Johnson&Johnson

Media contact:
Christie Corbett
+1 857-636-0211

Satu Glawe
+49 172-294-6264

Investor contact:
Raychel Kruper
investor-relations@its.jnj.com

U.S. medical inquiries:
+1 800 526-7736

For Immediate Release

TALVEY® (talquetamab-tgvs) demonstrates highly durable, longer-term responses in patients with relapsed or refractory multiple myeloma

24-month overall survival rate of 67 percent achieved with TALVEY® 0.8 mg/kg biweekly dosing in the Phase 1/2 MonumenTAL-1 study

MADRID (PRNewswire (June 14, 2024) – Johnson & Johnson (NYSE: JNJ) announced today that long-term data from the Phase 1/2 MonumenTAL-1 study showed that with 20 to 30 months of median follow-up, triple-class-exposed patients with relapsed or refractory multiple myeloma (RRMM) who were treated with TALVEY® (talquetamab-tgvs) maintained high overall response rates (ORR) and durable responses, irrespective of whether they had received prior T-cell redirection therapy.[1] These data, featured in a poster presentation at the 2024 European Hematology Association (EHA) Congress (Abstract #P915) demonstrate the efficacy and durability of TALVEY® when used before or after chimeric antigen receptor T-cell (CAR-T) therapy or bispecific antibody therapies in triple-class-exposed patients with RRMM.[1]

“Results from the MonumenTAL-1 study continue to show deeper response levels and a longer duration of response in patients treated with either of the approved dose options of talquetamab, while the median overall survival has yet to be reached at two years,” said Dr. Leo Rasche, attending physician on the myeloma service, University Hospital of Würzburg.* “It is encouraging to see no notable increases in treatment-related discontinuations with this longer follow-up across cohorts.”

In MonumenTAL-1, 297 patients with no prior exposure to T-cell redirection therapy received TALVEY® at the recommended Phase 2 dose (RP2D) of 0.8 mg/kg biweekly (Q2W) [n=154] or 0.4 mg/kg weekly (QW) [n=143].[1] At a median follow-up of 23.4 months, patients in the Q2W cohort demonstrated a median duration of response (DOR) of 17.5 months, with median DOR not reached in patients with complete response (CR) or better. For patients in the QW arm, a median follow-up of 29.8 months showed a median DOR of 9.5 months with a median DOR of 28.6 months in patients with a CR or better. At 24 months, 67.1 percent and 60.6 percent of patients were alive from the two dosing cohorts, respectively.[1]

At a median follow-up of 20.5 months, TALVEY® continued to show strong efficacy in patients with prior T-cell redirection therapy exposure (n=78), with 55.1 percent of patients achieving very good partial response (VGPR) or better and 57.3 percent alive at 24.2 months.[1]

Infection rates remained lower than in studies of B-cell maturation antigen–targeted bispecific antibodies (BsAbs), consistent with previous reports. No increase in grade 3/4 infections was observed, with longer follow-up GPRC5D-associated adverse events (AEs) led to few dose reductions and discontinuations. One additional patient discontinued treatment due to AEs since the previous report. Weight loss, as assessed by vital signs, was evident early but stabilized and improved over time, including in patients with oral toxicities. [1]

Data from MonumenTAL-2 support continued durable responses at one year with investigational combination of TALVEY® and pomalidomide in patients with RRMM who had ≥ two prior lines of therapy

Longer follow-up from the Phase 1b MonumenTAL-2 study of the investigational use of TALVEY® and pomalidomide show deep responses and a manageable safety profile in patients with RRMM and support the potential to combine TALVEY® with an immunomodulatory agent (IMiD). These updated data, from the first-ever study of a regimen combining a GPRC5D-targeted therapy and an immunomodulatory agent, were featured as a poster presentation at the 2024 EHA Congress (Abstract #P911).[2]

Patients in the Phase 1b MonumenTAL-2 study (n=35) were treated with subcutaneous (SC) TALVEY® at the RP2D of 0.8 mg/kg (Q2W) (n=19) or 0.4 mg/kg (QW) (n=16) with step-up doses, plus 2.0 mg of oral pomalidomide daily. At a median follow-up of 16.8 months (range, 1.2-25.1), response-evaluable patients demonstrated an ORR of 88.6 percent (≥ VGPR, 80 percent).[2]

“With multiple dosing options and the ability to be used both before or after CAR-T therapy and BCMA bispecifics, TALVEY is an important and versatile treatment option for the treatment of relapsed or refractory multiple myeloma,” said Jordan Schecter, M.D., Vice President, Disease Area Leader, Multiple Myeloma, at Johnson & Johnson Innovative Medicine. “The low rate of grade 3/4 infections seen in MonumenTAL-2 suggests the flexibility of TALVEY as a combination partner with an immunomodulatory agent for patients who continue to face limited treatment options with this complex hematologic disease.”

At 12 months, 80.4 percent of patients who achieved a CR or better maintained their response.[2] The progression-free survival (PFS) rate at 12 months was 72.6 percent.[2]

The most common grade 3/4 hematologic AEs were neutropenia (57.1 percent), anemia (25.7 percent), and thrombocytopenia (20 percent).[2] Taste, nail, skin, and rash toxicities occurred in 85.7 percent, 68.6 percent, 74.3 percent, and 20 percent of patients, respectively; the majority were grade 1/2 with few discontinuations.[2] Cytokine release syndrome (CRS) occurred in 74.3 percent and infections occurred in 80 percent (22.9 percent grade 3/4) of patients.[2]

*Dr. Leo Rasche has provided consulting, advisory, and speaking services to Johnson & Johnson; he has not been paid for any media work.

About TALVEY®

TALVEY® (talquetamab-tgvs) received approval from the U.S. FDA in August 2023 as a first-in-class GPRC5D-targeting bispecific antibody for the treatment of adult patients with relapsed or refractory multiple myeloma who have received at least four prior lines of therapy, including a proteasome inhibitor, an immunomodulatory agent, and an anti-CD38 antibody.[3] Since FDA approval, 1,500 patients were treated with TALVEY®. The European Commission (EC) granted conditional marketing authorization (CMA) of TALVEY® ▼ (talquetamab-tgvs) in August 2023 as monotherapy for the treatment of adult patients with relapsed and refractory multiple myeloma (RRMM) who have received at least three prior therapies, including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 antibody and have demonstrated disease progression on the last therapy.[4]

TALVEY® is a bispecific T-cell engaging antibody that binds to the CD3 receptor expressed on the surface of T-cells and G protein-coupled receptor class C group 5 member D (GPRC5D), a novel multiple myeloma target which is highly expressed on the surface of multiple myeloma cells and non-malignant plasma cells, as well as some healthy tissues such as epithelial cells of the skin and tongue.

For more information, visit www.TALVEY.com.

About MonumenTAL-1

MonumenTAL-1 (Phase 1: NCT03399799, Phase 2: NCT04634552) is a Phase 1/2 single-arm, open-label, multicohort, multicenter dose-escalation study involving more than 300 patients.[5,6] Phase 1 evaluated the safety and efficacy of TALVEY® in adults with relapsed or refractory multiple myeloma who received three or more prior lines of therapy, including a proteasome inhibitor, an immunomodulatory agent, and an anti-CD38 monoclonal antibody. The study excluded patients who experienced T-cell redirection therapy within 3 months, prior Grade 3 or higher CRS related to any T-cell redirection therapy, an autologous stem cell transplant within 12 weeks, an allogenic stem cell transplant within 6 months, Eastern Cooperative Oncology Group (ECOG) performance score of 3 or higher, stroke or seizure within 6 months, CNS involvement or clinical signs of meningeal involvement of multiple myeloma, plasma cell leukemia, or active or documented history of autoimmune disease (exception of vitiligo, resolved childhood atopic dermatitis or resolved Graves’ Disease that is euthyroid based on clinical and laboratory testing).

Phase 2 of the study evaluated the efficacy of TALVEY® in participants with relapsed or refractory multiple myeloma at the recommended Phase 2 dose(s) (RP2D), established as SC 0.4 mg/kg weekly and 0.8 mg/kg every two weeks, respectively. Efficacy was based on overall response rate (ORR) and duration of response (DOR) as assessed by an Independent Review Committee using the International Myeloma Working Group (IMWG) criteria.[1]

About MonumenTAL-2

The MonumenTAL-2 (NCT05050097) study is an ongoing Phase 1 study of subcutaneous talquetamab in combination with carfilzomib, daratumumab SC, lenalidomide or pomalidomide for the treatment of patients with multiple myeloma. The primary objective of the MonumenTAL-2 study is to identify and characterize the safety of the treatment combinations. Secondary objectives of the MonumenTAL-2 study include overall response rates, duration of response and time to response.[7]

About Multiple Myeloma

Multiple myeloma is an incurable blood cancer that affects a type of white blood cell called plasma cells, which are found in the bone marrow.[8] In multiple myeloma, these plasma cells change, spread rapidly and replace normal cells in the bone marrow with tumors.[9] Multiple myeloma is the third most common blood cancer and remains an incurable disease.[10] In 2023, it is estimated that more than 35,000 people will be diagnosed with multiple myeloma in the U.S. and more than 12,000 people will die from the disease.[11] People living with multiple myeloma have a five-year relative survival rate of 59.8 percent.[12] While some people diagnosed with multiple myeloma initially have no symptoms, most patients are diagnosed due to symptoms that can include bone fracture or pain, low red blood cell counts, tiredness, high calcium levels and kidney problems or infections.[13,14]

TALVEY® IMPORTANT SAFETY INFORMATION

INDICATION AND USAGE

TALVEY® (talquetamab-tgvs) is indicated for the treatment of adult patients with relapsed or refractory multiple myeloma who have received at least four prior lines of therapy, including a proteasome inhibitor, an immunomodulatory agent, and an anti-CD38 monoclonal antibody.

This indication is approved under accelerated approval based on response rate and durability of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).

IMPORTANT SAFETY INFORMATION

WARNING: CYTOKINE RELEASE SYNDROME and NEUROLOGIC TOXICITY, including IMMUNE EFFECTOR CELL-ASSOCIATED NEUROTOXICITY SYNDROME

Cytokine release syndrome (CRS), including life-threatening or fatal reactions, can occur in patients receiving TALVEY®. Initiate TALVEY® treatment with step-up dosing to reduce the risk of CRS. Withhold TALVEY® until CRS resolves or permanently discontinue based on severity.

Neurologic toxicity, including immune effector cell-associated neurotoxicity syndrome (ICANS), and serious and life-threatening or fatal reactions, can occur with TALVEY®. Monitor patients for signs and symptoms of neurologic toxicity including ICANS during treatment and treat promptly. Withhold or permanently discontinue TALVEY® based on severity.

Because of the risk of CRS and neurologic toxicity, including ICANS, TALVEY® is available only through a restricted program called the TECVAYLI® and TALVEY® Risk Evaluation and Mitigation Strategy (REMS).

CONTRAINDICATIONS: None.

WARNINGS AND PRECAUTIONS

Cytokine Release Syndrome (CRS): TALVEY® can cause cytokine release syndrome, including life-threatening or fatal reactions. In the clinical trial, CRS occurred in 76% of patients who received TALVEY® at the recommended dosages, with Grade 1 CRS occurring in 57% of patients, Grade 2 in 17%, and Grade 3 in 1.5%. Most events occurred following step-up dose 1 (29%) or step-up dose 2 (44%) at the recommended dosages. Recurrent CRS occurred in 30% of patients. CRS occurred in 33% of patients with step-up dose 3 in the biweekly dosing schedule (N=153). CRS occurred in 30% of patients with the first 0.4 mg/kg treatment dose and in 12% of patients treated with the first 0.8 mg/kg treatment dose. The CRS rate for both dosing schedules combined was less than 3% for each of the remaining doses in Cycle 1 and less than 3% cumulatively from Cycle 2 onward. The median time to onset of CRS was 27 (range: 0.1 to 167) hours from the last dose, and the median duration was 17 (range: 0 to 622) hours. Clinical signs and symptoms of CRS include but are not limited to pyrexia, hypotension, chills, hypoxia, headache, and tachycardia. Potentially life-threatening complications of CRS may include cardiac dysfunction, acute respiratory distress syndrome, neurologic toxicity, renal and/or hepatic failure, and disseminated intravascular coagulation (DIC).

Initiate therapy with step-up dosing and administer pre-treatment medications (corticosteroids, antihistamine, and antipyretics) prior to each dose of TALVEY® in the step-up dosing schedule to reduce the risk of CRS. Monitor patients following administration accordingly. In patients who experience CRS, pre-treatment medications should be administered prior to the next TALVEY® dose.

Counsel patients to seek medical attention should signs or symptoms of CRS occur. At the first sign of CRS, immediately evaluate patient for hospitalization and institute treatment with supportive care based on severity, and consider further management per current practice guidelines. Withhold TALVEY® until CRS resolves or permanently discontinue based on severity.

Neurologic Toxicity including ICANS: TALVEY® can cause serious or life-threatening neurologic toxicity, including immune effector cell-associated neurotoxicity syndrome (ICANS), including fatal reactions. In the clinical trial, neurologic toxicity occurred in 55% of patients who received the recommended dosages, with Grade 3 or 4 neurologic toxicity occurring in 6% of patients. The most frequent neurologic toxicities were headache (20%), encephalopathy (15%), sensory neuropathy (14%), and motor dysfunction (10%).

ICANS was reported in 9% of 265 patients where ICANS was collected and who received the recommended dosages. Recurrent ICANS occurred in 3% of patients. Most patients experienced ICANS following step-up dose 1 (3%), step-up dose 2 (3%), step-up dose 3 of the biweekly dosing schedule (1.8%), or the initial treatment dose of the weekly dosing schedule (2.6%) (N=156) or the biweekly dosing schedule (3.7%) (N=109). The median time to onset of ICANS was 2.5 (range: 1 to 16) days after the most recent dose with a median duration of 2 (range: 1 to 22) days. The onset of ICANS can be concurrent with CRS, following resolution of CRS, or in the absence of CRS. Clinical signs and symptoms of ICANS may include but are not limited to confusional state, depressed level of consciousness, disorientation, somnolence, lethargy, and bradyphrenia.

Monitor patients for signs and symptoms of neurologic toxicity during treatment and treat promptly. At the first sign of neurologic toxicity, including ICANS, immediately evaluate the patient and provide supportive care based on severity. Withhold or permanently discontinue TALVEY® based on severity and consider further management per current practice guidelines [see Dosage and Administration (2.5)].

Due to the potential for neurologic toxicity, patients receiving TALVEY® are at risk of depressed level of consciousness. Advise patients to refrain from driving or operating heavy or potentially dangerous machinery during the step-up dosing schedule and for 48 hours after completion of the step-up dosing schedule, and in the event of new onset of any neurological symptoms, until symptoms resolve.

TECVAYLI® and TALVEY® REMS: TALVEY® is available only through a restricted program under a REMS, called the TECVAYLI® and TALVEY® REMS because of the risks of CRS and neurologic toxicity, including ICANS.

Further information about the TECVAYLI® and TALVEY® REMS program is available at www.TEC-TALREMS.com or by telephone at 1-855-810-8064.

Oral Toxicity and Weight Loss: TALVEY® can cause oral toxicities, including dysgeusia, dry mouth, dysphagia, and stomatitis. In the clinical trial, 80% of patients had oral toxicity, with Grade 3 occurring in 2.1% of patients who received the recommended dosages. The most frequent oral toxicities were dysgeusia (49%), dry mouth (34%), dysphagia (23%), and ageusia (18%). The median time to onset of oral toxicity was 15 (range: 1 to 634) days, and the median time to resolution to baseline was 43 (1 to 530) days. Oral toxicity did not resolve to baseline in 65% of patients.

TALVEY® can cause weight loss. In the clinical trial, 62% of patients experienced weight loss of 5% or greater, regardless of having an oral toxicity, including 28% of patients with Grade 2 (10% or greater) weight loss and 2.7% of patients with Grade 3 (20% or greater) weight loss. The median time to onset of Grade 2 or higher weight loss was 67 (range: 6 to 407) days, and the median time to resolution was 50 (range: 1 to 403) days. Weight loss did not resolve in 57% of patients who reported weight loss.

Monitor patients for signs and symptoms of oral toxicity. Counsel patients to seek medical attention should signs or symptoms of oral toxicity occur and provide supportive care as per current clinical practice, including consultation with a nutritionist. Monitor weight regularly during therapy. Evaluate clinically significant weight loss further. Withhold TALVEY® or permanently discontinue based on severity.

Infections: TALVEY® can cause infections, including life-threatening or fatal infections. Serious infections occurred in 16% of patients, with fatal infections in 1.5% of patients. Grade 3 or 4 infections occurred in 17% of patients. The most common serious infections reported were bacterial infection (8%), which included sepsis and COVID-19 (2.7%).

Monitor patients for signs and symptoms of infection prior to and during treatment with TALVEY® and treat appropriately. Administer prophylactic antimicrobials according to local guidelines. Withhold or consider permanently discontinuing TALVEY® as recommended, based on severity.

Cytopenias: TALVEY® can cause cytopenias, including neutropenia and thrombocytopenia. In the clinical trial, Grade 3 or 4 decreased neutrophils occurred in 35% of patients, and Grade 3 or 4 decreased platelets occurred in 22% of patients who received TALVEY®. The median time to onset for Grade 3 or 4 neutropenia was 22 (range: 1 to 312) days, and the median time to resolution to Grade 2 or lower was 8 (range: 1 to 79) days. The median time to onset for Grade 3 or 4 thrombocytopenia was 12 (range: 2 to 183) days, and the median time to resolution to Grade 2 or lower was 10 (range: 1 to 64) days. Monitor complete blood counts during treatment and withhold TALVEY® as recommended, based on severity.

Skin Toxicity: TALVEY® can cause serious skin reactions, including rash, maculo-papular rash, erythema, and erythematous rash. In the clinical trial, skin reactions occurred in 62% of patients, with grade 3 skin reactions in 0.3%. The median time to onset was 25 (range: 1 to 630) days. The median time to improvement to grade 1 or less was 33 days.

Monitor for skin toxicity, including rash progression. Consider early intervention and treatment to manage skin toxicity. Withhold TALVEY® as recommended based on severity.

Hepatotoxicity: TALVEY® can cause hepatotoxicity. Elevated ALT occurred in 33% of patients, with grade 3 or 4 ALT elevation occurring in 2.7%; elevated AST occurred in 31% of patients, with grade 3 or 4 AST elevation occurring in 3.3%. Grade 3 or 4 elevations of total bilirubin occurred in 0.3% of patients. Liver enzyme elevation can occur with or without concurrent CRS.

Monitor liver enzymes and bilirubin at baseline and during treatment as clinically indicated. Withhold TALVEY® or consider permanent discontinuation of TALVEY®, based on severity [see Dosage and Administration (2.5)].

Embryo-Fetal Toxicity: Based on its mechanism of action, TALVEY® may cause fetal harm when administered to a pregnant woman. Advise pregnant women of the potential risk to the fetus. Advise females of reproductive potential to use effective contraception during treatment with TALVEY® and for 3 months after the last dose.

Adverse Reactions: The most common adverse reactions (≥20%) are pyrexia, CRS, dysgeusia, nail disorder, musculoskeletal pain, skin disorder, rash, fatigue, weight decreased, dry mouth, xerosis, dysphagia, upper respiratory tract infection, diarrhea, hypotension, and headache.

The most common Grade 3 or 4 laboratory abnormalities (≥30%) are lymphocyte count decreased, neutrophil count decreased, white blood cell decreased, and hemoglobin decreased.

Please read full Prescribing Information, including Boxed WARNING, for TALVEY®.

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 both Johnson & Johnson companies. Source: Johnson & Johnson

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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 TALVEY® (talquetamab-tgvs). 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.

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[2] Searle, E et al., Talquetamab, a GPRC5dxCD3 bispecific antibody, in combination with pomalidomide in patients with relapsed/refractory multiple myeloma: safety and efficacy results from the Phase 1b MonumenTAL-2 study. 2024 European Hematology Association Hybrid Congress. June 2024.
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