Jazz Pharmaceuticals Announces FDA Approval of Defitelio® (defibrotide sodium) for the Treatment of Hepatic Veno-Occlusive Disease (VOD) with Renal or Pulmonary Dysfunction Following Hematopoietic Stem-Cell Transplantation (HSCT)

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First and Only FDA-Approved Therapy for Patients with this Rare, Potentially Fatal Complication

DUBLIN, March 30, 2016 /PRNewswire/ -- Jazz Pharmaceuticals plc (Nasdaq: JAZZ) today announced that the United States (U.S.) Food and Drug Administration (FDA) granted marketing approval for Defitelio® (defibrotide sodium) for the treatment of adult and pediatric patients with hepatic VOD, also known as sinusoidal obstruction syndrome (SOS), with renal or pulmonary dysfunction following HSCT.[1]

"FDA's approval of Defitelio underscores the importance of Defitelio to children and adults as the first and only proven treatment for this rare and often deadly complication of stem-cell transplantation. Defitelio is a clinically significant therapeutic advance because it is a potentially curative intervention for patients with VOD, which may save lives with a single course of therapy. Before today, patients in the U.S. had no approved options," said Bruce Cozadd, chairman and chief executive officer of Jazz Pharmaceuticals. "The commercial availability of Defitelio in the U.S. demonstrates Jazz Pharmaceuticals' continued commitment to bringing meaningful new treatments to patients to fill high unmet medical needs."

The FDA approval of Defitelio is supported by efficacy data from three clinical studies in patients with hepatic VOD with renal or pulmonary dysfunction following HSCT who were treated with Defitelio at the recommended 6.25 mg/kg every 6 hours; results are provided in the table below.[1]

	Study Design	Patient Number	Survival Rate at Day +100 after HSCT	Confidence Interval (CI)
Study 1	Phase 3 Prospective Study	n=102	38%	95% CI: 29%, 48%
Study 2	Phase 2 Prospective Study	n=75	44%	95% CI: 33%, 55%
Study 3	Expanded Access Study	n=351	45%	95% CI: 40%, 51%

The safety of Defitelio to support approval is based on data from 176 patients in the clinical development program for the treatment of VOD with renal and/or pulmonary dysfunction following HSCT who were treated with Defitelio. The most common adverse reactions (incidence ≥10% and independent of causality) with Defitelio treatment were hypotension (low blood pressure), diarrhea, vomiting, nausea and epistaxis (nose bleeds).[1] The most common serious adverse reactions (incidence ≥5% and independent of causality) were hypotension (11%) and pulmonary alveolar hemorrhage (7%).[1]

"VOD/SOS is a devastating condition, which can develop without warning after stem-cell transplantation and can progress rapidly causing severe kidney or lung dysfunction and lead to multi-organ failure. Thus, it can derail a patient's recovery from the curative intent of a stem-cell transplant, with patients who develop VOD/SOS and multi-organ failure facing an overall mortality rate of over 80%," said Paul G. Richardson, M.D., director of clinical research at the LeBow Institute for Myeloma Therapeutics and the Jerome Lipper Multiple Myeloma Center at the Dana-Farber Cancer Institute and the RJ Corman Professor of Medicine at Harvard Medical School. "Defitelio thus fulfills an unmet need having shown a consistent Day +100 patient survival benefit across three large prospective studies. Importantly, Defitelio provides transplant teams with the first approved treatment option that can help return patients to the road to recovery."

"We applaud the FDA's approval of Defitelio and acknowledge Jazz Pharmaceuticals' commitment to bringing this meaningful new treatment to the small number of patients who develop VOD with renal or pulmonary dysfunction following stem-cell transplantation," said Susan K. Stewart, Executive Director at BMT InfoNet (Blood & Marrow Transplant Information Network).

Shipments of Defitelio to distribution channels will commence within a week.

Jazz Pharmaceuticals will offer patient support through its JumpStart program to help provide access to Defitelio. This program includes a reimbursement assistance program for providing information on benefit or reimbursement questions. Additionally, a patient assistance program (PAP) will be available to help qualified patients gain access to Defitelio. To learn more about these programs, contact 1-888-837-4397, Monday through Friday, 9 a.m. to 6 p.m. ET.

About Defitelio

Defitelio® (defibrotide sodium) injection 80mg/mL is indicated for the treatment of adult and pediatric patients with hepatic VOD, also known as SOS, with renal or pulmonary dysfunction following HSCT.[1] The FDA granted the Defitelio application priority review status. Defitelio also received orphan drug designation for the treatment of hepatic VOD.

Important Safety Information[1]

Defitelio should not be given to patients who are:

- Currently taking anticoagulants or fibrinolytics
- Allergic to Defitelio or any of its ingredients

Defitelio may increase the risk of bleeding in patients with VOD and should not be given to patients with active bleeding. During treatment with

Defitelio, patients should be monitored for signs of bleeding. In the event that bleeding occurs during treatment with Defitelio, treatment should be temporarily or permanently stopped. Patients should tell the doctor right away about any signs or symptoms of hemorrhage such as unusual bleeding, easy bruising, blood in urine or stool, headache, confusion, slurred speech, or altered vision.

Defitelio may cause allergic reactions including anaphylaxis. Patients who develop signs and symptoms of anaphylaxis such as trouble breathing, severe itching, skin rash or hives, or swelling of the face, lips, mouth or tongue should seek medical attention immediately.

The most common side effects of Defitelio are decreased blood pressure, diarrhea, vomiting, nausea and nose bleeds. Please see full **Prescribing Information** for Defitelio before prescribing.

In Europe, defibrotide is marketed under the name Defitelio®▼(defibrotide). In October 2013, the European Commission granted marketing authorization to Defitelio under exceptional circumstances for the treatment of severe VOD in patients undergoing HSCT therapy. It is the first and only approved treatment in Europe for severe VOD. In Europe, Defitelio is indicated in patients over one month of age. It is not indicated in patients with hypersensitivity to defibrotide or any of its excipients or with concomitant use of thrombolytic therapy.

▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system found under section 4.8 of the **SmPC.** (http://www.ema.europa.eu/ema/index.jsp?curl=/pages/medicines/human/medicines/002393/human_med_001646.jsp)

For more information about Defitelio in the U.S., please visit **www.Defitelio.com.**

About VOD

HSCT is an aggressive, potentially curative procedure to treat patients with malignant and non-cancerous hematologic disorders such as leukemia, lymphoma and aplastic anemia, and congenital immunodeficiency and autoimmune disorders.[2] VOD is a rare complication of HSCT, which occurs in approximately 9–14% of HSCT patients.[3,4] Hepatic VOD, also known as SOS, is an early and life-threatening complication affecting the sinusoidal endothelial cells of the liver, which can typically occur within the first 21 days following HSCT.[4,5] Hepatic VOD progresses to become life-threatening in approximately 30-50% of cases.[5] VOD with multi-organ dysfunction (MOD) is associated with an overall mortality (death) rate of 84%.[3] MOD is characterized by the presence of renal or pulmonary dysfunction.[6,7] VOD is often characterized by sudden weight gain, hepatomegaly (abnormally enlarged liver), and elevated bilirubin.[6,7]

About Jazz Pharmaceuticals plc

Jazz Pharmaceuticals plc (Nasdaq: JAZZ) is an international biopharmaceutical company focused on improving patients' lives by identifying, developing and commercializing meaningful products that address unmet medical needs. The company has a diverse portfolio of products and product candidates with a focus in the areas of sleep and hematology/oncology. In these areas, Jazz Pharmaceuticals markets Xyrem® (sodium oxybate) oral solution**,** Erwinaze® (asparaginase *Erwinia chrysanthemi*) and Defitelio® (defibrotide sodium) in the U.S. and markets Erwinase® and Defitelio® (defibrotide) in countries outside the U.S. For more information, please visit **www.jazzpharmaceuticals.com.**

"Safe Harbor" Statement under the Private Securities Litigation Reform Act of 1995

This press release contains forward-looking statements, including, but not limited to, statements related to the potential benefits and commercial availability of Defitelio in the U.S. and other statements that are not historical facts. These forward-looking statements are based on the company's current plans, objectives, estimates, expectations and intentions, and inherently involve significant risks and uncertainties. Actual results and the timing of events could differ materially from those anticipated in such forward-looking statements as a result of these risks and uncertainties, which include, without limitation, risks and uncertainties associated with the company's ability to effectively commercialize Defitelio in the U.S.; delays or problems in the supply or manufacture of Defitelio; obtaining and maintaining appropriate pricing and reimbursement; complying with the requirements of regulatory agencies; the challenges of achieving and maintaining commercial success of Defitelio; and other risks and uncertainties affecting the company, including those described from time to time under the caption "Risk Factors" and elsewhere in Jazz Pharmaceuticals plc's Securities and Exchange Commission filings and reports (Commission File No. 001-33500), including the company's Annual Report on Form 10-K for the year ended December 31, 2015 and future filings and reports by the company. Other risks and uncertainties of which the company is not currently aware may also affect the company's forward-looking statements and may cause actual results and timing of events to differ materially from those anticipated. The forward-looking statements herein are made only as of the date hereof or as of the dates indicated in the forward-looking statements, even if they are subsequently made available by the company on its website or otherwise. The company undertakes no obligation to update or supplement any forward-looking statements to reflect actual results, new information, future events, changes in its expectations or other circumstances that exist after the date as of which the forward-looking statements were made.

References:

1 Defitelio (defibrotide sodium) [package insert]. Palo Alto, CA: Jazz Pharmaceuticals; March 30, 2016.

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