Johnson&Johnson

NEWS RELEASE

RYBREVANT® (amivantamab-vmjw) plus LAZCLUZE™ (lazertinib) show strong favorable overall survival trend versus osimertinib in EGFR-mutated advanced lung cancer

2024-09-08

New longer-term data from the MARIPOSA study confirm superior outcomes of chemotherapy-free RYBREVANT® plus LAZCLUZE™ regimen compared to osimertinib monotherapy as first-line therapy

Results from an interim analysis featured in late-breaker oral presentation at WCLC

SAN DIEGO, Sept. 8, 2024 /PRNewswire/ -- Johnson & Johnson (NYSE: JNJ) today announced longer follow-up data from the landmark Phase 3 MARIPOSA study which showed first-line treatment with RYBREVANT® (amivantamab-vmjw) combined with LAZCLUZE™ (lazertinib) provided consistent benefit across long-term outcomes compared to osimertinib monotherapy in adult patients with advanced non-small cell lung cancer (NSCLC) with epidermal growth factor receptor (EGFR) exon 19 deletions (ex19del) or L858R substitution mutations. The data show a strong and improving overall survival (OS) trend favoring RYBREVANT® plus LAZCLUZE™ at approximately three years of follow-up. These results were presented in a late-breaking oral presentation at the **International Association for the Study of Lung Cancer (IASLC) 2024 World Conference on Lung Cancer (WCLC)** (**Abstract #1146**).[1]

At three years (a median follow-up of 31.1 months), 61 percent of patients receiving RYBREVANT® plus LACLUZE™ were alive compared to 53 percent of those treated with osimertinib based on an analysis performed at the request of a health authority (Median OS not estimable vs 37.3 months; hazard ratio [HR], 0.77; [95 percent confidence interval [CI], 0.61-0.96]; nominal P=0.019). Overall survival will continue to be assessed with longer term follow-up as a key secondary endpoint. The primary efficacy outcome measure was progression-free survival (PFS) as assessed by blinded independent central review (BICR).[1]

"By combining the multi-targeted mechanism of RYBREVANT with LAZCLUZE, a central nervous system-penetrant third-generation tyrosine kinase inhibitor, we are advancing a chemotherapy-free regimen for the first-line treatment of patients with EGFR-mutant NSCLC. This approach blocks EGFR and MET pathways and leverages the immune system, offering patients an opportunity for prolonged benefits," said Shirish M. Gadgeel, M.D., Chief of Division of Hematology and Oncology, Associate Director at Henry Ford Cancer Institute and presenting author.* "Even more encouraging is the marked improvement in the hazard ratio and the ongoing separation of survival curves, showing an eight percent improvement at three years for RYBREVANT plus LAZCLUZE compared to osimertinib. This supports the long-term benefit of the combination as a first-line treatment option in this setting."

Results further showed RYBREVANT® plus LAZCLUZE™ demonstrated a trend toward improved central nervous system disease control compared to osimertinib at three years (HR, 0.82; [95 percent CI, 0.62-1.09]; nominal P=0.165). At the three-year landmark, intracranial PFS was double for RYBREVANT® plus LAZCLUZE™ versus osimertinib (38 percent vs 18 percent, respectively). More patients remained on treatment at three years with the RYBREVANT® combination compared to osimertinib (40 percent vs 29 percent, respectively; HR, 0.80; [95 percent CI, 0.68-0.96]; nominal P=0.014). Additionally, more patients receiving RYBREVANT® and LAZCLUZE™ at the three-year follow-up had not started a subsequent therapy versus osimertinib (45 percent vs 32 percent, respectively; HR, 0.77; [95 percent CI, 0.65-0.93]; nominal P=0.005). Progression-free survival after first subsequent therapy was 57 percent for the RYBREVANT® combination compared to 49 percent for osimertinib (HR, 0.73; [95 percent CI, 0.59-0.91]; nominal P=0.004).[1]

"Promising results like these presented at WCLC reinforce our mission to improve the lives of patients diagnosed with lung cancer," said Joshua Bauml, M.D., Vice President, Lung Cancer Disease Area Stronghold Leader, Johnson & Johnson Innovative Medicine. "We are encouraged by the favorable overall survival trend observed with RYBREVANT plus LAZCLUZE and are eager to see how these data evolve as we continue to follow patients over time."

As previously reported in the MARIPOSA study, the safety profile was consistent with the safety profiles of the individual treatments. The rate of discontinuation of all study treatments due to treatment-related adverse events for RYBREVANT® plus LAZCLUZE™ was 10 percent. The rate of interstitial lung disease (including pneumonitis) was less than three percent in both arms.[2]

In August 2024, RYBREVANT® combined with LAZCLUZE™ was **approved** following a Priority Review by the U.S. Food and Drug Administration as a first-line therapy for patients with EGFR-mutated NSCLC based on the favorable efficacy and safety profile demonstrated in this study.

About the MARIPOSA Study

MARIPOSA (**NCT04487080**), which enrolled 1,074 patients, is a randomized, Phase 3 study evaluating RYBREVANT® in combination with LAZCLUZE™ versus osimertinib and versus LAZCLUZE™ alone in first-line treatment of patients with locally advanced or metastatic NSCLC with EGFR ex19del or L858R substitution mutations. The primary endpoint of the study is PFS (using RECIST v1.1 guidelines) as assessed by BICR. Secondary endpoints include OS, overall response rate (ORR), duration of response (DOR), second progression-free survival (PFS2) and intracranial PFS.[3]

About RYBREVANT®

RYBREVANT® (amivantamab-vmjw), a fully-human bispecific antibody targeting EGFR and MET with immune cell-directing activity, is approved in the **U.S.**, **Europe**, and in other markets around the world as monotherapy 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.[4]

RYBREVANT® is approved in the **U.S.**, **Europe** and in markets around the world in combination with chemotherapy (carboplatin and pemetrexed) for the first-line treatment of adult patients with locally advanced or metastatic NSCLC with EGFR exon 20 insertion mutations, as detected by an FDA-approved test.

RYBREVANT® is approved in the **U.S.** in combination with LAZCLUZE™ (lazertinib) for the first-line treatment of adult patients with locally advanced or metastatic NSCLC with EGFR exon 19 deletions or L858R substitution mutations, as detected by an FDA-approved test. A marketing authorization application (MAA) and type II extension of indication application were **submitted** to the European Medicines Agency (EMA) seeking approval of LAZCLUZE™ in combination with RYBREVANT® based on the MARIPOSA study.

In November 2023, Johnson & Johnson **submitted** a supplemental Biologics License Application (sBLA) to the U.S. FDA for RYBREVANT® in combination with chemotherapy for the treatment of patients with EGFR-mutated NSCLC who progressed on or after osimertinib based on the MARIPOSA-2 study. This indication was approved in **Europe** in August 2024.

In June 2024, Johnson & Johnson submitted a BLA to the U.S. FDA for the subcutaneous formulation of RYBREVANT® in combination with LAZCLUZE™ for all currently approved or submitted indications of intravenous (IV) RYBREVANT® in certain patients with NSCLC. A submission for the extension of the RYBREVANT® marketing authorization (line extension) was also **submitted** to the EMA seeking approval for this indication.

The NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for NSCLC§ prefer next-generation sequencing–based strategies over polymerase chain reaction–based approaches for the detection of EGFR exon 20 insertion variants. The NCCN Guidelines include:

- Amivantamab-vmjw (RYBREVANT®) plus chemotherapy as a preferred (Category 1 preferred recommendation) subsequent therapy for patients with locally advanced or metastatic NCSLC with EGFR exon 19 deletions or exon 21 L858R mutations who experienced disease progression after treatment with Osimertinib.[5] †‡
- Amivantamab-vmjw (RYBREVANT®) plus carboplatin and pemetrexed as a preferred (Category 1 preferred recommendation) first-line therapy in treatment-naive patients with newly diagnosed advanced or metastatic EGFR exon 20 insertion mutation-positive advanced NSCLC, or as a subsequent therapy option (Category 2A recommendation) for patients that have progressed on or after platinum-based chemotherapy with or without immunotherapy and have EGFR exon 20 insertion mutation-positive advanced NSCLC.[5] †‡
- Amivantamab-vmjw (RYBREVANT®) as a subsequent therapy option (Category 2A recommendation) for patients that have progressed on or after platinum-based chemotherapy with or without an immunotherapy and have EGFR exon 20 insertion mutation-positive NSCLC.[5] †‡

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

- The Phase 3 MARIPOSA-2 (**NCT04988295**) study assessing the efficacy of RYBREVANT® (with or without LAZCLUZE™) and carboplatin-pemetrexed versus carboplatin-pemetrexed alone in patients with locally advanced or metastatic EGFR ex19del or L858R substitution NSCLC after disease progression on or after osimertinib.[6]
- The Phase 3 PAPILLON (**NCT04538664**) study assessing RYBREVANT® in combination with carboplatin-pemetrexed versus chemotherapy alone in the first-line treatment of patients with advanced or metastatic NSCLC with EGFR exon 20 insertion mutations.[7]
- The Phase 3 PALOMA-3 (**NCT05388669**) study assessing LAZCLUZE™ with subcutaneous amivantamab compared to intravenous amivantamab in patients with EGFR-mutated advanced or metastatic NSCLC.[8]
- The Phase 2 PALOMA-2 (**NCT05498428**) study assessing subcutaneous amivantamab in patients with advanced or metastatic solid tumors including EGFR-mutated NSCLC.[9]
- The Phase 1 PALOMA (**NCT04606381**) study assessing the feasibility of subcutaneous administration of amivantamab based on safety and pharmacokinetics and to determine a dose, dose regimen and formulation for amivantamab subcutaneous delivery.[10]
- The Phase 1 CHRYSALIS (**NCT02609776**) study evaluating RYBREVANT® in patients with advanced NSCLC.[11]
- The Phase 1/1b CHRYSALIS-2 (**NCT04077463**) study evaluating RYBREVANT® in combination with LAZCLUZE™ and LAZCLUZE™ as a monotherapy in patients with advanced NSCLC with EGFR.[12]
- The Phase 1/2 METalmark (**NCT05488314**) study assessing RYBREVANT® and capmatinib combination therapy in locally advanced or metastatic NSCLC.[13]
- The Phase 1/2 PolyDamas (**NCT05908734**) study assessing RYBREVANT® and cetrelimab combination therapy

in locally advanced or metastatic NSCLC.[14]

- The Phase 2 SKIPPirr study (**NCT05663866**) exploring how to decrease the incidence and/or severity of first-dose infusion-related reactions with RYBREVANT® in combination with LAZCLUZE™ in relapsed or refractory EGFR-mutated advanced or metastatic NSCLC.[15]
- The Phase 1/2 swalloWTail (**NCT06532032**) study assessing RYBREVANT® and docetaxel combination therapy in patients with metastatic NSCLC.[16]
- The Phase 1b/2 OrigAMI-1 (**NCT05379595**) study assessing RYBREVANT® monotherapy and in addition to standard-of-care chemotherapy in patients with advanced or metastatic colorectal cancer.[17]
- The Phase 1b/2 OrigAMI-4 (**NCT06385080**) study assessing RYBREVANT® monotherapy and in addition to standard-of-care therapeutic agents in patients with recurrent/metastatic head and neck squamous cell carcinoma.[18]

For more information, visit: **https://www.RYBREVANT.com**.

About LAZCLUZE™

In 2018, Janssen Biotech, Inc., entered into a license and collaboration agreement with Yuhan Corporation for the development of LAZCLUZE™ (marketed as LACLAZA in Korea). LAZCLUZE™ 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 LAZCLUZE™ from the Phase 3 LASER301 study was published in **The Journal of Clinical Oncology** in 2023.

About Non-Small Cell Lung Cancer

Worldwide, lung cancer is one of the most common cancers, with NSCLC making up 80 to 85 percent of all lung cancer cases.[19,20] The main subtypes of NSCLC are adenocarcinoma, squamous cell carcinoma, and large cell carcinoma.[21] Among the most common driver mutations in NSCLC are alterations in EGFR, which is a receptor tyrosine kinase controlling cell growth and division.[22] 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.[21,22,23,24,25,26] EGFR ex19del or EGFR L858R mutations are the most common EGFR mutations.[27] The five- year survival rate for all people with advanced NSCLC and EGFR mutations treated with EGFR tyrosine kinase inhibitors (TKIs) is less than 20 percent.[28,29] EGFR exon 20 insertion mutations are the third most prevalent activating EGFR mutation.[30] Patients with EGFR exon 20 insertion mutations have a real-world five-year overall survival (OS) of eight percent in the frontline setting, which is worse than patients with EGFR ex19del or L858R mutations, who have a real-world five-year OS of 19 percent.[31]

IMPORTANT SAFETY INFORMATION[4,32]

WARNINGS AND PRECAUTIONS

Infusion-Related Reactions

RYBREVANT® can cause infusion-related reactions (IRR); signs and symptoms of IRR include dyspnea, flushing, fever, chills, nausea, chest discomfort, hypotension, and vomiting. The median time to IRR onset is approximately 1 hour.

RYBREVANT® with LAZCLUZE™

RYBREVANT® in combination with LAZCLUZE™ can cause infusion-related reactions. In MARIPOSA (n=421), IRRs occurred in 63% of patients treated with RYBREVANT® in combination with LAZCLUZE™, including Grade 3 in 5% and Grade 4 in 1% of patients. The incidence of infusion modifications due to IRR was 54% of patients, and IRRs leading to dose reduction of RYBREVANT® occurred in 0.7% of patients. Infusion-related reactions leading to permanent discontinuation of RYBREVANT® occurred in 4.5% of patients receiving RYBREVANT® in combination with LAZCLUZE™.

RYBREVANT® with Carboplatin and Pemetrexed

In PAPILLON (n=151), infusion-related reactions occurred in 42% of patients treated with RYBREVANT® in combination with carboplatin and pemetrexed, including Grade 3 (1.3%) adverse reactions. The incidence of infusion modifications due to IRR was 40%, and 0.7% of patients permanently discontinued RYBREVANT®.

RYBREVANT® as a Single Agent

In CHRYSALIS (n=302), IRR occurred in 66% of patients treated with RYBREVANT®. Among patients receiving treatment on Week 1 Day 1, 65% experienced an IRR, while the incidence of IRR was 3.4% with the Day 2 infusion, 0.4% with the Week 2 infusion, and cumulatively 1.1% with subsequent infusions. Of the reported IRRs, 97% were Grade 1-2, 2.2% were Grade 3, and 0.4% were Grade 4. The median time to onset was 1 hour (range 0.1 to 18 hours) after start of infusion. The incidence of infusion modifications due to IRR was 62% and 1.3% of patients permanently discontinued RYBREVANT® due to IRR.

Premedicate with antihistamines, antipyretics, and glucocorticoids and infuse RYBREVANT® as recommended. Administer RYBREVANT® via a peripheral line on Week 1 and Week 2 to reduce the risk of infusion-related reactions. Monitor patients for signs and symptoms of infusion reactions during RYBREVANT® infusion in a setting where cardiopulmonary resuscitation medication and equipment are available. Interrupt infusion if IRR is suspected. Reduce the infusion rate or permanently discontinue RYBREVANT® based on severity.

Interstitial Lung Disease/Pneumonitis

RYBREVANT® can cause severe and fatal interstitial lung disease (ILD)/pneumonitis.

RYBREVANT® with LAZCLUZE™

In MARIPOSA, ILD/pneumonitis occurred in 3.1% of patients treated with RYBREVANT® in combination with LAZCLUZE™, including Grade 3 in 1.0% and Grade 4 in 0.2% of patients. There was one fatal case (0.2%) of ILD/pneumonitis and 2.9% of patients permanently discontinued RYBREVANT® and LAZCLUZE™ due to ILD/pneumonitis.

RYBREVANT® with Carboplatin and Pemetrexed

In PAPILLON, Grade 3 ILD/pneumonitis occurred in 2.6% of patients treated with RYBREVANT® in combination with carboplatin and pemetrexed, all patients required permanent discontinuation.

RYBREVANT® as a Single Agent

In CHRYSALIS, ILD/pneumonitis occurred in 3.3% of patients treated with RYBREVANT®, with 0.7% of patients experiencing Grade 3 ILD/pneumonitis. Three patients (1%) discontinued RYBREVANT® due to ILD/pneumonitis.

Monitor patients for new or worsening symptoms indicative of ILD/pneumonitis (e.g., dyspnea, cough, fever). For patients receiving RYBREVANT® in combination with LAZCLUZE™, immediately withhold both drugs in patients with suspected ILD/pneumonitis and permanently discontinue if ILD/pneumonitis is confirmed. For patients receiving RYBREVANT® as a single agent or in combination with carboplatin and pemetrexed, immediately withhold RYBREVANT® in patients with suspected ILD/pneumonitis and permanently discontinue if ILD/pneumonitis is confirmed.

Venous Thromboembolic (VTE) Events with Concomitant Use of RYBREVANT® and LAZCLUZE™

RYBREVANT® in combination with LAZCLUZE™ can cause serious and fatal venous thromboembolic (VTEs) events, including deep vein thrombosis and pulmonary embolism. The majority of these events occurred during the first four months of therapy.

In MARIPOSA, VTEs occurred in 36% of patients receiving RYBREVANT® in combination with LAZCLUZE™, including Grade 3 in 10% and Grade 4 in 0.5% of patients. On-study VTEs occurred in 1.2% of patients (n=5) while receiving anticoagulation therapy. There were two fatal cases of VTE (0.5%), 9% of patients had VTE leading to dose

interruptions of RYBREVANT®, and 7% of patients had VTE leading to dose interruptions of LAZCLUZE™; 1% of patients had VTE leading to dose reductions of RYBREVANT®, and 0.5% of patients had VTE leading to dose reductions of LAZCLUZE™; 3.1% of patients had VTE leading to permanent discontinuation of RYBREVANT®, and 1.9% of patients had VTE leading to permanent discontinuation of LAZCLUZE™. The median time to onset of VTEs was 84 days (range: 6 to 777).

Administer prophylactic anticoagulation for the first four months of treatment. The use of Vitamin K antagonists is not recommended. Monitor for signs and symptoms of VTE events and treat as medically appropriate.

Withhold RYBREVANT® and LAZCLUZE™ based on severity. Once anticoagulant treatment has been initiated, resume RYBREVANT® and LAZCLUZE™ at the same dose level at the discretion of the healthcare provider. In the event of VTE recurrence despite therapeutic anticoagulation, permanently discontinue RYBREVANT® and continue treatment with LAZCLUZE™ at the same dose level at the discretion of the healthcare provider.

Dermatologic Adverse Reactions

RYBREVANT® can cause severe rash including toxic epidermal necrolysis (TEN), dermatitis acneiform, pruritus, and dry skin.

RYBREVANT® with LAZCLUZE™

In MARIPOSA, rash occurred in 86% of patients treated with RYBREVANT® in combination with LAZCLUZE™, including Grade 3 in 26% of patients. The median time to onset of rash was 14 days (range: 1 to 556 days). Rash leading to dose interruptions occurred in 37% of patients for RYBREVANT® and 30% for LAZCLUZE™, rash leading to dose reductions occurred in 23% of patients for RYBREVANT® and 19% for LAZCLUZE™, and rash leading to permanent discontinuation occurred in 5% of patients for RYBREVANT® and 1.7% for LAZCLUZE™.

RYBREVANT® with Carboplatin and Pemetrexed

In PAPILLON, rash occurred in 89% of patients treated with RYBREVANT® in combination with carboplatin and pemetrexed, including Grade 3 (19%) adverse reactions. Rash leading to dose reductions occurred in 19% of patients, and 2% permanently discontinued RYBREVANT® and 1.3% discontinued pemetrexed.

RYBREVANT® as a Single Agent

In CHRYSALIS, rash occurred in 74% of patients treated with RYBREVANT® as a single agent, including Grade 3 rash in 3.3% of patients. The median time to onset of rash was 14 days (range: 1 to 276 days). Rash leading to dose

reduction occurred in 5% of patients, and RYBREVANT® was permanently discontinued due to rash in 0.7% of patients.

Toxic epidermal necrolysis occurred in one patient (0.3%) treated with RYBREVANT® as a single agent.

Instruct patients to limit sun exposure during and for 2 months after treatment with RYBREVANT® or LAZCLUZE™ in combination with RYBREVANT®. Advise patients to wear protective clothing and use broad-spectrum UVA/UVB sunscreen. Alcohol-free (e.g., isopropanol-free, ethanol-free) emollient cream is recommended for dry skin.

When initiating RYBREVANT® treatment with or without LAZCLUZE™, administer alcohol-free emollient cream to reduce the risk of dermatologic adverse reactions. Consider prophylactic measures (e.g. use of oral antibiotics) to reduce the risk of dermatologic reactions. If skin reactions develop, start topical corticosteroids and topical and/or oral antibiotics. For Grade 3 reactions, add oral steroids and consider dermatologic consultation. Promptly refer patients presenting with severe rash, atypical appearance or distribution, or lack of improvement within 2 weeks to a dermatologist. For patients receiving RYBREVANT® in combination with LAZCLUZE™, withhold, dose reduce or permanently discontinue both drugs based on severity. For patients receiving RYBREVANT® as a single agent or in combination with carboplatin and pemetrexed, withhold, dose reduce or permanently discontinue RYBREVANT® based on severity.

Ocular Toxicity

RYBREVANT® can cause ocular toxicity including keratitis, blepharitis, dry eye symptoms, conjunctival redness, blurred vision, visual impairment, ocular itching, eye pruritus, and uveitis.

RYBREVANT® with LAZCLUZE™

In MARIPOSA, ocular toxicity occurred in 16% of patients treated with RYBREVANT® in combination with LAZCLUZE™, including Grade 3 or 4 ocular toxicity in 0.7% of patients. Withhold, reduce the dose, or permanently discontinue RYBREVANT® and continue LAZCLUZE™ based on severity.

RYBREVANT® with Carboplatin and Pemetrexed

In PAPILLON, ocular toxicity including blepharitis, dry eye, conjunctival redness, blurred vision, and eye pruritus occurred in 9%. All events were Grade 1-2.

RYBREVANT® as a Single Agent

In CHRYSALIS, keratitis occurred in 0.7% and uveitis occurred in 0.3% of patients treated with RYBREVANT®. All

events were Grade 1-2.

Promptly refer patients with new or worsening eye symptoms to an ophthalmologist. Withhold, dose reduce or permanently discontinue RYBREVANT® based on severity.

Embryo-Fetal Toxicity

Based on its mechanism of action and findings from animal models, RYBREVANT® and LAZCLUZE™ can cause fetal harm when administered to a pregnant woman. Advise females of reproductive potential of the potential risk to the fetus.

Advise female patients of reproductive potential to use effective contraception during treatment and for 3 months after the last dose of RYBREVANT®.

Advise females of reproductive potential to use effective contraception during treatment with LAZCLUZE™ and for 3 weeks after the last dose. Advise male patients with female partners of reproductive potential to use effective contraception during treatment with LAZCLUZE™ and for 3 weeks after the last dose.

Adverse Reactions

RYBREVANT® with LAZCLUZE™

For the 421 patients in the MARIPOSA clinical trial who received RYBREVANT® in combination with LAZCLUZE™, the most common adverse reactions (≥20%) were rash (86%), nail toxicity (71%), infusion-related reactions (RYBREVANT®, 63%), musculoskeletal pain (47%), stomatitis (43%), edema (43%), VTE (36%), paresthesia (35%), fatigue (32%), diarrhea (31%), constipation (29%), COVID-19 (26%), hemorrhage (25%), dry skin (25%), decreased appetite (24%), pruritus (24%), nausea (21%), and ocular toxicity (16%). The most common Grade 3 or 4 laboratory abnormalities (≥2%) were decreased albumin (8%), decreased sodium (7%), increased ALT (7%), decreased potassium (5%), decreased hemoglobin (3.8%), increased AST (3.8%), increased GGT (2.6%), and increased magnesium (2.6%).

Serious adverse reactions occurred in 49% of patients who received RYBREVANT® in combination with LAZCLUZE™. Serious adverse reactions occurring in ≥2% of patients included VTE (11%), pneumonia (4%), ILD/pneumonitis and rash (2.9% each), COVID-19 (2.4%), and pleural effusion and infusion-related reaction (RYBREVANT®) (2.1% each). Fatal adverse reactions occurred in 7% of patients who received RYBREVANT® in combination with LAZCLUZE™ due to death not otherwise specified (1.2%); sepsis and respiratory failure (1% each); pneumonia, myocardial infarction, and sudden death (0.7% each); cerebral infarction, pulmonary embolism (PE), and COVID-19 infection (0.5% each);

and ILD/pneumonitis, acute respiratory distress syndrome (ARDS), and cardiopulmonary arrest (0.2% each).

RYBREVANT® with Carboplatin and Pemetrexed

For the 151 patients in the PAPILLON clinical trial who received RYBREVANT® in combination with carboplatin and pemetrexed, the most common adverse reactions (≥20%) were rash (90%), nail toxicity (62%), stomatitis (43%), infusion-related reaction (42%), fatigue (42%), edema (40%), constipation (40%), decreased appetite (36%), nausea (36%), COVID-19 (24%), diarrhea (21%), and vomiting (21%). The most common Grade 3 to 4 laboratory abnormalities (≥2%) were decreased albumin (7%), increased alanine aminotransferase (4%), increased gamma-glutamyl transferase (4%), decreased sodium (7%), decreased potassium (11%), decreased magnesium (2%), and decreases in white blood cells (17%), hemoglobin (11%), neutrophils (36%), platelets (10%), and lymphocytes (11%).

Serious adverse reactions occurred in 37% of patients who received RYBREVANT® in combination with carboplatin and pemetrexed. Serious adverse reactions in ≥2% of patients included rash, pneumonia, ILD, pulmonary embolism, vomiting, and COVID-19. Fatal adverse reactions occurred in 7 patients (4.6%) due to pneumonia, cerebrovascular accident, cardio-respiratory arrest, COVID-19, sepsis, and death not otherwise specified.

RYBREVANT® as a Single Agent

For the 129 patients in the CHRYSALIS clinical trial who received RYBREVANT® as a single agent, the most common adverse reactions (≥20%) were rash (84%), IRR (64%), paronychia (50%), musculoskeletal pain (47%), dyspnea (37%), nausea (36%), fatigue (33%), edema (27%), stomatitis (26%), cough (25%), constipation (23%), and vomiting (22%). The most common Grade 3 to 4 laboratory abnormalities (≥2%) were decreased lymphocytes (8%), decreased albumin (8%), decreased phosphate (8%), decreased potassium (6%), increased alkaline phosphatase (4.8%), increased glucose (4%), increased gamma-glutamyl transferase (4%), and decreased sodium (4%).

Serious adverse reactions occurred in 30% of patients who received RYBREVANT®. Serious adverse reactions in ≥2% of patients included pulmonary embolism, pneumonitis/ILD, dyspnea, musculoskeletal pain, pneumonia, and muscular weakness. Fatal adverse reactions occurred in 2 patients (1.5%) due to pneumonia and 1 patient (0.8%) due to sudden death.

LAZCLUZE™ Drug Interactions

Avoid concomitant use of LAZCLUZE™ with strong and moderate CYP3A4 inducers. Consider an alternate concomitant medication with no potential to induce CYP3A4.

Monitor for adverse reactions associated with a CYP3A4 or BCRP substrate where minimal concentration changes

may lead to serious adverse reactions, as recommended in the approved product labeling for the CYP3A4 or BCRP substrate.

Please read full **Prescribing Information** for RYBREVANT®.

Please read full **Prescribing Information** for LAZCLUZE™.

About Johnson & Johnson

At Johnson & Johnson, we believe health is everything. Our strength in healthcare innovation empowers us to build a world where complex diseases are prevented, treated, and cured, where treatments are smarter and less invasive, and solutions are personal. Through our expertise in Innovative Medicine and MedTech, we are uniquely positioned to innovate across the full spectrum of healthcare solutions today to deliver the breakthroughs of tomorrow, and profoundly impact health for humanity. Learn more at **https://www.jnj.com/** or at **www.janssen.com/johnson-johnson-innovative-medicine**. Follow us at **@JanssenUS** and **@JNJInnovMed**. Janssen Research & Development, LLC, and Janssen Biotech, Inc. 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 RYBREVANT® (amivantamab-vmjw) and LAZCLUZE™ (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 Janssen Research & Development, LLC, Janssen Biotech, Inc. 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; manufacturing difficulties and delays; competition, including technological advances, new products and patents attained by competitors; challenges to patents; product efficacy or safety concerns resulting in product recalls or regulatory action; 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 December 31, 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 Research & Development, LLC,

Janssen Biotech, Inc. nor Johnson & Johnson undertakes to update any forward-looking statement as a result of new information or future events or developments.

*Dr. Shirish M. Gadgeel has provided consulting, advisory, and speaking services to Johnson & Johnson; he has not been paid for any media work.

†See the NCCN Guidelines for detailed recommendations, including other treatment options.

‡The NCCN Guidelines for NSCLC provide recommendations for certain individual biomarkers that should be tested and recommend testing techniques but do not endorse any specific commercially available biomarker assays or commercial laboratories.

§The NCCN Content does not constitute medical advice and should not be used in place of seeking professional medical advice, diagnosis or treatment by licensed practitioners. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.

---

[1] Gadgeel SM, et al. Amivantamab Plus LAZCLUZE™ vs Osimertinib in First-line EGFR-mutant Advanced NSCLC: Longer Follow-up of the MARIPOSA Study. IASLC WCLC 2024. September 8, 2024.
[2]Cho BC, et al. Amivantamab Plus LAZCLUZE™ vs Osimertinib as First-line Treatment in Patients With EGFR-mutated, Advanced Non-small Cell Lung Cancer (NSCLC): Primary Results From MARIPOSA, a Phase 3, Global, Randomized, Controlled Trial. 2023 European Society for Medical Oncology. October 23, 2023.
[3] ClinicalTrials.gov. A Study of Amivantamab and LAZCLUZE™ Combination Therapy Versus Osimertinib in Locally Advanced or Metastatic Non-Small Cell Lung Cancer (MARIPOSA). Available at: **https://classic.clinicaltrials.gov/ct2/show/NCT04487080**. Accessed September 2024.
[4] RYBREVANT® Prescribing Information. Horsham, PA: Janssen Biotech, Inc.
[5] Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Non-Small Cell Lung Cancer V.1.2024© National Comprehensive Cancer Network, Inc. All rights reserved. To view the most recent and complete version of the guideline, go online to **NCCN.org**. Accessed September 2024.
[6] ClinicalTrials.gov. A Study of Amivantamab and LAZCLUZE™ in Combination With Platinum-Based Chemotherapy Compared With Platinum-Based Chemotherapy in Patients With Epidermal Growth Factor Receptor (EGFR)-Mutated Locally Advanced or Metastatic Non-Small Cell Lung Cancer After Osimertinib Failure (MARIPOSA-2). Available at: https://classic.clinicaltrials.gov/ct2/show/study/NCT04988295. Accessed September 2024.
[7] ClinicalTrials.gov. A Study of Combination Amivantamab and Carboplatin-Pemetrexed Therapy, Compared With Carboplatin-Pemetrexed, in Participants With Advanced or Metastatic Non-Small Cell Lung Cancer Characterized by Epidermal Growth Factor Receptor (EGFR) Exon 20 Insertions (PAPILLON). Available at: https://clinicaltrials.gov/ct2/show/NCT04538664. Accessed September 2024.
[8] ClinicalTrials.gov. A Study of LAZCLUZE™ With Subcutaneous Amivantamab Compared With Intravenous Amivantamab in Participants With Epidermal Growth Factor Receptor (EGFR)-Mutated Advanced or Metastatic Non-small Cell Lung Cancer (PALOMA-3). https://clinicaltrials.gov/ct2/show/NCT05388669. Accessed September 2024.
[9] ClinicalTrials.gov. A Study of Amivantamab in Participants With Advanced or Metastatic Solid Tumors Including Epidermal Growth Factor Receptor (EGFR)-Mutated Non-Small Cell Lung Cancer (PALOMA-2). **https://clinicaltrials.gov/ct2/show/NCT05498428**. Accessed September 2024.
[10] ClinicalTrials.gov. A Study of Amivantamab Subcutaneous (SC) Administration for the Treatment of Advanced Solid Malignancies (PALOMA). Available at: https://clinicaltrials.gov/study/NCT04606381. Accessed September 2024.
[11] ClinicalTrials.gov. A Study of Amivantamab, a Human Bispecific EGFR and cMet Antibody, in Participants With Advanced Non-Small Cell Lung Cancer (CHRYSALIS). https://clinicaltrials.gov/ct2/show/NCT02609776. Accessed September 2024.
[12] ClinicalTrials.gov. A Study of LAZCLUZE™ as Monotherapy or in Combination With Amivantamab in Participants With Advanced Non-small Cell Lung Cancer (CHRYSALIS-2). https://clinicaltrials.gov/ct2/show/NCT04077463. Accessed September 2024.
[13] ClinicalTrials.gov. A Study of Amivantamab and Capmatinib Combination Therapy in Unresectable Metastatic Non-small Cell Lung Cancer (METalmark). https://clinicaltrials.gov/ct2/show/NCT05488314. Accessed September 2024.
[14] ClinicalTrials.gov. A Study of Combination Therapy With Amivantamab and Cetrelimab in Participants With Metastatic Non-small Cell Lung Cancer (PolyDamas). https://www.clinicaltrials.gov/study/NCT05908734?term=polydamas&rank=1. Accessed September 2024.
[15] ClinicalTrials.gov. Premedication to Reduce Amivantamab Associated Infusion Related Reactions (SKIPPirr). https://classic.clinicaltrials.gov/ct2/show/NCT05663866. Accessed September 2024.
[16] ClinicalTrials.gov. A Study of Combination Therapy With Amivantamab and Docetaxel in Participants With Metastatic Non-small Cell Lung Cancer (swalloWTail). **https://www.clinicaltrials.gov/study/NCT06532032?term=Swallowtail&intr=amivantamab&rank=1**. Accessed September 2024.
[17] ClinicalTrials.gov. A Study of Amivantamab Monotherapy and in Addition to Standard-of-Care Chemotherapy in Participants With Advanced or

Metastatic Colorectal Cancer (OrigAMI-1). **https://clinicaltrials.gov/study/NCT05379595?term=NCT05379595&rank=1**. Accessed September 2024.
[18] ClinicalTrials.gov. A Study of Amivantamab Alone or in Addition to Other Treatment Agents in Participants With Recurrent/ Metastatic Head and Neck Cancer (OrigAMI-4). **https://clinicaltrials.gov/study/NCT06385080?term=OrigAMI-4&limit=10&rank=1**. Accessed September 2024.
[19] The World Health Organization. Cancer. https://www.who.int/news-room/fact-sheets/detail/cancer. Accessed September 2024.
[20] American Cancer Society. What is Lung Cancer? https://www.cancer.org/content/cancer/en/cancer/lung-cancer/about/what-is.html. Accessed September 2024.
[21] Oxnard JR, et al. Natural history and molecular characteristics of lung cancers harboring EGFR exon 20 insertions. J Thorac Oncol. 2013 Feb;8(2):179-84. doi: 10.1097/JTO.0b013e3182779d18.
[22] Bauml JM, et al. Underdiagnosis of EGFR Exon 20 Insertion Mutation Variants: Estimates from NGS-based Real World Datasets. Abstract presented at: World Conference on Lung Cancer Annual Meeting; January 29, 2021; Singapore.
[23] Pennell NA, et al. A phase II trial of adjuvant erlotinib in patients with resected epidermal growth factor receptor-mutant non-small cell lung cancer. J Clin Oncol. 37:97-104.
[24] Burnett H, et al. Epidemiological and clinical burden of EGFR exon 20 insertion in advanced non-small cell lung cancer: a systematic literature review. Abstract presented at: World Conference on Lung Cancer Annual Meeting; January 29, 2021; Singapore.
[25] Zhang YL, et al. The prevalence of EGFR mutation in patients with non-small cell lung cancer: a systematic review and meta-analysis. Oncotarget. 2016;7(48):78985-78993.
[26] Midha A, et al. EGFR mutation incidence in non-small-cell lung cancer of adenocarcinoma histology: a systematic review and global map by ethnicity. Am J Cancer Res. 2015;5(9):2892-2911.
[27] American Lung Association. EGFR and Lung Cancer. **https://www.lung.org/lung-health-diseases/lung-disease-lookup/lung-cancer/symptoms-diagnosis/biomarker-testing/egfr**. Accessed March 2024.
[28] Howlader N, et al. SEER Cancer Statistics Review, 1975-2016, National Cancer Institute. Bethesda, MD, **https://seer.cancer.gov/csr/1975_2016/**, based on November 2018 SEER data submission, posted to the SEER web site.
[29] Lin JJ, et al. Five-Year Survival in EGFR-Mutant Metastatic Lung Adenocarcinoma Treated with EGFR-TKIs. J Thorac Oncol. 2016 Apr;11(4):556-65.
[30] Arcila, M. et al. EGFR exon 20 insertion mutations in lung adenocarcinomas: prevalence, molecular heterogeneity, and clinicopathologic characteristics. Mol Cancer Ther. 2013 Feb; 12(2):220-9.
[31] Girard N, et al. Comparative clinical outcomes for patients with NSCLC harboring EGFR exon 20 insertion mutations and common EGFR mutations. Abstract presented at: World Conference on Lung Cancer Annual Meeting; January 29, 2021; Singapore.
[32] LAZCLUZE™ Prescribing Information. Horsham, PA: Janssen Biotech, Inc.

Media contact:
Suzanne Frost
sfrost@its.jnj.com

Jackie Zima-Evans
jzimaev@ITS.JNJ.com

Investor contact:
Raychel Kruper
investor-relations@its.jnj.com

U.S. Medical Inquiries
+1 800 526-7736

View original content to download multimedia:**https://www.prnewswire.com/news-releases/rybrevant-amivantamab-vmjw-plus-lazcluze-lazertinib-show-strong-favorable-overall-survival-trend-versus-osimertinib-in-egfr-mutated-advanced-lung-cancer-302241208.html**

SOURCE Johnson & Johnson