Jazz Pharmaceuticals to Present Data at 2022 ASH Meeting Showcasing Commitment to Advancing Oncology Research

November 3, 2022

Key data includes results for intravenous administration of Rylaze® (asparaginase erwinia chrysanthemi (recombinant)-rywn) in Acute Lymphoblastic Leukemia or Lymphoblastic Lymphoma Patients

DUBLIN, Nov. 3, 2022 */PRNewswire/* -- Jazz Pharmaceuticals plc (Nasdaq: JAZZ) today announced that 13 abstracts will be presented at the American Society of Hematology (ASH) Annual Meeting from December 10-13, 2022. Research findings to be presented include data from company-sponsored, investigator-sponsored and collaborative trials for Rylaze® (asparaginase erwinia chrysanthemi (recombinant)-rywn)/asparaginase, Vyxeos® (daunorubicin and cytarabine), also known as JZP351, and Defitelio® (defibrotide sodium).

"We're excited about our continued progress in oncology, including the impact that *Rylaze* is having to provide patients with a much-needed, reliable therapeutic option for the treatment of acute lymphoblastic leukemia or lymphoblastic lymphoma," said Rob Iannone, M.D., M.S.C.E., executive vice president, global head of research and development of Jazz Pharmaceuticals. "The data at ASH from across *Rylaze*, *Vyxeos* and *Defitelio* demonstrate our commitment to continued evaluation of our products to make a difference for patients living with rare forms of leukemia and following hematopoietic stem cell transplant."

Highlights from Jazz and its investigational sponsors at the congress include:

- A poster featuring results from Part B of a Phase 2/3 trial conducted with the Children's Oncology Group, evaluating the efficacy, safety, and population pharmacokinetic modeling of *Rylaze* administered intravenously (IV) in patients living with acute lymphoblastic leukemia (ALL) or lymphoblastic lymphoma (LBL). Results demonstrate that IV administration of *Rylaze* at 25 mg/m^2 every 48 hours is feasible and efficacious with a safety profile consistent with other asparaginases.[1]
- A poster sharing a subgroup analysis from Arm B of the V-FAST Master Trial, evaluating outcomes of *Vyxeos* and midostaurin treatment in adults with newly diagnosed acute myeloid leukemia (*de novo* and secondary) with *FLT3* mutation. Preliminary results suggest the combination of *Vyxeos* + MID is feasible with a manageable safety profile and promising remission rates in adults with newly diagnosed, *FLT3*-mutated AML.[2]
- A poster from a pooled analysis of two registry studies (DEFIFrance and EBMT PASS) that collected real-world use of *Defitelio,* which describes the resolution of Veno-occlusive Disease/Sinusoidal Obstruction Syndrome (VOD/SOS) post hematopoietic cell transplantation (HCT). A substantial proportion of patients required >21 days of therapy to achieve resolution. Day 100 survival was higher in patients with VOD/SOS resolution versus without, regardless of severity, highlighting the importance of obtaining resolution of VOD/SOS symptoms to improve patient outcomes.[3]

The ASH abstracts are available online starting today, November 3, at:
https://ash.confex.com/ash/2022/webprogram/start.html

The full list of Jazz-supported presentations at the 2022 ASH Annual Meeting includes the below:

Rylaze/Asparaginase Presentations

Presentation Title	Author	Presentation Details
Efficacy, Safety, and Population Pharmacokinetic Modeling of Intravenous Recombinant *Erwinia* Asparaginase (JZP458) in Acute Lymphoblastic Leukemia/Lymphoblastic Lymphoma: Results from Study AALL1931	Maese L., et al.	**Type**: Poster **Session:** 614 **Date**: Monday, December 12, 2022, 6:00 PM-8:00 PM **Abstract number:** 4044
Comprehensive Plasma Amino Acid Analysis Following Administration of Short- and Long-Acting Erwinia Asparaginase (Crisantaspase) Demonstrated Significant Increase in Plasma Serine and Glycine Levels	Bollino, D., et al	**Type:** Poster **Session:** 604 **Date:** Monday, December 12, 2022, 6:00 PM-8:00 PM **Abstract number**: 3968
Phase 1 Dose Escalation Trial of Pegcrisantaspase in Combination with Venetoclax in Adults with Relapsed or Refractory Acute Myeloid Leukemia	Bollino, D., et al.	**Type:** Poster **Session:** 616 **Date:** Monday, December 12, 2022, 6:00 PM-8:00 PM **Abstract number**: 4075

Vyxeos Presentations

Presentation Title	Author	Presentation Details
V-FAST Master Trial: Subgroup Analysis of Outcomes with CPX-351 Plus Midostaurin in Adults with Newly Diagnosed Acute Myeloid Leukemia by *FLT3* Mutation Type	McCloskey J, et al.	**Type:** Poster **Session:** 615 **Date:** Saturday, December 10, 2022, 5:30 PM-7:30 PM **Abstract number**: 1436
Lower-Intensity CPX-351 + Venetoclax for Patients with Newly Diagnosed Acute Myeloid Leukemia Who Are Unfit for Intensive Chemotherapy: *Post Hoc* Analysis by Disease Risk Subgroups	Lin, T.L. et al.	**Type:** Poster **Session:** 615 **Date:** Saturday, December 10, 2022, 5:30 PM-7:30 PM **Abstract number:** 1423
CREST-UK: CPX-351 Real-World Effectiveness and Safety Study for the Treatment of Newly Diagnosed Therapy-Related AML and AML with Myelodysplasia-Related Changes in the UK	Mehta, P. et al.	**Type:** Poster **Session:** 615 **Date:** Sunday, December 11, 2022, 6:00 PM-8:00 PM **Abstract number:** 2739
Updated Results of CPX-351 in Combination with Gemtuzumab Ozogamicin (GO) in Relapsed Refractory (R/R) Acute Myeloid Leukemia (AML) and Post-Hypomethylating Agent (Post-HMA) Failure High-Risk Myelodysplastic Syndrome (HR-MDS)	Senapati, J. et al.	**Type:** Poster **Session:** 616 **Date:** Monday, December 12, 2022, 6:00 PM-8:00 PM **Abstract number:** 4078
Genomic Correlates of Outcome in a Randomised Comparison of CPX-351 and FLAG-Ida in High-Risk Acute Myeloid Leukaemia and Myelodysplastic Syndrome: Results from the UK NCRI AML19 Trial	Othman, J. et. al	**Type:** Oral Presentation **Session:** 617 **Date:** Sunday, December 11, 2022: 10:30 AM **Abstract number:** 431
Rapid and Reproducible Karyotyping with Nanopore Sequencing in AML Patients	Heuser, M. et al.	**Type:** Poster **Session:** 615 **Date:** Sunday, December 11, 2022, 6:00 PM-8:00 PM **Abstract number:** 2704
Outpatient Vyxeos Induction without Planned Admission for Select Patients with Secondary Acute Myeloid Leukemia (sAML): A Multicenter Analysis of Safety and Healthcare Resource Utilization	Keiffer, G. et al.	**Type:** Poster **Session:** 615 **Date:** Saturday, December 10, 2022, 5:30 PM-7:30 PM **Abstract number:** 1439
Molecular Response Analysis By High Throughput Sequencing in Higher Risk Myelodysplastic Syndrome (HR-MDS) Treated Intensively with CPX-351	Le Bris, Y. et al.	**Type:** Poster **Session:** 637 **Date:** Monday, December 12, 2022, 6:00 PM-8:00 PM **Abstract number:** 4413

Defitelio Presentations

Presentation Title	Author	Presentation Details
Treatment Duration, Symptom Resolution, and Survival in Defibrotide-Treated Patients with Veno-Occlusive Disease/Sinusoidal Obstruction Syndrome (VOD/SOS) after Hematopoietic Cell Transplantation: Pooled Analysis of DEFIFrance and EBMT PASS Registries	Mohty, M. et al.	**Type:** Poster **Session:** 721 **Date:** Saturday, December 10, 2022, 5:30 PM-7:30 PM **Abstract number:** 2067
A Phase II Study to Evaluate the Safety and Efficacy of Defibrotide in Sickle Cell Disease-Related Acute Chest Syndrome (IND 127812)	Schaefer, E. et al.	**Type:** Poster **Session:** 114 **Date:** Saturday, December 10, 2022, 5:30 PM-7:30 PM **Abstract number:** 1056

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.[4]

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

Important Safety Information for Rylaze

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 Vyxeos® (daunorubicin and cytarabine) liposome for injection
Vyxeos is a liposomal combination of daunorubicin, an anthracycline topoisomerase inhibitor, and cytarabine, a nucleoside metabolic inhibitor.

In the U.S., *Vyxeos* (daunorubicin and cytarabine) liposome for injection is indicated for the treatment of newly-diagnosed therapy-related acute myeloid leukemia (t-AML) or AML with myelodysplasia-related changes (AML-MRC) in adults and pediatric patients 1 year and older.[5]

More information about Vyxeos in the United States, including Full Prescribing Information, BOXED Warning and Medication Guide, is available here.

Important Safety Information for Vyxeos®

WARNING: VYXEOS has different dosage recommendations from other medications that contain daunorubicin and/or cytarabine. Do not substitute VYXEOS for other daunorubicin and/or cytarabine-containing products.

VYXEOS should not be given to patients who have a history of serious allergic reaction to daunorubicin, cytarabine, or any of its ingredients.

VYXEOS can cause a severe decrease in blood cells (red and white blood cells and cells that prevent bleeding, called platelets) which can result in serious infection or bleeding and possibly lead to death. Your doctor will monitor your blood counts during treatment with VYXEOS. Patients should tell the doctor about new onset fever or symptoms of infection or if they notice signs of bruising or bleeding.

VYXEOS can cause heart-related side effects. Tell your doctor about any history of heart disease, radiation to the chest, or previous chemotherapy. Inform your doctor if you develop symptoms of heart failure such as:

- shortness of breath or trouble breathing
- swelling or fluid retention, especially in the feet, ankles, or legs
- unusual tiredness

VYXEOS may cause allergic reactions including anaphylaxis. Seek immediate medical attention if you develop signs and symptoms of anaphylaxis such as:

- trouble breathing
- severe itching

- skin rash or hives
- swelling of the face, lips, mouth, or tongue

VYXEOS contains copper and may cause copper overload in patients with Wilson's disease or other copper-processing disorders.

VYXEOS can damage the skin if it leaks out of the vein. Tell your doctor right away if you experience symptoms of burning, stinging, or blisters and skin sores at the injection site.

VYXEOS can harm your unborn baby. Inform your doctor if you are pregnant, planning to become pregnant, or nursing. Do not breastfeed while receiving VYXEOS. Females and males of reproductive potential should use effective contraception during treatment and for 6 months following the last dose of VYXEOS.

The most common side effects were bleeding events, fever, rash, swelling, nausea, sores in the mouth or throat, diarrhea, constipation, muscle pain, tiredness, stomach pain, difficulty breathing, headache, cough, decreased appetite, irregular heartbeat, pneumonia, blood infection, chills, sleep disorders, and vomiting.

Call your doctor for medical advice about 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. You may also report side effects to Jazz Pharmaceuticals at 1-800-520-5568.

About Defitelio® (defibrotide sodium)
In the U.S., Defitelio® (defibrotide sodium) injection 80mg/mL received U.S. Food and Drug Administration (FDA) marketing approval on March 30, 2016, and it is indicated for the treatment of adult and pediatric patients with hepatic veno-occlusive disease (VOD), also known as sinusoidal obstruction syndrome (SOS), with renal or pulmonary dysfunction following hematopoietic stem-cell transplantation (HSCT) and is the first and only FDA-approved therapy for patients with this rare, potentially fatal complication. *Defitelio* is not approved for the prevention of VOD.[6]

Please see full Prescribing Information for Defitelio in the United States.

In Europe, defibrotide is marketed under the name Defitelio® ▼ (defibrotide). In October 2013, the European Commission granted marketing authorization to *Defitelio* under exceptional circumstances for the treatment of severe VOD in patients after HSCT therapy. In Europe, *Defitelio* is indicated in patients over one month of age. It is not indicated in patients with hypersensitivity to defibrotide or any of its excipients or with concomitant use of thrombolytic therapy.

▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system found under section 4.8 of the SmPC (http://www.ema.europa.eu/ema/index.jsp?curl=/pages/medicines/human/medicines/002393/human_med_001646.jsp)

The full Summary of Product Characteristics of Defitelio in Europe is available here.

Important Safety Information for Defitelio

Defitelio should not be given to patients who are:

- Currently taking anticoagulants or fibrinolytics
- Allergic to Defitelio or any of its ingredients

Defitelio may increase the risk of bleeding in patients with VOD and should not be given to patients with active bleeding. During treatment with Defitelio, patients should be monitored for signs of bleeding. In the event that bleeding occurs during treatment with Defitelio, treatment should be temporarily or permanently stopped. Patients should tell the doctor right away about any signs or symptoms of hemorrhage such as unusual bleeding, easy bruising, blood in urine or stool, headache, confusion, slurred speech, or altered vision.

Defitelio may cause allergic reactions including anaphylaxis. Patients who develop signs and symptoms of anaphylaxis such as trouble breathing, severe itching, skin rash or hives, or swelling of the face, lips, mouth or tongue should seek medical attention immediately.

The most common side effects of Defitelio are decreased blood pressure, diarrhea, vomiting, nausea and nose bleeds.

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 potentially addressing patient needs with our oncology portfolio 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, risks and uncertainties associated with pharmaceutical product development, and other risks and uncertainties affecting Jazz Pharmaceuticals and its development programs, including those described from time to time under the caption "Risk Factors" and elsewhere in Jazz Pharmaceuticals plc's 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 June 30, 2022 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.

Contacts:

Jazz Media Contact:
Kristin Bhavnani
Head of Global Corporate Communications
Jazz Pharmaceuticals plc
CorporateAffairsMediaInfo@jazzpharma.com
Ireland +353 1 637 2141
U.S. +1 215 867 4948

Jazz Investor Contact:
Andrea N. Flynn, Ph.D.
Vice President, Head, Investor Relations
Jazz Pharmaceuticals plc
investorinfo@jazzpharma.com
Ireland +353 1 634 3211
U.S. +1 650 496 2717

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[1] Maese L, Mignon LL, Choi MR, et al. Efficacy, Safety, and Population Pharmacokinetic Modeling of Intravenous Recombinant Erwinia Asparaginase (JZP458) in Acute Lymphoblastic Leukemia/Lymphoblastic Lymphoma: Results from Study AALL1931. *American Society of Hematology.* 2022. Available at: https://ash.confex.com/ash/2022/webprogram/Paper160192.html

[2] McCloskey J, Pullarkat V, Mannis G, et al. V-FAST Master Trial: Subgroup Analysis of Outcomes with CPX-351 Plus Midostaurin in Adults with Newly Diagnosed Acute Myeloid Leukemia by FLT3 Mutation Type. *American Society of Hematology.* 2022. Available at: https://ash.confex.com/ash/2022/webprogram/Paper159680.html

[3] Mohty M, Locatelli F, Blaise D, et al. Treatment Duration, Symptom Resolution, and Survival in Defibrotide-treated Patients with Veno-occlusive Disease/Sinusoidal Obstruction Syndrome after Hematopoietic Cell Transplantation: Pooled Analysis of DEFIFrance and EBMT PASS Registries. *American Society of Hematology.* 2022. Available at: https://ash.confex.com/ash/2022/webprogram/Paper162672.html

[4] Rylaze (asparaginase erwinia chrysanthemi (recombinant)-rywn) injection, for intramuscular use Prescribing Information. Palo Alto, CA: Jazz Pharmaceuticals, Inc.

[5] Vyxeos (daunorubicin and cytarabine) Prescribing Information. Palo Alto, CA: Jazz Pharmaceuticals, Inc.

[6] Defitelio (defibrotide sodium) Prescribing Information. Palo Alto, CA: Jazz Pharmaceuticals, Inc.

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