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For Immediate Release

Dexamethasone reduces infusion-related reactions in patients with *EGFR*-mutated non-small cell lung cancer treated with intravenous RYBREVANT® (amivantamab-vmjw)

Pre-medication regimen showed an infusion-related reaction rate of 22.5 percent with intravenous RYBREVANT®, a three-fold reduction from 67.4 percent historically seen with standard IRR management

SAN DIEGO, CA, September 10, 2024 – Johnson & Johnson (NYSE:JNJ) today announced results from the open-label Phase 2 SKIPPirr study, which evaluated additional prophylactic strategies to reduce the incidence of infusion-related reactions (IRRs) with intravenous (IV) RYBREVANT® (amivantamab-vmjw) in patients with advanced non-small cell lung cancer (NSCLC) with epidermal growth factor receptor (*EGFR*) exon 19 deletions (ex19del) or L858R substitution mutations. The study, which included 40 patients, showed that prophylaxis with 8-mg dexamethasone taken for two days prior to the first infusion met the primary endpoint of incidence of IRRs at Cycle 1 Day 1 (C1D1), with an all-grades IRR rate for IV RYBREVANT® of 22.5 percent.[1] This represents a three-fold reduction in the incidence of IRRs compared to standard management of IRRs with IV RYBREVANT®, where historic data has observed an all-grades incidence rate of 67.4 percent.[1,2] Data were presented as a mini-oral presentation at the International Association for the Study of Lung Cancer (IASLC) 2024 World Conference on Lung Cancer (WCLC).[1]

“These data offer important insights that may help improve the patient experience with intravenous amivantamab treatment,” said Gilberto Lopes, M.D., associate director of global oncology at Sylvester Comprehensive Cancer Center, part of the University of Miami Miller School of Medicine, and presenting author.* “This study shows us that an easily accessible approach of an increased dose regimen of dexamethasone as a pre-treatment prophylaxis can potentially help lower IRRs. It is encouraging to see a three-fold decrease in IRRs, when comparing the rates in SKIPPirr to historical data.”

In the study, patients received an at-home regimen of oral dexamethasone, taking an 8-mg dose twice daily on the two prior days and one hour prior to receiving IV RYBREVANT®. The RYBREVANT® treatment was combined with LAZCLUZE™ (lazertinib). All IRRs were Grade 1 or 2 with no patients

requiring hospitalization due to IRRs. There were no Grade 3 or higher IRR events reported. The safety profile of RYBREVANT® and LAZCLUZE™ with prophylactic dexamethasone at the initiation of treatment is consistent with previous studies, showing no significant increase in adverse events. The most common IRR-related symptoms observed in the study were nausea (8 percent), dyspnea (5 percent) and hypotension (5 percent).[1]

“Reducing the risk of IRRs is a critical aspect of improving the overall treatment experience for patients receiving intravenous RYBREVANT and oral LAZCLUZE,” said Mark Wildgust, Ph.D., Vice President of Oncology Global Medical Affairs, Johnson & Johnson Innovative Medicine. “Incorporating oral dexamethasone into the treatment regimen suggests we can help mitigate this risk, with the goal of allowing patients to continue their therapy with fewer interruptions.”

Additional studies are ongoing to evaluate prophylactic strategies to reduce IRRs for patients receiving IV RYBREVANT®. For more details and to view an infographic summarizing the study’s findings and dosing regimen, click here.

About the SKIPPirr Study

SKIPPirr (NCT05663866) is a Phase 2 study evaluating RYBREVANT® in combination with LAZCLUZE™ in patients with *EGFR*-mutated (Ex19del or L858R) advanced NSCLC after disease progression on osimertinib and platinum-based chemotherapy. All patients received oral LAZCLUZE™ and IV RYBREVANT®. The study used a Simon's 2-stage design to evaluate different preventive treatments across four groups. The first group received dexamethasone (4 mg) orally, taken twice daily on the day before treatment, for a total of two doses. The second group was given a higher dose of dexamethasone (8 mg), taken orally twice daily on the two days leading up to treatment and the morning of infusion (5 doses total). The third group received montelukast (10 mg) orally, starting four days before treatment and continuing through the day of treatment, totaling five doses. Lastly, the fourth group was treated with a single dose of methotrexate (25 mg), administered as a subcutaneous injection between days 7 and 3 before the treatment. The primary endpoint of the study is incidence of IRRs at C1D1.[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 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. 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 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 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.[5] †‡
- Amivantamab-vmjw (RYBREVANT®) plus chemotherapy as a Category 1 recommendation 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 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, or as a 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 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 2 SKIPPirr study, 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 L858R substitution mutations.[6]
- 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.[7]
- 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.[8]
- 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.[9]
- The Phase 2 PALOMA-2 (NCT05498428) study assessing subcutaneous amivantamab in patients with advanced or metastatic solid tumors including EGFR-mutated NSCLC.[10]
- 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.[11]
- The Phase 1 CHRYSALIS (NCT02609776) study evaluating RYBREVANT® in patients with advanced NSCLC.[12]
- 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.[13]
- The Phase 1/2 METalmark (NCT05488314) study assessing RYBREVANT® and capmatinib combination therapy in locally advanced or metastatic NSCLC.[14]
- The Phase 1/2 PolyDamas (NCT05908734) study assessing RYBREVANT® and cetrelimab combination therapy in locally 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 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]

RYBREVANT® 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, Janssen Biotech, Inc. and Janssen Global Services, 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 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., Janssen Global Services, LLC 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., Janssen Global Services, LLC 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. Gilberto Lopes 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.

Source: Johnson & Johnson

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[1] Lopes G, et al. Preventing Infusion-related Reactions with Intravenous Amivantamab: Primary Results From SKIPPirr, a Phase 2 Study. IASLC WCLC 2024. September 10, 2024.
[2] Park K, Sabari JK, Haura EB, et al. Management of infusion-related reactions (IRRs) in patients receiving amivantamab in the CHRYSALIS study. Lung Cancer. 2023;178:166-171.
[3] ClinicalTrials.gov. Premedication to Reduce Amivantamab Associated Infusion Related Reactions (SKIPPirr). https://classic.clinicaltrials.gov/ct2/show/NCT05663866. 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.9.2024© 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.
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