Jazz Pharmaceuticals Completes U.S. FDA Supplemental Biologics License Application for Rylaze™ (asparaginase erwinia chrysanthemi (recombinant)-rywn) Monday/Wednesday/Friday Dosing Schedule

February 02, 2022

Phase 2/3 trial data, the basis for submission, demonstrates Rylaze maintains a clinically meaningful level of nadir serum asparaginase activity throughout the entire duration of treatment for adult and pediatric patients with acute lymphoblastic leukemia and lymphoblastic lymphoma

Submission will be reviewed under FDA's Real-Time Oncology Review Program

DUBLIN, Feb. 2, 2022 /PRNewswire/ -- Jazz Pharmaceuticals plc (Nasdaq: JAZZ) today announced that the Company has completed the submission of a Supplemental Biologics License Application (sBLA) to the U.S. Food and Drug Administration (FDA) seeking approval for a Monday/Wednesday /Friday (M/W/F) intramuscular (IM) dosing schedule for Rylaze™ (asparaginase erwinia chrysanthemi (recombinant)-rywn), 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 and older who have developed hypersensitivity to *E. coli*-derived asparaginase. The submission will be reviewed under the Real-Time Oncology Review (RTOR) program, an initiative of FDA's Oncology Center of Excellence designed for efficient review of safe and effective cancer treatments, and follows *Rylaze's* initial approval under the RTOR program in June 2021.

"We were pleased *Rylaze*, a much-needed therapeutic option, was approved under the RTOR program while the clinical trial was ongoing. Our science-led and patient-focused development program has enabled us to deliver a clinically significant advancement for patients," said Rob Iannone, M.D., M.S.C.E., executive vice president, global head of research and development of Jazz Pharmaceuticals. "With a dosing schedule of *Rylaze* administered 25/25/50 mg/m^2 on Monday/Wednesday/Friday, patients maintain a clinically meaningful level of nadir serum asparaginase activity through the entire duration of treatment. We look forward to submitting two additional regulatory applications this year to ensure as many patients as possible can have access to a reliable and high-quality supply of this important therapy, including another regulatory application to FDA to support the intravenous route of administration and an additional application in Europe later this year."

The sBLA submitted by Jazz is supported by data from the three-cohort intramuscular administration part of the Phase 2/3 trial of *Rylaze* in adult and pediatric patients with ALL and LBL who have developed hypersensitivity to an *E. coli*-derived asparaginase. The trial studied three dosing regimens of *Rylaze,* with cohort 1a receiving 25 mg/m^2 administered M/W/F, cohort 1b receiving 37.5 mg/m^2 administered M/W/F and cohort 1c receiving 25 mg/m^2 administered Monday and Wednesday and 50 mg/m^2 administered on Friday. Initial results showed that in cohort 1c, a dosing regimen of *Rylaze* administered 25 mg/m^2 on Monday and Wednesday and 50 mg/m^2 on Friday demonstrated a positive benefit-to-risk profile, showing that *Rylaze* maintains a clinically meaningful level of nadir serum asparaginase activity (NSAA) ≥0.1 IU/mL at both 48 and 72 hours (from Friday to Monday). In addition, the safety profile of *Rylaze* was consistent with the reported safety information for patients with ALL/LBL receiving asparaginase with combination chemotherapy. Initial results from the trial were presented at the 63rd American Society of Hematology (ASH) Annual Meeting in December 2021.[1]

The sBLA follows FDA approval of *Rylaze* in June 2021 under the RTOR program.[2] *Rylaze* was also 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.[3]

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 recombinant erwinia asparaginase that uses a novel Pseudomonas fluorescens expression platform. 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, tiredness, infection, headache, fever, allergic reactions, fever with low white blood cell count, decreased appetite, mouth swelling (sometimes with sores), bleeding, and too much sugar in the 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.

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 (ALL)
ALL is a cancer of the blood and bone marrow that can progress quickly if not treated.[4] Leukemia is the most common cancer in children, and about three out of four of these cases are ALL.[5] 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.[6,7] 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 almost 6,000 new cases of ALL will be diagnosed in the United States in 2021.[5] Asparaginase is a core component of multi-agent chemotherapeutic regimens in ALL.[8] However, asparaginase treatments derived from *E. coli* are associated with the potential for development of hypersensitivity reactions.[9]

About Lymphoblastic Lymphoma (LBL)
LBL is a rare, fast-growing, aggressive subtype of Non-Hodgkin's lymphoma, most often seen in teenagers and young adults.[10] LBL is a very aggressive lymphoma – also called high-grade lymphoma – which means the lymphoma grows quickly with early spread to different parts of the body.[11,12]

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. For more information, please visit www.jazzpharmaceuticals.com and follow @JazzPharma on Twitter.

Caution Concerning Forward-Looking Statements
This press release contains forward-looking statements, including, but not limited to, statements related to Jazz Pharmaceuticals' belief in the potential of *Rylaze* to provide a reliable and consistently high-quality therapeutic option for adult and pediatric patients to maximize their chance for a cure, the availability of a reliable and consistently high-quality supply of *Rylaze*, 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, effectively launching and commercializing new products; obtaining and maintaining adequate coverage and reimbursement for the company's products; delays or problems in the supply or manufacture of the company's products; 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' Securities and Exchange Commission filings and reports (Commission File No. 001-33500), including Jazz Pharmaceuticals' Quarterly Report on Form 10-Q for the quarter ended September 30, 2021 and future filings and reports by Jazz Pharmaceuticals. Other risks and uncertainties of which Jazz Pharmaceuticals is not currently aware may also affect Jazz Pharmaceuticals' 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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