



PharmaMar and Jazz Pharmaceuticals announce initiation of confirmatory phase III clinical trial of Zepzelca® (lurbinectedin) for the treatment of patients with relapsed Small Cell Lung Cancer

- **The confirmatory trial is designed to secure full approval in the U.S. and serve as a registrational trial for the European Medicines Agency.**
- **The multi-center, open-label global trial will enroll 705 patients from over 100 centers mainly in North America and Europe.**

MADRID and DUBLIN, December 13th, 2021. – PharmaMar (MSE:PHM) and partner Jazz Pharmaceuticals plc (Nasdaq:JAZZ) today announced the initiation of a confirmatory Phase III clinical trial, LAGOON, evaluating Zepzelca® (lurbinectedin) for the treatment of patients with relapsed Small Cell Lung Cancer (SCLC). The trial will measure Overall Survival (OS) as primary endpoint and Progression-Free Survival (PFS) as one of the secondary endpoints of lurbinectedin monotherapy or lurbinectedin in combination with irinotecan, compared with investigator’s choice of topotecan or irinotecan, in patients with SCLC whose disease has progressed following prior platinum-containing chemotherapy with or without anti-PD-1 or anti-PD-L1 agents.

"We are very excited about this trial, which is designed to reinforce lurbinectedin as a second-line treatment of choice in the U.S. and has the potential to bring our treatment to European patients," said **Ali Zeaiter, M.D.**, director of Clinical Development, PharmaMar Oncology Business Unit.

"There has been a strong clinical demand for lurbinectedin following the FDA’s accelerated approval, which demonstrates that this important therapy is filling a significant unmet need for the metastatic small cell lung cancer community," said **Rob Iannone, M.D., M.S.C.E.**, executive vice president, research and development



and chief medical officer at Jazz Pharmaceuticals. *"We are committed to working with PharmaMar and the FDA to further demonstrate the clinical benefit of lurbinectedin and support conversion to full regulatory approval in the U.S."*

LAGOON is a Phase III, randomized (1:1:1), multicenter, open-label clinical trial with three arms: one arm to receive lurbinectedin 3.2 mg/m² as monotherapy (the approved dose in the U.S.), the second arm to receive lurbinectedin 2.0 mg/m² in combination with irinotecan 75 mg/m² and the third arm to receive topotecan or irinotecan based on the investigators' choice. The trial will be conducted in patients with SCLC, whose disease has progressed following prior platinum-containing chemotherapy with or without anti-PD-1 or anti-PD-L1 agents. LAGOON is expected to enroll 705 patients from more than 100 sites mainly in North America and Europe.

The FDA approved lurbinectedin under accelerated approval in June 2020 for the treatment of adult patients with metastatic SCLC with disease progression on or after platinum-based chemotherapy. The approval is based on Overall Response Rate (ORR) and Duration of Response (DoR) demonstrated in an open-label, monotherapy clinical study. If successful, LAGOON will serve as the confirmatory trial for lurbinectedin to secure full approval in the U.S. LAGOON will also be used as a registrational trial with the European Medicines Agency (EMA) to obtain marketing authorization in Europe. Jazz Pharmaceuticals holds the commercial rights for lurbinectedin in North America.

In 2021, lurbinectedin received marketing authorization in the United Arab Emirates, Canada, Australia and Singapore. Additional marketing authorizations are expected in 2022 and beyond.

Legal warning

This press release does not constitute an offer to sell or the solicitation of an offer to buy securities, and shall not constitute an offer, solicitation or sale in any jurisdiction in which such offer, solicitation or sale would be unlawful prior to registration or qualification under the securities laws of that jurisdiction.

About PharmaMar

PharmaMar is a biopharmaceutical company focused on the research and development of new oncology treatments, whose mission is to improve the healthcare outcomes of patients afflicted by serious diseases with our innovative medicines. The Company is inspired by the sea, driven by science, and motivated by patients with serious diseases to improve their lives by delivering novel medicines to them. PharmaMar intends to continue to be the world leader in marine medicinal discovery, development and innovation. PharmaMar has developed and now commercializes Yondelis® in Europe by itself, as well as Zepzelca® (lurbinectedin), in the US; and Aplidin® (plitidepsin), in Australia, with different partners. In addition, it



has a pipeline of drug candidates and a robust R&D oncology program. PharmaMar has other clinical-stage programs under development for several types of solid cancers: lurbinectedin and PM14. Headquartered in Madrid (Spain), PharmaMar has subsidiaries in Germany, France, Italy, Belgium, Austria, Switzerland and The United States. PharmaMar also wholly owns other companies: GENOMICA, a molecular diagnostics company; and Sylentis, dedicated to researching therapeutic applications of gene silencing (RNAi). To learn more about PharmaMar, please visit us at www.pharmamar.com.

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 Jazz Pharmaceuticals' belief in the potential of Zepzelca to provide a potentially new SCLC therapeutic option in the first-line setting 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, effectively launching and commercializing new products; obtaining and maintaining adequate coverage and reimbursement for the company's products; delays or problems in the supply or manufacture of the company's products; 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 (Commission File No. 001-33500), including Jazz Pharmaceuticals' Quarterly Report on Form 10-Q for the quarter ended September 30, 2021 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.

About lurbinectedin

Lurbinectedin (Zepzelca[®]), also known as PM1183, is an analog of the marine compound ET-736 isolated from the sea squirt *Ecteinacidia turbinata* in which a hydrogen atom has been replaced by a methoxy group. It is a selective inhibitor of the oncogenic transcription programs on which many tumors are



particularly dependent. Together with its effect on cancer cells, lurbinectedin inhibits oncogenic transcription in tumor-associated macrophages, downregulating the production of cytokines that are essential for the growth of the tumor. Transcriptional addiction is an acknowledged target in those diseases, many of them lacking other actionable targets.

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