



News Release

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Janssen Submits Supplemental New Drug Application to the U.S. Food and Drug Administration Seeking Full Approval of BALVERSA® (erdafitinib) for the Treatment of Patients with Locally Advanced or Metastatic Urothelial Carcinoma and Selected Fibroblast Growth Factor Receptor Gene Alterations

Submission Based on Confirmatory Data from Cohort 1 of the Phase 3 THOR Study, Which Showed a 36 Percent Reduction in the Risk of Death in Patients Treated with BALVERSA® Versus Chemotherapy

RARITAN, N.J., August 28, 2023 – The Janssen Pharmaceutical Companies of Johnson & Johnson today announced the submission of a supplemental New Drug Application (sNDA) to the U.S. Food and Drug Administration (FDA) seeking full approval of BALVERSA® (erdafitinib), a kinase inhibitor, for the treatment of adult patients with locally advanced or metastatic urothelial carcinoma (mUC) that has susceptible fibroblast growth factor receptor (FGFR)3 genetic alterations, and progressed during or following at least one line of a programmed death receptor-1 (PD-1) or programmed death-ligand 1 (PD-L1) inhibitor in the locally advanced or metastatic setting or within 12 months of neoadjuvant or adjuvant therapy.¹

BALVERSA® received Breakthrough Therapy Designation from the U.S. FDA in 2018 and received [accelerated approval](#) in 2019 for the treatment of adults with locally advanced or 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. The sNDA submission for BALVERSA® is intended to satisfy the regulatory requirements to confirm the clinical benefit of BALVERSA® based on the randomized data from Cohort 1 of the Phase 3 THOR study.²

“BALVERSA continues to generate promising clinical findings for patients with FGFR-altered metastatic urothelial cancer, who often face poor disease outcomes,” said Peter Lebowitz, M.D., Ph.D., Global Therapeutic Area Head, Oncology, Janssen Research & Development, LLC. “Through the ongoing development of this targeted therapy, we are committed to transforming bladder cancer treatment to positively impact the lives of patients.”

The sNDA is based upon data from Cohort 1 of the randomized, controlled, open-label, multicenter Phase 3 THOR ([NCT03390504](#)) study evaluating the efficacy and safety of BALVERSA®. The study met its primary endpoint of overall survival (OS), with patients who received BALVERSA® achieving a median OS of over one year at the prespecified interim analysis data cutoff.²

As the interim results met the predefined criteria for superiority of treatment with BALVERSA® over chemotherapy, the independent data safety monitoring committee recommended that the study be stopped, and that patients randomized to chemotherapy be offered the opportunity to cross over to BALVERSA®. The safety profile of BALVERSA® observed in THOR was consistent with the known safety profile of BALVERSA® in mUC. Results from Cohort 1 were [presented](#) in a Late-Breaking Presentation Session (Abstract # [LBA4619](#)) at the 2023 [American Society of Clinical Oncology](#) Annual Meeting.³

The current full prescribing information is available at www.BALVERSA.com.

About THOR

THOR ([NCT03390504](#)) is a Phase 3 randomized, open-label, multicenter study evaluating the efficacy and safety of BALVERSA®. All patients included in the study had metastatic or unresectable UC, with selected FGFR genetic alterations, and showed disease progression during or after one or two prior lines of treatment. The study compared 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). The trial consists of screening, a treatment phase (from randomization until disease progression, intolerable toxicity, withdrawal of consent or decision by investigator to discontinue treatment) and a post-treatment follow-up (from end-of-treatment to participant's death, withdraws consent, lost to follow-up study completion for the respective cohort, whichever comes first). A long-term extension period is planned for after the clinical cutoff date is achieved for the final analysis of each cohort for patients who continue to benefit from the study intervention. The primary endpoint of the study is OS; progression free survival (PFS), objective response rate (ORR), duration of response (DOR), patient-reported outcomes, safety and pharmacokinetics (PK) are secondary endpoints. Results from Cohort 1 were presented at the 2023 ASCO Annual Meeting earlier this year; findings from Cohort 2 will be presented at an upcoming medical meeting.^{2,3}

About BALVERSA[®]

BALVERSA[®] (erdafitinib) is a once-daily, oral FGFR kinase inhibitor that is approved by the U.S. FDA for the treatment of adults with locally advanced or mUC that have susceptible FGFR3 or FGFR2 genetic alterations and have progressed during or following at least one line of 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>. This indication is approved under accelerated approval based on tumor response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.^{1,4}

In addition to the Phase 3 THOR study, BALVERSA[®] is being studied in the Phase 2 THOR-2/BLC2003 study ([NCT04172675](https://clinicaltrials.gov/ct2/show/study/NCT04172675)) study examining BALVERSA[®] versus investigator choice of intravesical chemotherapy in participants who received Bacillus Calmette-Guérin and recurred with high risk non-muscle-invasive bladder cancer and the Phase 1 study ([NCT05316155](https://clinicaltrials.gov/ct2/show/study/NCT05316155)) investigating BALVERSA[®] in patients with non-muscle invasive or muscle invasive bladder cancer with select FGFR alterations, given via the TARIS intravesical drug delivery system (TAR-210), which is designed to release BALVERSA[®] in the bladder to treat localized bladder cancer, while reducing systemic toxicities.^{1,2,5}

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 Urothelial Carcinoma

Urothelial carcinoma, also known as transitional cell carcinoma, starts in the innermost lining of the bladder.⁶ It is the most common and frequent form of bladder cancer, representing more than 90 percent of all bladder cancers.⁷ Metastatic or unresectable disease is identified in approximately 20 percent of patients presenting with urothelial cancer, or an estimated five to eight percent of all bladder cancers. Approximately one in five patients (20 percent) diagnosed with mUC have an FGFR genetic alteration.^{8,9} Fibroblast growth factor receptors are a family of receptor tyrosine kinases that can be activated by genetic alterations in a variety of tumor types, and these alterations may lead to increased tumor cell growth and survival.^{6,10,11,12,13} Select FGFR genetic alterations can be detected through an FDA-approved companion diagnostic. The five-year survival rate for patients with Stage IV metastatic bladder cancer that has spread to distant parts of the body is currently eight percent.¹⁴

BALVERSA® IMPORTANT SAFETY INFORMATION

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 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: Cardiovascular, Metabolism & Retina; Immunology; Infectious Diseases & Vaccines; Neuroscience; Oncology; and Pulmonary Hypertension.

Learn more at www.janssen.com. Follow us at [@JanssenGlobal](#) and [@JanssenUS](#). Janssen Research & Development, LLC, and Janssen Biotech, Inc., are part of the Janssen Pharmaceutical Companies of Johnson & Johnson.

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., 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 BALVERSA Prescribing Information.

² Clinicaltrials.gov. A Study of Erdafitinib in Participants With Advanced Solid Tumors and Fibroblast Growth Factor Receptor (FGFR) Gene Alterations. <https://www.clinicaltrials.gov/ct2/show/NCT04083976>. Accessed May 2023.

³ ASCO Publications. Phase 3 THOR study: Results of erdafitinib (erda) versus chemotherapy (chemo) in patients (pts) with advanced or metastatic urothelial cancer (mUC) with select fibroblast growth factor receptor alterations (FGFRalt). Available at: https://ascopubs.org/doi/10.1200/JCO.2023.41.17_suppl.LBA4619

⁴ U.S. Food & Drug Administration. FDA grants accelerated approval to erdafitinib for metastatic urothelial carcinoma. Available at: <https://www.fda.gov/drugs/resources-information-approved-drugs/fda-grants-accelerated-approval-erdafitinib-metastatic-urothelial-carcinoma>. Accessed September 2021.

⁵ Clinicaltrials.gov. A Study of Erdafitinib in Participants with Metastatic or Locally Advanced Urothelial Cancer. <https://clinicaltrials.gov/ct2/show/NCT03473743>. Accessed May 2023.

⁶ American Cancer Society. "What is Bladder Cancer." Available at <https://www.cancer.org/cancer/bladder-cancer/about/what-is-bladder-cancer.html>. Accessed May 2023.

⁷ National Cancer Institute. "Bladder Cancer Treatment (PDQ®)—Health Professional Version". Available at: https://www.cancer.gov/types/bladder/hp/bladder-treatment-pdq#link/21_toc. Accessed May 2023.

⁸ Tomlinson et al. FGFR3 protein expression and its relationship to mutation status and prognostic variables in bladder cancer. *J Pathol.* 2007;213(1):91-98.

⁹ De Santis M, et al. *J Clin Oncol.* 2011;30:191-199.

¹⁰ Helsten et al. The FGFR Landscape in Cancer: Analysis of 4,853 Tumors by Next-Generation Sequencing. *Clin Cancer Res.* 2015;22(1):259-267.

¹¹ Eisenhauer E.A. et al. New response evaluation criteria in solid tumours: Revised RECIST guideline (version 1.1). *European Journal of Cancer.* 2009. 45: 228 – 247

¹² Janssen Pharmaceuticals, Inc. Data on file.

¹³ U.S. and World Population Clock. <https://www.census.gov/popclock/>. Accessed May 2023.

¹⁴ Bladder Cancer: Statistics. Available at: <https://www.cancer.net/cancer-types/bladder-cancer/statistics>. Accessed May 2023.