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News Release

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New RYBREVANT®▼ (amivantamab) Data Showed Long-Term Clinical Response and Safety Profile in Patients with Advanced Non-Small Cell Lung Cancer with EGFR Exon 20 Insertion Mutations Who Have Failed Prior Platinum-Based Chemotherapy

Additional analyses of data from the CHRYSALIS study evaluate progression-free survival and overall survival with amivantamab when compared to other anti-cancer therapies frequently used in real-world settings in the EU and U.S.[1,2]

BEERSE, BELGIUM, March 29, 2023 – The Janssen Pharmaceutical Companies of Johnson & Johnson today announced new long-term data from the CHRYSALIS study, evaluating RYBREVANT®▼ (amivantamab) in patients with advanced non-small cell lung cancer (NSCLC) and epidermal growth factor receptor (EGFR) exon 20 insertion mutations whose disease progressed on prior platinum-based chemotherapy.[1] Data from the study showed long-term response and safety profile in this population, and were presented in an oral presentation at the **2023 European Lung Cancer Congress (ELCC)** (Abstract #779),[1] taking place from 29 March – 1 April in Copenhagen, Denmark.

In the analysis of the CHRYSALIS study, investigators assessed the efficacy and safety of amivantamab in patients (n=114) with NSCLC and EGFR exon 20 insertion mutations, who had progressed on prior platinum-based chemotherapy, and were treated at the recommended Phase 2 dose of 1050 mg (1400 mg for a patient weight of at least 80 kg).[1] The primary endpoint was overall response rate (ORR) per Response Evaluation Criteria in Solid Tumours Version 1.1* (RECIST v1.1).[1] Additional endpoints included duration of response (DOR), clinical benefit rate, progression-free survival (PFS) and overall survival

(OS).[1]

After a median follow-up of 19.2 months, the median OS with amivantamab treatment was 23 months (95 percent confidence interval [CI], 18.5–29.5) with a two-year OS rate of 47 percent.[1] The investigator-assessed ORR was 37 percent (95 percent CI, 28–46) with a median DOR of 12.5 months (95 percent CI, 6.9–19.3), and median PFS of 6.9 months (95 percent CI, 5.6–8.8).[1] Across subgroups, treatment with amivantamab resulted in consistent efficacy across post-platinum patients with EGFR exon 20 insertion mutations, including the elderly, regardless of prior therapies or response to prior platinum chemotherapy.[1] Forty-eight patients (42 percent) had sustained clinical response measured by ORR on amivantamab for at least 12 cycles.[1] The median duration of treatment was 7.5 months and treatment is ongoing in 15 patients (13 percent) who have received amivantamab for a median of 2.6 years.[1] Of these patients, seven are progression-free and eight are receiving treatment beyond progression.[1]

No new safety signals were identified and rash (all group, 89 percent), infusion-related reactions (IRR; 67 percent) and paronychia (58 percent) remained the most common treatment emergent adverse events (AEs).[1] The incidence of treatment-related AEs leading to dose interruption, reduction and discontinuation was 29 percent, 18 percent and seven percent, respectively.[1]

"With these new data, amivantamab showed long-term consistent efficacy regardless of prior therapies or response to prior platinum chemotherapy," said Pilar Garrido[†], M.D., Associate Professor of Medical Oncology at Universidad de Alcalá, Head of Medical Oncology Department at the University Hospital Ramón y Cajal in Madrid, Spain and principal investigator. "Due to the aggressive nature of NSCLC with EGFR exon 20 insertion mutations, treatment with targeted therapies is an important consideration when identifying a treatment option for patients."

NSCLC driven by EGFR exon 20 insertion mutations carries a worse prognosis and shorter survival rates compared with lung cancer driven by more common EGFR mutations, such as exon 19 deletions and L858R substitutions.[3] The standard of care for common EGFR mutations, such as EGFR tyrosine kinase inhibitors (TKIs), are generally inactive against exon 20 insertion mutations.[3]

"Despite treatment advances, patients with advanced NSCLC with EGFR exon 20 insertion mutations continue to face poor clinical outcomes," said Martin Vogel, EMEA Therapeutic Area Lead Oncology, Janssen-Cilag GmbH. "These insights reinforce the potential of amivantamab as a targeted and effective option for these patients, and our commitment to lead the way in precision medicine approaches, whereby we are better able to identify the distinct patient populations most likely to benefit from specific treatments."

Results from Analysis of Real-World Datasets Comparing Amivantamab to Alternative Anti-Cancer Therapies in the EU and U.S.

An analysis of results from the CHRYSALIS study compared to alternative anti-cancer treatments used in real-world settings for patients with NSCLC with EGFR exon 20 insertion mutations (Abstract #422) highlighted the relative effectiveness of amivantamab versus EGFR TKIs, immunotherapy, non-platinum chemotherapy and vascular endothelial growth factor inhibitors (VEGFi) plus chemotherapy.[2] The comparative analyses assessed OS, PFS, time to next treatment (TTNT), and ORR by investigator (ORR-INV).[2]

"The long-term CHRYSALIS data presented at ELCC support amivantamab as an important treatment option for patients with EGFR exon 20 insertion mutation-positive NSCLC, providing valuable clinical insights that may help inform treatment decisions," said Kiran Patel, M.D., Vice President, Clinical Development, Solid Tumors, Janssen Research & Development, LLC. "We're committed to transforming the treatment of lung cancer through continued research and the development of targeted therapies for genetic-mutated disease where high unmet needs continue to exist."

About the CHRYSALIS Study

CHRYSALIS (NCT02609776) is a Phase 1 open-label, multicentre, first-in-human study to evaluate the safety, pharmacokinetics and preliminary efficacy of amivantamab as a monotherapy, in combination with lazertinib** and in combination with platinum-based chemotherapy, in patients with advanced NSCLC with various EGFR mutations.[4] In the study, investigators assessed efficacy using overall response rate per Response Evaluation Criteria in Solid Tumours Version 1.1* (RECIST v1.1), clinical benefit rate, median duration of response and median progression-free survival, as well as the safety profile of amivantamab.[4]

The study enrolled 780 patients with advanced NSCLC.[4] The study consists of two parts:

amivantamab monotherapy and combination dose escalations (Part 1), and amivantamab monotherapy and combination dose expansions (Part 2).[4]

About Amivantamab

Amivantamab is a fully-human EGFR-mesenchymal-epithelial transition factor (MET) bispecific antibody with immune cell-directing activity that targets tumours with activating and resistance EGFR mutations and MET mutations and amplifications.[5,6,7,8,9] The European Commission granted Conditional Marketing Authorisation for amivantamab in December 2021 for the treatment of adult patients with advanced NSCLC with activating epidermal growth factor receptor (EGFR) exon 20 insertion mutations, after failure of platinum-based therapy.[10] Amivantamab is the first approved treatment in the European Union specifically targeting EGFR exon 20 insertion mutations for NSCLC.[3,10,11] Amivantamab also received accelerated approval by the U.S. Food and Drug Administration (FDA) in May 2021 for the treatment of adult patients with locally advanced or metastatic NSCLC with EGFR exon 20 insertion mutations, as detected by an FDA-approved test, whose disease has progressed on or after platinum-based chemotherapy.[12]

Amivantamab is being studied in multiple clinical trials in NSCLC, including:

- As first-line therapy in the Phase 3 MARIPOSA (NCT04487080) study assessing amivantamab in combination with lazertinib, a novel third generation EGFR TKI, against osimertinib and against lazertinib alone in untreated advanced EGFR-mutated NSCLC.[13]
- The Phase 3 MARIPOSA-2 (NCT04988295) study assessing the efficacy of lazertinib, amivantamab and carboplatin-pemetrexed versus carboplatin-pemetrexed in patients with locally advanced or metastatic EGFR exon 19 deletion or exon 21 L858R substitution NSCLC after osimertinib failure.[14]
- The Phase 1/1b CHRYSALIS-2 (NCT04077463) study evaluating amivantamab in combination with lazertinib and lazertinib as a monotherapy in patients with advanced NSCLC with EGFR mutations.[15]
- The Phase 3 PAPILLON (NCT04538664) study assessing amivantamab in combination with carboplatin-pemetrexed versus chemotherapy alone in patients with advanced or metastatic EGFR-mutated NSCLC and exon 20 insertion mutations.[16]
- The Phase 1 PALOMA (NCT04606381) study assessing the feasibility of subcutaneous (SC) administration of amivantamab based on safety and pharmacokinetics and to determine a dose, dose regimen and formulation for amivantamab SC delivery.[17]

- The Phase 2 PALOMA-2 (NCT05498428) study assessing amivantamab in participants with advanced or metastatic solid tumours including EGFR-mutated NSCLC.[18]
- The Phase 3 PALOMA-3 (NCT05388669) study assessing lazertinib with SC amivantamab as compared to intravenous amivantamab in participants with EGFR-mutated advanced or metastatic NSCLC.[19]
- The Phase 1/2 METalmark (NCT05488314) study assessing amivantamab and capmatinib combination therapy in unresectable metastatic NSCLC.[20]

About Non-Small Cell Lung Cancer (NSCLC)

In Europe, it is estimated that 477,534 patients were diagnosed with lung cancer in 2020, with around 85 percent diagnosed with NSCLC.[21,22] Lung cancer is Europe's biggest cancer killer, with more deaths than breast cancer and prostate cancer combined.[21]

The main subtypes of NSCLC are adenocarcinoma, squamous cell carcinoma and large cell carcinoma.[22] Among the most common driver mutations in NSCLC are alterations in EGFR, which is a receptor tyrosine kinase supporting cell growth and division.[23] EGFR mutations are present in 16 to 19 percent of Caucasian patients with NSCLC and present in 37 to 41 percent of Asian patients who have NSCLC adenocarcinoma.[24] The five-year survival rate for all people with advanced NSCLC and EGFR mutations treated with EGFR TKIs is less than 20 percent.[25] Patients with EGFR exon 20 insertion mutations have a real-world five-year OS of eight percent in the frontline setting, which is worse than patients with EGFR exon 19 deletions or L858R mutations, who have a real-world five-year OS of 19 percent.[26]

About the Janssen Pharmaceutical Companies of Johnson & Johnson

At Janssen, we're creating a future where disease is a thing of the past. We're the Pharmaceutical Companies of Johnson & Johnson, working tirelessly to make that future a reality for patients everywhere by fighting sickness with science, improving access with ingenuity, and healing hopelessness with heart. We focus on areas of medicine where we can make the biggest difference: Cardiovascular, Metabolism & Retina; Immunology; Infectious Diseases & Vaccines; Neuroscience; Oncology; and Pulmonary Hypertension.

Learn more at www.janssen.com/emea. Follow us at www.twitter.com/JanssenEMEA for our latest news. Janssen Pharmaceutica NV, Janssen-Cilag GmbH, Janssen Research & Development, LLC, and Janssen Biotech, Inc. are part of the Janssen Pharmaceutical Companies of Johnson & Johnson.

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†Dr. Garrido has served as a consultant to Janssen; she has not been paid for any media work.

*RECIST (version 1.1) refers to Response Evaluation Criteria in Solid Tumours, which is a standard way to measure how well solid tumours respond to treatment and is based on whether tumours shrink, stay the same or get bigger.[4]

**In 2018, Janssen Biotech, Inc. entered into a license and collaboration agreement with Yuhan Corporation for the development of lazertinib.

Cautions Concerning Forward-Looking Statements

This press release contains "forward-looking statements" as defined in the Private Securities Litigation Reform Act of 1995 regarding product development and the potential benefits and treatment impact of amivantamab. The reader is cautioned not to rely on these forward-looking statements. These statements are based on current expectations of future events. If underlying assumptions prove inaccurate or known or unknown risks or uncertainties materialize, actual results could vary materially from the expectations and projections of Janssen Pharmaceutica NV, Janssen Research and Development, LLC, Janssen Biotech, Inc., Janssen-Cilag GmbH and/or Johnson & Johnson. Risks and uncertainties include, but are not limited to: challenges and uncertainties inherent in product research and development, including the uncertainty of clinical success and of obtaining regulatory approvals; uncertainty of commercial success; competition, including technological advances, new products and patents attained by competitors; challenges to patents; changes in behavior and spending patterns of purchasers of health care products and services; changes to applicable laws and regulations, including global health care reforms; and trends toward health care cost containment. A further list and descriptions of these risks, uncertainties and other factors can be found in Johnson & Johnson's Annual Report on Form 10-K for the fiscal year ended January 1, 2023, including in the sections captioned "Cautionary Note Regarding Forward-Looking Statements" and "Item 1A. Risk Factors," and in Johnson & Johnson's subsequent Quarterly Reports on Form 10-Q and other filings with the Securities and Exchange Commission. Copies of these filings are available online at www.sec.gov, www.jnj.com or on request from Johnson & Johnson. None of Janssen Pharmaceutica NV, Janssen Research and Development, LLC, Janssen Biotech, Inc., the Janssen Pharmaceutical Companies nor Johnson & Johnson undertakes to update any forward-looking statement as a result of new information or future events or developments.

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