Background TMEFF2 is a transmembrane protein with epidermal growth factor-like and 2 follistatin-like domains. The enriched expression of TMEFF2 in prostate cancer and its restricted expression in healthy brain and prostate make it an attractive candidate for targeted prostate cancer therapy. JNJ-70218902 (JNJ-902) is a bispecific TMEFF2 × CD3 antibody that binds to human TMEFF2 on prostate cancer cells and to human CD3 on T cells to promote T cell-mediated killing of tumor cells. Given the 100% sequence homology and analogous biodistribution of TMEFF2 in humans and monkey, the pharmacodynamics of JNJ-902 was studied in cynomolgus monkeys.

Methods Two dosing regimens of JNJ-902 were evaluated in cynomolgus monkeys: single, fixed dosing (0.075 mg/kg) and step-up dosing (0.075 mg/kg followed by 0.3 mg/kg 1 week later). Blood, serum, and prostate tissue were collected for flow cytometry to assess number of T cell infiltrates and myeloid cells, and surface markers of T cell function (activation, proliferation, and suppression).

Results An approximately dose proportional increase in JNJ-902 exposure was observed in this study. Both dosing regimens increased CD4+ and CD8+ T cell infiltration in the prostate, including activation and proliferation of CD4+ and CD8+ T cells (measured by granzyme B, CD25, CD69, and Ki-67), and in the periphery, minimal suppressive biomarkers (CD4+CD25hi Foxp3+) were observed. Interestingly, greater infiltration of CD8+ T cells was observed with step-up dosing. Both dosing regimens led to an influx of pro-inflammatory cells (dendritic cells, myeloid cells, macrophages, and B cells) into the prostate.

Conclusions Redirecting T cell activity to TMEFF2-expressing tumors by JNJ-902 is a promising immunotherapy for prostate cancers. In cynomolgus monkeys, treatment with JNJ-902 induced the infiltration of activated and proliferating T cells and inflammatory cells into the prostate, suggesting the potential to mediate an effective immune response. The clinical evaluation of JNJ-902 is currently underway in a phase 1 dose escalation trial in patients with metastatic castration-resistant prostate cancer (NCT04397276).

Ethics Approval The procedures involving the care and use of animals in this study were reviewed and approved by CRMWN Institutional Animal Care and Use Committee before conduct (Testing Facility Study Number 886-526). During the study, the care and use of animals were conducted with guidance from the guidelines of the USA National Research Council.