



News Release

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Janssen Announces New Data Supporting Safety and Efficacy of RYBREVANT® and Lazertinib Combination for Patients with Non-Small Cell Lung Cancer and EGFR Mutations

Presentations at the International Association for the Study of Lung Cancer (IASLC) 2022 World Conference on Lung Cancer (WCLC) Span Relapsed/Refractory Disease and Frontline Treatment in Patients with EGFR-Positive Non-Small Cell Lung Cancer

July 26, 2022 (RARITAN, N.J.) – The Janssen Pharmaceutical Companies of Johnson & Johnson today announced new data from the Phase 1b/2 CHRYSALIS-2 study ([NCT04077463](https://clinicaltrials.gov/ct2/show/study/NCT04077463)) cohort evaluating the safety and tolerability of the combination of RYBREVANT® (amivantamab-vmjw) with the third-generation epidermal growth factor receptor (EGFR) tyrosine kinase inhibitor (TKI) lazertinib and platinum-based chemotherapy (carboplatin and pemetrexed) in patients with relapsed/refractory non-small cell lung cancer (NSCLC) and EGFR mutations.¹ These findings and additional updates, including data on RYBREVANT® in combination with lazertinib in the frontline setting for patients with NSCLC will be

presented at the IASLC 2022 WCLC hosted by the IASLC August 6-9 in Vienna, Austria.

CHRYSALIS-2 ([NCT04077463](#)) is an ongoing clinical trial evaluating RYBREVANT® in combination with lazertinib in patients with advanced NSCLC with EGFR exon 19 deletion mutations or L858R activating mutations.² One cohort of CHRYSALIS-2 evaluates the combination of RYBREVANT® and lazertinib with carboplatin and pemetrexed.¹ Results from the RYBREVANT®, lazertinib, carboplatin and pemetrexed combination cohort (n=20) will be featured in a mini oral presentation ([Abstract #MA07.04](#)) at the IASLC 2022 WCLC.¹ Enrolled participants received a median of two prior lines of therapy.¹ Prior therapies included osimertinib (n=14), gefitinib (n=3), afatinib (n=3), and platinum-based chemotherapy (n=5), among others.¹

After a median follow-up of 7.1 months, the combination of RYBREVANT® and lazertinib with carboplatin and pemetrexed yielded an overall response rate (ORR) of 50 percent (95 percent confidence interval [CI];27-73), with 15 out of 20 patients remaining on treatment.¹ The observed safety profile of this treatment combination was consistent with the previously reported safety profile of each individual agent; no evidence of new safety signals or additional toxicity was observed.¹ The most common treatment-emergent adverse events (AEs) included neutropenia (85 percent), rash (75 percent), infusion-related reaction and stomatitis (60 percent), fatigue and paronychia (50 percent each), and thrombocytopenia and nausea (40 percent each).¹

“Patients with relapsed/refractory non-small cell lung cancer with EGFR mutations currently have few treatment options. For them, the promise of precision medicine has the potential to change the trajectory of their disease,” said Alexander Spira, M.D., Ph.D., FACP, CEO and Clinical Director of NEXT Oncology Virginia and study investigator.[‡] “The data we’ve seen with the combination of amivantamab with lazertinib and chemotherapy further demonstrate the potential of this treatment regimen for these patients, and we are optimistic about future study to improve outcomes for those with EGFR-positive non-small cell lung cancer.”

Janssen is currently recruiting patients for the Phase 3 MARIPOSA-2 ([NCT04988295](#)) study to evaluate the combination of RYBREVANT® and lazertinib with platinum-based chemotherapy in patients with EGFR-mutated NSCLC after disease progression on or after osimertinib.³

Separately, updated data from the frontline, treatment-naïve cohort of the Phase 1 CHRYSALIS study ([NCT02609776](#)) will be featured in a poster presentation ([Abstract #P1.16-01](#)).⁴ CHRYSALIS is an ongoing study evaluating the safety, pharmacokinetics and preliminary efficacy of RYBREVANT® as a monotherapy and in combination, including with lazertinib, in patients with advanced NSCLC with various EGFR mutations.⁵ Patients enrolled in the treatment-naïve cohort had NSCLC characterized by either an EGFR exon 19 deletion (n=11) or L858R mutation (n=9), with 50 percent having co-mutations in the TP53 gene.⁴ All 20 patients had confirmed response (ORR of 100%). After a median follow-up of 22.3 months, 14 patients (70 percent) were progression free and remained on therapy with median duration of response and median progression-free survival not reached.⁴ Two patients with L858R mutations remained on treatment after their disease progressed.⁴ Based upon the last data cutoff on June 1, 2022 (median follow-up and treatment duration of 28 months), 12 patients (60 percent; 9 exon 19 deletion, 3 exon 21 L858R) remain progression free and on treatment.⁴

The safety profile of the combination of RYBREVANT® and lazertinib was consistent with previous reports, and no new safety signals were identified.⁴ Treatment-related AEs of Grade ≥ 3 severity occurred in seven patients (35 percent).⁴ Treatment-related AEs leading to dose reduction of either RYBREVANT® or lazertinib occurred in seven patients, most commonly due to rash (n=5).⁴ One patient had a treatment-related AE of interstitial lung disease which led to treatment discontinuation.⁴ Janssen is evaluating the combination of RYBREVANT® and lazertinib in the frontline setting for patients with EGFR-mutated NSCLC in the ongoing Phase 3 MARIPOSA study ([NCT04487080](#)).⁶

"Janssen's presence at this year's World Conference on Lung Cancer is a testament to our continuous effort to improve outcomes for people with non-small cell lung cancer, especially those whose disease is characterized by specific genetic mutations and who tend to be underserved by the current standard of care," said Joshua Bauml, M.D., Executive Medical Director, Janssen Research & Development, LLC. "We are committed to evaluating the potential of combination regimens in delaying disease progression in the treatment-naïve setting and addressing the ongoing challenge of treatment resistance in patients with relapsed/refractory disease."

Janssen will also share data that highlight the utility of next-generation sequencing (NGS) testing in identifying patients with NSCLC who may benefit from targeted treatment in a mini oral presentation ([Abstract #MA12.05](#)).⁷ Results showed that compared with single-gene testing strategies, NGS testing resulted in a higher percentage of identified mutations, a shorter time to appropriate targeted therapy and lower total testing costs per patient.⁷

About RYBREVANT®

RYBREVANT® (amivantamab-vmjw) [received](#) accelerated approval by the U.S. Food and Drug Administration (FDA) in May 2021 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.⁸ This indication is approved under accelerated approval based on overall response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in the confirmatory trials. RYBREVANT® has also received approval from health authorities in [Europe](#), as well as other markets around the world.

The NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Non-Small Cell Lung Cancer* prefer NGS-based strategies over PCR-based approaches for the detection of EGFR exon 20 insertion variants and include amivantamab-vmjw (RYBREVANT®) as a subsequent therapy option with 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.^{9†^}

RYBREVANT® is being studied in multiple clinical trials, including for untreated advanced EGFR-mutated NSCLC in the Phase 3 MARIPOSA ([NCT04487080](https://clinicaltrials.gov/ct2/show/study/NCT04487080)) study assessing RYBREVANT® in combination with lazertinib as an alternative to osimertinib for frontline treatment; the Phase 3 MARIPOSA-2 ([NCT04988295](https://clinicaltrials.gov/ct2/show/study/NCT04988295)) study to evaluate the combination of RYBREVANT® and lazertinib with platinum-based chemotherapy in patients with EGFR-mutated NSCLC after disease progression on or after osimertinib; the Phase 1/1b CHRYSALIS-2 ([NCT04077463](https://clinicaltrials.gov/ct2/show/study/NCT04077463)) study assessing the combination of RYBREVANT® and lazertinib in patients who have progressed after treatment with osimertinib and chemotherapy; the Phase 3 PAPILLON ([NCT04538664](https://clinicaltrials.gov/ct2/show/study/NCT04538664)) study assessing RYBREVANT® in combination with carboplatin-pemetrexed versus chemotherapy alone in patients with advanced or metastatic EGFR-mutated NSCLC and exon 20 insertion mutations; and the Phase 1 PALOMA ([NCT04606381](https://clinicaltrials.gov/ct2/show/study/NCT04606381)) study assessing the feasibility of subcutaneous (SC) administration of RYBREVANT® based on safety and pharmacokinetics and to determine a dose, dose regimen and formulation for RYBREVANT® SC delivery.^{2,3,5,6,10,11}

*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.⁹

^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.

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

About Lazertinib

Lazertinib is an oral, third-generation, brain-penetrant, EGFR TKI that targets both the T790M mutation and activating EGFR mutations while sparing wild type-EGFR.¹² Interim safety and efficacy results from the lazertinib Phase 1/2 study were published in [*The Lancet Oncology*](#) in 2019. In 2018, Janssen Biotech, Inc. entered into a license and collaboration agreement with Yuhan Corporation for the development of lazertinib.

About Non-Small Cell Lung Cancer

Worldwide, lung cancer is one of the most common cancers, and NSCLC makes up 80 to 85 percent of all lung cancers.^{13,14} The main subtypes of NSCLC are adenocarcinoma, squamous cell carcinoma and large cell carcinoma.¹⁴ Among the most common driver mutations in NSCLC are alterations in EGFR, which is a receptor tyrosine kinase supporting cell growth and division.¹⁵ EGFR mutations are present in 10 to 15 percent^{15,16,17,18,19} of people with NSCLC adenocarcinoma and occur in 40 to 50 percent of Asians.^{20,21} The five-year survival rate for all people with metastatic NSCLC and EGFR mutations treated with EGFR TKIs is less than 20 percent.^{22,23}

RYBREVANT® IMPORTANT SAFETY INFORMATION⁸

WARNINGS AND PRECAUTIONS

Infusion Related Reactions⁸

RYBREVANT® can cause infusion-related reactions (IRR); signs and symptoms of IRR include dyspnea, flushing, fever, chills, nausea, chest discomfort, hypotension, and vomiting.

Based on the safety population, 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. Monitor patients for any 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/Pneumonitis⁸

RYBREVANT® can cause interstitial lung disease (ILD)/pneumonitis. Based on the safety population, 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). Immediately withhold RYBREVANT® in patients with suspected ILD/pneumonitis and permanently discontinue if ILD/pneumonitis is confirmed.

Dermatologic Adverse Reactions⁸

RYBREVANT® can cause rash (including dermatitis acneiform), pruritus and dry skin. Based on the safety population, rash occurred in 74% of patients treated with RYBREVANT®, 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®.

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 emollient cream is recommended for dry skin.

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. Withhold, dose reduce or permanently discontinue RYBREVANT® based on severity.

Ocular Toxicity⁸

RYBREVANT® can cause ocular toxicity including keratitis, dry eye symptoms, conjunctival redness, blurred vision, visual impairment, ocular itching, and uveitis. Based on the safety population, 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 presenting with eye symptoms to an ophthalmologist. Withhold, dose reduce or permanently discontinue RYBREVANT® based on severity.

Embryo Fetal Toxicity⁸

Based on its mechanism of action and findings from animal models, RYBREVANT® 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 final dose of RYBREVANT®.

Adverse Reactions⁸

The most common adverse reactions ($\geq 20\%$) 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 ($\geq 2\%$) 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%).

Please read full [Prescribing Information](#) for RYBREVANT®.

About the Janssen Pharmaceutical Companies of Johnson & Johnson

At Janssen, we're creating a future where disease is a thing of the past. We're the Pharmaceutical Companies of Johnson & Johnson, working tirelessly to make that future a reality for patients everywhere by fighting sickness with science, improving access with ingenuity, and healing hopelessness with heart. We focus on areas of medicine where we can make the biggest difference: Cardiovascular, Metabolism, & Retina; Immunology; Infectious Diseases & Vaccines; Neuroscience; Oncology; and Pulmonary Hypertension.

Learn more at www.janssen.com. Follow us at [@JanssenGlobal](https://twitter.com/JanssenGlobal) and [@JanssenUS](https://twitter.com/JanssenUS). Janssen Research & Development, LLC and Janssen Biotech, Inc. are part of the Janssen Pharmaceutical Companies of Johnson & Johnson.

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‡Dr. Spira has served as a consultant to Janssen; he has not been paid for any media work.

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 lazertinib. The reader is cautioned not to rely on these forward-looking statements. These statements are based on current expectations of future events. If underlying assumptions prove inaccurate or known or unknown risks or uncertainties

materialize, actual results could vary materially from the expectations and projections of Janssen Research & Development, LLC, or any of the other Janssen Pharmaceutical Companies 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 January 2, 2022, including in the sections captioned "Cautionary Note Regarding Forward-Looking Statements" and "Item 1A. Risk Factors," and in Johnson & Johnson's subsequent Quarterly Reports on Form 10-Q and other filings with the Securities and Exchange Commission. Copies of these filings are available online at www.sec.gov, www.jnj.com or on request from Johnson & Johnson. None of the Janssen Pharmaceutical Companies nor Johnson & Johnson undertakes to update any forward-looking statement as a result of new information or future events or developments.

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- ⁸ RYBREVANT® Prescribing Information. Horsham, PA: Janssen Biotech, Inc.
- ⁹ Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Non-Small Cell Lung Cancer V.3.2022. © National Comprehensive Cancer Network, Inc. 2022. All rights reserved. Accessed March 18, 2022. To view the most recent and complete version of the guideline, go online to NCCN.org.
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