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U.S. Food and Drug Administration Grants Full Approval for BALVERSA® to Treat Locally Advanced or Metastatic Bladder Cancer with Select Genetic Alterations

BALVERSA® is the First and Only Targeted Therapy for Patients with Locally Advanced or Metastatic Urothelial Carcinoma and Susceptible Fibroblast Growth Factor Receptor Alterations

Phase 3 THOR Study Showed a 36 Percent Reduction in the Risk of Death with BALVERSA® Versus Chemotherapy in Patients

Data were featured at the European Society for Medical Oncology (ESMO) 2023 Congress and in The New England Journal of Medicine

RARITAN, N.J., JANUARY 19, 2024 – Johnson & Johnson announced today that the U.S. Food and Drug Administration (FDA) approved a supplemental New Drug Application (sNDA) for BALVERSA® (erdafitinib) for the treatment of adult patients with locally advanced or metastatic urothelial carcinoma (mUC) with susceptible fibroblast growth factor receptor 3 (FGFR3) genetic alterations whose disease has progressed on or after at least one line of prior systemic therapy. BALVERSA® is not recommended for the treatment of patients who are eligible for and have not received prior PD-1 or PD-L1 inhibitor therapy. This FDA action converts the April 2019 accelerated approval of BALVERSA® to a full approval based on the clinical and overall survival benefit observed in the Phase 3 THOR study. BALVERSA® is the first oral FGFR kinase inhibitor to be approved, and the first and only targeted treatment for patients with mUC and FGFR alterations.

Approximately 20 percent of patients with mUC have FGFR3 genetic alterations. After one or more lines of systemic therapy, including a checkpoint inhibitor, these patients generally have a poor prognosis with few available treatment options. This approval is based on results from Cohort 1 of the randomized, controlled, open-label, multicenter Phase 3 THOR study (NCT03390504) confirming the clinical benefit of BALVERSA® in extending overall survival (OS) compared to chemotherapy in the second-line setting. Results from the study showed a 36 percent reduction in the risk of death with BALVERSA® versus chemotherapy in patients previously treated with a PD-1 or PD-(L)1 inhibitor, with those in the BALVERSA® arm living a median of over four months longer (Hazard Ratio (HR) 0.64; [95 percent Confidence Interval (CI), 0.47-0.88]; p=0.0050).[1]

“Based on results from randomized Phase 3 data, BALVERSA continues to demonstrate the promise of targeted therapy in the treatment of patients with advanced bladder cancer,” said Kiran Patel, M.D., Vice President, Clinical Development, Solid Tumors, Johnson & Johnson Innovative Medicine. “This important milestone reinforces our commitment to advance innovative, precision therapies in oncology and confirm the role of targeted therapy in the treatment of bladder cancer.”

Warnings and Precautions in the U.S. Prescribing Information include ocular disorders, hyperphosphatemia and embryo-fetal toxicity. The most common (>20%) adverse reactions, including laboratory abnormalities, were increased phosphate, nail disorders, stomatitis, diarrhea, increased creatinine, increased alkaline phosphate, increased alanine aminotransferase, decreased hemoglobin, decreased sodium, increased aspartate aminotransferase, fatigue, dry mouth, dry skin, decreased phosphate, decreased appetite, dysgeusia, constipation, increased calcium, dry eye, palmar-plantar erythrodysesthesia syndrome, increased potassium, alopecia, and central serous retinopathy.[2]

Johnson & Johnson is offering BALVERSA® and associated patient services through a single-source specialty pharmacy provider, US Bioservices. This model is part of the Company’s ongoing commitment to provide high-quality products, services, access, and support to healthcare professionals and patients.

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 (investigator’s choice of docetaxel or

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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, or 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 in a Late-Breaking Presentation Session (Abstract #LBA4619) at the 2023 American Society of Clinical Oncology Annual Meeting.[1] In June 2023, based on the recommendation of the independent data safety monitoring committee, the THOR study was stopped at the interim analysis for efficacy and all patients randomized to chemotherapy were offered the opportunity to cross over to BALVERSA®. Results from Cohort 1 and Cohort 2 of the confirmatory, Phase 3, randomized study were presented at ESMO 2023 (Abstract #2359O), and results of Cohort 1 were published in the *New England Journal of Medicine* in November 2023.

About BALVERSA®

BALVERSA® (erdafitinib) is a once-daily, oral FGFR kinase inhibitor indicated for the treatment of adult patients with locally advanced or metastatic urothelial carcinoma (mUC) with susceptible fibroblast growth factor receptor 3 (FGFR3) genetic alterations whose disease progressed on or after at least one line of prior systemic therapy. BALVERSA® is not recommended for the treatment of patients who are eligible for and have not received prior PD-1 or PD-(L)1 inhibitor therapy.[2] 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.

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.[3]

The Company submitted a marketing authorization application to the European Medicines Agency in September 2023 for BALVERSA® as a treatment for adult patients with FGFR3-altered, locally advanced unresectable or metastatic urothelial carcinoma that has progressed following therapy with a PD-(L)1 inhibitor.

In 2008, Janssen Pharmaceuticals 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.[4] It is the most common form of bladder cancer, representing more than 90 percent of all bladder cancers.[5] Metastatic or unresectable disease is identified in approximately 20 percent of patients presenting with urothelial cancer, and 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.[6,7] 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.[6,8,9,10,11] 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.[12]

BALVERSA® IMPORTANT SAFETY INFORMATION

WARNING 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 occurred in 22% of patients treated with BALVERSA, with a median time to first onset of 46 days. In 104 patients with CSR, 40% required dose interruptions and 56% required dose reductions; 2.9% of BALVERSA-treated patients required permanent discontinuation for CSR. Of the 24 patients who restarted BALVERSA after dose interruption with or without dose reduction, 67% had recurrence and/or worsening of CSR after restarting. CSR was ongoing in 41% of the 104 patients at the time of last evaluation.

Dry eye symptoms occurred in 26% of BALVERSA®-treated 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 or permanently discontinue BALVERSA® based on severity and/or ophthalmology exam findings *[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*

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Pharmacodynamics (12.2)]. Increased phosphate occurred in 73% of BALVERSA®-treated patients. The median onset time of increased phosphate was 16 days (range: 8–421) after initiating BALVERSA®. Twenty-four percent of patients received phosphate binders during treatment with BALVERSA®. Vascular calcification was observed in 0.2% of patients treated with BALVERSA®.

Monitor for hyperphosphatemia throughout treatment. In all patients, restrict phosphate intake to 600-800 mg daily and avoid concomitant use of agents that may increase serum phosphate levels. If serum phosphate is above 7.0 mg/dL, consider adding an oral phosphate binder until serum phosphate level returns to <7.0 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 female. In a rat embryo-fetal toxicity study, erdafitinib caused malformations and embryo-fetal death at maternal exposures that were less than the human exposures at the maximum human recommended dose. Advise pregnant patients 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)]*.

Adverse Reactions

In this pooled safety population of 479 patients who received BALVERSA®, the median duration of treatment was 4.8 months (range: 0.1 to 43 months). The most common (>20%) adverse reactions were: increased phosphate, nail disorders, stomatitis, diarrhea, increased creatinine, increased alkaline phosphatase, increased alanine aminotransferase, decreased hemoglobin, decreased sodium, increased aspartate aminotransferase, fatigue, dry mouth, dry skin, decreased phosphate, decreased appetite, dysgeusia, constipation, increased calcium, dry eye, palmar-plantar erythrodysesthesia syndrome, increased potassium, alopecia, and central serous retinopathy.

In Cohort 1 of the BLC3001 study:

- Serious adverse reactions occurred in 41% of patients who received BALVERSA®. Serious reactions in >2% of patients included urinary tract infection (4.4%), hematuria (3.7%), hyponatremia (2.2%), and acute kidney injury (2.2%). Fatal adverse reactions occurred in 4.4% of patients who received BALVERSA®, including sudden death (1.5%), pneumonia (1.5%), renal failure (0.7%), and cardiorespiratory arrest (0.7%).

- Permanent discontinuation of BALVERSA® due to an adverse reaction occurred in 14% of patients. Adverse reactions which resulted in permanent discontinuation of BALVERSA® in >2% of patients included nail disorders (3%) and eye disorders (2.2%).

- Dosage interruptions of BALVERSA® due to an adverse reaction occurred in 72% of patients. Adverse reactions which required dosage interruption in >4% of patients included nail disorders (22%), stomatitis (19%), eye disorders (16%), palmar-plantar erythrodysesthesia syndrome (15%), diarrhea (10%), hyperphosphatemia (7%), increased aspartate aminotransferase (6%), and increased alanine aminotransferase (5%).

- Dose reductions of BALVERSA® due to an adverse reaction occurred in 69% of patients. Adverse reactions which required dose reductions in >4% of patients included nail disorders (27%), stomatitis (19%), eye disorders (17%), palmar-plantar erythrodysesthesia syndrome (12%), diarrhea (7%), dry mouth (4.4%), and hyperphosphatemia (4.4%).

- Clinically relevant adverse reactions in <15% of patients who received BALVERSA® included nausea (15%), pyrexia (15%), epistaxis (13%), vomiting (10%), and arthralgia (10%).

Drug Interactions

- Moderate CYP2C9 or Strong CYP3A4 Inhibitors: Consider alternative agents; however, if co-administration is unavoidable monitor closely for adverse reactions. (7.1)
- Strong CYP3A4 inducers: Avoid co-administration use with BALVERSA®. (7.1)
- Moderate CYP3A4 inducers: If co-administration is required at the start of BALVERSA® treatment, administer BALVERSA® at a dose of 9 mg daily. (7.1)
- Serum phosphate level-altering agents: Avoid co-administration use with agents that can alter serum phosphate levels before the initial dose modification period based on serum phosphate levels. (2.3, 7.1)
- P-gp substrates: If co-administration is unavoidable 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 patients not to breastfeed during treatment with BALVERSA® and for one month following the last dose.

Please click here to see full BALVERSA® Prescribing Information.

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

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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 and Janssen Biotech, Inc. are both 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®. 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.

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