Johnson&Johnson

NEWS RELEASE

RYBREVANT® (amivantamab-vmjw) plus LAZCLUZE® (lazertinib) prevents acquired resistance versus osimertinib in first-line EGFR-mutated non-small cell lung cancer

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RYBREVANT® combination extends survival and significantly reduces common EGFR and MET resistance mutations seen with osimertinib-based treatment

BARCELONA, Spain, Sept. 6, 2025 /PRNewswire/ -- Johnson & Johnson (NYSE:JNJ) today announced new analyses from the Phase 3 MARIPOSA study showing that first-line treatment with RYBREVANT® (amivantamab-vmjw) plus LAZCLUZE® (lazertinib) significantly reduces the development of epidermal growth factor receptor (EGFR)- and MET-driven resistance compared with osimertinib in patients with EGFR-mutated non-small cell lung cancer (NSCLC) with exon 19 deletion (ex19del) or L858R mutations (Poster Abstract PT1.03).[1] These resistance data build on the combination's previously reported and unmatched overall survival benefit in a chemotherapy-free regimen, which is projected to exceed four years, one year beyond the median observed with osimertinib, and underscore its potential to change the biology of the disease by preventing acquired resistance.[2,3] Late-breaking results are being presented at the **International Association for the Study of Lung Cancer (IASLC) 2025 World Congress on Lung Cancer (WCLC)**.

Resistance to third-generation EGFR tyrosine kinase inhibitors (TKIs), such as osimertinib given alone or with chemotherapy, remains a common and major barrier to long-term disease control.[4] This ongoing challenge underscores the need for next-generation strategies that can more effectively prevent the development of resistance to EGFR and MET and extend survival for patients with EGFR-mutated lung cancer.

"We now have a body of evidence that suggests TKI monotherapy is no longer enough in the first-line treatment of

EGFR-mutated lung cancer," said Professor Sanjay Popat*, FRCP, Ph.D., medical oncologist at the Royal Marsden Hospital and the Institute of Cancer Research in the United Kingdom. "The MARIPOSA results show that combining RYBREVANT with LAZCLUZE is an important step forward, reducing EGFR- and MET-driven resistance seen with TKI-based therapy and giving patients a longer, stronger first response."

Consistent with prior data presented at the European Society for Medical Oncology (ESMO) 2024 Congress,[5] these updated analyses from the MARIPOSA study confirm that patients treated with RYBREVANT® plus LAZCLUZE® were less likely to develop the two main types of resistance (MET amplification and EGFR mutations) compared to those treated with osimertinib alone. MET amplifications occurred in three percent of patients on the combination versus 13 percent on osimertinib (P=0.002), and secondary EGFR mutations (such as C797S) were significantly lower for RYBREVANT® plus LAZCLUZE® (1 percent vs 8 percent; P=0.01). Acquired MET amplification led to early discontinuation in 23 percent of patients on osimertinib within six months, compared with four percent on RYBREVANT® plus LAZCLUZE®. Among patients who stayed on the combination for at least six months, acquired resistance was rare, with two percent developing MET amplification and no EGFR C797S mutations observed. The analysis also found greater overall genetic diversity of resistance in patients treated with osimertinib, particularly among patients with EGFR- and MET-based alterations.[1]

"Choosing the first treatment for EGFR-mutated NSCLC is one of the most important decisions we make. It can influence how the disease progresses over time," said Joshua Bauml, M.D., Vice President, Lung Cancer Disease Area Leader, Johnson & Johnson Innovative Medicine. "These data show RYBREVANT plus LAZCLUZE changes the biology of disease by blocking the resistance pathways cancers typically use to overcome treatment. By preventing resistance in the frontline, we can extend survival and keep future treatment options open for patients. These are benefits not seen with prior therapies or emerging combinations."

The safety profile of RYBREVANT® plus LAZCLUZE® was consistent with the primary analysis and no new safety signals emerged with longer-term follow-up. Most AEs (grade 3 or higher) occurred early in treatment. RYBREVANT® studies suggest that using preemptive or prophylactic measures can help lower the overall number and severity of skin reactions, infusion-related reactions and venous thromboembolic events.[6,7,8]

RYBREVANT® plus LAZCLUZE® is approved in the United States, Europe and other markets around the world for patients with first-line EGFR-mutated NSCLC based on the Phase 3 MARIPOSA 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 exon 19 deletion (ex19del) or

substitution mutations. The primary endpoint of the study is progression-free survival (PFS) (using RECIST v1.1 guidelines**) as assessed by BICR. Secondary endpoints include overall survival, overall response rate, duration or response, progression-free survival after first subsequent therapy (PFS2) and intracranial PFS.[9]

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 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.[10]

RYBREVANT® is approved in the **U.S.**, **Europe** and other 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., Europe** and other markets around the world 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 exon 21 L858R substitution mutations, as detected by an FDA-approved test.

RYBREVANT® is approved in the **U.S.**, **Europe** and other markets around the world in combination with chemotherapy (carboplatin-pemetrexed) for the treatment of adult patients with locally advanced or metastatic NSCLC with EGFR exon 19 deletions or L858R substitution mutations, whose disease has progressed on or after treatment with an EGFR TKI.

Subcutaneous amivantamab is approved in **Europe** in combination with LAZCLUZE® for the first-line treatment of adult patients with advanced NSCLC with EGFR exon 19 deletions or exon 21 L858R substitution mutations, and as a monotherapy for the treatment of adult patients with advanced NSCLC with activating EGFR exon 20 insertion mutations after failure of platinum-based therapy. A Biologics License Application (BLA) was submitted to the U.S. FDA for this indication.

The National Comprehensive Cancer Network® (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 lazertinib (LAZCLUZE®) as a Category 1 recommendation for first-line therapy in patients with locally advanced or metastatic NSCLC with EGFR exon 19 deletions or exon 21 L858R mutations.[11†‡]
- Amivantamab-vmjw (RYBREVANT®) plus chemotherapy as a Category 1 recommendation for patients with

locally advanced or metastatic NSCLC with EGFR exon 19 deletions or exon 21 L858R mutations who experienced disease progression after treatment with osimertinib.[11 †‡]

- Amivantamab-vmjw (RYBREVANT®) plus chemotherapy as a Category 1 recommendation for first-line therapy in treatment-naive patients with newly diagnosed advanced or metastatic EGFR exon 20 insertion mutation-positive advanced NSCLC.[11 †‡]
- Amivantamab-vmjw (RYBREVANT®) as a 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. [11 †‡]

RYBREVANT® is being studied in multiple clinical trials in NSCLC, including:

- The Phase 3 MARIPOSA (**NCT04487080**) study assessing RYBREVANT® in combination with LAZCLUZE® versus osimertinib and versus LAZCLUZE® alone in the first-line treatment of patients with locally advanced or metastatic NSCLC with EGFR ex19del or substitution mutations.[12]
- 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 NSCLC with EGFR exon 19 deletions or L858R substitution mutations after disease progression on or after osimertinib.[13]
- 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.[14]
- The Phase 3 PALOMA-3 (**NCT05388669**) study assessing LAZCLUZE® with subcutaneous (SC) amivantamab compared to RYBREVANT® in patients with EGFR-mutated advanced or metastatic NSCLC.[15]
- The Phase 2 PALOMA-2 (**NCT05498428**) study assessing SC amivantamab in patients with advanced or metastatic solid tumors including EGFR-mutated NSCLC.[16]
- The Phase 1 PALOMA (**NCT04606381**) study assessing the feasibility of SC amivantamab based on safety and pharmacokinetics and to determine a dose, dose regimen and formulation for SC amivantamab delivery.[17]
- The Phase 1 CHRYSALIS (**NCT02609776**) study evaluating RYBREVANT® in patients with advanced NSCLC.[18]
- 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 mutations.[19]
- The Phase 1/2 METalmark (**NCT05488314**) study assessing RYBREVANT® and capmatinib combination therapy in locally advanced or metastatic NSCLC.[20]
- The Phase 1/2 swalloWTail (**NCT06532032**) study assessing RYBREVANT® and docetaxel combination therapy in patients with metastatic NSCLC.[21]
- The Phase 1/2 PolyDamas (**NCT05908734**) study assessing RYBREVANT® and cetrelimab combination therapy in locally advanced or metastatic NSCLC.[22]

- 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.[23]
- The Phase 2 COPERNICUS (**NCT06667076**) study combining developments in treatment administration and prophylactic supportive care in representative US patients with common EGFR-mutated NSCLC treated with SC amivantamab in combination with LAZCLUZE® or chemotherapy.[24]
- The Phase 2 COCOON (**NCT06120140**) study assessing the effectiveness of a proactive dermatologic management regimen given with first-line RYBREVANT® and LAZCLUZE® in patients with EGFR-mutated advanced NSCLC.[25]

The legal manufacturer for RYBREVANT® is Janssen Biotech, Inc.

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 LECLAZA in South 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.[26]

The legal manufacturer for LAZCLUZE® is Janssen Biotech, Inc. and Yuhan Corporation.

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.[27,28] The main subtypes of NSCLC are adenocarcinoma, squamous cell carcinoma, and large cell carcinoma.[29] Among the most common driver mutations in NSCLC are alterations in EGFR, which is a receptor tyrosine kinase controlling cell growth and division.[30] 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.[27,28,31,32,33,34] EGFR ex19del or EGFR L858R mutations are the most common EGFR mutations.[35] 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.[36,37] EGFR exon 20 insertion mutations are the third most prevalent activating EGFR mutation.[38] 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.[39]

IMPORTANT SAFETY INFORMATION[10,40]

WARNINGS AND PRECAUTIONS

Infusion-Related Reactions

RYBREVANT® can cause infusion-related reactions (IRR) including anaphylaxis; 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

Based on the pooled safety population (n=281), IRR occurred in 50% of patients treated with RYBREVANT® in combination with carboplatin and pemetrexed, including Grade 3 (3.2%) adverse reactions. The incidence of infusion modifications due to IRR was 46%, and 2.8% of patients permanently discontinued RYBREVANT® due to IRR.

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. If an anaphylactic reaction occurs, permanently discontinue RYBREVANT®.

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

Based on the pooled safety population, ILD/pneumonitis occurred in 2.1% treated with RYBREVANT® in combination with carboplatin and pemetrexed with 1.8% of patients experiencing Grade 3 ILD/pneumonitis. 2.1% discontinued RYBREVANT® due to ILD/pneumonitis.

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%) permanently 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 (VTE) 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

Based on the pooled safety population, rash occurred in 82% of patients treated with RYBREVANT® in combination with carboplatin and pemetrexed, including Grade 3 (15%) adverse reactions. Rash leading to dose reductions

occurred in 14% of patients, and 2.5% permanently discontinued RYBREVANT® and 3.1% 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, reduce the dose, 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

Based on the pooled safety population, ocular toxicity occurred in 16% of patients treated with RYBREVANT® in combination with carboplatin and pemetrexed. All events were Grade 1 or 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, reduce the dose, 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 130 patients in the MARIPOSA-2 clinical trial who received RYBREVANT® in combination with carboplatin and pemetrexed, the most common adverse reactions (≥20%) were rash (72%), infusion-related reactions (59%), fatigue (51%), nail toxicity (45%), nausea (45%), constipation (39%), edema (36%), stomatitis (35%), decreased appetite (31%), musculoskeletal pain (30%), vomiting (25%), and COVID-19 (21%). The most common Grade 3 to 4 laboratory abnormalities (≥2%) were decreased neutrophils (49%), decreased white blood cells (42%), decreased lymphocytes (28%), decreased platelets (17%), decreased hemoglobin (12%), decreased potassium (11%), decreased sodium (11%), increased alanine aminotransferase (3.9%), decreased albumin (3.8%), and increased gamma-glutamyl transferase (3.1%).

In MARIPOSA-2, serious adverse reactions occurred in 32% of patients who received RYBREVANT® in combination with carboplatin and pemetrexed. Serious adverse reactions in >2% of patients included dyspnea (3.1%), thrombocytopenia (3.1%), sepsis (2.3%), and pulmonary embolism (2.3%). Fatal adverse reactions occurred in 2.3% of patients who received RYBREVANT® in combination with carboplatin and pemetrexed; these included respiratory failure, sepsis, and ventricular fibrillation (0.8% each).

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%).

In PAPILLON, 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 **http://www.innovativemedicine.jnj.com/**. Follow us at **@JNJInnovMed**.

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® or LAZCLUZE®. 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 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 most recent Annual Report on Form 10-K, 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 **http://www.sec.gov**, **http://www.jnj.com**, or on request from Johnson & Johnson. Johnson & Johnson does not undertake to update any forward-looking statement as a result of new information or future events or developments.

*Professor Sanjay Popat has served as a consultant to Johnson & Johnson; he has not been paid for any media work.

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

[§]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.

[†]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.

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