Talvey™ (talquetamab-tgvs) – New orphan drug approval

- On August 10, 2023, Janssen announced the FDA approval of Talvey (talquetamab-tgvs), 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).
- Multiple myeloma is the third most common blood cancer. 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.
- 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 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.
- The efficacy of Talvey was established in a single-arm, open-label study (MMY1001) in patients with relapsed or refractory multiple myeloma. The study included 187 patients who were not exposed to prior T cell redirection therapy and 32 patients who were exposed to prior T cell redirection therapy. Efficacy was based on overall response rate (ORR) and duration of response (DOR).
    - In T cell redirection therapy naïve patients, the ORR was 73% (95% CI: 63.2, 81.4) with Talvey 0.4 mg/kg weekly and 73.6% (95% CI: 63.0, 82.4) with Talvey 0.8 mg/kg biweekly. The median DOR was 9.5 months (95% CI: 6.5, not estimable) and not estimable, respectively.
    - In patients previously exposed to T cell redirection therapy, the ORR was 72% (95% CI: 53, 86) with Talvey 0.4 mg/kg weekly and an estimated 59% of responders maintained response for at least 9 months.
- Talvey carries a boxed warning for cytokine release (CRS) and neurologic toxicity, including immune effector cell-associated neurotoxicity syndrome (ICANS).
    - Talvey is available only through a restricted program called the Tecvayli and Talvey Risk Evaluation and Mitigation Strategy (REMS).
- Additional warnings and precautions for Talvey include oral toxicity and weight loss; infections; cytopenias; skin toxicity; hepatotoxicity; and embryo-fetal toxicity.
- The most common adverse reactions (≥ 20%) with Talvey use were pyrexia, CRS, dysgeusia, nail disorder, musculoskeletal pain, skin disorder, rash, fatigue, decreased weight, dry mouth, xerosis, dysphagia, upper respiratory tract infection, diarrhea, hypotension, and headache. The most common grade 3 or 4 laboratory abnormalities (≥ 30%) were decreased lymphocyte count, decreased neutrophil count, decreased white blood cell, and decreased hemoglobin.

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- Talvey is administered subcutaneously (SC) on a weekly or biweekly (every 2 weeks) dosing schedule according to the tables below. Treatment should continue until disease progression or unacceptable toxicity.
    - Talvey should only be administered by a qualified healthcare professional with appropriate medical support to manage severe reactions such as CRS and ICANS.
    - Due to the risk of CRS and neurologic toxicity, including ICANS, patients should be hospitalized for 48 hours after administration of all doses within the Talvey step-up dosing schedule.

Talvey weekly dosing schedule

Dosing schedule	Day	Dose	
Step-up dosing schedule	Day 1	Step-up dose 1	0.01 mg/kg
	Day 4	Step-up dose 2	0.06 mg/kg
	Day 7	First treatment dose	0.4 mg/kg
Weekly dosing schedule	One week after first treatment dose and weekly thereafter	Subsequent treatment doses	0.4 mg/kg once weekly

Talvey biweekly dosing schedule

Dosing schedule	Day	Dose	
Step-up dosing schedule	Day 1	Step-up dose 1	0.01 mg/kg
	Day 4	Step-up dose 2	0.06 mg/kg
	Day 7	Step-up dose 3	0.4 mg/kg
	Day 10	First treatment dose	0.8 mg/kg
Biweekly dosing schedule	Two weeks after first treatment dose and every 2 weeks thereafter	Subsequent treatment doses	0.8 mg/kg every 2 weeks

- Janssen's launch plans for Talvey are pending. Talvey will be available as a 3 mg/1.5 mL (2 mg/mL) single-dose vial and 40 mg/mL single-dose vial.