Jazz Pharmaceuticals enters into Letter of Intent with the pan-Canadian Pharmaceutical Alliance (pCPA) for Rylaze®, helping address the unmet need of acute lymphoblastic leukemia and lymphoblastic lymphoma patients across Canada

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MISSISSAUGA, ON, Aug. 2, 2023 /CNW/ - Jazz Pharmaceuticals Canada Inc. today announced that the Company has entered into a Letter of Intent (LOI) with the pan-Canadian Pharmaceutical Alliance (pCPA) regarding Rylaze® (crisantaspase recombinant) in Canada.[1] This allows for individual jurisdictions in Canada to begin formalizing access for eligible patients. *Rylaze* is indicated 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 year or older who have developed hypersensitivity to *E. coli*-derived asparaginase.[2] ALL and LBL are two forms of cancer that most often impact children and young adults.[3]

A study by the Children's Oncology Group (COG), published in the Journal of Clinical Oncology, demonstrated that completion of a full course of asparaginase treatment is important for patient survival, with high-risk children who do not receive their complete asparaginase treatment being at greater risk of their cancer recurring.[4] However, hypersensitivity reactions can affect up to 30% of patients who receive an *E. coli*-derived asparaginase,[5] meaning patients are unable to complete their treatment course.[6] As a result, these patients need a consistent supply of asparaginase with no expected immunologic cross-reactivity to *E. coli* in order to complete their entire course of therapy.

Rylaze is the only Health Canada-approved non-*E. coli* derived asparaginase. The recombinant technology used to produce *Rylaze* provides a sustainable supply of therapy through reliable manufacture.[7] As a result, this can support the anticipated needs of eligible ALL and LBL patients in Canada, allowing them to complete their planned asparaginase treatment.

"We would like to thank the pCPA and its membership who recognized the need for a sustainable treatment option and worked in an expedited and collaborative manner throughout the negotiations," says Paul Petrelli, General Manager of Jazz Pharmaceuticals Canada Inc. "*Rylaze* helps address the critical unmet need for a high-quality and consistently manufactured non-*E. coli* asparaginase treatment option, should a patient experience a hypersensitivity reaction to pegaspargase."

"Access to a non-*E. coli* derived asparaginase is important for patients to complete their chemotherapy treatment without disruption, which can improve their outcome," says Dr. Thai Hoa Tran, pediatric oncologist and researcher at Sainte-Justine Hospital in Montreal, Quebec. "*Rylaze* can achieve therapeutically effective serum activity levels and provides a reliable source of non-*E. coli* asparaginase for clinicians when treating patients who developed hypersensitivity to *E. coli* asparaginase."

In the Phase 2/3 pivotal trial, *Rylaze* demonstrated efficacy with over 90% of patients, who received intramuscular *Rylaze*, maintaining therapeutic levels of asparaginase activity through optimized dosing. The trial also demonstrated that *Rylaze* presents a safety profile that is consistent with other asparaginase treatments.[7]

"Pediatric Oncology Group of Ontario (POGO) is pleased to recognize this important milestone towards public funding of Rylaze for children and young adults in Ontario and across Canada," says Dr. Paul Gibson, Associate Medical Director, POGO. "This announcement is in keeping with POGO's goal to support evidence-based, optimal and equitable therapy for childhood cancer in Ontario and beyond."

Acute lymphoblastic leukemia, a rare form of cancer impacting 385 Canadians each year according to the most recent incidence data,[8] is the most common type of leukemia diagnosed in children.[9] ALL is a cancer of the blood and bone marrow that can progress quickly if not treated.[10,11] Unlike chronic leukemias, which usually develop over months, acute leukemias like ALL start to develop within days or weeks.[8] In the case of ALL, the cancer starts in abnormal lymphoid stem cells and rapidly spreads.[8] Adults can also develop ALL, and about four of every 10 cases of ALL diagnosed are in adults.[12]

Lymphoblastic lymphoma is a rare, fast-growing subtype of non-Hodgkin's lymphoma (NHL), most often seen in teenagers and young adults.[13] 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.[14]

About *Rylaze* (crisantaspase recombinant)
Rylaze, also known as JZP458, is approved in Canada for use as a component of a multi-agent chemotherapeutic regimen for the treatment of ALL and LBL in adult and pediatric patients one year or older who have developed hypersensitivity to *E. coli*-derived asparaginase.[2] *Rylaze* is a recombinant crisantaspase manufactured via a novel *Pseudomonas fluorescens* expression platform.[7]

The Health Canada approval of *Rylaze* was based on the review of an open-label, multi-cohort, multicenter, Phase 2/3 trial that assessed efficacy and safety in adult and pediatric patients with ALL or LBL who had developed hypersensitivity/silent inactivation to *E. coli*-derived asparaginase.[2,7]

The clinical package demonstrated efficacy through achievement and maintenance of Nadir Serum Asparaginase Activity (NSAA) levels on therapeutic target (≥0.1IU/mL) in over 90% of patients at both 48 and 72 hours (observed and modeled) with an optimized Monday-Wednesday-Friday dosing to sustain therapeutic levels over the weekend.[2,7]

For more information, please refer to the product monograph for *Rylaze* located here.

Rylaze was approved by Health Canada in September 2022[15] and received a positive CADTH recommendation on May 15, 2023.[1] The pCPA engagement letter was issued on June 2, 2023 and the negotiations were completed on July 4, 2023.

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.

References

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[1] Canadian Journal of Health Technologies. CADTH Reimbursement Recommendation: Crisantaspase Recombinant (Rylaze). CADTH.ca; Updated May, 2023.Vol 3. Issue 5.. Accessed July 25, 2023.https://www.cadth.ca/sites/default/files/DRR/2023/PC0301%20Rylaze%20-%20CADTH%20Final%20Recommendation%20Final.pdf

[2] Health Canada. Product information. Canada.ca. Updated May 25, 2023. Accessed July 25, 2023. https://health-products.canada.ca/dpd-bdpp/info?lang=eng&code=101958

[3] McNeer JL, Bleyer A (2018) Acute lymphoblastic leukemia and lymphoblastic lymphoma in adolescents and young adults. Pediatr Blood Cancer 65:e26989. https://doi.org/10.1002/pbc.26989

[4] Gupta S, Wang C, Raetz EA,et al.. Impact of Asparaginase Discontinuation on Outcome in Childhood Acute Lymphoblastic Leukemia: A Report From the Children's Oncology Group. *J Clin Oncol*. 2020 Jun 10;38(17):1897-1905. DOI: 10.1200/JCO.19.03024. Epub 2020 Apr 10. PMID: 32275469; PMCID: PMC7280050.

[5] Vrooman LM, Supko JG, Neuberg DS, et al. Erwinia asparaginase after allergy to E. coli asparaginase in children with acute lymphoblastic leukemia. *Pediatr Blood Cancer*. 2010 Feb;54(2):199-205. DOI: 10.1002/pbc.22225. PMID: 19672973; PMCID: PMC3706086.

[6] Hijiya N, van der Sluis IM. Asparaginase-associated toxicity in children with acute lymphoblastic leukemia. Leuk Lymphoma. 2016;57(4):748-757. DOI 10.3109/10428194.2015.1101098

[7] Maese L, Loh ML, Choi MR, et al. Recombinant Erwinia asparaginase (JZP458) in acute lymphoblastic leukemia: results from the phase 2/3 AALL1931 study. *Blood*. 2023;141(7):704-712. doi:10.1182/blood.2022016923

[8] Canadian Cancer Society. Acute lymphoblastic leukemia statistics. Cancer.ca. Updated 2023. Accessed July 25, 2023. https://cancer.ca/en/cancer-information/cancer-types/acute-lymphoblastic-leukemia-all/statistics.

[9] Canadian Cancer Society. What is acute lymphoblastic leukemia? Cancer.ca. Updated 2023. Accessed July 25, 2023. https://cancer.ca/en/cancer-information/cancer-types/acute-lymphoblastic-leukemia-all/what-is-acute-lymphoblastic-leukemia

[10] National Cancer Institute. Adult acute lymphoblastic leukemia treatment (PDQ®)–Patient Version. Cancer.gov. Updated November 19, 2021. Accessed July 2, 2023. www.cancer.gov/types/leukemia/patient/adult-all-treatment-pdq

[11] National Cancer Institute. Childhood acute lymphoblastic leukemia treatment (PDQ®)–Patient Version. Cancer.gov. Updated September 2, 2022. Accessed July 02, 2023. https://www.cancer.gov/types/leukemia/patient/child-all-treatment-pdq

[12] American Cancer Society. Key Statistics for Acute Lymphocytic Leukemia. Cancer.org. Updated January 12, 2023. Accessed July 25, 2023. https://www.cancer.org/cancer/acute-lymphocytic-leukemia/about/key-statistics.html.

[13] Leukemia Foundation. Lymphoblastic Lymphoma. Leukaemia.org. Updated June 18, 2019. Accessed July 25, 2023. https://www.leukaemia.org.au/blood-cancer/lymphoma/non-hodgkin-lymphoma/lymphoblastic-lymphoma/

[14] Leukemia Foundation. Non-Hodgkin lymphoma. Leukemia.org. Updated July 2, 2020. Accessed July 25, 2023. https://www.leukaemia.org.au/disease-information/lymphomas/non-hodgkin-lymphoma/other-non-hodgkin-lymphomas/lymphoblastic-lymphoma

[15] Health Canada. Notice of Compliance. Canada.ca. Updated November 25, 2022. Accessed July 19, 2023.https://health-products.canada.ca/noc-ac/nocInfo?no=28897

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