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News Release

Media Contacts:
Zayn Qureshi
+44 7760 334666
Email: zqureshi@its.jnj.com

Investor Relations:
Raychel Kruper
+1 732 524 6164
investor-relations@its.jnj.com

Landmark Phase 3 MARIPOSA Study Shows RYBREVANT®▼(amivantamab) Plus Lazertinib Resulted in 30 Percent Reduction in Risk of Disease Progression or Death Compared to Osimertinib in Patients with EGFR-Mutated Non-Small Cell Lung Cancer

Early data show an overall survival trend favoring the combination of amivantamab and lazertinib compared to osimertinib; consistent results seen in patients with and without brain metastases[1]

Late-breaking results from the MARIPOSA study featured in a Presidential Symposium at 2023 ESMO Congress[1]

BEERSE, BELGIUM, 23 October, 2023 – The Janssen Pharmaceutical Companies of Johnson & Johnson today announced results from the Phase 3 MARIPOSA study showing RYBREVANT®▼ (amivantamab) in combination with lazertinib compared to osimertinib resulted in a 30 percent reduction in the risk of disease progression or death (Hazard Ratio [HR]=0.70; 95 percent Confidence Interval [CI], 0.58–0.85; *P*<0.001) in the first-line treatment of patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) with either epidermal growth factor receptor (EGFR) exon 19 deletions (ex19del) or L858R substitution.[1] Results also showed a favourable trend in overall survival (OS) for amivantamab and lazertinib in these patients compared to osimertinib (HR=0.80; 95 percent CI, 0.61–1.05; *P*=0.11) at a first interim analysis.[1] These data were presented in a Presidential Symposium

at the European Society for Medical Oncology (ESMO) 2023 Congress taking place 20-24 October in Madrid, Spain (Abstract #LBA14).[1]

"Despite advances in EGFR-mutated NSCLC treatment, novel targeted therapies and regimens are needed to address resistance and disease progression, which are nearly inevitable with current treatments," said Byoung Chul Cho*, M.D., Ph.D., medical oncologist and professor in the Division of Medical Oncology at Yonsei Cancer Center, Yonsei University College of Medicine in Seoul, Republic of Korea, and presenting author. "With the combination of amivantamab and lazertinib in the MARIPOSA study, progression free survival was significantly improved in patients with previously untreated EGFR-mutated NSCLC compared to osimertinib. These results support the potential of this amivantamab combination to be a future standard of care."

At a median follow-up of 22 months, median progression-free survival (PFS) for amivantamab and lazertinib was 23.7 months compared to 16.6 months for osimertinib (HR=0.70; 95 percent CI, 0.58–0.85; *P*<0.001).[1] Other secondary endpoints showed consistent and clinically meaningful benefits for the combination of amivantamab and lazertinib versus osimertinib across prespecified patient subgroups, including race, type of EGFR mutation, history of brain metastasis, and performance status.[1†] Lazertinib was included in the MARIPOSA study to determine its contribution to the combination with amivantamab, and lazertinib monotherapy was shown to provide a clinically meaningful median PFS of 18.5 months (95 percent CI, 14.8–20.1).[1]

The MARIPOSA study required all patients to have serial brain imaging with MRIs in order to detect or monitor brain metastases, a measure not implemented in most prior studies for EGFR-mutated NSCLC.[1] The primary endpoint of PFS in MARIPOSA included these central nervous system (CNS) events detected by serial brain MRIs.[1] Extracranial PFS, which may more closely approximate what would be seen in other trials, was also explored in MARIPOSA.[1] The median PFS when censoring CNS-only first progressions was 27.5 months for the combination of amivantamab and lazertinib, compared with 18.5 months for osimertinib (HR=0.68; 95% CI, 0.56–0.83; *P*<0.001).[1] The median duration of response (DOR), or the length of time that a tumour continues to respond to treatment without the cancer growing or spreading, was significantly longer for patients receiving amivantamab plus lazertinib compared to osimertinib, with a nine-month improvement in median DOR (25.8 vs. 16.8 months).[1]

"Lung cancer remains the leading cause of cancer death worldwide and for patients with certain oncogenic driver mutations, the survival rate with the current standard of care, tyrosine kinase inhibitors, is still too low," said Martin Vogel, EMEA Therapeutic Area Lead Oncology, Janssen-Cilag GmbH. "There are many known actionable mutations within NSCLC, and alterations in EGFR are amongst the most common and challenging to treat. Identifying patients whose advanced NSCLC is driven by genetic mutations and providing targeted-first line treatments, such as the combination of amivantamab and lazertinib, may help address this area of particularly high unmet medical need."

The safety profile of the combination of amivantamab and lazertinib was consistent with the safety profiles of the individual treatments, with mostly Grade 1 or 2 adverse events (AEs).[1]Toxicity was largely manageable with dose interruptions and reductions, along with supportive care measures commonly used in the treatment of patients with NSCLC. The most common Grade 3 or higher treatment-related AEs were rash and paronychia.[1] Amivantamab plus lazertinib had higher rates of EGFR- and MET-related AEs (hypoalbuminemia and peripheral oedema) and venous thromboembolism compared to osimertinib, with higher rates of diarrhoea being observed with osimertinib.[1] The rate of discontinuation of all study treatments due to treatment-related AEs for the amivantamab combination was 10 percent. The rate of interstitial lung disease (including pneumonitis) was less than three percent in both arms.[1]

"Amivantamab is the first fully-human bispecific antibody that targets two major oncogenic driver pathways and, when combined with lazertinib, we believe, may lead to a more complete response against the tumour," said Peter Lebowitz, M.D., Ph.D., Global Therapeutic Area Head, Oncology, Janssen Research & Development, LLC. "The prolonged duration of progression-free survival and favourable trend in overall survival observed in the MARIPOSA study show the potential of amivantamab in combination with lazertinib to transform first-line treatment in EGFR-mutated NSCLC."

Amivantamab is a bispecific antibody targeting EGFR and MET with immune cell-directing activity, and in the MARIPOSA study, was combined with lazertinib, an oral third-generation EGFR tyrosine kinase inhibitor (TKI), to treat patients with locally advanced or metastatic EGFR-mutated NSCLC.[1,2,3,4,5,6,7] In the study, 1,074 patients were randomised to receive treatment with amivantamab plus lazertinib, osimertinib alone or lazertinib alone.[1] The

primary endpoint was PFS following treatment with amivantamab plus lazertinib compared to osimertinib as assessed by blinded independent central review (BICR) according to RECIST v1.1.[1‡] Secondary endpoints included OS, objective response rate (ORR), DOR and intracranial PFS.[1]

Results from MARIPOSA will support future planned health authority submissions.

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About the MARIPOSA Study

MARIPOSA (NCT04487080), which enrolled 1,074 patients, is a randomised, Phase 3 study evaluating amivantamab in combination with lazertinib versus osimertinib and versus lazertinib alone in first-line treatment of patients with locally advanced or metastatic NSCLC with EGFR ex19del or substitution mutations.[1] The primary endpoint of the study is PFS (using RECIST v1.1 guidelines) as assessed by blinded independent central review.[1] Secondary endpoints include OS, ORR, DOR, second progression free survival (PFS2) and intracranial PFS.[1]

About Amivantamab

Amivantamab is a fully-human EGFR-MET bispecific antibody with immune cell-directing activity that targets tumours with activating and resistance EGFR mutations and MET mutations and amplifications.[2,3,4,5,6] The European Commission granted Conditional Marketing Authorisation of amivantamab in December 2021 for the treatment of adult patients with advanced NSCLC with activating EGFR exon 20 insertion mutations, after failure of platinum-based therapy.[2] Amivantamab is the first approved treatment in the European Union specifically targeting EGFR exon 20 insertion mutations for NSCLC.[2] In October 2023, a marketing authorisation application was submitted to the European Medicines Agency seeking approval for the combination of amivantamab in combination with chemotherapy (carboplatin-pemetrexed) for the first-line treatment of patients with NSCLC with EGFR exon 20 insertion mutations.[8]

In addition to the Phase 3 MARIPOSA study, amivantamab is being studied in multiple clinical trials in NSCLC, including:

- The Phase 3 MARIPOSA-2 (NCT04988295) study assessing the efficacy of amivantamab (with or without lazertinib) and carboplatin-pemetrexed versus

carboplatin-pemetrexed in patients with locally advanced or metastatic EGFR ex19del or L858R substitution NSCLC after disease progression on or after osimertinib. Topline data for this randomised Phase 3 study demonstrated statistically significant and clinically meaningful improvement in PFS in patients receiving amivantamab plus chemotherapy with and without lazertinib versus chemotherapy.[1,9,10]

- The Phase 3 PAPILLON (NCT04538664) study assessing amivantamab in combination with carboplatin-pemetrexed versus carboplatin-pemetrexed in the first-line treatment of patients with advanced or metastatic NSCLC with EGFR exon 20 insertion mutations. Topline data for this randomised Phase 3 study demonstrated statistically significant and clinically meaningful improvement in PFS in patients receiving amivantamab versus chemotherapy.[11,12]
- The Phase 1 CHRYSALIS (NCT02609776) study evaluating amivantamab in participants with advanced NSCLC.[13]
- 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.[14]
- 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.[15]
- The Phase 2 PALOMA-2 (NCT05498428) study assessing subcutaneous amivantamab in participants with advanced or metastatic solid tumors including EGFR-mutated NSCLC.[16]
- The Phase 3 PALOMA-3 (NCT05388669) study assessing lazertinib with subcutaneous amivantamab compared to intravenous amivantamab in participants with EGFR-mutated advanced or metastatic NSCLC.[17]
- The Phase 1/2 METalmark (NCT05488314) study assessing amivantamab and capmatinib combination therapy in locally advanced or metastatic NSCLC.[18]
- The Phase 2 SKIPPirr study (NCT05663866) exploring how to decrease the incidence and/or severity of first-dose infusion-related reactions with amivantamab in combination with lazertinib in relapsed or refractory EGFR-mutated advanced or metastatic NSCLC.[19]

For a full list of adverse events and information on dosage and administration, contraindications and other precautions when using amivantamab please refer to the Summary of Product Characteristics.[2]

▼ In line with EMA regulations for new medicines and those given conditional approval, amivantamab is subject to additional monitoring.

About Lazertinib

Lazertinib is an oral, third-generation, brain-penetrant EGFR TKI that targets both the T790M mutation and activating EGFR mutations while sparing wild-type EGFR. An analysis of the efficacy and safety of lazertinib from the Phase 3 study LASER301 was published in *The Journal of Clinical Oncology* in 2023.[7] In 2018, Janssen Biotech, Inc., entered into a license and collaboration agreement with Yuhan Corporation for the development of lazertinib.

About Non-Small Cell Lung Cancer

In Europe, it is estimated that 477,534 patients were diagnosed with lung cancer in 2020, with around 85 percent diagnosed with NSCLC.[20,21] 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 controlling cell growth and division.[23] EGFR mutations are present in 10 to 15 percent of Western patients with NSCLC with adenocarcinoma histology and occur in 40 to 50 percent of Asian patients.[24,25,26,27] EGFR ex19del or EGFR L858R mutations are the most common EGFR mutations.[28] The five-year survival rate for all people with advanced NSCLC and EGFR mutations treated with EGFR TKIs is less than 20 percent.[29,30] Patients with EGFR ex19del or L858R mutations have a real-world five-year OS of 19 percent.[31]

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: Oncology, Immunology, Neuroscience, Cardiovascular, Pulmonary Hypertension, and Retina.

Learn more at www.janssen.com/emea. Follow us at www.linkedin.com/janssenEMEA for our latest news. Janssen Pharmaceutica NV, Janssen-Cilag GmbH, and Janssen Research & Development, LLC are Johnson & Johnson companies.

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 and lazertinib. 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 Research and Development, LLC, Janssen Biotech, Inc., Jannsen-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 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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*Dr. Cho has served as a consultant to Janssen; he has not been paid for any media work.

†The ECOG Performance Status Scale is a score that estimates a patient's ability to perform certain activities of daily living without the help of others.

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‡RECIST (version 1.1) refers to Response Evaluation Criteria in Solid Tumors, 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.

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