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

SAN DIEGO--(BUSINESS WIRE)-- **Ligand Pharmaceuticals Incorporated (NASDAQ: LGND)** announced that its partner Jazz Pharmaceuticals plc (Nasdaq: JAZZ), ("Jazz") has been granted marketing authorization by the European Commission (EC) 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 (one month and older) who have developed hypersensitivity or silent inactivation to E. coli-derived asparaginase. 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.

"We congratulate our partner Jazz on its receipt of approval for Enrylaze® from the European Commission, expanding the market opportunity for one of our key commercial-stage products," said Todd Davis, CEO of Ligand Pharmaceuticals. "Jazz has executed on a successful launch of the product in the U.S., and we look forward to contributions from sales in the European Union."

Ligand is eligible to receive milestone payments and tiered low- to mid-single digit royalties based on worldwide net sales of any products resulting from its collaboration with Jazz, including Rylaze.

Enrylaze may be given by both intravenous infusion (IV) and intramuscular injection (IM) and is dosed either on alternate days (every 48 hours) or via a Monday/Wednesday/Friday (MWF) dosing schedule. 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.

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. The determination of efficacy was based on demonstration of the

achievement and maintenance of nadir serum asparaginase activity (NSAA) levels ≥ 0.1 U/mL.

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.

Overall, the safety profile of JZP458 was consistent with the reported safety information for patients with ALL/LBL receiving asparaginase with combination chemotherapy. 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.

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®

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. 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.

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.

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. ALL is the most common childhood malignancy, accounting for 80% of leukemia diagnoses in children, compared to 20% of adults. 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. The estimated overall incidence of ALL and lymphoblastic lymphoma (LBL) in Europe is 1.28 per 100,000. The number of ALL global cases in children was 59,100 in 2017. Asparaginase is a core component of multi-agent chemotherapeutic regimens in ALL, however, up to 30% of patients develop hypersensitivity to E. coli-derived asparaginase, necessitating treatment discontinuation or a switch to a non-E. coli-derived asparaginase preparation. Patients not receiving asparaginase due to hypersensitivities and those not receiving all prescribed doses have been shown to have poor outcomes.

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. LBL is a type of high-grade lymphoma – which means the lymphoma grows quickly with early spread to different parts of the body. LBL is the second most common type of NHL in childhood and adolescence, accounting for 25-35% of cases.

About Ligand Pharmaceuticals

Ligand is a biopharmaceutical company enabling scientific advancement through supporting the clinical development of high-value medicines. Ligand does this by providing financing, licensing our technologies or both. Our business model generates value for stockholders by creating a diversified portfolio of biotech and pharmaceutical product revenue streams that are supported by an efficient and low corporate cost structure. Our goal is to offer investors an opportunity to participate in the promise of the biotech industry in a profitable and diversified manner. Our business model is based on funding programs in mid- to late-stage drug development in return for economic rights and licensing our technology to help partners discover and develop medicines. We partner with other pharmaceutical companies to leverage what they do best (late-stage development, regulatory management and commercialization) in order to generate our revenue. Our Captisol® platform technology is a chemically modified cyclodextrin with a structure designed to optimize the solubility and stability of drugs. We have established multiple alliances, licenses and other business relationships with the world's leading pharmaceutical companies including Amgen, Merck, Pfizer, Jazz, Takeda, Gilead Sciences and Baxter International. For more information, please visit www.ligand.com.

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SEC filings, public conference calls and webcasts.

Forward-Looking Statements

This news release contains forward-looking statements by Ligand that involve risks and uncertainties and reflect Ligand's judgment as of the date of this release. Words such as "plans," "believes," "expects," "anticipates," and "will," and similar expressions, are intended to identify forward-looking statements. These forward-looking statements include: the efficacy and safety of Enrylaze and the timing and amount of royalties Ligand may receive in connection with the commercialization of Enrylaze. Actual events or results may differ from Ligand's or its partner's expectations due to risks and uncertainties inherent in Ligand's and its partner's business, including, without limitation: changes in the size and nature of the market for Enrylaze, including potential competition, patient and payer perceptions and reimbursement determinations; that Enrylaze will continue to demonstrate requisite safety and efficacy following commercial launch; Ligand is dependent on Jazz for the development and commercialization of Enrylaze; Ligand or its partners may not be able to protect their intellectual property, and patents covering certain products and technologies may be challenged or invalidated; and other risks described in Ligand and Jazz's prior press releases and filings with the Securities and Exchange Commission available at www.sec.gov. Ligand disclaims any intent or obligation to update these forward-looking statements beyond the date of this release. This caution is made under the safe harbor provisions of the Private Securities Litigation Reform Act of 1995.

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Ligand Pharmaceuticals Incorporated
Simon Latimer
investors@ligand.com
(858) 550-7766
X Handle: @Ligand_LGND

LifeSci Advisors
Bob Yedid
bob@lifesciadvisors.com
(516) 428-8577

Source: Ligand Pharmaceuticals Incorporated