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For Immediate Release

First results from late-breaking Phase 3 PALOMA-3 study show five-fold reduction in infusion-related reactions with five-minute subcutaneous amivantamab administration

New formulation showed non-inferiority to intravenous administration in fourth positive Phase 3 study in RYBREVANT® clinical program

Longer overall survival, progression-free survival and duration of response shown with subcutaneous amivantamab; featured in Best of ASCO 2024

RYBREVANT® marketing application submitted to European Medicines Agency based on PALOMA-3 study

CHICAGO (May 31, 2024) – Johnson & Johnson announced today first data from the Phase 3 PALOMA-3 study evaluating subcutaneous (SC) amivantamab combined with lazertinib in patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) with epidermal growth factor receptor (EGFR) exon 19 deletion (ex19del) or L858R mutations. Study results showed non-inferior efficacy and pharmacokinetics for SC amivantamab combined with lazertinib compared to intravenous (IV) administration, the currently approved formulation of RYBREVANT® (amivantamab-vmjw). Administration time for SC amivantamab was reduced to approximately five minutes from five hours (across two days) and showed a five-fold reduction in infusion-related reactions (IRRs). These late-breaking results, which are the Company's fourth positive Phase 3 readout for the RYBREVANT® clinical program, were featured as an oral presentation at the 2024 American Society of Clinical Oncology (ASCO) Annual Meeting (Abstract #LBA8505).[1] Data were also selected for the Best of ASCO 2024 Meetings, highlighting the cutting-edge science and leading research in oncology from Johnson & Johnson.

"The PALOMA-3 data show that subcutaneous amivantamab offers shorter infusion times and lower rates of infusion-related reactions and venous thromboembolism with pharmacokinetics and efficacy comparable to the current IV administration," said Dr. Natasha B. Leighl*, medical oncologist at the Princess Margaret Cancer Centre in Toronto, Canada, and the presenting author. "I look forward to seeing how these findings can make a meaningful difference in clinical practice by potentially improving the treatment experience for patients with EGFR-mutated non-small cell lung cancer."

Results showed SC amivantamab was non-inferior to IV amivantamab, meeting both co-primary pharmacokinetic (PK) efficacy endpoints as measured by amivantamab levels in the blood (C_{trough} and area under the serum concentration time curve from day 1 to 15).[1]

At a median follow-up of seven months, the overall response rate was 30 percent (95 percent confidence interval [CI], 24–37) in the subcutaneous arm and 33 percent (95 percent CI, 26–39) for IV (relative risk, 0.92; 95 percent CI, 0.70-1.23; *P*=0.001), meeting the noninferiority criteria. SC amivantamab also demonstrated longer duration of response (DoR), progression-free survival (PFS) and significant improvement in overall survival (OS) compared to IV administration during this time. Specifically, median DoR was numerically longer for SC amivantamab combined with lazertinib compared to IV (median, 11.2 vs 8.3 months among confirmed responders) as was PFS (median, 6.1 vs 4.3 months; hazard ratio [HR], 0.84; 95 percent CI, 0.64–1.10; *P*=0.20). A pre-specified exploratory endpoint showed patients treated with SC amivantamab had significantly longer OS compared with IV (HR, 0.62; 95 percent CI, 0.42–0.92; nominal *P*=0.02). At 12 months, 65 percent of patients who received SC amivantamab combined with lazertinib were alive compared with 51 percent of those treated with the IV regimen. It is theorized that the efficacy seen with SC amivantamab may be linked to SC absorption via the lymphatic system, potentially enhancing immune-mediated activity.[1]

Of particular note, administration time was substantially shorter for SC amivantamab (median less than approximately five minutes) compared to IV administration (up to five hours), with significantly more patients reporting convenience with the SC administration (85 percent with SC amivantamab vs 35 percent with IV administration at end of treatment; *P*<0.001).[1]

The overall safety profile of SC amivantamab is consistent with the known profile of IV administration. The most common all-grade adverse events (≥ 20 percent) for SC amivantamab compared to IV were paronychia (54 percent vs 51 percent), hypoalbuminemia (47 percent vs 37 percent) and rash (46 percent vs 43 percent), respectively. No Grade 4 or 5 IRRs were reported. The rate of IRRs for patients treated with SC amivantamab combined with lazertinib was shown to be approximately five-fold lower than that observed with the IV formulation (13 percent vs 66 percent, respectively). Prophylactic anticoagulation was used in most patients in the study and was found to be safe and effective in reducing the rate of venous thromboembolic events (VTE). Patients receiving prophylactic anticoagulation had lower rates of VTE (10 percent) than those without prophylaxis (21 percent). Furthermore, VTE incidence was lower in the SC arm compared to the IV arm (9 percent vs 14 percent, respectively) regardless of anticoagulation use. Severe bleeding risk was low and similar among patients receiving anticoagulants in the SC (2 percent) and IV (1 percent) arms.[1]

“We are always exploring innovative approaches to meet the urgent needs of patients living with EGFR-mutated non-small cell lung cancer and these compelling findings reinforce the potential for a new route of administration for amivantamab,” said Yusri Elsayed, M.D., M.H.Sc., Ph.D., Global Therapeutic Area

Head, Oncology, Johnson & Johnson Innovative Medicine. “We look forward to pursuing regulatory submissions for this formulation, as we advance our ambition to transform the first-line treatment of EGFR-mutated NSCLC.”

Today, Janssen-Cilag International NV, a Johnson & Johnson company, announced the submission of an application for the extension of the RYBREVANT® marketing authorization (line extension) to the European Medicines Agency (EMA) seeking approval of SC amivantamab in combination with lazertinib for the first-line treatment of adult patients with locally advanced or metastatic NSCLC with EGFR ex19del or L858R mutations and as monotherapy in adult patients with advanced NSCLC with activating EGFR exon 20 insertion mutations after failure of platinum-based therapy based on the PALOMA-3 data. Johnson & Johnson will submit regulatory applications seeking the approval of SC amivantamab in other markets, including the United States.

About PALOMA-3

PALOMA-3 (NCT05388669), which enrolled 418 patients, is a randomized, open-label Phase 3 study evaluating the pharmacokinetics (PK), efficacy and safety of subcutaneous amivantamab (administered via manual injection) combined with lazertinib compared to IV amivantamab and lazertinib in patients with EGFR-mutated advanced or metastatic NSCLC after progression on osimertinib and chemotherapy. The co-primary PK endpoints of the study were trough concentration (C_{trough} on Cycle [C] 2 Day [D] 1 or C4D1) and C2 area under the curve (AUCD1-D15). Key secondary endpoints were objective response rate and progression-free survival. Overall survival was a predefined exploratory endpoint. Prophylactic anticoagulation was recommended for the first four months of treatment.[2]

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

RYBREVANT® is also 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 October 2023, a type II extension of indication application was submitted to the European Medicines Agency (EMA) seeking approval of RYBREVANT® for this indication.

In December 2023, Johnson & Johnson submitted a supplemental Biologics License Application (sBLA) together with a New Drug Application (NDA) to the U.S. FDA for RYBREVANT® in combination with 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. This submission is based on the Phase 3 MARIPOSA study and was granted Priority Review in February 2024. A marketing authorization application (MAA) and type II extension of indication application were also submitted to the EMA seeking approval of lazertinib in combination with RYBREVANT® based on the MARIPOSA study.

In November 2023, Johnson & Johnson submitted an 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. A type II extension of indication application was also submitted to the EMA seeking approval of RYBREVANT® 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 carboplatin and pemetrexed as a preferred (Category 1 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.[4] †‡
- Amivantamab-vmjw (RYBREVANT®) plus chemotherapy as a preferred (Category 1 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.[4] †‡

- 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.[4] †‡

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

- The Phase 3 PALOMA-3 (NCT05388669) study assessing lazertinib with subcutaneous amivantamab compared to intravenous amivantamab in patients with EGFR-mutated advanced or metastatic NSCLC.[2]
- The Phase 2 PALOMA-2 (NCT05498428) study assessing subcutaneous amivantamab in patients with advanced or metastatic solid tumors including EGFR-mutated NSCLC.[5]
- 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.[6]
- 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.[7]
- The Phase 3 MARIPOSA-2 (NCT04988295) study assessing the efficacy of RYBREVANT® (with or without lazertinib) 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.[8]
- The Phase 3 MARIPOSA (NCT04487080) study assessing RYBREVANT® in combination with lazertinib versus osimertinib and versus lazertinib alone in the first-line treatment of patients with locally advanced or metastatic NSCLC with EGFR ex19del or L858R substitution mutations.[9]
- The Phase 1 CHRYSALIS (NCT02609776) study evaluating RYBREVANT® in patients with advanced NSCLC.[10]
- The Phase 1/1b CHRYSALIS-2 (NCT04077463) study evaluating RYBREVANT® in combination with lazertinib and lazertinib as a monotherapy in patients with advanced NSCLC with EGFR mutations.[11]
- The Phase 1/2 METalmark (NCT05488314) study assessing RYBREVANT® and capmatinib combination therapy in locally advanced or metastatic NSCLC.[12]
- The Phase 1/2 PolyDamas (NCT05908734) study assessing RYBREVANT® and cetrelimab combination therapy in locally advanced or metastatic NSCLC.[13]
- 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 lazertinib in relapsed or refractory EGFR-mutated advanced or metastatic NSCLC.[14]

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.[15, 16] The main subtypes of NSCLC are adenocarcinoma, squamous cell carcinoma, and large cell carcinoma.[17] Among the most common driver mutations in NSCLC are alterations in EGFR, which is a receptor tyrosine kinase controlling cell growth and division.[18] 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.[17,18,19,20,21,22] EGFR ex19del or EGFR L858R mutations are the most common EGFR mutations.[23] 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.[24,25] EGFR exon 20 insertion mutations are the third most prevalent activating EGFR mutation.[26] 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.[27]

RYBREVANT® IMPORTANT SAFETY INFORMATION[3]

WARNINGS AND PRECAUTIONS

The safety population of RYBREVANT® with carboplatin and pemetrexed described in Warnings and Precautions was based on 151 patients in the PAPILLON study.

The safety population of RYBREVANT® as a single agent described in Warnings and Precautions was based on 129 patients in the CHRYSALIS study.

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.

RYBREVANT® with Carboplatin and Pemetrexed

RYBREVANT® in combination with carboplatin and pemetrexed can cause infusion-related reactions. Based on the safety population, 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

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/Pneumonitis

RYBREVANT® can cause interstitial lung disease (ILD)/pneumonitis.

RYBREVANT® with Carboplatin and Pemetrexed

Based on the safety population, 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

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 Reactions

RYBREVANT® can cause rash (including dermatitis acneiform), pruritus, and dry skin.

RYBREVANT® with Carboplatin and Pemetrexed

RYBREVANT® in combination with carboplatin and pemetrexed can cause dermatologic adverse reactions. Based on the safety population, 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; 2% permanently discontinued RYBREVANT®, and 1.3% discontinued pemetrexed.

RYBREVANT® as a Single Agent

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® 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 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 Toxicity

RYBREVANT® can cause ocular toxicity including keratitis, dry eye symptoms, conjunctival redness, blurred vision, visual impairment, ocular itching, and uveitis.

RYBREVANT® with Carboplatin and Pemetrexed

Based on the safety population, RYBREVANT® in combination with carboplatin and pemetrexed can cause ocular toxicity including blepharitis, dry eye, conjunctival redness, blurred vision, and eye pruritus. All events were Grade 1-2.

RYBREVANT® as a Single Agent

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 Toxicity

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 last dose of RYBREVANT®.

Adverse Reactions

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.

Please read the full Prescribing Information for RYBREVANT®.

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 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 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; competition, including technological advances, new products and patents attained by competitors; challenges to patents; 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 undertake to update any forward-looking statement as a result of new information or future events or developments.

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*Dr. Leighl has served as a consultant to Johnson & Johnson; she 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.

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