

RYLAZETM

(asparaginase erwinia chrysanthemi (recombinant)-rywn)

INVESTOR CALL

JULY 20, 2021



Life-Changing Medicines. Redefining Possibilities.

Caution Concerning Forward Looking Statements

This slide deck and the accompanying oral presentation contain forward-looking statements, including, but not limited to, statements related to Jazz Pharmaceuticals' belief in the potential of Rylaze to provide a reliable therapeutic option for adult and pediatric patients to maximize positive treatment outcomes; growth prospects for Rylaze, including plans for a U.S. label expansion, international geographic expansion and approval of additional indications for Rylaze; the availability of a reliable supply of Rylaze; and other statements that are not historical facts. These forward-looking statements are based on the Company's current plans, objectives, estimates, expectations 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: effectively launching and commercializing Rylaze; maintaining or increasing sales of and revenue from Rylaze; the costly and time-consuming pharmaceutical product development process and the uncertainty of clinical success, including risks related to failure or delays in successfully initiating or completing clinical trials and assessing patients such as those being experienced, and expected to continue to be experienced, by the Company as a result of the effects of the COVID-19 pandemic; the time-consuming and uncertain regulatory approval process, including the risks that the Company may be unable to submit anticipated regulatory filings on the timeframe anticipated, or at all, or that the Company may be unable to obtain regulatory approvals of Rylaze for additional indications and label expansion, in a timely manner or at all; regulatory initiatives and changes in tax laws; market volatility; the ultimate duration and severity of the COVID-19 pandemic and resulting global economic, financial, and healthcare system disruptions and the current and potential future negative impacts to the Company's business operations and financial results; protecting and enhancing the Company's intellectual property rights; delays or problems in the supply or manufacture of Rylaze; complying with applicable U.S. and non-U.S. regulatory requirements; government investigations, legal proceedings and other actions; obtaining and maintaining adequate coverage and reimbursement for Rylaze; the Company's ability to achieve expected future financial performance and results and the uncertainty of future tax, accounting and other provisions and estimates; 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, including the Company's Form 10-K for the year ended December 31, 2020, and future filings and reports by the Company. In addition, while the Company expects the COVID-19 pandemic to continue to adversely affect its business operations and financial results, the extent of the impact on the Company's ability to generate sales of and revenues from its approved products, execute on new product launches, its clinical development and regulatory efforts, its corporate development objectives and the value of and market for its ordinary shares, will depend on future developments that are highly uncertain and cannot be predicted with confidence at this time, such as the ultimate duration and severity of the pandemic, governmental "stay-at-home" orders and travel restrictions, quarantines, social distancing and business closure requirements in the U.S., Ireland, UK and other countries, and the effectiveness of actions taken globally to contain and treat the disease. Moreover, other risks and uncertainties of which the Company is not currently aware may also affect the Company's forward-looking statements and may cause actual results and the timing of events to differ materially from those anticipated.





Now Available

High Quality, Reliably Supplied Erwinia Asparaginase

The only recombinant erwinia asparaginase manufactured product that maintains a clinically meaningful level of asparaginase activity throughout the entire duration of treatment



Please see full prescribing information at www.rylaze.com



Agenda

1. Introduction

Bruce Cozadd, Chairman and Chief Executive Officer

2. Pediatric ALL and the Role of Asparaginase

Luke Maese, D.O.

Associate Professor of Pediatrics, University of Utah - Huntsman Cancer Institute Division of Pediatric Hematology/Oncology, Primary Children's Hospital

3. Rylaze: Clinical, Development and Manufacturing Overview

Rob lannone, M.D., M.S.C.E., Executive Vice President, R&D and Chief Medical Officer

4. Rylaze: Commercial Overview

Kim Sablich, Executive Vice President and General Manager, North America

5. Q&A



Rylaze – Driven by Patient Need

From Concept to Launch

INNOVATE

High-quality recombinant product with reliable, consistent supply



EXECUTE

Accelerated clinical development; CMC/manufacturing excellence



TRANSFORM

Optimize treatment; save lives

RAPID PROGRESSION FROM PHASE 1 INITIATION TO LAUNCH IN ~2.5 YEARS



Patient-Centric Innovation Drives our Strategy

Putting Patients Front-and-Center of Everything We Do

Quickly advancing Rylaze from concept-to-approval is a critical advance for patients



Drive to address significant unmet needs for ALL patients



Innovation, dedication and excellence by the Jazz team



Highly productive collaboration with both COG and FDA



Strategic investments in growing our conceptto-approval capabilities



Leighton (JZP458 trial participant) and her mom, Allison

PEDIATRIC ACUTE LYMPHOBLASTIC LEUKEMIA AND THE ROLE OF ASPARAGINASE

LUKE MAESE, D.O.
ASSOCIATE PROFESSOR OF PEDIATRICS
UNIVERSITY OF UTAH - HUNTSMAN CANCER INSTITUTE
DIVISION OF PEDIATRIC HEMATOLOGY/ONCOLOGY
PRIMARY CHILDREN'S HOSPITAL



Acute Lymphoblastic Leukemia (ALL)



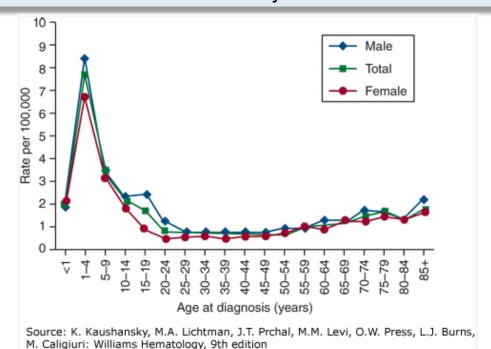


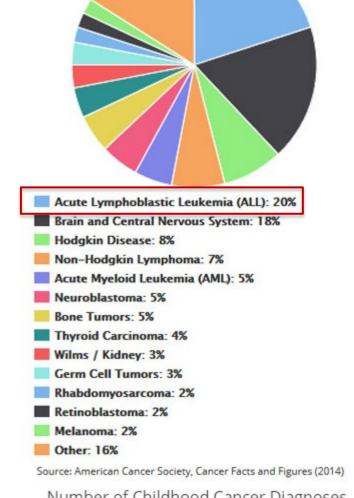
Acute Lymphoblastic Leukemia

- Malignant clonal disease of the bone marrow in which early lymphoid precursors proliferate and replace the normal hematopoietic cells of the marrow
- Occurs across the age spectrum
- Most common childhood cancer
 - ~6000 new US cases/year (~3000 children)
 - 30 cases/million < 20 y/o

www.accessmedicine.com

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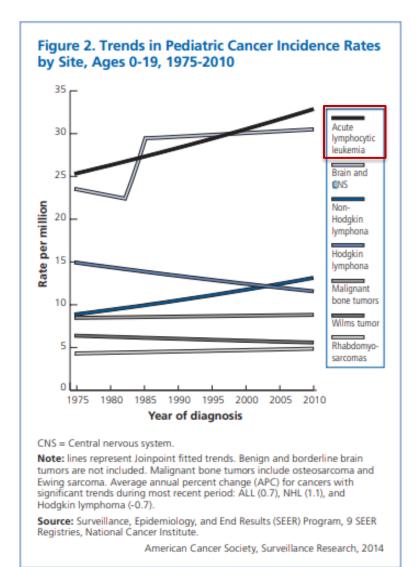
Number of Childhood Cancer Diagnoses Per Year

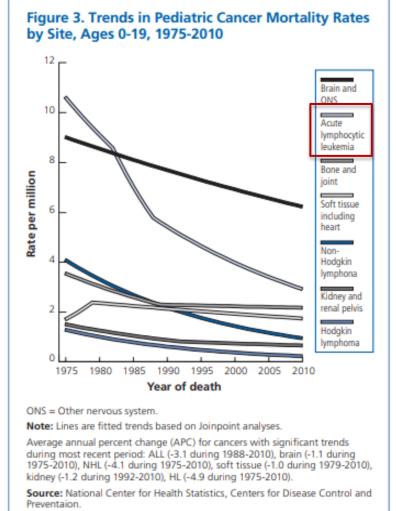
Total = 15,780, Age 0-19



Acute Lymphoblastic Leukemia

2nd most lethal cancer in children





American Cancer Society, Surveillance Research, 2014

ALL Survival

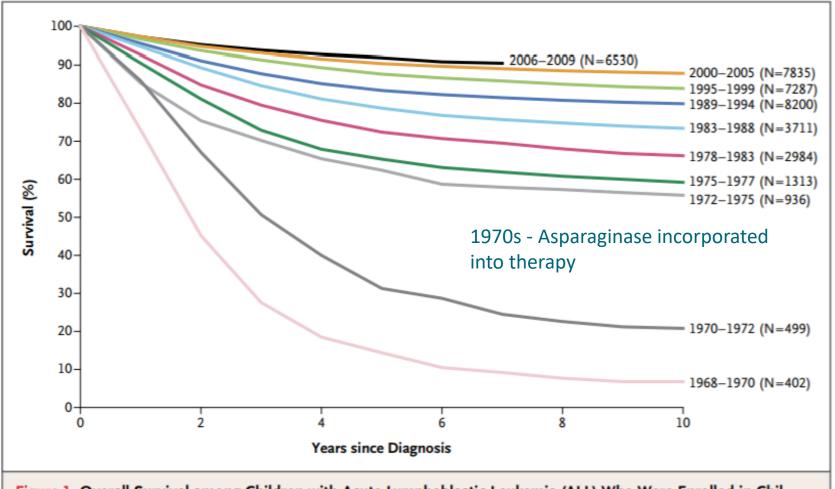


Figure 1. Overall Survival among Children with Acute Lymphoblastic Leukemia (ALL) Who Were Enrolled in Children's Cancer Group and Children's Oncology Group Clinical Trials, 1968–2009.





Pediatric ALL treatment

- **Cooperative Groups**
 - 3 major US ALL cooperative groups (Children's Oncology Group, Dana-Farber Cancer Institute, St. Jude Children's Research Hospital)
 - Foundation of treatment advances in pediatric oncology
 - Smaller numbers necessitate large partnerships

age-adjusted ITT^a

- Risk classification
- Chemotherapeutic backbones



National Cancer Network®

Comprehensive NCCN Guidelines Version 2.2021 Pediatric Acute Lymphoblastic Leukemia

Hetwork				
Ph-Negative ALL	Induction	Consolidation		
COG AALL0932 regimen ¹⁶ (SR)	SR arm: dexamethasone, vincristine, pegaspargase; IT therapy: cytarabine then methotrexate	SR-Low/Avg arm: 6-MP,b vincristine; IT therapy: methotrexate		
		SR-Avg/High arm: cyclophosphamide, cytarabine, 6-MP, b vincristine, pegaspargase; IT therapy: methotrexate		
COG AALL01131 regimen ¹⁷ (HR)	HR arm: prednisone or dexamethasone, vincristine, pegaspargase, daunorubicin; IT therapy: cytarabine then methotrexate	HR arm: cyclophosphamide, cytarabine, 6-MP, ^b vincristine, pegaspargase; IT therapy: methotrexate		
DFCI ALL Protocol 11-001 ¹⁸	Prednisone, vincristine, pegaspargase, doxorubicin, IT cytarabine, then triple IT therapy (ITT) ^a	SR arm: high-dose methotrexate, vincristine, pegasparagase, 6-MP,b dexamethasone; IT therapy: methotrexate or ITTa		
		HR/VHR ^h arms: high-dose methotrexate, vincristine, pegasparagase, 6-MP, dexamethasone, doxorubicin, dexrazoxane; IT therapy: methotrexate or ITT ^a		
Total Therapy XVI regimen ⁵	Prednisone, vincristine, daunorubicin, pegaspargase, cyclophosphamide, cytarabine, 6-mercaptopurine (6-MP), ^b	LR arm: high-dose methotrexate, 6-MP,b ITTa		
),	SR/HR arm: high-dose methotrexate, 6-MP. ^b ITT ^a		





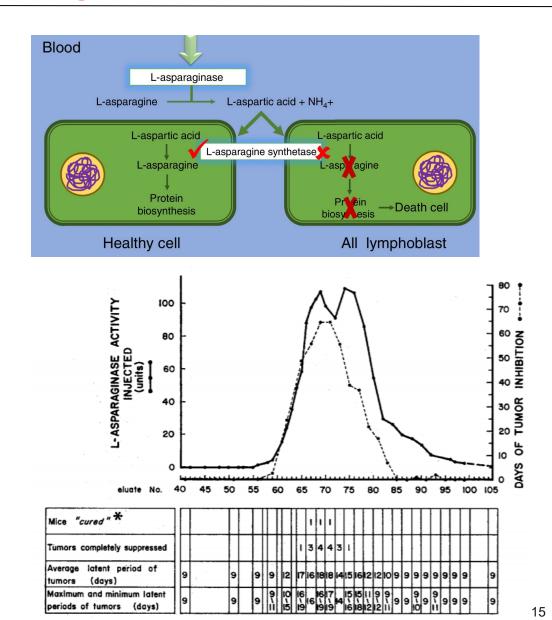
Asparaginase





Asparaginase Background

- L-asparaginase is produced in animals, plants, and microorganisms
- Normal cells can synthesize L-asparagine (asparagine synthetase), many malignant cells cannot (lack asparagine synthetase)
- Asparaginase shown to have anti-tumor properties as far back as the 1960s

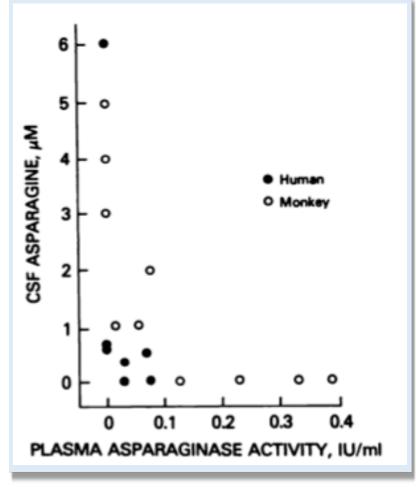




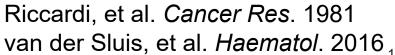


Measurement of Effectiveness

- Therapeutic Drug Monitoring (TDM)
 - Serum asparagine
 - Accurate measurement in patients undergoing asparaginase therapy is challenging due to the continued hydrolyzation of asparagine
 - Serum asparaginase activity (SAA)
 - Inverse relationship with asparagine concentrations
 - Standard for monitoring
 - 0.1 IU/mL most widely accepted threshold for therapeutic SAA









Asparaginase Preparations

Host	Escherichia Coli (E. coli)			Erwinia chrysanthemi	
Preparation	Native <i>E. coli</i> asparaginase	Pegylated asparaginase		Erwinia asparaginase	Recombinant <i>Erwinia</i> asparaginase
Drug	Elspar	Oncaspar (SS-PEG)	Asparlas (SC-PEG)	Erwinaze	Rylaze™ (asparaginase erwinia chrysanthemi (recombinant)-rywn)
Decade developed	1960s	1980s	2000s	1970s	2021
Notable Items	 Not currently supplied in US 	 First long acting product Decreased hypersensitivity 	More stableExtended half life	 Substitute for patients with hypersensitivity to <i>E. coli</i> derived asparaginase Manufacturing limitations Global shortage since 2016 	 Recombinant manufacturing process Phase 2/3 clinical trial ongoing





Therapeutic Role

 Asparagine depletion is a hallmark of ALL and LBL therapy and improves outcomes

Table 2

Protocols of trials showing improved efficacy with addition of L-asparaginase

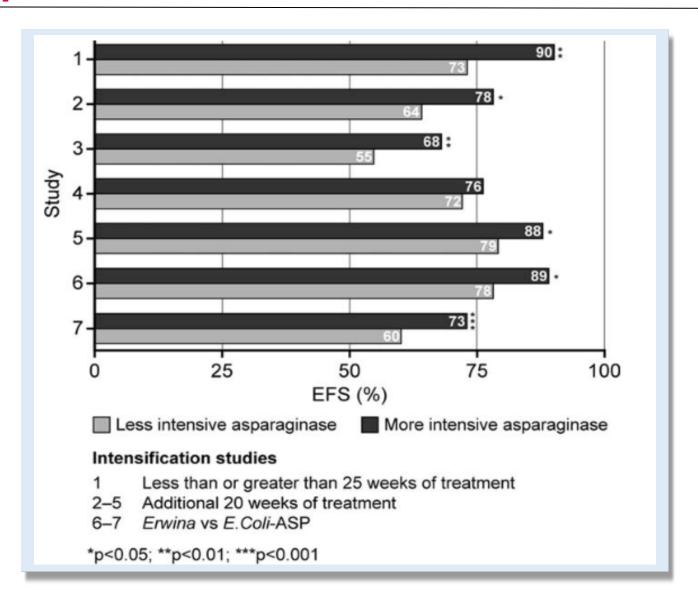
Protocol ^a	Treatment phase	L-asparaginase dose	Frequency	Principal finding
CCG 101/143 ^[23]	Induction	6000 IU/m² IM	3×/week for 3 weeks	Overall induction remission rate of 93% versus 86% ^[24]
DFCI 77-01 ^{b[25,26]}	Induction Intensification	50,000 IU/m ² IV (<6 years) 25,000 IU/m ² IV (≥6 years) 50,000 IU/m ² IV (<6 years) 25,000 IU/m ² IV (≥6 years)	q 2 days × 5 doses q week (until doxorubicin completed)	Significantly greater DFS in patients assigned to asparaginase arm (72% vs. 42%; <i>P</i> =0.04)
POG 8704 ^{b[27]}	Induction Continuation	10,000 IU/m ² IM 25,000 IU/m ² IM	Day 27, 29, and 31 q week × 20 doses	Significantly greater 4-year CCR rate with asparaginase vs. control (71% vs. 58%; <i>P</i> <0.001)
IDH-ALL-91 ^{b[28]}	Induction Reinduction Continuation	10,000 IU/m ² 10,000 IU/m ² 25,000 IU/m ²	8 × over 3 weeks 4 × over 2 weeks q week × 20 doses	Significantly greater 9-year DFS in patients assigned to asparaginase arm (88% vs. 79%; P=0.03)

^aAll protocols used native *E. coli* asparaginase, except IDH-ALL-91, in which >90% of patients received *Erwinia* asparaginase, ^bRandomized clinical trial. ALL=Acute lymphoblastic leukemia, CCG=Children's Cancer Group, CCR=Continuous complete remission, CR=Complete remission, DFCI=Dana–Farber Cancer Institute, DFS=Disease-free survival, *E. coli=Escherichia coli*, IDH=Italian, Dutch, Hungarian, IM=Intramuscular, IV=Intravenous, POG=Pediatric Oncology Group, q=Every





Therapeutic Role

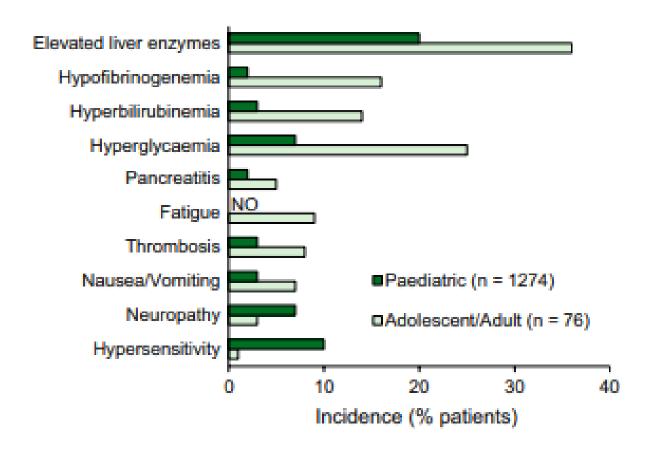






Asparaginase Toxicities

- Major
 - Hypersensitivity
 - Pancreatitis
 - Thrombosis
 - Hepatotoxicity
- Others
 - Hyperglycemia
 - Encephalopathy
 - Myelosuppression
 - Hypertriglyceridemia







Asparaginase Hypersensitivity

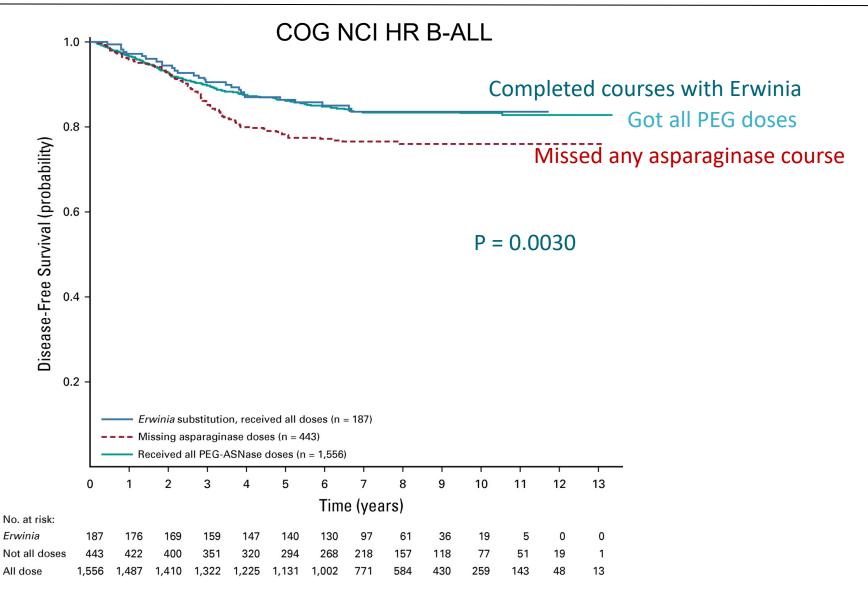
- L-asparaginase hypersensitivity rates
 - Short acting *E. coli*: 10-30%
 - Long-acting *E.coli* (Pegaspargase or Calaspargase pegol): 3-24%
 - Erwinia chrysanthemi: 3-37%

Pegaspargase hypersensitivity				
Consortium/Study	N	Hypersensitivity rate (%)		
CCG-1962	118	3		
CCG-1991	3054	16		
POG 9203	34	24		
NOPHO ALL2008	615	13		
DFCI 11-001	120	12		
Total XVI	598	13.5		
AALL0232 (consolidation)	2369	14		
AALL1131 (consolidation)	902	13		





Asparaginase Importance in Therapy







Summary

- ALL is the most common cancer of childhood
- Significant improvement in ALL survival over the past century
 - Achieved through cooperative group research and optimization of chemotherapeutic strategy
- Asparaginase is an integral component of ALL therapy
 - Importance of asparaginase depletion has been definitively established
 - Side effects are frequently encountered with long acting asparaginase products
 - Second line asparaginase products are essential





RYLAZE: CLINICAL, DEVELOPMENT AND MANUFACTURING OVERVIEW

ROBERT IANNONE, M.D., M.S.C.E.
EXECUTIVE VICE PRESIDENT, RESEARCH & DEVELOPMENT AND CHIEF
MEDICAL OFFICER



HCPs Have Been Forced to Make Difficult Choices

Missed Asparaginase Doses Can Lead to Compromised Patient Outcomes¹



Reducing the number of Erwinia asparaginase doses or omitting entire courses





Asparaginase treatment is delayed until product is available

Supply Management Compromises

Prioritizing Patients



Prioritizing patients based on severity of disease and / or severity of HSR

Borrowing Supply



Pharmacy directors call other institutions to source Erwinia asparaginase

Rechallenge / **Desensitization**



Retreating with *E. coli*-derived asparaginase in the ICU with multiple premeds



A Scalable, High Quality, Modern Process

Rylaze Recombinant Protein Manufacturing





EFFICIENT AND HIGH YIELD PRODUCTION

in as little as 3 weeks

Chilled cell paste

Extraction of *Erwinia* asparaginase

Extract

Purification of *Erwinia*asparaginase and final formulation

Frozen drug substance



CONSISTENT PRODUCTION STANDARDS

with advanced quality control

- One year of global supply on hand at launch
- Further inventory build post-launch to ensure security of supply
- Working with long established and worldclass manufacturing partners

Filling of drug product "ready to use" solution in low particulate filling components

Product is ready to use





A READILY AVAILABLE SUPPLY

with a shelf life of 24 months



HIGHLY PURIFIED product



that requires no filtration



Rylaze Asparaginase Activity

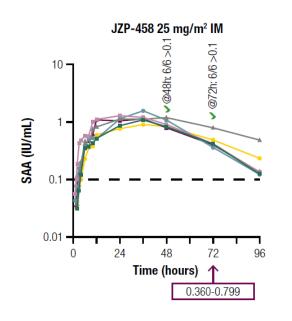
Preclinical & analytical data

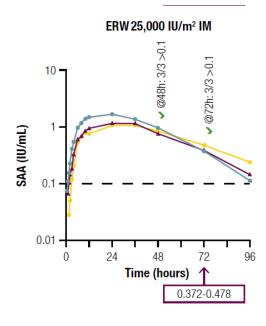
- Identical amino acid sequence
- In vitro asparaginase activity comparable to Erwinaze

Rylaze	Erwinaze	
Drug Substance	Drug Product	
Activity U/mg	Activity U/mg	
658	693	
Batch A	Batch X	
663	610	
Batch B	Batch Y	

Phase 1 healthy volunteer trial – JZP458 101

- Comparability between 25,000 IU Erwinaze and 25mg JZP458
- Basis for starting dose in Phase 2/3 clinical trial







Pivotal Trial Design¹

Part A: IM dose confirmation Part B: IV dose confirmation



M W F M W F

Patients

- Peds & adults w/1L ALL/LBL
- <u>></u> Gr3 allergic reaction to *E. coli* asparaginase or silent inactivation

Assessments include:

- Blood samples (NSAA levels); pre- and post-dose
- Safety data

1° Endpoint

- % patients with last 72-hr NSAA ≥ 0.1 IU/mL²
- Safety and tolerability

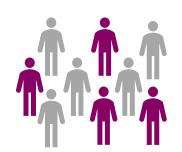
Key 2º Endpoint

% patients with last 48-hr NSAA ≥ 0.1 IU/mL²

2º Endpoints

• PK, exposure-response modeling, immunogenicity

Open-label, multicenter¹, Phase 2/3, dose confirmation and pharmacokinetic study; planned enrollment complete^{2,3}



Patients with ALL or LBL
who develop ≥ Grade 3
allergic reactions to longacting *E. coli*-derived
asparaginase or have silent
inactivation and have ≥1
dose remaining in their
treatment plan

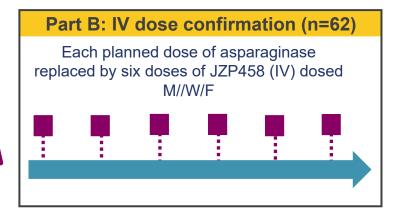
Pivotal part A: IM dose confirmation Each planned dose of asparaginase replaced by six doses of JZP458 (IM) dosed M/W/F

Part A IM dosing cohorts (n=168)				
Dosing schedule	M	W	F	
Cohort 1a	25mg/m ²	25mg/m ²	25mg/m ²	
Cohort 1b	37.5mg/m ²	37.5mg/m ²	37.5mg/m ²	
Cohort 1c	25mg/m ²	25mg/m ²	50mg/m ²	

M/W/F, Monday, Wednesday, Friday

Initiated with confirmed IM dose





IM = intramuscular
IV = intravenous



Rylaze Label: Indication, Dosage and Administration

INDICATIONS AND USAGE:

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
1 month or older who have developed hypersensitivity to E. coli-derived asparaginase.

DOSAGE AND ADMINISTRATION:

• When replacing a long-acting asparaginase product, the recommended dosage of RYLAZE is 25 mg/m² administered intramuscularly every 48 hours. See the full prescribing information for the long-acting asparaginase product to determine the duration of administration of RYLAZE as replacement therapy.



Rylaze Label: Efficacy

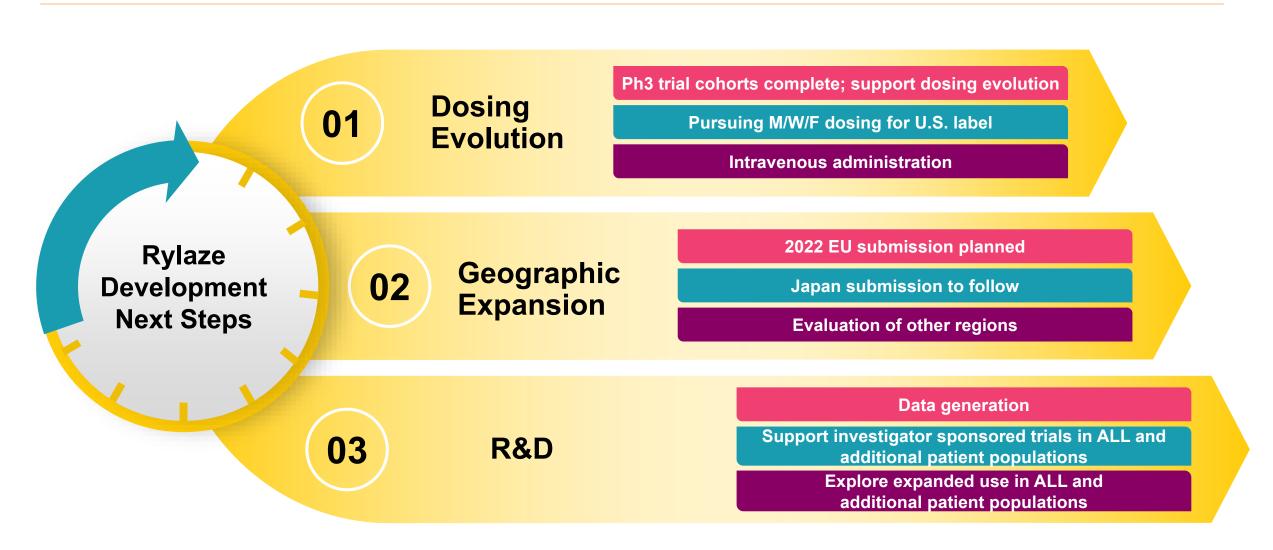
- Determination of efficacy was based on a demonstration of the achievement and maintenance of nadir serum asparaginase activity (NSAA) above the level of 0.1 U/mL
- The results of modeling and simulations showed that for a dosage of 25 mg/m² administered intramuscularly every 48 hours, the proportion of patients maintaining NSAA ≥ 0.1 U/mL at 48 hours after a dose of RYLAZE was 93.6% (95% CI: 92.6%, 94.6%)
- No clinically meaningful differences in safety or NSAA across pediatric age groups (infants, children, adolescents)



Rylaze Label: Safety

- The most common adverse reactions (incidence >15%) were abnormal liver test, nausea, musculoskeletal pain, fatigue, infection, headache, pyrexia, drug hypersensitivity, febrile neutropenia, decreased appetite, stomatitis, bleeding and hyperglycemia.
- In patients treated with the Rylaze, a fatal adverse reaction (infection) occurred in one patient and serious adverse reactions occurred in 55% of patients.
- The most frequent serious adverse reactions (in ≥5% of patients) were febrile neutropenia, dehydration, pyrexia, stomatitis, diarrhea, drug hypersensitivity, infection, nausea and viral infection.
- Permanent discontinuation due to an adverse reaction occurred in 9% of patients who received Rylaze.
- Adverse reactions resulting in permanent discontinuation included hypersensitivity (6%) and infection $(3\%).^{1}$

Continuing to Enhance and Expand Rylaze Use





Summary and Conclusions

- Jazz developed a high quality, efficient and consistent manufacturing process to meet global demand
- Pre-clinical analytical data predict comparable asparaginase activity to Erwinaze, which was used to establish the dose for the JZP458 Phase 1 trial in healthy volunteers
- JZP485 Phase 2/3 clinical trial was designed to improve 72-hour asparaginase activity to optimally support M/W/F dosing
- Plan to follow the current approval, based on 48-hour dosing data, with data from the completed cohort 1c (25/25/50 mg/m² M/W/F) to support a label update
- Enrollment in the IV cohort is complete and data from this cohort support global submissions
- Planning for additional indication development is underway





Rylaze: Key Events Timeline

U.S. Commercial Product Availability as of Thursday, July 15, 2021



Price

High-quality recombinant product with reliable, consistent, supply



The Rylaze Wholesale Acquisition Price, or WAC, is \$4,390 per vial; per vial pricing is comparable to the historic cost of Erwinaze



Jazz Has Served ALL Patients for Nearly a Decade

U.S. Market Overview



FOCUSED EXECUTION

Focus on Pediatric Oncologists at Launch

The majority of ALL incidence and asparaginase treatment is in the pediatric setting

Concentrated Prescriber Base

Focused on ~280 accounts covering 90% of current asparaginase treatment

Well Defined Pediatric Treatment Paradigm

90% of all pediatric cancer patients are treated in COG institutions

Treatment Landscape

- ~6,000 new cases of ALL in the U.S annually¹
- ~20% of patients will have a hypersensitivity reaction to E. coli-derived asparaginase²

Rely on Rylaze

Ready to Deliver for Patients and Drive Confidence in Completing Asparaginase Therapy



Drive Awareness and Establish Confidence

Rylaze is a high-quality product with modern manufacturing and reliable supply to complete course of therapy: Rely on Rylaze

Completing Asparaginase Therapy

Educate and reinforce understanding that completing asparaginase therapy and continued asparagine depletion are critical to optimal patient outcomes

Physicians have been forced to make difficult decisions in the absence of reliable supply





Multi-Pronged Approach Drives Success

Maximizing Our Reach to Ensure Every Patient in Need Can Get Rylaze



Jazz Knows ALL Prescribers

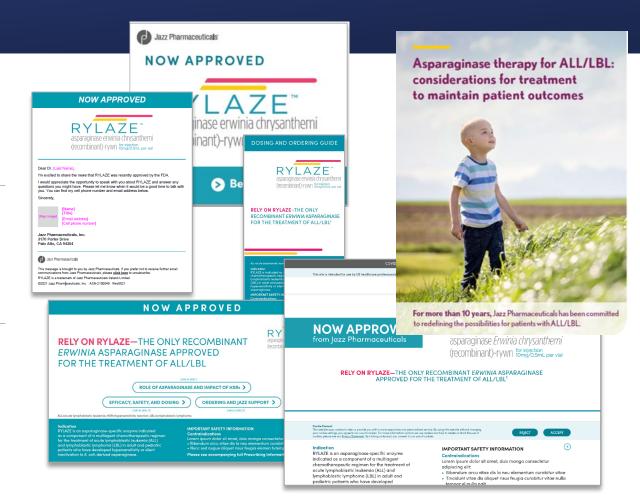
Jazz has been addressing ALL needs for nearly a decade; existing Leukemia OAM team

Strategic Engagement

Experienced MSL, ARM and RMM teams will engage with thought leaders and key decision makers to enable launch success.

Surround Sound Support

Disease awareness education as well as websites and other digital assets to reinforce awareness





Well-Positioned to Address Global Needs

Focus on pediatric oncologists at launch

> U.S. Launch

Expand

- European submission expected 2022
- Japan: Working with our partner on regulatory approach



- Significant AYA population not currently receiving or completing asparaginase therapy
- Treatment paradigm in AYA more fragmented than in pediatrics
- Opportunity to investigate asparaginase use in other indications





Patient-Centric Innovation Drives our Strategy

Putting Patients Front-and-Center of Everything We Do

Quickly advancing Rylaze from concept-to-approval is a critical advance for patients



Drive to address significant unmet needs for ALL patients



Innovation, dedication and excellence by the Jazz team



Highly productive collaboration with both COG and FDA



Strategic investments in growing our conceptto-approval capabilities



Leighton (JZP458 trial participant) and her mom, Allison

