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NEWS RELEASE

Neoadjuvant TAR-200 plus cetrelimab nearly doubles the pathological complete response rate compared to cetrelimab alone in patients with muscle-invasive bladder cancer

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TAR-200 plus cetrelimab effective in reducing tumor size in those with muscle-invasive disease, potentially improving surgical outcomes and lowering risk of recurrence

BARCELONA, Spain, Sept. 16, 2024 /PRNewswire/ -- Johnson & Johnson (NYSE: JNJ) announced today interim data from the ongoing Phase 2 SunRISe-4 study showing neoadjuvant treatment with investigational TAR-200 plus cetrelimab (CET) achieved nearly double the pathological complete response (pCR) rate compared to CET alone in patients with muscle-invasive bladder cancer (MIBC) who are ineligible or refuse neoadjuvant platinum-based chemotherapy and scheduled for radical cystectomy (RC).[1] These data were featured as a late-breaking oral presentation at the **European Society of Medical Oncology (ESMO) 2024 Congress** (Abstract #LBA84).

"These findings from the SunRISe-4 study show for the first time that an intravesical treatment with TAR-200, combined with a systemic PD-1 inhibitor, could potentially result in a complete pathological response in a high proportion of patients, as well as allowing a tolerable approach," said Andrea Necchi, M.D., of Italy's Vita-Salute San Raffaele University and the IRCCS San Raffaele Hospital and Scientific Institute and a presenting author of the study. "These preliminary findings show a potential for a future change in the local treatment of muscle-invasive bladder carcinoma using TAR-200."

In the interim analysis of the SunRISe-4 study, neoadjuvant TAR-200 plus CET (n=53) showed overall efficacy with a centrally confirmed pathologic complete response (pCR, [T0]) rate of 42 percent compared to 23 percent (95 percent CI, 28-56; 10-41, respectively) with CET alone (n=31) in patients with histologically proven, non-metastatic

MIBC. The pathological overall response (pOR) rate (defined as the proportion of patients ≤ pT1) was 60 percent compared to 36 percent, respectively (CI 95 percent, 46-74; 19-55).[1]

In a subgroup analysis of patients with organ-confined disease (cT2), those treated with TAR-200 plus CET (n=40) showed a 48 percent pCR rate compared to 23 percent pCR with CET alone (n=26, 95 percent CI, 32-64; 9-44, respectively) and 68 percent were downstaged (≤ pT1) at the time of radical cystectomy, potentially improving surgical outcomes and reducing risk of recurrence.[1]

"With these promising results, TAR-200 plus cetrelimab as a neoadjuvant therapy before radical cystectomy could potentially alter how bladder cancer is treated," said Kiran Patel, M.D., Vice President, Clinical Development, Solid Tumors, Innovative Medicine, Johnson & Johnson. "This investigational innovative approach may offer a possible alternative for many patients who are not eligible for the current standard of pre-operative treatments."

Treatment-related adverse events (TRAEs) occurred in 72 percent of patients treated with TAR-200 combined with CET and 44 percent of patients treated with CET alone, with the majority being Grade 1-2. Nine percent of patients discontinued treatment with TAR-200 and eight percent discontinued treatment with CET in the combined treatment cohort due to TRAEs; no patients discontinued treatment due to TRAEs when treated with CET alone.[1]

Bladder cancer is the ninth most common cancer in the world.[2] Although BCG immunotherapy has been accepted as the standard of care for nearly five decades, 30-40 percent of patients do not respond to BCG and experience disease recurrence or progression.[3] In such scenarios, radical cystectomy (removal of the bladder and neighboring structures and organs) emerges as the primary treatment option. This major abdominal procedure requires a urinary diversion to be created to collect and store urine.[4]

TAR-200 is an investigational targeted releasing system designed to provide extended local release of gemcitabine into the bladder. It is installed in a physician's office setting during a 2-3 minute procedure with no anesthesia. In December 2023, the FDA **granted** TAR-200 Breakthrough Therapy Designation (BTD) for the potential future treatment of patients with BCG-unresponsive HR-NMIBC, who are ineligible for or elected not to undergo radical cystectomy (surgical removal of the bladder).

About SunRISe-4

SunRISe-4 (**NCT04919512**) is an open-label, multicenter, randomized Phase 2 study assessing the efficacy and safety of neoadjuvant TAR-200 + cetrelimab (CET) (anti-programmed death-1 antibody) or neoadjuvant CET alone in patients with MIBC scheduled for RC who are ineligible for or refuse neoadjuvant platinum-based chemotherapy.

About TAR-200

TAR-200 is an investigational targeted releasing system, enabling extended release of gemcitabine into the bladder,

increasing the amount of time the drug delivery system spends in the bladder and sustaining local drug exposure. The safety and efficacy of TAR-200 are being evaluated in Phase 2 and Phase 3 studies in patients with MIBC in **SunRISe-2** and **SunRISe-4**, and NMIBC in **SunRISe-1**, **SunRISe-3** and **SunRISe-5**.

About Cetrelimab

Cetrelimab is an investigational programmed cell death receptor-1 (PD-1) monoclonal antibody being studied for the treatment of bladder cancer, prostate cancer, melanoma, and multiple myeloma as part of a combination treatment. Cetrelimab is also being evaluated in multiple other combination regimens.

About Muscle-Invasive Bladder Cancer

Muscle-invasive bladder cancer (MIBC) is a severe form of bladder cancer where the tumor penetrates the muscular layer of the bladder wall, significantly increasing the risk of metastasis.[5] Approximately 25 percent of bladder cancer cases are diagnosed as MIBC at the time of initial presentation.[6] Early detection and timely intervention are crucial for managing MIBC, as delayed treatment can lead to poor prognosis.

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, Janssen Biotech, Inc., and Janssen Global Services, LLC 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 TAR-200 or cetrelimab. 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., Janssen Global Services, LLC 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., Janssen Global Services, LLC, nor Johnson & Johnson undertakes to update any forward-looking statement as a result of new information or future events or developments.

*Dr. Andrea Necchi has provided consulting, advisory, and speaking services to Johnson & Johnson; they have not been paid for any media work.

[1] Necchi A., et al. TAR-200 Plus Cetrelimab or Cetrelimab Alone as Neoadjuvant Therapy in Patients With Muscleinvasive Bladder Cancer Who Are Ineligible for or Refuse Neoadjuvant Cisplatin-based Chemotherapy: Interim Analysis of SunRISe-4. ESMO 2024. September 16, 2024.
[2] Globocan 2022 **https://gco.iarc.who.int/media/globocan/factsheets/populations/900-world-fact-sheet.pdf**
[3] Zlotta AR, Fleshner NE, Jewett MA. The management of BCG failure in non-muscle-invasive bladder cancer: an update. Can Urol Assoc J. 2013;3(6-S4):199.
[4] Bladder removal surgery: What is a radical cystectomy? Bladder Cancer Advocacy Network. Accessed April 1, 2024. **https://bcan.org/bladder-removal-surgery/**.
[5] National Collaborating Centre for Cancer (UK). Bladder Cancer: Diagnosis and Management. London: National Institute for Health and Care Excellence (NICE); 2015 Feb. (NICE Guideline, No. 2.) 5, Managing muscle-invasive bladder cancer. Available from: **https://www.ncbi.nlm.nih.gov/books/NBK356289/**
[6] Krishna SR, Konety BR. Current concepts in the management of muscle invasive bladder cancer. Indian J Surg Oncol. 2017 Mar;8(1):74-81. doi: 10.1007/s13193-016-0586-1. Epub 2016 Dec 15. PMID: 28127187; PMCID: PMC5236024.

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