Jazz Pharmaceuticals Presents Positive Data from Phase 2/3 Trial of Rylaze® (asparaginase erwinia chrysanthemi (recombinant)-rywn) in Acute Lymphoblastic Leukemia or Lymphoblastic Lymphoma at the ASCO 2022 Annual Meeting

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Oral presentation confirms patients achieved clinically meaningful nadir serum asparaginase activity throughout the course of Rylaze treatment with intramuscular dosing regimen administered 25/25/50 mg/m^2 on Monday/Wednesday/Friday

DUBLIN, June 7, 2022 /PRNewswire/ -- Jazz Pharmaceuticals plc (Nasdaq: JAZZ) today announced positive results from a Phase 2/3 trial, developed and conducted in close collaboration with the Children's Oncology Group (COG), evaluating the intramuscular (IM) administration of Rylaze® (asparaginase erwinia chrysanthemi (recombinant)-rywn) in adult and pediatric patients with acute lymphoblastic leukemia (ALL) and lymphoblastic lymphoma (LBL) who have developed hypersensitivity to an *E. coli*-derived asparaginase. These results will be presented as an oral presentation today at the American Society of Clinical Oncology (ASCO) 2022 Annual Meeting.

These results confirm the interim trial analysis presented in December 2021 at the 63rd American Society of Hematology (ASH) Annual Meeting, and demonstrated that ≥90% of patients in Cohort 1c receiving the IM dosing regimen of 25/25/50 mg/m^2 administered Monday/Wednesday/Friday (MWF) achieved nadir serum asparaginase activity (NSAA) levels ≥0.1 IU/mL at 48 and 72 hours, with a safety profile consistent with what has been described for other asparaginases.

"We are excited to share these results from the Phase 2/3 trial of *Rylaze* highlighting the clinically meaningful nadir serum asparaginase activity from the Monday/Wednesday/Friday dosing regimen, which supports a new dosing schedule that aligns with current clinical practice," said Rob Iannone, M.D., M.S.C.E., executive vice president, global head of research and development of Jazz Pharmaceuticals. "*Rylaze* is an example of how Jazz and the Children's Oncology Group have advanced a critically needed treatment from development through FDA approval, and then continue to explore additional dosing and administration options to address the needs of patients."

"Asparaginase-based therapies remain a cornerstone in ALL and LBL treatment, and *Rylaze* has been an important option for patients who develop a hypersensitivity to an *E. coli*-derived asparaginase since its approval last year," said trial primary investigator Dr. Luke Maese, associate professor of pediatric hematology-oncology at the University of Utah, Primary Children's Hospital and Huntsman Cancer Institute. "It's encouraging to see these data further support an IM Monday/Wednesday/Friday dosing schedule for *Rylaze,* which is more in line with clinical practice in the U.S., in addition to the currently approved schedule of every 48 hours."

Rylaze was approved in the U.S. in 2021 for use as a component of a multi-agent chemotherapeutic regimen for the treatment of ALL and LBL in adult and pediatric patients one month or older who have developed hypersensitivity to *E. coli*-derived asparaginase. It was approved with an IM dosing schedule of 25 mg/m^2 every 48 hours based on observed data from the Phase 2/3 trial, in conjunction with data produced by a population pharmacokinetic (PPK) model. Data from the Phase 2/3 trial supported additional regulatory filings for *Rylaze*, including two supplemental Biologics Licensing Applications (sBLA) to the U.S. FDA to support MWF IM dosing completed in January 2022 and IV administration options completed in April 2022.

Trial Results

Data presented at ASCO include efficacy and safety results from the Phase 2/3 open-label, multicenter, pharmacokenitic (PK) trial of Rylaze (also known as JZP458) in patients with ALL/LBL who developed hypersensitivity or silent inactivation to a long-acting *E. coli*-derived asparaginase. These results are from Part A of the trial, which investigated three cohorts via IM administration:

- Cohort 1a (n=33): studied a dose of 25 mg/m^2 Monday/Wednesday/Friday
- Cohort 1b (n=83): studied a dose of 37.5 mg/m^2 Monday/Wednesday/Friday
- Cohort 1c (n=51): studied a dose of 25 mg/m^2 on Monday and Wednesday and 50 mg/m^2 on Friday

Efficacy Findings

The primary efficacy endpoint of the trial was the proportion of patients with NSAA levels ≥0.1 IU/mL at the last 72-hours during the first treatment course.

The key secondary endpoint was the proportion of patients with NSAA levels ≥0.1 IU/mL at the last 48-hours during the first treatment course.

A population PK (PPK) model was developed based on SAA data from the clinical trial to characterize the PK of JZP458 when given IM and to inform dosing decisions. Simulated data from the PPK model matched the observed data well.

Based on a PPK modeling and simulation analysis, the proportion of patients predicted to achieve NSAA levels ≥0.1 IU/mL with a 95% CI in Cohort 1c at the last 72- and 48-hour in Course 1 were 92% (91%, 93%) and 94% (93%, 95%) respectively, based on modeled data.

Safety Findings

In Cohort 1c in this trial, the following treatment-related adverse events (TRAEs) leading to discontinuation were observed:

Patients, n (%)	Cohort 1c: 25/25/50 mg/m^2 MWF (n = 51)
Any TRAE leading to study drug discontinuation	5 (10)
Pancreatitis	4 (8)
Drug hypersensitivity	1 (2)
Anaphylactic reaction	0
Increased ALT	0
Hyperammonemia	0

There were no TRAEs leading to death.

The safety profile of JZP458 is consistent with the published literature on asparaginase given as a component of a multiagent chemotherapeutic regimen.[1,2,3,4,5]

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 (RTOR) 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.[6] Leukemia is the most common cancer in children, and about three out of four of these cases are ALL.[7] 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.[8,9] Adults can also develop ALL, and about four of every 10 cases of ALL diagnosed are in adults.[10] The American Cancer Society estimates that about 6,600 new cases of ALL will be diagnosed in the United States in 2022.[10] Asparaginase is a core component of multi-agent chemotherapeutic regimens in ALL.[11] However, asparaginase treatments derived from *E. coli* are associated with the potential for development of hypersensitivity reactions.[1]

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.[6] 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.[12,13]

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.

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References

[1] Hijiya N, van der Sluis IM. Asparaginase-associated toxicity in children with acute lymphoblastic leukemia. *Leuk Lymphoma*. 2016;57(4):748–757.

[2] Raetz EA, et al. Tolerability and efficacy of L-asparaginase therapy in pediatric patients with acute lymphoblastic leukemia. *J Pediatr Hematol Oncol.* 2010;32(7):554-563

[3] Vrooman LM, et al. Activity and Toxicity of Intravenous Erwinia Asparaginase Following Allergy to E. coli-Derived Asparaginase in Children and Adolescents With Acute Lymphoblastic Leukemia. *Pediatr Blood Cancer*. 2016;63(2):228-233.

[4] Avramis VI, et al. A randomized comparison of native Escherichia coli asparaginase and polyethylene glycol conjugated asparaginase for treatment of children with newly diagnosed standard-risk acute lymphoblastic leukemia: a Children's Cancer Group study. *Blood.* 2002;99(6):1986-1994.

[5] van der Sluis IM, et al. Efficacy and safety of recombinant E. coli asparaginase in children with previously untreated acute lymphoblastic leukemia: A randomized multicenter study of the Dutch Childhood Oncology Group. *Pediatr Blood Cancer.* 2018;65(8):e27083.

[6] National Cancer Institute. Adult Acute Lymphoblastic Leukemia Treatment (PDQ®)–Patient Version. Available at: www.cancer.gov/types/leukemia /patient/adult-all-treatment-pdq. Accessed May 5, 2022.

[7] American Cancer Society. Key Statistics for Childhood Leukemia. Available at https://www.cancer.org/cancer/leukemia-in-children/about /key-statistics.html. Accessed Accessed May 5, 2022.

[8] American Cancer Society. Cancer Facts & Figures 2022. Available at: https://www.cancer.org/research/cancer-facts-statistics/all-cancer-facts-figures/cancer-facts-figures-2022.html. Accessed May 5, 2022.

[9] Pui C, Evans W. A 50-Year Journey to Cure Childhood Acute Lymphoblastic Leukemia. Seminars in Hematology. 2013;50(3), 185-196.

[10] American Cancer Society. Key 2022 Statistics for Acute Lymphocytic Leukemia (ALL). Available at: https://www.cancer.org/cancer/acute-lymphocytic-leukemia/about/key-statistics.html#references. Accessed May 25, 2022.

[11] Salzer W, Bostrom B, Messinger Y et al. 2018. Asparaginase activity levels and monitoring in patients with acute lymphoblastic leukemia. Leukemia & Lymphoma. 59:8, 1797-1806, DOI: 10.1080/10428194.2017.1386305.

[12] Leukemia Foundation. Lymphoblastic Lymphoma. Available at https://www.leukaemia.org.au/disease-information/lymphomas/non-hodgkin-lymphoma/other-non-hodgkin-lymphomas/lymphoblastic-lymphoma/. Accessed May 5, 2022.

[13] Cancer Research UK. High-Grade NHL. Available at https://www.cancerresearchuk.org/about-cancer/non-hodgkin-lymphoma/types/high-grade. Accessed May 5, 2022.

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