Johnson&Johnson

NEWS RELEASE

RYBREVANT® (amivantamab-vmjw) plus LAZCLUZE™ (lazertinib) approved in the U.S. as a first-line chemotherapy-free treatment for patients with EGFR-mutated advanced lung cancer

8/20/2024

RYBREVANT® plus LAZCLUZE™ is the first and only chemotherapy-free regimen showing superior progression-free survival versus osimertinib

Following Priority Review, approval is based on Phase 3 MARIPOSA results showing RYBREVANT® plus LAZCLUZE™ reduced the risk of disease progression or death by 30 percent versus osimertinib, with a nine-month-longer median duration of response

RARITAN, N.J., Aug. 20, 2024 /PRNewswire/ -- Johnson & Johnson (NYSE: JNJ) announced today that the U.S. Food and Drug Administration (FDA) approved RYBREVANT® (amivantamab-vmjw) plus LAZCLUZE™ (lazertinib) for the first-line treatment of adult patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) with epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 L858R substitution mutations, as detected by an FDA-approved test.[1,2]

With this milestone, RYBREVANT® plus LAZCLUZE™ becomes the first and only multitargeted, chemotherapy-free combination regimen with demonstrated superiority versus osimertinib approved for the first-line treatment of patients with EGFR-mutated NSCLC.[1,2] RYBREVANT® is an EGFR- and MET*-directed bispecific antibody that engages the immune system, and LAZCLUZE™ is a highly selective, brain-penetrant, third-generation oral EGFR TKI**. RYBREVANT® plus LAZCLUZE™ is the only multitargeted regimen targeting both the common EGFR mutations directly.[1,2]

"This approval is a crucial development for patients with EGFR-mutated NSCLC, who have faced significant unmet needs for far too long," said Jill Feldman[†], lung cancer survivor and co-founder of the EGFR Resisters, a patient advocacy group. "Having witnessed firsthand the remarkable evolution in lung cancer treatment, this profoundly important milestone brings a novel therapeutic approach to patients and their families. I'm thrilled that more patients can now experience the progression-free survival benefits seen in the MARIPOSA study."

Lung cancer is the leading cause of cancer mortality worldwide, resulting in 1.8 million deaths each year, with NSCLC accounting for 80 to 85 percent of all cases.[3,4] Of patients with EGFR-mutated NSCLC, between 25 and 39 percent never receive second-line therapy, due to disease progression and lack of treatment options.[5,6,7] The five-year survival rate is less than 20 percent for all people with advanced EGFR-mutated NSCLC treated with current standard of care TKI monotherapy.[8,9] Acquired resistance mechanisms after TKI monotherapy makes subsequent treatment more difficult.[8,9]

"The unique combination of RYBREVANT and LAZCLUZE demonstrated superior efficacy in the first-line treatment of certain patients with EGFR-mutated advanced NSCLC as shown with the MARIPOSA study," said Alexander Spira[‡], M.D., Ph.D., FACP, Director, Virginia Cancer Specialists Research Institute, and study investigator. "Patients will now have the option of a potential new first-line standard of care with significant clinical benefits over osimertinib. This first-line therapy uses a targeted approach aiming to achieve the best possible patient outcomes while reserving chemotherapy for later stages of treatment when resistance becomes more complex."

The FDA approval is based on positive results from the Phase 3 MARIPOSA study, which showed RYBREVANT® plus LAZCLUZE™ reduced the risk of disease progression or death by 30 percent compared to osimertinib (median progression-free survival [PFS]: 23.7 months versus 16.6 months) in the first-line treatment of patients with locally advanced or metastatic NSCLC with EGFR exon 19 deletions or exon 21 L858R substitution mutations.[1,2] The median duration of response (DOR) was nine months longer with RYBREVANT® plus LAZCLUZE™ versus osimertinib (25.8 months versus 16.7 months), a secondary endpoint of the study.

"Building on more than three decades of oncology innovation, we are uniquely positioned to build best-in-class treatments where survival rates have remained stagnant for years," said Jennifer Taubert, Executive Vice President, Worldwide Chairman, Innovative Medicine, Johnson & Johnson. "RYBREVANT plus LAZCLUZE establishes a new benchmark in the advanced first-line setting, and we look forward to bringing this new chemotherapy-free treatment regimen to patients."

"Johnson & Johnson is deeply committed to setting new standards of care for people living with some of the most devastating and complex diseases of our time," said John Reed, M.D., Ph.D., Executive Vice President, Innovative Medicine, R&D, Johnson & Johnson. "Today's FDA approval of chemotherapy-free RYBREVANT plus LAZCLUZE in the first line is an incredible step towards our goal of altering the trajectory of lung cancer and reducing the impact of

the world's leading cause of cancer mortality."

The safety profile of RYBREVANT® plus LAZCLUZE™ was consistent with the profiles of the individual treatments. Venous thromboembolic events (VTE) were observed with the combination. Adverse event (AE) rates were consistent in this arm as compared to other RYBREVANT® regimens.

MARIPOSA Publications & Presentations

Results from MARIPOSA were first **presented** at the European Society of Medical Oncology 2023 Congress and recently **published** in The New England Journal of Medicine. Results **presented** at the 2024 American Society of Clinical Oncology annual meeting and **published** in Annals of Oncology demonstrated the combination's significant benefit for patients who have at least one high-risk feature, which represents 85 percent of all EGFR-mutated NSCLC cases.[10]

Longer-term follow-up data from MARIPOSA will be presented at the International Association for the Study of Lung Cancer (IASLC) 2024 World Congress on Lung Cancer (WCLC) in September.

Regulatory Milestones

This approval marks the second new indication this year for RYBREVANT®, following the March 1, 2024, U.S. FDA **approval** of RYBREVANT® in combination with chemotherapy (carboplatin-pemetrexed) for the first-line treatment of patients with locally advanced or metastatic NSCLC with EGFR exon 20 insertion mutations, based on the Phase 3 PAPILLON study.[1]

On June 17, Johnson & Johnson announced the **submission** of a Biologics License Application (BLA) to the U.S. FDA for a fixed combination of amivantamab and recombinant human hyaluronidase for subcutaneous administration (SC amivantamab) for all currently approved or submitted indications of intravenous (IV) RYBREVANT®. This application is based on the Phase 3 PALOMA-3 study, with preliminary results showing a five-fold reduction in infusion-related reactions (IRR) with a five-minute administration of SC amivantamab.[11] Longer overall survival (OS), PFS and DOR were also observed with SC amivantamab.[11] On August 14, the U.S. FDA designated this application for Priority Review.

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 deletions or substitution mutations. The primary

endpoint of the study is PFS (using RECIST v1.1 guidelines) as assessed by blinded independent central review (BICR). Secondary endpoints include OS, overall response rate (ORR), DOR, second progression-free survival (PFS2) and intracranial PFS.[12]

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.[1] In the subcutaneous formulation, amivantamab is co-formulated with recombinant human hyaluronidase PH20 (rHuPH20), Halozyme's ENHANZE® drug delivery technology.

RYBREVANT® is approved in the **U.S.** 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. In April 2024, the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) **recommended** the approval of RYBREVANT® in Europe for this indication.

RYBREVANT® is approved in the U.S. in combination with LAZCLUZE™ 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 EMA seeking approval of LAZCLUZE™ in combination with RYBREVANT® based on the MARIPOSA study.

In November 2023, Johnson & Johnson **submitted** a supplemental BLA 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. A type II extension of indication application was also **submitted** to the EMA seeking approval of RYBREVANT® for this indication.

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. In August 2024, the U.S. FDA designated this application for Priority Review.

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 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.[13 §¶]
- 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.[13 §¶]
- 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.[13 §¶]

In addition to MARIPOSA, 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.[14]
- 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.[15]
- 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.[11]
- The Phase 1 CHRYSALIS (**NCT02609776**) study evaluating RYBREVANT® in patients with advanced NSCLC.[16]
- 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.[17]
- 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.[18]
- The Phase 2 PALOMA-2 (**NCT05498428**) study assessing subcutaneous amivantamab in patients with advanced or metastatic solid tumors including EGFR-mutated NSCLC.[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 PolyDamas (**NCT05908734**) study assessing RYBREVANT® and cetrelimab combination therapy

in locally advanced or metastatic NSCLC.[21]

- 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.[22]

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™ (lazertinib, 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.

Access to RYBREVANT® and LAZCLUZE™

J&J offers comprehensive access and support information and resources to assist patients in gaining access to RYBREVANT® and LAZCLUZE™. Our patient support program, J&J withMe, is available to provide personalized support to help patients start and stay on their J&J medicines. J&J withMe offers providers help supporting their patients by verifying patients' insurance coverage, providing information on Prior Authorization and Appeals processes and educating on reimbursement processes. Patients can connect to RYBREVANT withMe to receive cost support, regardless of insurance type, free, personalized one-on-one support from a Care Navigator, and resources and community connections. Learn more at **RYBREVANTwithMe.com** or by calling 833-JNJ-wMe1 (833-565-9631).♠

About Non-Small Cell Lung Cancer (NSCLC)

Lung cancer is one of the most common cancers worldwide, with NSCLC making up 80 to 85 percent of all cases.[3,4] The main subtypes of NSCLC are adenocarcinoma, squamous cell carcinoma and large cell carcinoma.[23] Among the most common driver mutations in NSCLC are alterations in EGFR, which is a receptor tyrosine kinase controlling cell growth and division.[24] 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.[23,24,25,26,27,28] EGFR ex19del or EGFR L858R mutations are the most common EGFR mutations.[29] The five-year survival rate for all people with advanced NSCLC and EGFR mutations treated with EGFR tyrosine kinase inhibitors is less than 20 percent.[8,9] 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 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[1,2]

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=129), 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®. 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. Continue LAZCLUZE™ 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 (4.3%), ILD/pneumonitis and rash (2.9% each), COVID-19 (2.4%), 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.

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* Mesenchymal-epithelial transition

** Tyrosine kinase inhibitor

† Jill Feldman has not been paid for any media work.

‡ Dr. Alexander Spira 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.

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♣ The patient support and resources provided by J&J withMe are not intended to provide medical advice, replace a treatment plan from the patient's doctor or nurse, provide case management services, or serve as a reason to prescribe a J&J medicine.

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