# Jazz Pharmaceuticals Announces Availability of DefitelioTM (defibrotide sodium) for the Treatment of Hepatic Veno-Occlusive Disease (VOD) with Renal or Pulmonary Dysfunction Following Hematopoietic Stem-Cell Transplantation (HSCT) Therapy

August 28, 2017

DUBLIN, August 28, 2017 -- Jazz Pharmaceuticals plc (Nasdaq: JAZZ) today announced the Canadian availability of DefitelioTM (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 therapy.[1]

"VOD/SOS is a devastating condition, which can develop without warning after stem-cell transplantation and can progress rapidly, cause severe kidney or lung dysfunction, and potentially lead to multi-organ failure," said Iain McGill, senior vice president, Europe and Rest of World, Jazz Pharmaceuticals. "The availability of Defitelio is great news for patients in Canada as it provides a new treatment option in a disease that previously had no approved treatments."

Jazz filed a New Drug Submission (NDS) to Health Canada on November 29, 2016. The application received priority review status. Priority review is typically granted when there is an unmet medical need for a serious, life-threatening or severely debilitating disease or condition. The product was approved by Health Canada on July 10, 2017.

Health Canada's approval of Defitelio was 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.

"The availability of Defitelio fills a significant need in the transplantation community to treat VOD/SOS with renal or pulmonary dysfunction, a rare but frequently fatal complication in patients who receive HSCT therapy," said Denis-Claude Roy, M.D., F.R.C.P, Director, CellCAN Regenerative Medicine and Cell Therapy Network, Director, Maisonneuve-Rosemont Hospital Research Centre and Professor of Medicine at the Université de Montreal.

With the approval and availability of Defitelio in Canada, Jazz Pharmaceuticals, in discussion with Health Canada, will stop making Defitelio available through the Special Access Program. Patients currently receiving treatment through the Special Access Program will be able to complete their course of therapy.

**About Defitelio**

Defitelio™ (defibrotide sodium) solution for intravenous infusion is indicated for the treatment of adult and pediatric patients with hepatic VOD, also known as SOS, with renal or pulmonary dysfunction following HSCT therapy.[1]

Defitelio is also approved in the U.S., Europe, Israel, and South Korea. Please refer to the local label for the approved indication and prescribing information.

**Important Safety Information for Canada**[1]

DefitelioTM should not be given to patients who are:

- Currently taking anticoagulants or fibrinolytics
- Allergic to DefitelioTM or ingredient in the formulation or component of the container

Defitelio™ must be prescribed and administered to patients by specialised physicians experienced in the diagnosis and treatment of complications of HSCT. 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.

Defitelio™ may cause allergic reactions including anaphylaxis. If a severe hypersensitivity reaction occurs, discontinue Defitelio™ permanently.

The most common side effects of Defitelio™ are decreased blood pressure, diarrhea, vomiting, nausea and nose bleeds. Please see **Product Monograph** for Defitelio™ in Canada before prescribing information.

**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 that 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), when left untreated, can be 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 in Canada**

With a leadership team based in Ontario, a partner distribution facility in Montreal, and a research facility in Vancouver, Jazz Pharmaceuticals' Canadian offices contribute to the company's commercial, medical and research initiatives, and support its growing global business.

**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 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 Canada 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 Canada; delays or problems in the supply or manufacture of Defitelio; obtaining and maintaining appropriate pricing and reimbursement for Defitelio in Canada; complying with the requirements of regulatory agencies; and achieving and maintaining commercial success of Defitelio in Canada; 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 Quarterly Report on Form 10-Q for the quarter ended June 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 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) Product Monograph. Jazz Pharmaceuticals Ireland Limited; July 10, 2017.

2 Ikehara S. New strategies for BMT and organ transplantation. Int J Hematol. 2002;76 (Suppl 1):161-4.

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4 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.

5 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.

6 Carreras E. How I manage sinusoidal obstruction syndrome after haematopoietic cell transplantation. Brit J Haematol. 2015 Feb.; 168 (4); 481-91.

7 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.

SOURCE Jazz Pharmaceuticals plc

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