News Release

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Results from Phase 2 THOR-2 Study Show Improved Rates of Recurrence-Free Survival in Patients with High-Risk Non-Muscle-Invasive Bladder Cancer with Select Fibroblast Growth Factor Receptor Alterations Treated with BALVERSA® (erdafitinib) Versus Chemotherapy

Data from Cohort 1 of the Phase 2 THOR-2 study showed oral erdafitinib reduced the risk of disease recurrence or death compared with intravesical standard-of-care chemotherapy

MADRID, Spain, October 21, 2023 – The Janssen Pharmaceutical Companies of Johnson & Johnson today announced results from the Phase 2 randomized, open-label THOR-2 study evaluating BALVERSA® versus investigator choice of intravesical chemotherapy in patients with high-risk non-muscle-invasive bladder cancer (HR-NMIBC) and select fibroblast growth factor receptor (FGFR) alterations which recurred after Bacillus Calmette-Guérin (BCG) therapy. Data from Cohort 1 of the study were featured today in a Proffered Paper Late-Breaking Session (Abstract #LBA102) at the European Society for Medical Oncology (ESMO) 2023 Congress taking place October 20-24 in Madrid, Spain, and simultaneously published in *Annals of Oncology*.[1,2]

Of the 73 patients included in Cohort 1, 49 were randomized to BALVERSA® and 24 were randomized to chemotherapy. Oral erdafitinib reduced the risk of recurrence of disease or

death by 72 percent compared with intravesical chemotherapy in patients with high-risk resected papillary Ta/T1 NMIBC harboring FGFR mutations or fusions with recurrence after BCG treatment and who refused or were ineligible for radical cystectomy.

With a median follow-up of 13.4 months at the data cutoff, median recurrence-free survival (RFS) was not met in patients who received BALVERSA® and was 11.6 months for patients who received chemotherapy (Hazard Ratio [HR]=0.28; 95 percent Confidence Interval [CI], 0.13-0.62; nominal p=0.0008). The six-month RFS in patients randomized to BALVERSA® was 96 percent compared to 73 percent in those assigned to chemotherapy. The 12-month RFS in patients assigned to BALVERSA® was 77 percent compared to 41 percent in patients who received chemotherapy.

Grade 3 or 4 serious treatment-related adverse events (TRAEs) were observed in fifteen patients (31 percent) who received BALVERSA® and one patient (4 percent) randomized to chemotherapy. Fourteen patients (29 percent) assigned to BALVERSA® and zero patients who received intravesical chemotherapy had TRAEs that lead to discontinuation of treatment. Central serous retinopathy occurred in 19 patients (39 percent) who received BALVERSA® and resolved in 11 patients (58 percent).

"Patients with NMIBC who experience disease recurrence after BCG treatment have limited treatment options, and those eligible patients with FGFR alterations who received erdafitinib in the THOR-2 trial had far fewer recurrences against patients treated by the current standard of care," said James W.F. Catto*, Ph.D., Department of Oncology and Metabolism, University of Sheffield, Sheffield, UK and presenting author of the study. "Our findings underscore the importance of detecting certain genetic biomarkers to identify patients who may benefit from treatment with a targeted therapy like erdafitinib."

"Janssen's ongoing development of BALVERSA reinforces our commitment to bringing targeted, precision medicines to patients with FGFR-driven bladder cancer," said Kiran Patel, M.D., Vice President, Clinical Development, Solid Tumors, Janssen Research & Development, LLC. "These results support the importance of testing for FGFR in early-stage bladder cancer and potential benefit with BALVERSA in patients with high-risk non-muscle-invasive bladder cancer where disease progression and poor outcomes are common."

About THOR-2

THOR-2 (NCT04172675) is a Phase 2 randomized, open-label study evaluating BALVERSA® versus investigator choice of intravesical chemotherapy in participants with NMIBC who recurred after BCG therapy. Patients are categorized to one of three cohorts based on their disease presentation: patients with HR-NMIBC and a papillary tumour only, where early cancer cells are still confined within the innermost layer of the bladder lining (Cohort 1), patients with HR-NMIBC presenting as carcinoma in situ (CIS) with or without a concurrent papillary tumour (Cohort 2), or patients with intermediate-risk NMIBC presenting with papillary disease only (Cohort 3).Patients in Cohort 1 are randomized to receive either BALVERSA® or chemotherapy (mitomycin C or gemcitabine) in a 2:1 ratio and all patients in Cohorts 2 and 3 will receive BALVERSA®. The Cohort 1 primary endpoint is RFS; secondary endpoints include RFS at six- and 12-months, time to progression, overall survival, plasma concentration of BALVERSA® and number of patients with adverse events. The study consists of screening period, treatment phase, follow-up phase and long-term extension phase.

About BALVERSA®

BALVERSA® (erdafitinib) is a once-daily, oral FGFR kinase inhibitor that received accelerated approval in 2019 for the treatment of adults with locally advanced or metastatic urothelial carcinoma (mUC) which has susceptible FGFR3 or FGFR2 genetic alterations and who have progressed during or following at least one line of prior platinum-containing chemotherapy, including within 12 months of neoadjuvant or adjuvant platinum-containing chemotherapy. Patients are selected for therapy based on an FDA-approved companion diagnostic for BALVERSA®. Information on FDA-approved tests for the detection of FGFR genetic alterations in urothelial cancer is available at: http://www.fda.gov/CompanionDiagnostics.[3]

In addition to the Phase 2 THOR-2 study, BALVERSA® is being studied in the Phase 3 THOR (NCT03390504) study comparing BALVERSA® in two cohorts; BALVERSA® versus standard of care chemotherapy (investigators choice of docetaxel or vinflunine) after at least one line of treatment including an anti-programmed death (ligand) 1 (PD-[L]1) agent (Cohort 1); and BALVERSA® compared to pembrolizumab after one prior treatment not containing an anti-PD-(L)1 agent (Cohort 2) in patients with metastatic or unresectable urothelial carcinoma, with selected FGFR genetic alterations, who showed disease progression during or after one or two prior lines of treatment.[4,5]

In August 2023, Janssen submitted a Supplemental New Drug Application to the U.S. Food and Drug Administration seeking the full approval of BALVERSA® based upon data from Cohort

1 Phase 3 THOR study. The Company also submitted a marketing authorization application to the European Medicines Agency in September 2023.

In 2008, Janssen Pharmaceutica NV entered into an exclusive worldwide license and collaboration agreement with Astex Pharmaceuticals to develop and commercialize BALVERSA®.

For more information, visit www.BALVERSA.com.

About High-Risk Non-Muscle-Invasive Bladder Cancer

High-risk non-muscle-invasive bladder cancer (HR-NMIBC) is a type of non-invasive bladder cancer that is more likely to recur or spread beyond the lining of the bladder, called the urothelium, and progress to invasive bladder cancer compared to low-risk NMIBC.[6,7] HR-NMIBC makes up 15–44 percent of patients with NMIBC and is characterized by a high-grade, large tumor size, presence of multiple tumors, and CIS. Radical cystectomy is currently recommended for NMIBC patients who fail BCG therapy, with over 90 percent cancer-specific survival if performed before muscle-invasive progression.[8,9] Given that NMIBC typically affects older patients, many may be unwilling or unfit to undergo radical cystectomy.[10] The high rates of recurrence and progression can pose significant morbidity and distress for these patients.[9,11]

BALVERSA® IMPORTANT SAFETY INFORMATION[12]

WARNINGS AND PRECAUTIONS

Ocular Disorders – BALVERSA® can cause ocular disorders, including central serous retinopathy/retinal pigment epithelial detachment (CSR/RPED) resulting in visual field defect.

CSR/RPED was reported in 25% of patients treated with BALVERSA®, with a median time to first onset of 50 days. Grade 3 CSR/RPED, involving central field of vision, was reported in 3% of patients. CSR/RPED resolved in 13% of patients and was ongoing in 13% of patients at the study cutoff. CSR/RPED led to dose interruptions and reductions in 9% and 14% of patients, respectively, and 3% of patients discontinued BALVERSA®. Dry eye symptoms occurred in 28% of patients during treatment with BALVERSA® and were Grade 3 in 6% of patients. All patients should receive dry eye prophylaxis with ocular demulcents as needed.

Perform monthly ophthalmological examinations during the first 4 months of treatment and every 3 months afterwards, and urgently at any time for visual symptoms. Ophthalmological examination should include assessment of visual acuity, slit lamp examination, fundoscopy, and optical coherence tomography. Withhold BALVERSA® when CSR occurs and permanently discontinue if it does not resolve within 4 weeks or if Grade 4 in severity. For ocular adverse reactions, follow the dose modification guidelines *[see Dosage and Administration (2.3)].*

Hyperphosphatemia and Soft Tissue Mineralization – BALVERSA® can cause hyperphosphatemia leading to soft tissue mineralization, cutaneous calcinosis, non-uremic calciphylaxis and vascular calcification. Increases in phosphate levels are a pharmacodynamic effect of BALVERSA® *[see Pharmacodynamics (12.2)].* Hyperphosphatemia was reported as an adverse reaction in 76% of patients treated with BALVERSA®. The median onset time for any grade event of hyperphosphatemia was 20 days (range: 8–116) after initiating BALVERSA®. Thirty-two percent of patients received phosphate binders during treatment with BALVERSA®. Cutaneous calcinosis, non-uremic calciphylaxis and vascular calcification have been observed in 0.3% of patients treated with BALVERSA®.

Monitor for hyperphosphatemia throughout treatment. In all patients, restrict phosphate intake to 600-800 mg daily. If serum phosphate is above 7.0 mg/dL, consider adding an oral phosphate binder until serum phosphate level returns to <5.5 mg/dL. Withhold, dose reduce, or permanently discontinue BALVERSA® based on duration and severity of hyperphosphatemia *[see Dosage and Administration (2.3), Table 2: Dose Modifications for Adverse Reactions]*.

Embryo-Fetal Toxicity – Based on the mechanism of action and findings in animal reproduction studies, BALVERSA® can cause fetal harm when administered to a pregnant woman. In a rat embryo-fetal toxicity study, erdafitinib was embryotoxic and teratogenic at exposures less than the human exposures at all doses studied. Advise pregnant women of the potential risk to the fetus. Advise female patients of reproductive potential to use effective contraception during treatment with BALVERSA® and for one month after the last dose. Advise male patients with female partners of reproductive potential to use effective contraception during treatment with BALVERSA® and for one month after the last dose *[see Use in Specific Populations (8.1, 8.3) and Clinical Pharmacology (12.1)]*.

Most common adverse reactions including laboratory abnormalities ≥20%:
Phosphate increased (76%), stomatitis (56%), fatigue (54%), creatinine increased (52%), diarrhea (47%), dry mouth (45%), nail disorder (45%), alanine aminotransferase increased (41%), alkaline phosphatase increased (41%), sodium decreased (40%), decreased appetite (38%), albumin decreased (37%), dysgeusia (37%), hemoglobin decreased (35%), dry skin (34%), aspartate aminotransferase increased (30%), magnesium decreased (30%), dry eye (28%), alopecia (26%), palmar-plantar erythrodysesthesia syndrome (26%), constipation (28%), phosphate decreased (24%), abdominal pain (23%), calcium increased (22%), nausea (21%), and musculoskeletal pain (20%). The most common Grade 3 or greater adverse reactions (>1%) were stomatitis (9%), nail dystrophy*, palmar-plantar erythrodysesthesia syndrome (6%), paronychia (3%), nail disorder (10%), keratitis†, and hyperphosphatemia (1%).

*Included within nail disorder. †Included within dry eye.

- An adverse reaction with a fatal outcome in 1% of patients was acute myocardial infarction.
- Serious adverse reactions occurred in 41% of patients, including eye disorders (10%).
- Permanent discontinuation due to an adverse reaction occurred in 13% of patients. The most frequent reasons for permanent discontinuation included eye disorders (6%).
- Dosage interruptions occurred in 68% of patients. The most frequent adverse reactions requiring dosage interruption included hyperphosphatemia (24%), stomatitis (17%), eye disorders (17%), and palmar-plantar erythrodysesthesia syndrome (8%).
- Dose reductions occurred in 53% of patients. The most frequent adverse reactions for dose reductions included eye disorders (23%), stomatitis (15%), hyperphosphatemia (7%), palmar-plantar erythrodysesthesia syndrome (7%), paronychia (7%), and nail dystrophy (6%).

Drug Interactions

- Moderate CYP2C9 or strong CYP3A4 Inhibitors: Consider alternative agents or monitor closely for adverse reactions. (7.1)
- Strong CYP2C9 or CYP3A4 inducers: Avoid concomitant use with BALVERSA®. (7.1)
- Moderate CYP2C9 or CYP3A4 inducers: Increase BALVERSA® dose up to 9 mg. (7.1)
- Serum phosphate level-altering agents: Avoid concomitant use with agents that can alter serum phosphate levels before the initial dose modification period. (2.3, 7.1)
- CYP3A4 substrates: Avoid concomitant use with sensitive CYP3A4 substrates with narrow

therapeutic indices. (7.2)

- OCT2 substrates: Consider alternative agents or consider reducing the dose of OCT2 substrates based on tolerability. (7.2)
- P-gp substrates: Separate BALVERSA® administration by at least 6 hours before or after administration of P-gp substrates with narrow therapeutic indices. (7.2)

Use in Specific Populations

Lactation – Because of the potential for serious adverse reactions from erdafitinib in a breastfed child, advise lactating women not to breastfeed during treatment with BALVERSA® and for one month following the last dose.

Please see the full Prescribing Information for BALVERSA®.

About the Janssen Pharmaceutical Companies of Johnson & Johnson

At Janssen, we're 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: Oncology, Immunology, Neuroscience, Cardiovascular, Pulmonary Hypertension, and Retina.

Learn more at www.janssen.com. Follow us at @JNJInnovMed and @JanssenUS. Janssen Research & Development, LLC and Janssen Biotech, Inc. 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 BALVERSA® (erdafitinib). 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; competition, including technological advances, new products and patents attained by competitors; challenges to patents; 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 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.

*Dr. Catto has not been paid for any media work.

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[1] Catto J, et al. THOR-2 Cohort 1: Results of Erdafitinib (Erda) vs Intravesical Chemotherapy (Chemo) in Patients (Pts) With High-Risk Non–Muscle-Invasive Bladder Cancer (HR NMIBC) With Select Fibroblast Growth Factor Receptor Alterations (FGFRalt) Who Received Prior Bacillus Calmette-Guérin (BCG) Treatment. 2023 European Society for Medical Oncology Congress. Presented at the 2023 European Society for Medical Oncology Congress.
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[10] Guancial EA, et al. Bladder cancer in the elderly patient: challenges and solutions. *Clin Interv Aging.* 2015; 10: 939–949.

[11] Chamie K, et al. Recurrence of high-risk bladder cancer: A population-based analysis. *Cancer.* 2013. 119(17): 3219–3227.
[12] BALVERSA Prescribing Information.