Jazz Pharmaceuticals to Present Data on Defibrotide, an Investigational Treatment, in Patients with Hepatic Veno-Occlusive Disease (VOD) at BMT Tandem Meetings

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Three Oral Presentations Provide New Analyses of the Efficacy and Safety of Defibrotide in Patients with VOD, Including Post-Hoc Sub-Group Analyses in Children, Adults, and Allograft and Autograft Recipients

DUBLIN, Feb. 12, 2015 /PRNewswire/ -- Jazz Pharmaceuticals plc (Nasdaq: JAZZ) announced today that researchers will present data on the use of defibrotide, an investigational medicine being studied in the United States (U.S.) for the treatment of hepatic veno-occlusive disease (VOD), a rare, potentially life-threatening, early complication in patients undergoing hematopoietic stem-cell transplantation (HSCT) therapy. The three presentations include an update from an ongoing treatment investigational new drug (T-IND) study in the U.S., as well as updates from a number needed to treat (NNT, an epidemiological measure of effectiveness) analysis from a historically controlled pivotal Phase 3 trial in patients undergoing HSCT therapy, and from an international defibrotide compassionate use program.

Data from the three defibrotide studies will be presented today in an oral abstract session at the 2015 BMT (Bone Marrow Transplantation) Tandem meetings, the combined annual meetings of the American Society of Blood and Marrow Transplantation (ASBMT) and the Center for International Blood and Marrow Transplant Research (CIBMTR), in San Diego, California. BMT Tandem is one of the largest international forums dedicated specifically to HSCT.

"VOD is a potentially life-threatening complication in patients undergoing HSCT therapy, and there are currently no approved therapies for VOD in the U.S," said Jeffrey Tobias, M.D., executive vice president and chief medical officer of Jazz Pharmaceuticals. "The data presented at the BMT Tandem meetings build upon existing evidence showing that, when recognized and diagnosed, severe VOD may be effectively treated with defibrotide. The data also provide additional information on defibrotide's efficacy and safety profile in important subgroups of patients such as children, adults, and allograft and autograft recipients."

In 2014, Jazz Pharmaceuticals acquired the rights to defibrotide in the U.S. and other markets in North America, South America and Central America. Defibrotide has a Fast Track regulatory path designation in the U.S. for the treatment of severe VOD. The company has initiated a rolling new drug application submission to the U.S. Food and Drug Administration for defibrotide for the treatment of severe VOD and anticipates completing the submission in the first half of 2015.

In Europe, defibrotide is marketed under the name Defitelio®▼ (defibrotide). Defitelio is the first and only licensed product in Europe for the treatment of severe VOD in patients over one month of age undergoing HSCT therapy.

The three defibrotide oral presentations will be presented today during the BMT Tandem "Scientific" meeting, Session F - Allogeneic Transplants & Supportive Care & Graft Processing in the Harbor Ballroom ABC at the Manchester Grand Hyatt from 4:45 pm to 6:45 pm PST. Details are as follows:

- **Paul G. Richardson, M.D., "Defibrotide for the Treatment of Severe Hepatic Veno-Occlusive Disease: An Analysis of Clinical Benefit As Determined By Number Needed to Treat (NNT) to Achieve Complete Response and to Improve Survival."** Dr. Richardson and co-authors will present an NNT analysis from a Phase 3 study that formed the basis of the approval of defibrotide for the treatment of severe VOD following HSCT in the European Union. Dr. Richardson is the clinical program leader and 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.
- **Paul G. Richardson, M.D., "Updated Results from the Ongoing US Treatment IND Study Using Defibrotide for Patients with Hepatic Veno-Occlusive Disease."** Researchers will present an interim analysis update from the T-IND study, which is gathering data on the safety and efficacy of defibrotide in patients with severe and non-severe VOD post-HSCT, as well as post-chemotherapy.
- **Selim Corbachioglu, M.D., "Defibrotide for the Treatment of Hepatic Veno-Occlusive Disease: An Update from the International Compassionate Use Program in 710 Patients."** Dr. Corbachioglu, of the University of Regensburg, Germany, will present the final results of a large, international defibrotide compassionate use program conducted from 1998-2009 in Europe, the U.S., Asia and the Middle East.

Full details of the 2015 BMT Tandem meetings can be found at https://bmt.confex.com/tandem/2015/webprogram/programs.html.

About Defibrotide

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

Please consult the Defitelio Summary of Product Characteristics (SmPC) **http://www.ema.europa.eu/ema/index.jsp?curl=/pages/medicines/human/medicines/002393/human_med_001646.jsp** before prescribing, particularly in relation to use of medicinal products that increase the risk of hemorrhage, concomitant systemic anticoagulant therapy, medicinal products that affect platelet aggregation, use in patients who have or develop clinically significant acute bleeding requiring blood transfusion, and patients who have hemodynamic instability.

The most frequent adverse events observed during pre-marketing use were hemorrhage, hypotension and coagulopathy, as noted in the Defitelio SmPC. Please consult the Defitelio SmPC for the full list of all side effects reported with Defitelio.

▼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.

An ongoing expanded access program through a Treatment IND is enrolling patients diagnosed with VOD in the U.S. Expanded access programs are part of an effort by the U.S. Food and Drug Administration (FDA) and the pharmaceutical industry to make investigational drugs available for the treatment of serious or life threatening diseases in people with limited treatment options. For information about the defibrotide study contact Darcy Fay at (1.650.496.3051; darcy.fay@jazzpharma.com) or Lam Calderon (1.312.706.6240; 0265-002Gentium@iconplc.com); or visit www.clinicaltrials.gov (Identifier: NCT00628498).

About VOD
VOD, also known as sinusoidal obstruction syndrome (SOS), is a complication in patients undergoing HSCT therapy. The condition is characterized by blockage in some of the small blood vessels in the liver, resulting in decreased blood flow within the liver and possibly leading to liver damage. Signs and symptoms include weight gain, jaundice and enlargement of the liver. VOD may also occur after a patient undergoes radiation therapy to the liver or receives anticancer chemotherapy before HSCT.[1]

In its severe form, VOD can be life-threatening and is associated with multi-organ failure, and can be fatal in over 80% of patients.[2,3] Although the disease appears most often within 21 days post-HSCT, its onset can occur later in the course of the patient's recovery from HSCT, even after discharge from the hospital.[2] Early clinical signs such as percent weight gain, mean total bilirubin (indicative of jaundice) and the rate of change in these measures may predict progression to severe VOD.[4,5] However, other conditions may mimic VOD, making early differential diagnosis challenging, yet crucial to successful patient outcomes.[6]

Specific groups of HSCT patients, including children, people who have suffered a previous injury to the liver, and recipients of allogenic (i.e., from another individual) hematopoietic stem cells, are at higher risk of developing VOD.[3] Current treatment approaches usually involve monitoring of clinical lab values, as well as supportive care.

Studies have reported a wide range of incidence rates for VOD in HSCT patients, from as low as 0% to as high as 62%.[3] Generally, data indicate that approximately 14% of patients undergoing HSCT develop VOD.[2,7,8]

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/or product candidates with a focus in the areas of sleep and hematology/oncology. In these areas, Jazz Pharmaceuticals markets Xyrem® (sodium oxybate) oral solution and Erwinaze® (asparaginase *Erwinia chrysanthemi*) in the U.S., and markets Erwinase® and Defitelio® (defibrotide) in Europe and other 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 effectiveness of defibrotide for treating severe VOD, Jazz Pharmaceuticals' plans to complete a rolling NDA submission for defibrotide in the U.S. and the timing thereof and other statements that are not historical facts. These forward-looking statements are based on Jazz Pharmaceuticals' current expectations 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 inherent uncertainty associated with regulatory approval process, including the risks that the company may be required to conduct additional time-consuming and costly clinical trials as a condition of regulatory approval of defibrotide in the U.S. and that the company may otherwise be unable to obtain or maintain any regulatory approval for defibrotide in the U.S., and those other risks detailed 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 Quarterly Report on Form 10-Q for the quarter ended September 30, 2014 and future filings and reports by the company. Jazz Pharmaceuticals undertakes no duty or obligation to update any forward-looking statements contained in this press release as a result of new information, future events or changes in its expectations.

References

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