Jazz Pharmaceuticals Announces U.S. FDA Approval of Monday/Wednesday/Friday Intramuscular Dosing Schedule for Rylaze® (asparaginase erwinia chrysanthemi (recombinant)-rywn)

November 18, 2022

Rylaze dosing options provide sustained asparaginase activity throughout the entire course of treatment for adult and pediatric patients with acute lymphoblastic leukemia or lymphoblastic lymphoma

DUBLIN, Nov. 18, 2022 /PRNewswire/ -- Jazz Pharmaceuticals plc (Nasdaq: JAZZ) today announced the U.S. Food and Drug Administration (FDA) approval of a supplemental Biologics License Application (sBLA) to add a Monday/Wednesday/Friday (MWF) intramuscular (IM) dosing schedule for Rylaze® (asparaginase erwinia chrysanthemi (recombinant)-rywn). *Rylaze* is approved for use in the U.S. as a component of a multi-agent chemotherapeutic regimen for the treatment of acute lymphoblastic leukemia (ALL) and lymphoblastic lymphoma (LBL) in adult and pediatric patients one month or older who have developed hypersensitivity to *E. coli*-derived asparaginase.

Rylaze was first approved in the U.S. in June 2021 under the FDA Real-Time Oncology Review (RTOR) program. The approval with a dosing schedule of 25 mg/m^2 administered IM every 48 hours met the immediate patient need for a non-*E.coli*-derived asparaginase treatment option while the clinical trial was still ongoing to evaluate additional dosing and administration options.

"With the addition of a Monday/Wednesday/Friday dosing schedule for *Rylaze*, patients will have another dosing option, which provides sustained asparaginase activity throughout the entire course of *Rylaze* treatment," said Rob Iannone, M.D., M.S.C.E., executive vice president, global head of research and development of Jazz Pharmaceuticals. "Jazz has been consistently committed to ensuring access to the reliable, high-quality supply of this important therapy so patients and healthcare providers have the opportunity to complete the full course of asparaginase therapy. As part of our efforts to improve patient and healthcare provider experience with *Rylaze*, we have evaluated additional dosing and administration options, and are also seeking approval for *Rylaze* globally."

"The expansion of the *Rylaze* label to include a Monday/Wednesday/Friday dosing schedule provides another option to support patients in completing their planned asparaginase treatment regimen. The benefit of completing the full course of asparaginase has been shown in various publications, and discontinuation of asparaginase has been associated with inferior disease-free survival," said Dr. Luke Maese, associate professor at the University of Utah, Primary Children's Hospital and Huntsman Cancer Institute. "*Rylaze* is an effective and reliable treatment option for patients with ALL and LBL that have developed hypersensitivity to an *E. coli*-derived asparaginase."

The MWF dosing option was approved by the FDA under the RTOR program based on data from the intramuscular administration part of the Phase 2/3 trial (JZP458-201 or AALL1931), which was developed and conducted in close collaboration with the Children's Oncology Group (COG) and was the basis for the initial approval of *Rylaze* in June 2021.

Results show that a dosing regimen of 25 mg/m^2 administered intramuscularly on Monday morning and Wednesday morning, and 50 mg/m^2 administered on Friday afternoon demonstrated a positive benefit-to-risk profile, with ≥90% of the patients achieving nadir serum asparaginase activity (NSAA) ≥0.1 U/mL by simulation.[1]

Overall, the safety profile of *Rylaze* was consistent with the reported safety information for patients with ALL/LBL receiving asparaginase with combination chemotherapy. There were no new safety signals observed in the trial.[1]

Rylaze was granted orphan drug designation for the treatment of ALL/LBL in June 2021 and was added to the National Comprehensive Cancer Network® Clinical Practice Guidelines in Oncology (NCCN Guidelines®) in July 2021. Jazz also completed the submission of an sBLA to the FDA seeking approval for an intravenous route of administration for *Rylaze* as well as the submission of a Marketing Authorisation Application (MAA) to the European Medicines Agency for JZP458.

About Rylaze® (asparaginase erwinia chrysanthemi (recombinant)-rywn)
Rylaze, also known as JZP458, is approved in the U.S. for use as a component of a multi-agent chemotherapeutic regimen for the treatment of acute lymphoblastic leukemia (ALL) and lymphoblastic lymphoma (LBL) in adult and pediatric patients one month or older who have developed hypersensitivity to *E. coli*-derived asparaginase. *Rylaze* has orphan drug designation for the treatment of ALL/LBL in the United States. *Rylaze* is a distinct recombinant *Erwinia asparaginase* that uses a novel *Pseudomonas fluorescens* expression platform for production. JZP458 was granted Fast Track designation by the U.S. Food and Drug Administration (FDA) in October 2019 for the treatment of this patient population. *Rylaze* was approved as part of the Real-Time Oncology Review program, an initiative of the FDA's Oncology Center of Excellence designed for efficient delivery of safe and effective cancer treatments to patients.

The full U.S. Prescribing Information for *Rylaze* is available at: **<https://pp.jazzpharma.com/pi/rylaze.en.USPI.pdf>**

Important Safety Information

***Rylaze* should not be given to people who have had:**

- Serious allergic reactions to *Rylaze*
- Serious swelling of the pancreas (stomach pain), serious blood clots, or serious bleeding during previous asparaginase treatment

***Rylaze* may cause serious side effects, including:**

- Allergic reactions (a feeling of tightness in your throat, unusual swelling/redness in your throat and/or tongue, or trouble breathing), some of which may be life-threatening
- Swelling of the pancreas (stomach pain)
- Blood clots (may have a headache or pain in leg, arm, or chest)
- Bleeding
- Liver problems

Contact your doctor immediately if any of these side effects occur.

Some of the most common side effects with *Rylaze* include: liver problems, nausea, bone and muscle pain, infection, tiredness, headache, fever with low white blood cell count, fever, bleeding, mouth swelling (sometimes with sores), pain in the abdomen, decreased appetite, serious allergic reactions, a high blood sugar level, diarrhea, swelling of the pancreas and low levels of potassium in your blood.

Rylaze can harm your unborn baby. Inform your doctor if you are pregnant, planning to become pregnant, or nursing. Females of reproductive potential should use effective contraception (other than oral contraceptives) during treatment and for 3 months following the final dose. Do not breastfeed while receiving *Rylaze* and for 1 week after the final dose.

Tell your healthcare provider if there are any side effects that are bothersome or that do not go away.

These are not all the possible side effects of *Rylaze*. For more information, ask your healthcare provider.

Call your doctor for medical advice about any 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 (1-800-332-1088).

About Acute Lymphoblastic Leukemia

Acute lymphoblastic leukemia (ALL) is a cancer of the blood and bone marrow that can be fast growing.[2] Leukemia is the most common cancer in children, and about three out of four of these cases are ALL.[3] Although it is one of the most common cancers in children, ALL is among the most curable of the pediatric malignancies due to recent advancements in treatment.[4] Adults can also develop ALL, and about four of every 10 cases of ALL diagnosed are in adults.[5] The American Cancer Society estimates that about 6,600 new cases of ALL will be diagnosed in the United States in 2022.[5]

About Lymphoblastic Lymphoma

Lymphoblastic lymphoma (LBL) is a rare, fast-growing, aggressive subtype of non-Hodgkin's lymphoma (NHL), most often seen in children and teenagers.[6] In LBL, the abnormal lymphocytes are present in the lymph nodes or thymus gland, whereas in ALL, the abnormal lymphocytes are mainly in the blood and bone marrow.[6]

About Jazz Pharmaceuticals plc

Jazz Pharmaceuticals plc (NASDAQ: JAZZ) is a global biopharmaceutical company whose purpose is to innovate to transform the lives of patients and their families. We are dedicated to developing life-changing medicines for people with serious diseases—often with limited or no therapeutic options. We have a diverse portfolio of marketed medicines and novel product candidates, from early- to late-stage development, in neuroscience and oncology. Within these therapeutic areas, we are identifying new options for patients by actively exploring small molecules and biologics, and through innovative delivery technologies and cannabinoid science. Jazz is headquartered in Dublin, Ireland and has employees around the globe, serving patients in nearly 75 countries. Please visit www.jazzpharmaceuticals.com for more information.

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References

[1] Maese L, Loh M.L., Li Rim Choi L. et al. Efficacy and Safety of Intramuscular (IM) Recombinant Erwinia Asparaginase in Acute Lymphoblastic Leukemia (ALL) or Lymphoblastic Lymphoma (LBL): The Children's Oncology Group (COG) AALL1931 Study. Journal of Clinical Oncology 2022 40:16_suppl, 7001-7001. DOI: 10.1200/JCO.2022.40.16_suppl.7001

[2] National Cancer Institute. Dictionary of Cancer Terms. Available at: https://www.cancer.gov/publications/dictionaries/cancer-terms/def/acute-lymphoblastic-leukemia. Accessed Nov. 17, 2022.

[3] American Cancer Society. Key Statistics for Childhood Leukemia. https://www.cancer.org/cancer/leukemia-in-children/about/key-statistics.html. Accessed Nov. 17, 2022.

[4] Pui C, Evans W. A 50-Year Journey to Cure Childhood Acute Lymphoblastic Leukemia. Seminars in Hematology. 2013;50(3), 185-196.
[5] American Cancer Society. Key Statistics for Acute Lymphocytic Leukemia. Available at: https://www.cancer.org/cancer/acute-lymphocytic-leukemia/about/key-statistics.html. Accessed Nov. 17, 2022.
[6] Leukaemia Foundation. Lymphoblastic Lymphoma. Available at https://www.leukaemia.org.au/disease-information/lymphomas/non-hodgkin-lymphoma/other-non-hodgkin-lymphomas/lymphoblastic-lymphoma/. Accessed Nov. 17, 2022.

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