Jazz Pharmaceuticals Announces FDA Approval of Additional Indication for Vyxeos® (daunorubicin and cytarabine) for the Treatment of Secondary Acute Myeloid Leukemia in Pediatric Patients

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DUBLIN, March 30, 2021 /PRNewswire/ -- Jazz Pharmaceuticals plc (Nasdaq: JAZZ) today announced that the U.S. Food and Drug Administration (FDA) approved a revised label for Vyxeos® (daunorubicin and cytarabine) to include a new indication to treat newly-diagnosed therapy-related acute myeloid leukemia (t-AML) or AML with myelodysplasia-related changes (AML-MRC) in pediatric patients aged one year and older. The approval of *Vyxeos* for this indication is supported by safety data from two single-arm trials: AAML1421, conducted by the Children's Oncology Group (COG) and CPX-MA-1201, conducted by Cincinnati Children's Hospital (CCH) and evidence of effectiveness from an adequate and well-controlled study in adults.

"At Jazz Pharmaceuticals, we believe all patients living with complex conditions deserve solutions, and work diligently to expand the science behind our therapies to ensure the greatest number of patients can benefit from our medicines," said Robert Iannone, M.D., M.S.C.E., executive vice president, research and development and chief medical officer of Jazz Pharmaceuticals. "While pediatric patients represent a relatively small percentage of total AML patients, there is a critical need for more effective therapies in this setting. With the expansion of the *Vyxeos* label to include the pediatric population, Jazz demonstrates our continued commitment to broadening our cancer research and focusing on the people for whom we can have the greatest impact."

Safety and pharmacokinetics of *Vyxeos* in children and young adults were established in two clinical studies that enrolled patients with AML or relapsed/refractory hematologic malignancies. Thirty-eight pediatric patients aged one to 21 years of age with AML in first relapse were enrolled in the Phase 1/2 AAML1421 study conducted by COG, and 27 patients aged one to 19 years with relapsed/refractory hematologic malignancies were enrolled in the Phase 1 CPX-MA-1201 study conducted by CCH. Both studies found no differences in the safety profile based on age. [1] The use of *Vyxeos* for this indication is supported by evidence of effectiveness from study CPX351-301 in adult patients.

Vyxeos has a Boxed Warning as it cannot be substituted with other daunorubicin and/or cytarabine-containing products. In the Phase 3 study, 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.[2]

"The expansion of the *Vyxeos* label to include children is a welcome and necessary advancement in support of some of our most vulnerable patients," said Dr. Edward Anders Kolb, M.D., director of the Center for Cancer and Blood Disorders at Nemours/Alfred I. DuPont Hospital for Children and chair of myeloid disease committee at COG. "Jazz has been a wonderful partner in pediatric drug development and we are grateful for the continued work being done to provide safe and effective therapies for children."

About Vyxeos® (daunorubicin and cytarabine)
Vyxeos is a liposomal combination of daunorubicin, an anthracycline topoisomerase inhibitor, and cytarabine, a nucleoside metabolic inhibitor, that is indicated for the treatment of newly-diagnosed therapy-related acute myeloid leukemia (t-AML) or AML with myelodysplasia-related changes (AML-MRC) in adults and pediatric patients 1 year and older. For more information about Vyxeos in the United States, please visit https://vyxeos.com.

More information about Vyxeos, including Full Prescribing Information, BOXED Warning and Medication Guide, is available here.

Important Safety Information
WARNING: VYXEOS has different dosage recommendations from other medications that contain daunorubicin and/or cytarabine. Do not substitute VYXEOS for other daunorubicin and/or cytarabine-containing products.

VYXEOS should not be given to patients who have a history of serious allergic reaction to daunorubicin, cytarabine, or any of its ingredients.

VYXEOS can cause a severe decrease in blood cells (red and white blood cells and cells that prevent bleeding, called platelets) which can result in serious infection or bleeding and possibly lead to death. Your doctor will monitor your blood counts during treatment with VYXEOS. Patients should tell the doctor about new onset fever or symptoms of infection or if they notice signs of bruising or bleeding.

VYXEOS can cause heart-related side effects. Tell your doctor about any history of heart disease, radiation to the chest, or previous chemotherapy. Inform your doctor if you develop symptoms of heart failure such as:

- shortness of breath or trouble breathing
- swelling or fluid retention, especially in the feet, ankles, or legs
- unusual tiredness

VYXEOS may cause allergic reactions including anaphylaxis. Seek immediate medical attention if you develop signs and symptoms of anaphylaxis such as:

- trouble breathing
- severe itching
- skin rash or hives
- swelling of the face, lips, mouth, or tongue

VYXEOS contains copper and may cause copper overload in patients with Wilson's disease or other copper-processing disorders.

VYXEOS can damage the skin if it leaks out of the vein. Tell your doctor right away if you experience symptoms of burning, stinging, or blisters and skin sores at the injection site.

VYXEOS can harm your unborn baby. Inform your doctor if you are pregnant, planning to become pregnant, or nursing. Do not breastfeed while receiving VYXEOS. Females and males of reproductive potential should use effective contraception during treatment and for 6 months following the last dose of VYXEOS.

The most common side effects 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.

Call your doctor for medical advice about side effects. You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088. You may also report side effects to Jazz Pharmaceuticals at 1-800-520-5568.

About AML

Acute myeloid leukemia (AML) is a type of cancer in which the bone marrow makes abnormal myeloblasts (a type of white blood cell), red blood cells, or platelets.[3] It can sometimes spread to other parts of the body including the lymph nodes, liver, spleen, central nervous system (brain and spinal cord), and testicles.[4] AML is a relatively rare disease representing 1.1 percent of all new cancer cases.[5] It is estimated that more than 19,500 people will be diagnosed with AML in the United States this year with the potential for more than 11,000 people to die from the disease.[6] The median age at diagnosis is 68 years old,[6] with rising age associated with a progressively worsening prognosis.[7] AML in children makes up a small portion of the overall AML population (4.5% occurs in patients < 20 years old). Further, t-AML and AML-MRC in pediatric AML are very rare subtypes of this group accompanied by poor prognosis.[5] There is also a reduced tolerance for intensive chemotherapy as patients age.[8] AML has the lowest survival rate of any other form of leukemia.[5] Patients with newly diagnosed therapy-related AML or AML with myelodysplasia-related changes may have a particularly poor prognosis.[9-11] A hematopoietic stem cell transplant may be a curative treatment option for patients.[12]

About Jazz Pharmaceuticals plc

Jazz Pharmaceuticals plc (Nasdaq: JAZZ) is a global biopharmaceutical company dedicated to developing life-changing medicines for people with serious diseases — often with limited or no options. We have a diverse portfolio of marketed medicines and novel product candidates, from early- to late-stage development, in key therapeutic areas. Our focus is in neuroscience, including sleep medicine and movement disorders, and in oncology, including hematologic malignancies and solid tumors. We actively explore new options for patients including novel compounds, small molecule advancements, biologics and innovative delivery technologies. Jazz is headquartered in Dublin, Ireland and has employees around the globe, serving patients in more than 90 countries. For more information, please visit www.jazzpharmaceuticals.com and follow @JazzPharma on Twitter.

Jazz Pharmaceuticals "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 Jazz Pharmaceuticals' expectations regarding broadening our cancer research; expanding the science behind our therapies; the estimated completion date of clinical trials and other statements that are not historical facts. These forward-looking statements are based on Jazz Pharmaceuticals' 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: risks related to the impact of COVID-19 pandemic on our research activities; and other risks and uncertainties affecting Jazz Pharmaceuticals, 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 Annual Report on Form 10-K for the year ended December 31, 2020 and future filings and reports by the company. Other risks and uncertainties of which Jazz Pharmaceuticals 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 Jazz Pharmaceuticals on its website or otherwise. Jazz Pharmaceuticals 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.

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