most common serious adverse reactions (> 1 patient, 1.6%) were pyrexia, hematochezia, febrile neutropenia, and renal failure.
- In a randomized clinical trial studying the palliative treatment of patients with multiple myeloma, severe myelotoxicity (WBC ≤1,000 and/or platelets ≤25,000) was more common in the IV melphalan arm (28%) than in the oral melphalan arm (11%).

Drug Interactions

- No formal drug interaction studies have been conducted. When nalidixic acid and IV melphalan are given simultaneously, the incidence of severe hemorrhagic necrotic enterocolitis has been reported to increase in pediatric patients.

Use in Specific Populations

- It is not known whether melphalan is present in human milk. Because many drugs are excreted in human milk and because of the potential for serious adverse reactions in nursing infants from melphalan, breastfeeding is not recommended during treatment with EVOMELA.
- Advise females of reproductive potential to avoid pregnancy, which may include the use of effective contraception methods, during and after treatment with EVOMELA.
- For Palliative Treatment, consider dose reduction for patients with renal impairment receiving EVOMELA.

About Captisol®

Captisol is a patent-protected, chemically modified cyclodextrin with a structure designed to optimize the solubility and stability of drugs. Captisol was invented and initially developed by scientists in the laboratories of Dr. Valentino Stella at the University of Kansas' Higuchi Biosciences Center for specific use in drug development and formulation. This unique technology has enabled six FDA-approved products, including Onyx Pharmaceuticals' Kyprolis®, Baxter International's Nexterone® and Merck's NOXAFIL IV. There are also more than 30 Captisol-enabled products currently in clinical development.

About Spectrum Pharmaceuticals, Inc.

Spectrum Pharmaceuticals is a leading biotechnology company focused on acquiring, developing, and commercializing drug products, with a primary focus in Hematology and Oncology. Spectrum currently markets six hematology/oncology drugs, and expects an FDA decision on another drug in the second half of 2016. Additionally, Spectrum's pipeline includes two drugs targeting blockbuster markets in advanced stages of clinical development. Spectrum's strong track record for in-licensing and acquiring differentiated drugs, and expertise in clinical development have generated a robust, diversified, and growing pipeline of product candidates in advanced-stage Phase 2 and Phase 3 studies. More information on Spectrum is available at www.sppirx.com.

Forward-looking statement — This press release may contain forward-looking statements regarding future events and the future performance of Spectrum Pharmaceuticals that involve risks and uncertainties that could cause actual results to differ materially. These statements are based on management's current beliefs and expectations. These statements include, but are not limited to, statements that relate to our business and its future, including certain company milestones, Spectrum's ability to identify, acquire, develop and commercialize a broad and diverse pipeline of late-stage clinical and commercial products, leveraging the expertise of partners and employees around the world to assist us in the execution of our strategy, and any statements that relate to the intent, belief, plans or expectations of Spectrum or its management, or that are not a statement of historical fact. Risks that could cause actual results to differ include the possibility that our existing and new drug candidates may not prove safe or effective, the possibility that our existing and new applications to the FDA and other regulatory agencies may not receive approval in a timely manner or at all, the possibility that our existing and new drug candidates, if approved, may not be more effective, safer or more cost efficient than competing drugs, the possibility that our efforts to acquire or in-license and develop additional drug candidates may fail, our lack of sustained revenue history, our limited marketing experience, our dependence on third parties for clinical trials, manufacturing, distribution and quality control and other risks that are described in further detail in the Company's reports filed with the Securities and Exchange Commission. We do not plan to update any such forward-looking statements and expressly disclaim any duty to update the information contained in this press release except as required by law.

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Spectrum Pharmaceuticals
Shiv Kapoor, 702-835-6300
Vice President, Strategic Planning & Investor Relations
InvestorRelations@sppirx.com

Source: Spectrum Pharmaceuticals

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