Jazz Pharmaceuticals Receives European Commission Approval for Enrylaze® (a recombinant Erwinia asparaginase or crisantaspase) for the Treatment of Acute Lymphoblastic Leukemia and Lymphoblastic Lymphoma

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DUBLIN, Sept. 21, 2023 /PRNewswire/ -- Jazz Pharmaceuticals plc (Nasdaq: JAZZ) today announced that the European Commission (EC) has granted marketing authorization for Enrylaze® (JZP458; a recombinant *Erwinia* asparaginase or crisantaspase) 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 (1 month and older) who developed hypersensitivity or silent inactivation to *E. coli*-derived asparaginase.[1] *Enrylaze*, approved as Rylaze® in the United States and Canada, is a new *Erwinia*-derived asparaginase developed using a next-generation recombinant technology with a safety profile consistent with that of other asparaginase preparations.[1,2,3,4,5]

"Asparaginase is a core component of multi-agent chemotherapeutic regimens for the treatment of ALL, however, up to 30% of patients develop hypersensitivity to *E. coli*-derived asparaginase, resulting in a delay or disruption in treatment," said Professor Carmelo Rizzari, Department of Pediatrics, University of Milano-Bicocca, Head of the Pediatric Hematology Oncology Unit, Foundation IRCCS San Gerardo dei Tintori, Monza, Italy. "The ability to complete a full course of asparaginase treatment is of critical importance when treating ALL and LBL, as it is strongly linked to improved outcomes for patients. The approval of *Enrylaze* now provides an important option to support patients in completing their planned asparaginase treatment regimen."

Enrylaze may be given by both intravenous infusion (IV) and intramuscular injection (IM) and is dosed on either alternate days (every 48 hours) or via a Monday/Wednesday/Friday (MWF) dosing schedule.[1] The use of recombinant technology to manufacture *Enrylaze* delivers a scalable supply – able to meet global demand, and a ready-to-use solution that avoids the need for reconstitution in the clinic.[2]

"This approval is a testament to Jazz's commitment to developing an *Erwinia*-derived asparaginase using innovative recombinant technology to deliver a scalable supply, and we look forward to making *Enrylaze* available to those who need it," said Robert Iannone, MD., M.S.C.E., executive vice president, global head of research and development of Jazz Pharmaceuticals. "Healthcare professionals in the European Union will now have access to a new, recombinant *Erwinia*-derived asparaginase with multiple dosing and administration options to address their patients' individual needs, which allows them to complete their treatment program as prescribed."

The EC approval is based on data from a Phase 2/3 trial conducted in collaboration with the Children's Oncology Group (COG) in a cohort of 228 pediatric and adult patients with ALL and LBL who have developed hypersensitivity or silent inactivation to *E. coli*-derived asparaginase. The study was conducted in two parts to assess the IV and IM routes of administration.[1,3] The determination of efficacy was based on demonstration of the achievement and maintenance of nadir serum asparaginase activity (NSAA) levels ≥ 0.1 U/mL.[1]

The study showed that for the IV administration of JZP458 (a recombinant *Erwinia* asparaginase or crisantaspase) (25/25/50 mg/m^2 MWF), the proportion of patients maintaining NSAA ≥ 0.1 U/mL at 48 hours after a dose was 89.8% (95% CI: 82.1%, 97.5%) and 40% at 72 hours post-dose (95% CI: 26.4%, 53.6%). The IM administration of JZP458 (25/25/50 mg/m^2 MWF) achieved sustained asparagine activity in 95.9% of patients at 48 hours after a dose (95% CI: 90.4%, 100.0%) and 89.8% of patients at 72 hours post-dose (95% CI: 81.3%, 98.3%). The other dosing schedules were based on interpolation from pharmacokinetic (PK) and response rates observed with the very similar investigated regimens.[1]

Overall, the safety profile of JZP458 was consistent with the reported safety information for patients with ALL/LBL receiving asparaginase with combination chemotherapy.[1,3] The most common adverse reactions were anemia, vomiting, thrombocytopenia, neutropenia, nausea, febrile neutropenia, fatigue, pyrexia, decreased appetite, transaminase increased, abdominal pain, white blood cell count decreased, headache, diarrhea, and lymphocyte count decreased. The most frequent serious adverse reactions were febrile neutropenia, pyrexia, vomiting, sepsis, medicinal product hypersensitivity, nausea, and pancreatitis.[1]

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

For a full list of side effects and information on dosage and administration, contraindications, and other precautions when using *Enrylaze*, please refer to the Summary of Product Characteristics for further information.

About Enrylaze® (JZP458) *Enrylaze*, also known as JZP458 and approved as Rylaze® in the United States and Canada, is the only recombinant *Erwinia* asparaginase or crisantaspase that is derived from a *Pseudomonas fluorescens* expression platform.[2,4,5] It is approved 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 (1 month and older) who developed hypersensitivity or silent inactivation to *E. coli*-derived asparaginase products. JZP458 was approved by the U.S. Food and Drug Administration (FDA) in June 2021 for the treatment of this patient population and became commercially available in July of the same year in the U.S.[4]

About Study JZP458-201

The EC approval of *Enrylaze* is based on clinical data from the pivotal Phase 2/3 single-arm, open-label, multicenter, dose confirmation study evaluating 228 pediatric and adult patients with ALL or LBL who have developed hypersensitivity or silent inactivation to *E. coli*-derived asparaginases and have not previously received *Erwinia*-derived asparaginase. The study was designed to assess the safety, tolerability, and efficacy of JZP458. The determination of efficacy was measured by serum asparaginase activity (SAA) levels. The Phase 2/3 study was conducted in two parts. The first part

investigated the intramuscular (IM) route of administration, including a Monday-Wednesday-Friday dosing schedule. The second investigated the dose and schedule for the intravenous (IV) route of administration.[1,3]

About Acute Lymphoblastic Leukemia (ALL)

Acute lymphoblastic leukemia (ALL) is a cancer of the blood and bone marrow that can progress quickly if not treated.[6,7] ALL is the most common childhood malignancy, accounting for 80% of leukemia diagnoses in children, compared to 20% of adults.[8] Long-term survival rates for pediatric patients have improved significantly over the last few decades, which is in part a result of crafting effective combinations of multi-agent chemotherapeutics with an asparaginase backbone.[9] The estimated overall incidence of ALL and lymphoblastic lymphoma (LBL) in Europe is 1.28 per 100,000.[10] The number of ALL global cases in children was 59,100 in 2017.[11]

Asparaginase is a core component of multi-agent chemotherapeutic regimens in ALL,[12] however, up to 30% of patients develop hypersensitivity to *E. coli*-derived asparaginase,[13] necessitating treatment discontinuation or a switch to a non-*E. coli*-derived asparaginase preparation.[14] Patients not receiving asparaginase due to hypersensitivities and those not receiving all prescribed doses have been shown to have poor outcomes.[2,15]

About Lymphoblastic Lymphoma (LBL)

Lymphoblastic Lymphoma (LBL) is a rare, fast-growing, aggressive subtype of non-Hodgkin's lymphoma (NHL), which is very rare in adults and is most often seen in teenagers and young adults under the age of 35.[16,17] LBL is a type of high-grade lymphoma – which means the lymphoma grows quickly with early spread to different parts of the body.[17] LBL is the second most common type of NHL in childhood and adolescence, accounting for 25-35% of cases.[18]

About Jazz Pharmaceuticals

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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