Jazz Pharmaceuticals Announces First Patient Enrolled in Phase 2 Clinical Trial Evaluating Defibrotide for the Prevention of Acute Graft-versus-Host Disease

February 23, 2018 8:31 AM ET

DUBLIN, Feb. 23, 2018 /PRNewswire/ -- Jazz Pharmaceuticals plc (Nasdaq: JAZZ) today announced that the first patient has been enrolled in a Phase 2 clinical trial evaluating the efficacy and safety of defibrotide for the prevention of acute Graft-versus-Host-Disease (aGvHD) in adult and pediatric patients after allogeneic hematopoietic stem cell transplant (HSCT). The defibrotide clinical trial will be conducted across approximately 60 medical centers in the United States (U.S.), Canada and European Union.

"Potential complications of hematopoietic stem cell transplant such as acute Graft-versus-Host Disease can be life threatening and even fatal," said Karen Smith, M.D., Ph.D., executive vice president, research and development and chief medical officer at Jazz Pharmaceuticals. "Despite the use of current immunoprophylaxis strategies, Graft-versus-Host Disease remains a leading cause of non-relapse mortality after allogeneic stem cell transplant. Jazz is committed to advancing our understanding of how defibrotide may address this unmet need."

The Phase 2 clinical trial is a prospective, randomized, open-label study of the efficacy and safety of defibrotide added to standard of care immunoprophylaxis for the prevention of aGvHD, compared to the standard of care alone. Jazz expects to enroll approximately 150 adult and pediatric patients who have undergone allogeneic HSCT from an unrelated donor. The primary endpoint is cumulative incidence of Grade B-D aGvHD by day +100 post-allogeneic HSCT. Additional information about the trial, including eligibility criteria and a list of clinical trial sites can be found at: https://clinicaltrials.gov (ClinicalTrials.gov Identifier: NCT03339297).

This Phase 2 trial complements the company's ongoing Phase 3 clinical trial evaluating defibrotide for prevention of hepatic veno-occlusive disease (VOD) in high-risk adult and pediatric patients undergoing hematopoietic stem cell transplant.

About GvHD

Graft-versus-Host-Disease (GvHD) is a life-threatening complication of HSCT, a potentially curative option for several malignant and non-malignant disorders, and occurs when immune cells from a non-identical donor (graft) recognize the transplant recipient (host) as foreign. GvHD is the most frequent cause of morbidity and non-relapse mortality following allogeneic HSCT.[1] One in five patients receiving a transplant from an unrelated donor dies from GvHD. Approximately 24,000 allogeneic patients in the United States and Europe are at risk for acute GvHD (aGvHD), which usually occurs within the first 100 days following HSCT and typically involves damage to the skin, gastrointestinal tract and/or liver.[1,2,3,4] The International Bone Marrow Transplant Registry (IBMTR) Severity Index grades aGvHD as follows: Grade A includes patients with stage 1 skin aGvHD only; B includes those with stage 2 skin and no visceral aGvHD or stage 0-2 skin with stage 1 or 2 visceral aGvHD; C includes patients with stage 3 skin, liver and/or gut aGvHD; D includes those with stage 4 skin, liver and/or gut aGvHD.[5]

About Defitelio® (defibrotide sodium)

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 not approved for the treatment of prevention of GvHD or prevention of VOD.

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.[6] VOD is a rare complication of HSCT that occurs in approximately 9-14% of HSCT patients.[7,8] 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.[8,9] Hepatic VOD progresses to become life-threatening in approximately 30-50% of cases.[9] VOD with multi-organ dysfunction (MOD), when left untreated, can be associated with an overall mortality (death) rate of 84%.[7] MOD is characterized by the presence of renal or pulmonary dysfunction.[10,11] VOD is often characterized by sudden weight gain, hepatomegaly (abnormally enlarged liver), and elevated bilirubin.[10,11]

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*), Defitelio® (defibrotide sodium) and Vyxeos® (daunorubicin and cytarabine) liposome for injection in the U.S. and markets Erwinase® and Defitelio® (defibrotide) in countries outside the U.S. For country-specific product information, please visit www.jazzpharmaceuticals.com/products. For more information, please visit www.jazzpharmaceuticals.com and follow us on Twitter at @JazzPharma.

"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 defibrotide as a potential treatment for the prevention of aGvHD in adult and pediatric patients after allogeneic HSCT 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: pharmaceutical product development and clinical success thereof; and the regulatory approval process; 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, 2017 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. Pasquini MC, Zhu X. Current use and outcome of hematopoietic stem cell transplantation: CIBMTR summary slides, 2015. Available at: http://www.cibmtr.org
2. Passweg JR, Baldomero H, Bader P, et al. Hematopoietic stem cell transplantation in Europe 2014: more than 4000 transplants annually. *Bone Marrow Transplantation*. 2016;51:786-92.
3. Jagasia M, et al. Blood. 2012;119: 296-307.
4. Jacobsohn DA, *Bone Marrow Transplantation*. 2008;41: 215-221.
5. Rowlings PA, Przepiorka D, et al. IBMTR Severity Index for grading acute graft-versus-host disease: retrospective comparison with Glucksberg grade. *British Journal of Haematology*. 1997;97:855-64.
6. Ikehara S. New strategies for BMT and organ transplantation. Int J Hematol. 2002;76(Suppl 1):161-4.
7. Coppell JA, Richardson PG, Soiffer R, et al. Hepatic veno-occlusive disease following stem cell transplantation: incidence, clinical course, and outcome. Biol Blood Marrow Transplant. 2010;16(2):157-168.
8. Tsirigotis PD, Resnick IB, Avni B, et al. Incidence and risk factors for moderate-to-severe veno-occlusive disease of the liver after allogeneic stem cell transplantation using a reduced intensity conditioning regimen. Bone Marrow Transplant. 2014;49(11):1389-1392.
9. Carreras E, Díaz-Beyá M, Rosiñol L, et al. The incidence of veno-occlusive disease following allogeneic hematopoietic stem cell transplantation has diminished and the outcome improved over the last decade. Biol Blood MarrowTransplant. 2011;17(11):1713-1720.
10. Carreras E. How I manage sinusoidal obstruction syndrome after haematopoietic cell transplantation. Brit J Haematol. 2015 Feb.; 168 (4); 481-91.
11. Mohty M, Malard F, Abecassis M, et al. Sinusoidal obstruction syndrome/veno‐occlusive disease: current situation and perspectives—a position statement from the European Society for Blood and Marrow Transplantation (EBMT). Bone Marrow Transplant. 2015;50(6):781‐789.

View original content with multimedia:http://www.prnewswire.com/news-releases/jazz-pharmaceuticals-announces-first-patient-enrolled-in-phase-2-clinical-trial-evaluating-defibrotide-for-the-prevention-of-acute-graft-versus-host-disease-300603339.html

SOURCE Jazz Pharmaceuticals plc

Media Contact: Jacqueline Kirby, Vice President, Corporate Affairs & Government Relations, Ireland +353 1 697 2141, U.S. +1 215 867 4910 or Investor Contact: Kathee Littrell, Vice President, Investor Relations, Ireland +353 1 634 7887, U.S. +1 650 496 2717