Jazz Pharmaceuticals Announces First Patient Enrolled in Phase 3 Clinical Trial Evaluating Defibrotide for the Potential Prevention of VOD in High Risk Patients

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DUBLIN, Jan. 17, 2017 /PRNewswire/ -- Jazz Pharmaceuticals plc (Nasdaq: JAZZ) today announced that the first patient has been enrolled in a Phase 3 clinical trial comparing the efficacy and safety of defibrotide versus best supportive care (BSC) in the prevention of hepatic veno-occlusive disease (VOD) in adult and pediatric patients undergoing hematopoietic stem cell transplant (HSCT) who are at high risk or at very high risk of developing VOD. The defibrotide clinical trial will be conducted across approximately 100 medical centers in the United States (U.S.), Canada, Asia Pacific and countries in the European Union (EU).

"The initiation of this trial is another step forward in Jazz's development program for defibrotide as a treatment option for patients who are at high risk or very high risk of developing this life-threatening condition," said Karen Smith, M.D., Ph.D., global head of research and development and chief medical officer of Jazz Pharmaceuticals. "If the data from this trial are positive, they may be used to pursue regulatory approval of a label expansion for defibrotide in both the U.S. and EU to include the prevention of hepatic VOD in high risk patients following HSCT."

The Phase 3 trial is a randomized, open-label, multi-center trial with an adaptive design comparing the efficacy of defibrotide vs. BSC in the prevention of hepatic VOD. The trial is expected to enroll approximately 400 adult and pediatric patients undergoing HSCT who are at high risk or very high risk of developing VOD. High (or very high) risk patients are identified due to the clinical regimen required to prepare them for HSCT, as well as their prior medical history and concomitant disease. The adaptive design allows for an interim analysis with pre-defined stopping points for early success or failure as well as the option to increase enrollment if needed to preserve the statistical power of the trial.

For patients randomized to receive defibrotide prophylaxis, defibrotide will be administered starting on the day before the first day of the conditioning regimen for a recommended minimum of 21 days and ending no later than Day +30 post HSCT. The primary endpoint is VOD-free survival at Day +30 post-HSCT. Additional information about the trial, including eligibility criteria and a list of clinical trial sites can be found at: www.clinicaltrials.gov (ClinicalTrials.gov Identifier: NCT02851407).

About Defitelio® (defibrotide sodium)[1]
Defibrotide has orphan drug designation from the U.S. Food and Drug Administration (FDA) and European Medicines Agency (EMA) for the prevention of hepatic VOD. In the U.S. Defitelio® (defibrotide sodium) injection 80mg/mL received U.S. FDA marketing approval on March 30, 2016 for the treatment of adult and pediatric patients with hepatic veno-occlusive disease (VOD), also known as sinusoidal obstruction syndrome (SOS), with renal or pulmonary dysfunction following hematopoietic stem-cell transplantation (HSCT) and is the first and only FDA-approved therapy for patients with this rare, potentially fatal complication.

Defitelio is contraindicated in patients currently taking anticoagulants or fibrinolytics and in patients who are allergic to Defitelio or any of its ingredients. Defitelio may increase the risk of bleeding and should be withheld or stopped if significant bleeding occurs. Patients should be monitored for allergic reactions, especially if there is a history of previous exposure to Defitelio. The most common side effects of Defitelio are decreased blood pressure, diarrhea, vomiting, nausea and nose bleeds.

Please see full **Prescribing Information** for Defitelio.

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)

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 multi-organ dysfunction 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
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 of defibrotide as a treatment for the prevention of VOD in adult and pediatric patients undergoing HSCT who are at high risk or very high risk of developing VOD, the potential for label expansion for defibrotide, 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 of pharmaceutical product development and clinical success thereof, the uncertainty of regulatory approval, and other risks and uncertainties affecting the company and its development programs, 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 Quarterly Report on Form 10-Q for the quarter ended September 30, 2016 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 the 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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SOURCE Jazz Pharmaceuticals plc

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