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NEWS RELEASE

RYBREVANT® (amivantamab-vmjw) plus LAZCLUZE™ (lazertinib) show statistically significant and clinically meaningful improvement in overall survival versus osimertinib

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Median overall survival improvement expected to exceed one year

First and only regimen with a survival benefit over current standard of care in first-line treatment of EGFR-mutated lung cancer

RARITAN, N.J., Jan. 7, 2025 /PRNewswire/ -- Johnson & Johnson (NYSE:JNJ) today announced positive topline results for the gold standard endpoint in cancer treatment of overall survival (OS) from the Phase 3 MARIPOSA study, evaluating RYBREVANT® (amivantamab-vmjw) plus LAZCLUZE™ (lazertinib) as a first-line therapy for patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) with epidermal growth factor receptor (EGFR) exon 19 deletions (ex19del) or L858R substitution mutations. The chemotherapy-free combination regimen met the final pre-specified secondary endpoint of OS and demonstrated clinically meaningful and statistically significant improvement in OS versus the current standard of care osimertinib. Improvement in median OS is expected to exceed one year.

Unlike progression-free survival (PFS), which tracks the time a treatment keeps a patient's cancer from progressing, OS helps patients understand the impact therapy could have on the ability to live longer from the start of treatment. Extending life expectancy is the most meaningful indicator of a treatment's impact.

"The combination of these two agents previously demonstrated an improvement in progression-free survival, but this does not always capture the impact on the entire treatment course. Evaluation of overall survival can better

demonstrate the benefit of a first-line treatment regimen," said Stephen Liu, M.D.*, Associate Professor of Medicine at Georgetown University School of Medicine and Director of Thoracic Oncology and Head of Developmental Therapeutics at Georgetown's Lombardi Comprehensive Cancer Center. "Seeing this increase in overall survival in a trial with mature data is powerful and reaffirms that first-line treatment with RYBREVANT and LAZCLUZE can lead to better patient outcomes."

"Every milestone in clinical trials and every approval of a new drug or regimen brings hope and progress for EGFR-positive patients and their families," said Marcia Horn**, President of International Cancer Advocacy Network. "These topline data from the MARIPOSA trial offer renewed optimism in the journey to extend life for EGFR-mutated patients, adding another important option for patients and oncologists."

"These new findings reinforce the clinically meaningful impact this chemotherapy-free regimen can have for patients worldwide with non-small cell lung cancer and represent the first overall survival benefit over the current standard of care," said Yusri Elsayed, M.D., M.H.Sc., Ph.D., Global Therapeutic Area Head, Oncology, Johnson & Johnson Innovative Medicine. "With less than 20 percent of patients living beyond five years, an incredible unmet need remains for EGFR-positive lung cancer. These MARIPOSA results show RYBREVANT plus LAZCLUZE can extend survival beyond the current standard of care, providing patients with more time and hope in their fight against this devastating disease. Extending median overall survival by more than a year could be transformative for these patients."

Results from the final OS analysis build upon **previously reported** data from the interim analysis and positive results from the PFS analysis. **MARIPOSA**, which enrolled 1,074 patients, is a randomized, Phase 3 study evaluating RYBREVANT® in combination with LAZCLUZE™ versus osimertinib as a first-line treatment of patients with EGFR-mutated NSCLC. The study's primary endpoint was PFS (using RECIST v1.1 guidelines***) as assessed by blinded independent central review (BICR). Secondary endpoints included OS, objective response rate (ORR), duration of response (DOR), second progression-free survival (PFS2) and intracranial PFS.

The safety profile of RYBREVANT® plus LAZCLUZE™ was generally consistent with the profiles of the individual treatments. Adverse event rates were consistent in this arm as compared to other RYBREVANT® regimens. Venous thromboembolic events were observed with the combination. Subsequent studies showed that administering oral anticoagulant medicines prophylactically during the initial four months of the RYBREVANT® and LAZCLUZE™ regimen significantly reduced the risk of thrombosis.

Due to the impact of these data on patient care, these OS results will be presented at an upcoming major medical meeting, and will be shared with global health authorities. RYBREVANT® combined with LAZCLUZE™ is approved in the United States and **Europe** for the first-line treatment of patients with EGFR-mutated NSCLC based on the MARIPOSA Phase 3 study.

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.[1]

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.** and **Europe** 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.

RYBREVANT® is approved in the **U.S.**, **Europe** and other markets around the world in combination with chemotherapy (carboplatin and 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 tyrosine kinase inhibitors (TKI).

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.[2†‡]
- 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.[2†‡]
- 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.[2†‡]
- 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.[2†‡]

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

About LAZCLUZE™

In 2018, Janssen Biotech, Inc., entered into a license and collaboration agreement with Yuhan Corporation for the development of LAZCLUZE™ (marketed as LACLAZA in Korea). LAZCLUZE™ is an oral, third-generation, brain-penetrant EGFR TKI that targets both the T790M mutation and activating EGFR mutations while sparing wild-type EGFR. An analysis of the efficacy and safety of LAZCLUZE™ from the Phase 3 LASER301 study was published in **The Journal of Clinical Oncology** in 2023.

About Non-Small Cell Lung Cancer

Worldwide, lung cancer is one of the most common cancers, with NSCLC making up 80 to 85 percent of all lung cancer cases.[3,4] The main subtypes of NSCLC are adenocarcinoma, squamous cell carcinoma, and large cell carcinoma.[5] Among the most common driver mutations in NSCLC are alterations in EGFR, which is a receptor tyrosine kinase controlling cell growth and division.[6] 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.[5,6,7,8,9,10] EGFR ex19del or EGFR L858R mutations are the most common EGFR mutations.[11] The five-year survival rate for all people with advanced NSCLC and EGFR mutations treated with EGFR TKIs is less than 20 percent.[12,13] EGFR exon 20 insertion mutations are the third most prevalent activating EGFR mutation.[14] 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.[15]

IMPORTANT SAFETY INFORMATION[1,16]

Before you receive RYBREVANT® as a single agent or in combination, tell your healthcare provider about all of your medical conditions, including if you:

- have a history of lung or breathing problems.
- are pregnant or plan to become pregnant. RYBREVANT® and LAZCLUZE™ can harm your unborn baby.

Females who are able to become pregnant:

- Your healthcare provider should do a pregnancy test before you start treatment with RYBREVANT® or RYBREVANT® in combination with LAZCLUZE™.
- You should use effective birth control (contraception) during treatment and for 3 months after your final dose of RYBREVANT®.

- For patients receiving LAZCLUZE™: You should use effective birth control (contraception) during treatment and for 3 weeks after your last dose of LAZCLUZE™.
- Tell your healthcare provider right away if you become pregnant or think you might be pregnant during treatment with RYBREVANT® or LAZCLUZE™.

Males who have female partners who are able to become pregnant:

- You should use effective birth control during treatment and for 3 weeks after your last dose of LAZCLUZE™.
- are breastfeeding or plan to breastfeed. It is not known if RYBREVANT® passes into your breast milk. Do not breastfeed during treatment and for 3 months after your last dose of RYBREVANT®. It is not known if LAZCLUZE™ passes into your breast milk. Do not breastfeed during treatment and for 3 weeks after your last dose of LAZCLUZE™.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

LAZCLUZE™ may affect the way other medicines work, and other medicines may affect how LAZCLUZE™ works.

You should not start or stop any medicine before you talk with your healthcare provider that prescribed LAZCLUZE™.

How will I receive RYBREVANT®?

- RYBREVANT® will be given to you by your healthcare provider by intravenous infusion into your vein.
- Your healthcare provider will decide the time between doses as well as how many treatments you will receive.
- Your healthcare provider will give you medicines before each dose of RYBREVANT® to help reduce the risk of infusion-related reactions.
- RYBREVANT® may be given in combination with the medicines carboplatin and pemetrexed. If you have any questions about these medicines, ask your healthcare provider.
- If your treatment with RYBREVANT® is given in combination with LAZCLUZE™ (lazertinib), you should take your dose of LAZCLUZE™ by mouth anytime before your infusion with RYBREVANT®.
- If you miss any appointments, call your healthcare provider as soon as possible to reschedule your appointment.

How should I take LAZCLUZE™?

- Take LAZCLUZE™ exactly as your healthcare provider tells you to take it.
- Take LAZCLUZE™ one (1) time each day. On the day RYBREVANT® is also given, take LAZCLUZE™ anytime

before receiving the RYBREVANT® infusion.

- You can take LAZCLUZE™ with or without food.
- Swallow LAZCLUZE™ tablets whole. Do not crush, cut, or chew the tablets.
- If you miss a dose of LAZCLUZE™ and:
  - it has been less than 12 hours, take the missed dose.
  - it has been more than 12 hours, skip the dose and take your next dose at your regularly scheduled time.
- If you vomit a dose of LAZCLUZE™, do not take an extra dose. Take your next dose at your regularly scheduled time.
- LAZCLUZE™ may be given in combination with other anti-cancer medicines. If you have any questions about these medicines, ask your healthcare provider.

What should I avoid while receiving RYBREVANT® and/or LAZCLUZE™?

RYBREVANT® and RYBREVANT® in combination with LAZCLUZE™ can cause skin reactions. You should limit your time in the sun during and for 2 months after your treatment with RYBREVANT® and/or LAZCLUZE™. Wear protective clothing and use sunscreen during treatment with RYBREVANT® and/or LAZCLUZE™.

What are the possible side effects of RYBREVANT® or LAZCLUZE™?

RYBREVANT® and LAZCLUZE™ may cause serious side effects, including:

- infusion-related reactions. Infusion-related reactions are common with RYBREVANT® and can be severe or serious. Tell your healthcare provider right away if you get any of the following symptoms during your infusion of RYBREVANT®:

- shortness of breath
- fever
- chills
- nausea
- flushing
- chest discomfort
- lightheadedness
- vomiting

- lung problems. RYBREVANT® may cause lung problems that may lead to death. LAZCLUZE™ may also cause lung problems that may lead to death. Symptoms may be similar to those symptoms from lung cancer. Tell your healthcare provider right away if you get any new or worsening lung symptoms, including shortness of breath, cough, or fever.

- blood clot problems. Blood clots are a serious, but common side effect of RYBREVANT®, when given together with LAZCLUZE™, may cause blood clots in the veins of your legs (deep vein thrombosis) or lungs (pulmonary embolism) that may lead to death. Your healthcare provider will start you on medicine to prevent blood clots for the first 4 months of treatment. Tell your healthcare provider right away if you have any signs and symptoms of blood clots, including swelling, pain or tenderness in the leg, sudden unexplained chest pain, or shortness of breath.

- skin problems. RYBREVANT® can cause severe rash; including blisters, peeling, skin pain and sores, redness, raised acne-like bumps, itching, and dry skin. LAZCLUZE™ may cause severe rash including redness, raised acne-like bumps, itching, and dry skin. You may use alcohol-free (isopropanol-free, ethanol-free) moisturizing cream to reduce the risk of skin problems. Tell your healthcare provider right away if you get any skin reactions. Your healthcare provider may treat you with a medicine(s) or send you to see a skin specialist (dermatologist) if you get skin reactions during treatment with RYBREVANT® or LAZCLUZE™. See "What should I avoid while receiving RYBREVANT® and/or LAZCLUZE™?"

- eye problems. RYBREVANT® may cause eye problems. LAZCLUZE™ may also cause eye problems. Tell your healthcare provider right away if you get symptoms of eye problems which may include:

- eye pain
- inflammation of eye lids
- inflamed cornea (front part of the eye)
- dry eyes
- eye redness
- blurred vision
- changes in vision
- itchy eyes
- excessive tearing
- sensitivity to light
- new or worsening problems with vision

Your healthcare provider may send you to see an eye specialist (ophthalmologist) if you get new or worsening eye problems during treatment with RYBREVANT® or LAZCLUZE™. You should not use contact lenses until your eye symptoms are checked by a healthcare provider.

The most common side effects of RYBREVANT® in combination with LAZCLUZE™ (lazertinib) include:

- rash
- infected skin around the nail
- muscle and joint pain
- sores in the mouth
- diarrhea
- constipation
- COVID-19
- dry skin

- swelling of hands, ankles, feet, face, or all of your body
- unusual feeling in the skin (such as tingling or a crawling feeling)
- feeling very tired
- bleeding
- decreased appetite
- itchy skin
- nausea
- changes in certain blood tests

The most common side effects of RYBREVANT® when given in combination with carboplatin and pemetrexed include:

- rash
- infected skin around the nail
- feeling very tired
- nausea
- sores in the mouth
- constipation
- swelling of hands, ankles, feet, face, or all of your body
- decreased appetite
- muscle and joint pain
- vomiting
- COVID-19
- changes in certain blood tests

The most common side effects of RYBREVANT® when given alone:

- rash
- infected skin around the nail
- muscle and joint pain
- shortness of breath
- nausea
- feeling very tired
- swelling of hands, ankles, feet, face, or all of your body
- sores in the mouth
- cough
- constipation
- vomiting
- changes in certain blood tests

LAZCLUZE™ may cause fertility problems in males and females, which may affect your ability to have children. Talk to your healthcare provider if this is a concern for you.

Your healthcare provider may temporarily stop, decrease your dose, or completely stop your treatment with RYBREVANT® or LAZCLUZE™ if you have serious side effects.

These are not all of the possible side effects of RYBREVANT® or LAZCLUZE™.

Call your doctor for medical advice about side effects. You may report side effects to FDA at **1-800-FDA-1088**.

General information about the safe and effective use of RYBREVANT®:

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet.

You can ask your healthcare provider or pharmacist for information about RYBREVANT® that is written for health professionals.

General information about the safe and effective use of LAZCLUZE™:

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. Do not use LAZCLUZE™ for a condition for which it was not prescribed. Do not give LAZCLUZE™ to other people, even if they have the same symptoms that you have. It may harm them.

You can ask your pharmacist or healthcare provider for information about LAZCLUZE™ that is written for health professionals.

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 of Janssen Research & Development, LLC, Janssen Biotech, Inc. and/or Johnson & Johnson. Risks and uncertainties include, but are not limited to: challenges and uncertainties inherent in product research and development, including the uncertainty of clinical success and of obtaining regulatory approvals; uncertainty of commercial success; manufacturing difficulties and delays; competition, including technological

advances, new products and patents attained by competitors; challenges to patents; product efficacy or safety concerns resulting in product recalls or regulatory action; changes in behavior and spending patterns of purchasers of health care products and services; changes to applicable laws and regulations, including global health care reforms; and trends toward health care cost containment. A further list and descriptions of these risks, uncertainties and other factors can be found in Johnson & Johnson's Annual Report on Form 10-K for the fiscal year ended December 31, 2023, including in the sections captioned "Cautionary Note Regarding Forward-Looking Statements" and "Item 1A. Risk Factors," and in Johnson & Johnson's subsequent Quarterly Reports on Form 10-Q and other filings with the Securities and Exchange Commission. Copies of these filings are available online at **www.sec.gov**, **www.jnj.com** or on request from Johnson & Johnson. None of Janssen Research & Development, LLC, Janssen Biotech, Inc. nor Johnson & Johnson undertakes to update any forward-looking statement as a result of new information or future events or developments.

*Dr. Liu has served as a consultant to J&J; he has not been paid for any media work.

**Marcia Horn 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.

†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

[1] RYBREVANT® Prescribing Information. Horsham, PA: Janssen Biotech, Inc.
[2] 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 December 2024.
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