# Results from Phase 3 Trial of Defibrotide for the Treatment of Severe Veno-Occlusive Disease and Multi-Organ Failure Published Online in BLOOD

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**Data show that defibrotide improved survival and complete response compared with historical controls**

DUBLIN, Feb. 1, 2016 /PRNewswire/ -- Jazz Pharmaceuticals plc (Nasdaq: JAZZ) today announced that data from the phase 3 pivotal study of defibrotide were published online in *BLOOD*, the Journal of the American Society of Hematology (ASH). The data demonstrated that defibrotide use in patients with hepatic veno-occlusive (VOD), also known as sinusoidal obstruction syndrome (SOS), with multi-organ failure (MOF) post-hematopoietic stem-cell transplantation (HSCT) was associated with a statistically significant improvement in Day +100 survival and in rate of complete response (CR) by Day +100, compared with rigorously selected historical controls.

"Based on the results of this pivotal phase 3 study, we believe defibrotide provides a promising treatment option for patients with this urgent unmet need," said lead author and principal investigator, Paul G. Richardson, M.D., director of clinical research and clinical program leader at the Jerome Lipper Multiple Myeloma Center, Dana-Farber Cancer Institute and the RJ Corman Professor of Medicine at Harvard Medical School, Boston MA. "Although HSCT has improved substantially over the last decade, hepatic VOD/SOS with MOF remains a very real and life-threatening complication post-HSCT, and for which there are no currently approved therapies."

Defibrotide is an investigational agent in the United States (U.S.). A new drug application (NDA) is under review by the U.S. Food and Drug Administration (FDA). Hepatic VOD/SOS can be a life-threatening complication of HSCT. Hepatic VOD/SOS with MOF has been associated with 84% mortality rate.[1]

**About the Study**

The phase 3 study investigated the safety and efficacy of defibrotide in adult and pediatric patients with established hepatic VOD/SOS with MOF. Patients (n=102) given 25 mg/kg/day defibrotide were compared with 32 historical controls identified from review of medical charts of HSCT patients by an independent medical review committee, blinded to outcome. Baseline characteristics between groups were well balanced. The historical-control methodology offers a novel approach for phase 3 evaluation of orphan diseases associated with high mortality, where a placebo control would be unethical.

Defibrotide was associated with a statistically significant improvement in Day +100 post-HSCT survival, the primary endpoint, compared to the historical controls. The estimated between-group difference in Day +100 survival was 23.0% (95.1% confidence interval (CI): 5.2%-40.8%; P=.0109), using a propensity-adjusted analysis. The difference of complete response (CR) rates by Day +100 post-HSCT, a secondary endpoint, resulted in an estimated between-group difference adjusted for propensity score of 19.0% (95.1% CI: 3.5 – 34.6; P=.0160). Median duration of treatment with defibrotide was 21.5 days.

Hypotension was the most common adverse event in both groups (39.2% with defibrotide and 50.0% for historical controls). Related adverse events included hemorrhage and hypotension. There was no difference in the incidence of common hemorrhagic events between defibrotide and the historical controls.

**About VOD**

HSCT is a potentially curative procedure to treat patients with malignant and non-cancerous hematologic disorders such as leukemia, lymphoma and aplastic anemia, congenital immunodeficiency and autoimmune disorders.[2] Hepatic VOD, also known as SOS, is a rare, early and life-threatening complication of HSCT.

**About Defibrotide**

In the U.S., defibrotide is an investigational drug for the treatment of patients with hepatic VOD with multi-organ dysfunction (MOD), defined as renal or pulmonary dysfunction, following HSCT. Defibrotide was granted Orphan Drug Designation by the FDA in May 2003 and has Fast Track designation.

Defibrotide is being made available as an investigational new drug (IND) free of charge through an expanded access Treatment Protocol. The ongoing expanded access Treatment Protocol is currently enrolling patients diagnosed with VOD in the U.S. Expanded access programs are part of an effort by the 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 expanded access defibrotide study, contact Erin Tokunaga at erin.tokunaga@jazzpharma.com or Lam Calderon (1.312.706.6240; 0265-002Gentium@iconplc.com); or visit www.clinicaltrials.gov (Identifier: NCT00628498).

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 hepatic VOD in patients undergoing HSCT therapy. Defitelio received an approval in Israel in May 2015 for the same indication as in the EU.

**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 and Erwinaze® (asparaginase *Erwinia chrysanthemi*) in the U.S., and markets Erwinase® and Defitelio® (defibrotide) in countries outside the U.S. For more information, please visit www.jazzpharmaceuticals.com.

References:
1. Coppell JA et al.  Biol Blood Marrow Transplant. 2010; 16 (2): 157-168.
2. Ikehara S. New strategies for BMT and organ transplantation. Int J Hematol. 2002;76(Suppl 1):161-4.

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To view the original version on PR Newswire, visit:http://www.prnewswire.com/news-releases/results-from-phase-3-trial-of-defibrotide-for-the-treatment-of-severe-veno-occlusive-disease-and-multi-organ-failure-published-online-in-blood-300212651.html

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