Vyxeos® Receives Marketing Authorisation in the European Union for Treatment of Certain Types of High-Risk Acute Myeloid Leukaemia

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DUBLIN, Aug. 27, 2018 /PRNewswire/ -- Jazz Pharmaceuticals plc (Nasdaq: JAZZ) today announced that the European Commission approved Vyxeos® 44 mg/100 mg powder for concentrate for solution for infusion for the treatment of adults with newly diagnosed, therapy-related acute myeloid leukaemia (t-AML) or AML with myelodysplasia-related changes (AML-MRC). *Vyxeos* is an advanced liposomal formulation that delivers a synergistic molar ratio of daunorubicin and cytarabine.

"*Vyxeos* is the first chemotherapy to demonstrate an overall survival advantage versus the standard of care in a Phase 3 study of older adult patients with newly diagnosed therapy- related AML or AML with myelodysplasia-related changes," said Daniel Swisher, president and chief operating officer at Jazz Pharmaceuticals. "Jazz is committed to making *Vyxeos* available to patients in the EU and we will now pursue rolling launches of *Vyxeos* across the European Union on a country-by-country basis as pricing and reimbursement decisions are made."

The European Commission approval extends to all European Union Member States, as well as Iceland, Norway and Liechtenstein.

"AML is a rare cancer in Europe and patients with therapy-related AML or AML with myelodysplasia-related changes have a particularly poor prognosis compared to people with other forms of leukaemia," said Professor Charles Craddock CBE, Academic Director, Centre for Clinical Haematology at University Hospitals Birmingham NHS Foundation Trust. "*Vyxeos* is a new and clinically meaningful treatment option that provides a welcome advance for patients and health care professionals across the European Union."

The Marketing Authorisation Application (MAA) for *Vyxeos* included clinical data from five studies, including the pivotal Phase 3 study. Data from the Phase 3 study was published in the *Journal of Clinical Oncology* in July 2018. The study evaluated the efficacy and safety of *Vyxeos* compared to 7+3 chemotherapy in 309 patients 60 to 75 years of age with newly diagnosed t-AML or AML-MRC, a rapidly progressing and life-threatening blood cancer.

The study met its primary endpoint as *Vyxeos* demonstrated a superior improvement in overall survival compared to the 7+3 treatment regimen. The median overall survival for the *Vyxeos* treatment group was 9.6 months compared with 5.9 months for the 7+3 treatment group (2-sided p-value = 0.005; HR [95% confidence interval] = 0.69 [0.52, 0.90]). *Vyxeos* was also associated with a significantly higher remission rate than 7+3 with a complete response rate of 37% versus 26%; p=0.036. In addition, the overall rate of hematopoietic stem cell transplant (HSCT) was 34% in the *Vyxeos* arm and 25% in the 7+3 arm. The reported adverse reactions with *Vyxeos* were generally consistent with the known safety profile of cytarabine and daunorubicin therapy.

The incidences of non-haematologic adverse events were comparable between arms, despite a longer treatment phase and prolonged time to neutrophil and platelet count recovery with *Vyxeos*. Fatal treatment-emergent CNS hemorrhage not in the setting of progressive disease occurred in 2% of patients in the *Vyxeos* arm and 0.7% of patients in the control arm. Six percent of patients in both the *Vyxeos* and control arm had a fatal adverse reaction on treatment or within 30 days of therapy that was not in the setting of progressive disease. The most common adverse reactions (incidence ≥ 25%) were bleeding events, fever, rash, swelling, nausea, sores in the mouth or throat, diarrhea, constipation, muscle pain, tiredness, stomach pain, difficulty breathing, headache, cough, decreased appetite, irregular heartbeat, pneumonia, blood infection, chills, sleep disorders and vomiting.

About Vyxeos®
Vyxeos 44 mg/100 mg powder for concentrate for solution for infusion is an advanced liposomal formulation that delivers a synergistic combination of daunorubicin and cytarabine to leukaemia cells for a prolonged period of time. Based on data in animals, *Vyxeos* liposomes accumulate and persist in high concentration in the bone marrow, where they are preferentially taken up intact by leukaemia cells. *Vyxeos* is the first product developed with the company's proprietary CombiPlex® platform, which enables the design and rapid evaluation of various combinations of therapies. *Vyxeos* received Orphan Drug Designation (ODD) by the European Commission in January 2012 with retention of the ODD reaffirmed in July 2018 following assessment by the Committee for Orphan Medicinal Products (COMP) and by the U.S. Food and Drug Administration (FDA) in September 2008 for the treatment of AML. *Vyxeos* received Promising Innovative Medicine (PIM) designation from the Medicines and Healthcare Products Regulatory Agency in the United Kingdom. The European Medicines Agency's Committee for Medicinal Products for Human Use (CHMP) issued a positive opinion in June 2018 recommending marketing authorisation for *Vyxeos. Vyxeos* received U.S. FDA approval and orphan drug exclusivity in August 2017.

About CombiPlex®
The CombiPlex proprietary technology enables the design and rapid evaluation of various combinations of therapies to deliver enhanced anti-cancer activity. The CombiPlex technology seeks to identify the most synergistic ratio of drugs in vitro and fix this ratio in a nano-scale delivery complex that maintains the synergistic combination after administration. CombiPlex utilizes two proprietary nano-scale delivery platforms: liposomes to control the release and distribution of water-soluble drugs and drugs that are both water- and fat-soluble (amphipathic), and nanoparticles to control the release and distribution of non-water-soluble (hydrophobic) drugs.

About AML
Acute myeloid leukaemia (AML) is a blood cancer that begins in the bone marrow, which produces most of the body's new blood cells. AML cells crowd out healthy cells and move into the bloodstream to spread cancer to other parts of the body. [1] The median age at diagnosis is 68 years old, with rising age associated with a progressively worsening prognosis.[2-3] There is also a reduced tolerance for intensive chemotherapy as patients age.[4] Patients with t-AML or AML-MRC have few treatment options and some of the lowest survival rates compared to people with other forms of leukaemia.[5-6] A hematopoietic stem cell transplant (HSCT) may be a curative treatment option for patients.[7]

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®, Defitelio® (defibrotide) and Vyxeos® 44 mg/100 mg powder for concentrate for solution for infusion in countries outside the U.S. For country-specific product labels, 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 the commercial availability and launch of Vyxeos in the European Union 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 Vyxeos in the European Union; delays or problems in the supply or manufacture of Vyxeos; obtaining and maintaining appropriate pricing and reimbursement for Vyxeos; complying with applicable regulatory requirements; 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, 2018 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. National Cancer Institute. General Information About Adult Acute Myeloid Leukemia https://www.cancer.gov/types/leukemia/patient/adult-aml-treatment-pdq Accessed July 23, 2018.
2. SEER Stat Facts: AML. 2017.
3. Baer MR, et al., Leukemia, 2011 May; 25(5):10.1038/eu.2011.9.
4. Klepin HD. Hematology Am Soc Hematol Educ Program. 2014 (1):8-13.
5. Pinto AC, et al. Current Cancer Treatment - Novel Beyond Conventional Approaches. 2011; 693-714.
6. Smith SM, et al. *Blood*. 2003; 102(1):43-52.
7. Peccatori, J and Ciceri, F. Haematologica. 2010 Jun; 95(6): 857–859. doi: 10.3324/haematol.2010.023184.

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