

News Release

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U.S. FDA Approves TALVEY™ (talquetamab-tgvs), a First-in-Class Bispecific Therapy for the Treatment of Patients with Heavily Pretreated Multiple Myeloma

Bispecific antibody targeting GPRC5D receptor showed an overall response rate of more than 70 percent with durable responses, including in patients previously treated with a bispecific antibody or CAR-T cell therapy

HORSHAM, Pa., Aug. 10, 2023 – The Janssen Pharmaceutical Companies of Johnson & Johnson announced today that the U.S. Food and Drug Administration (FDA) has granted accelerated approval of TALVEY™ (talquetamab-tgvs), a first-in-class 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.¹ This indication is approved under accelerated approval based on response rate and durability of response.¹ Continued approval for this indication is contingent upon verification and description of clinical benefit in confirmatory trial(s).¹

TALVEY™ is a bispecific T-cell engaging antibody that binds to the CD3 receptor on the surface of T cells and G protein-coupled receptor class C group 5 member D (GPRC5D) expressed on the surface of multiple myeloma cells, non-malignant plasma cells and healthy tissue such as epithelial cells in

keratinized tissues of the skin and tongue.¹ TALVEY™ is approved as a weekly or biweekly subcutaneous (SC) injection after an initial step-up phase, offering physicians the flexibility to determine the optimal treatment regimen for patients.¹

“The clinically meaningful efficacy and safety profile observed with talquetamab in heavily pretreated patients in this clinical trial, which included patients treated with prior BCMA-targeted bispecific or CAR-T cell therapy, has been notable,” said Ajai Chari, M.D., Director of Multiple Myeloma Program, Professor of Clinical Medicine at the University of California, San Francisco.* “Patients at this stage of disease have a poor prognosis. Talquetamab as a first-in-class therapy is a new option for patients with this difficult-to-treat blood cancer.”

The talquetamab Phase 2 MonumentAL-1 study, which included patients who had received at least four prior lines of therapy and who were not exposed to prior T-cell redirection therapy (n=187), showed meaningful overall response rates (ORR).¹ At the SC biweekly dose of 0.8 mg/kg, 73.6 percent of patients (95 percent Confidence Interval [CI], range, 63.0 to 82.4) achieved an ORR.¹ With a median follow-up of nearly 6 (range, 0 to 9.5) months from first response among responders, 58 percent of patients achieved a very good partial response (VGPR) or better, including 33 percent of patients achieving a complete response (CR) or better.¹ At the SC weekly dose of 0.4 mg/kg, 73.0 percent of patients (95 percent CI, range, 63.2 to 81.4) achieved an ORR.¹ With a median follow-up of nearly 14 (range, 0.8 to 15.4) months from first response among responders, 57 percent of patients achieved a VGPR or better, including 35 percent of patients achieving a CR or better.¹ Responses were durable with a median duration of response not reached in the 0.8 mg/kg SC biweekly dose group and 9.5 months in the 0.4 mg/kg SC weekly dose group.¹ Among patients receiving the 0.8 mg/kg SC biweekly dose, an estimated 85 percent of responders maintained response for at least 9 months.¹

The MonumentAL-1 study also included 32 patients who were exposed to prior bispecific antibody or CAR-T cell therapy (94 percent B-cell maturation antigen [BCMA]-directed therapy) and had received at least four prior lines of therapy, including a proteasome inhibitor, an immunomodulatory agent, and an anti-CD38 monoclonal antibody, received TALVEY at the 0.4 mg/kg SC weekly dose.¹ With a median duration of follow-up of 10.4 months, 72 percent of patients (95 percent CI, range, 53 to 86) achieved an ORR per an Independent Review Committee assessment, and an estimated 59 percent of responders maintained response for at least 9 months.¹

The Safety Profile for TALVEY™ includes a Boxed Warning for cytokine release syndrome (CRS) and neurologic toxicity including immune effector cell-associated neurotoxicity syndrome (ICANS); Warnings and Precautions include Oral Toxicity and Weight Loss, Infections, Cytopenias, Skin Toxicity, Hepatotoxicity and Embryo-fetal toxicity. The most common adverse reactions (≥20 percent) 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 percent) are lymphocyte count decreased, neutrophil count decreased, white blood cell decreased, and hemoglobin decreased.¹

"Although options for the treatment of multiple myeloma have expanded significantly in recent years, the disease remains incurable, and therefore, patients are in need of new treatment options," said Michael Andreini, President and Chief Executive Officer, Multiple Myeloma Research Foundation.[†] "Today's approval of talquetamab provides patients with a new treatment approach for relapsed or refractory disease that is a welcome addition to the myeloma community."

"The approval of TALVEY, our fifth innovative therapy and second bispecific antibody approved for the treatment of multiple myeloma, demonstrates our commitment to expanding our portfolio of medicines to help address unmet needs for patients who continue to face challenges with this complex hematologic malignancy," said Peter Lebowitz, M.D., Ph.D., Global Therapeutic Area Head, Oncology, Janssen Research & Development, LLC. "Our team of scientists never settles in their determination to discover and develop effective therapies. With the discovery of this new antigen, we continue to strive for research breakthroughs while remaining focused on delivering curative regimens in our commitment to eliminate cancer."

TALVEY™ is available only through a restricted program called the TECVAYLI® and TALVEY™ Risk Evaluation and Mitigation Strategy (REMS).¹ Details of the Important Safety Information are included below.

The most common non-hematologic adverse events observed in the study were oral toxicities, which occurred in 80 percent of patients, with Grade 3 occurring in 2.1 percent of patients.¹ The most frequent oral toxicities were dysgeusia (49 percent), dry mouth (34 percent), dysphagia (23 percent), and ageusia (18 percent).¹ In addition, 62 percent of patients experienced weight loss, including 29 percent with Grade 2 weight loss and 2.7 percent with Grade 3 weight loss.¹ Serious infections occurred in 16 percent of patients, with fatal infections occurring in 1.5 percent of patients.¹

Grade 3 or 4 serious infections occurred in 17 percent of patients.¹ Grade 3 or 4 decreased neutrophils occurred in 35 percent of patients and decreased platelets occurred in 22 percent of patients.¹ Skin reactions occurred in 62 percent of patients, with Grade 3 skin reactions in 0.3 percent.¹ Permanent discontinuation of TALVEY™ due to an adverse reaction occurred in 9 percent of patients.¹

About the MonumentAL-1 Study

MonumentAL-1 (Phase 1: [NCT03399799](#), Phase 2: [NCT04634552](#)) is a Phase 1/2 single-arm, open-label, multicohort, multicenter dose-escalation study involving over 300 patients.^{2,3} 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.^{1,2} 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 the past 12 weeks, an allogeneic stem cell transplant within the past 6 months, Eastern Cooperative Oncology Group (ECOG) performance score of 3 or higher, stroke or seizure within the past 6 months, CNS involvement or clinical signs of meningeal involvement of multiple myeloma, and plasma cell leukemia, active or documented history of autoimmune disease (exception of vitiligo, resolved childhood atopic dermatitis or resolved Grave's Disease that is euthyroid based on clinical and laboratory testing).^{1,2}

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) (RP2Ds), established at SC 0.4 mg/kg weekly and 0.8 mg/kg every two weeks, respectively.³ Efficacy was based on overall response rate (ORR) and duration of response (DOR) as assessed by an Independent Review Committee using IMWG criteria.³

TALVEY™ 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. Withhold or 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%. Recurrent CRS occurred in 30% of patients. Most events occurred following step-up dose 1 (29%), step-up dose 2 (44%), or the initial treatment dose for the weekly dosing schedule (30%) (N=186) and the third step-up dose for the biweekly dosing schedule (33%) (N=153). CRS occurred in 12% of patients treated with the first 0.8 mg/kg dose of the biweekly dosing schedule. 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, life-threatening or fatal neurologic toxicity, including ICANS. In the clinical trial, neurologic toxicity including ICANS 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%), 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. 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] in the full Prescribing Information*).

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, regardless of having an oral toxicity, including 29% 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 permanently discontinue 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 or permanently discontinue TALVEY™ based on severity.

Hepatotoxicity: TALVEY™ can cause hepatotoxicity. In the clinical trial, 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] in the full Prescribing Information*).

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.

Please read full [Prescribing Information](#) including Boxed Warning for TALVEY™.

About TALVEY™

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 (GPC5D), 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.¹

TALVEY™ is currently being investigated in combination and in sequence across all lines of multiple myeloma in studies with other bispecific antibodies as well as with existing standards of care. In addition to a Phase 1/2 clinical study of TALVEY™ for the treatment of relapsed or refractory multiple myeloma, TALVEY™ is also being evaluated in combination studies ([NCT04586426](#), [NCT04108195](#), [NCT05050097](#), [NCT05338775](#)) and in a randomized Phase 3 study ([NCT05455320](#)).

In May 2021 and August 2021, TALVEY™ was granted Orphan Drug Designation for the treatment of multiple myeloma by the U.S. FDA and the European Commission, respectively. TALVEY™ was also granted Breakthrough Therapy Designation from the U.S. FDA in June 2022 for the treatment of adult patients with relapsed or refractory multiple myeloma who have previously received at least four prior lines of therapy, including a proteasome inhibitor, an immunomodulatory agent, and an anti-CD38 antibody. The approval follows the FDA's decision in February 2023 to initiate a Priority Review of the Biologics License Application (BLA) submitted in December 2022.

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.⁴ In multiple myeloma, these plasma cells change, spread rapidly and replace normal cells in the bone marrow with tumors.⁵ Multiple myeloma is the third most common blood cancer and remains an incurable disease.⁶ 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.⁷ People living with multiple myeloma have a 5-year relative survival rate of 59.8 percent.⁸ 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.^{9,10}

About the Janssen Pharmaceutical Companies of Johnson & Johnson

At Janssen, we are 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 [@JanssenUS](https://twitter.com/JanssenUS) and [@JanssenGlobal](https://twitter.com/JanssenGlobal). Janssen Biotech, Inc., and Janssen Research & Development, LLC, are part of the Janssen Pharmaceutical Companies of Johnson & Johnson.

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

† Mr. Andreini 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 of TALVEY™. 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 Biotech, Inc., Janssen Research & Development, LLC, 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 1, 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 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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¹ TALVEY™ U.S. Prescribing Information.

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- ² ClinicalTrials.gov Identifier NCT03399799. Accessed July 6, 2023. <https://clinicaltrials.gov/ct2/show/NCT03399799>
- ³ ClinicalTrials.gov Identifier NCT04634552. Accessed July 6, 2023. <https://clinicaltrials.gov/ct2/show/NCT04634552>
- ⁴ Rajkumar SV. Multiple myeloma: 2020 update on diagnosis, risk-stratification and management. *Am J Hematol.* 2020;95(5):548-567. <http://www.ncbi.nlm.nih.gov/pubmed/32212178>
- ⁵ National Cancer Institute. Plasma Cell Neoplasms. Accessed July 9, 2023. Available at: <https://www.cancer.gov/types/myeloma/patient/myeloma-treatment-pdq>
- ⁶ Multiple myeloma. City of Hope, 2022. Multiple Myeloma: Causes, Symptoms & Treatments. Accessed July 18, 2023. <https://www.cancercenter.com/cancer-types/multiple-myeloma>
- ⁷ American Cancer Society. Key Statistics About Multiple Myeloma. Accessed July 9, 2023. Available at: <https://www.cancer.org/cancer/multiple-myeloma/about/key-statistics.html#:~:text=Multiple%20myeloma%20is%20a%20relatively,men%20and%2015%2C37%20in%20women>
- ⁸ SEER*Explorer: An interactive website for SEER cancer statistics [Internet]. Surveillance Research Program, National Cancer Institute. Accessed June 30, 2023. <https://seer.cancer.gov/explorer/>
- ⁹ American Cancer Society. What is Multiple Myeloma? Accessed July 9, 2023. Available at: <https://www.cancer.org/cancer/multiple-myeloma/about/what-is-multiple-myeloma.html>
- ¹⁰ American Cancer Society. Multiple Myeloma Early Detection, Diagnosis, and Staging. Accessed July 19, 2023. Available at: <https://www.cancer.org/cancer/types/multiple-myeloma/detection-diagnosis-staging/detection.html>