News Release

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Janssen Presents Results from Phase 1b/2 NORSE Study in Patients with Metastatic or Locally Advanced Urothelial Carcinoma Treated with BALVERSA® (erdafitinib) in Combination with Cetrelimab, a PD-1 Inhibitor

Oral presentation at ESMO Annual Congress 2021 – featured in a late-breaking abstract – reports efficacy and safety of BALVERSA® in combination with a PD-1 inhibitor in bladder cancer

September 17, 2021 (RARITAN, N.J.) – The Janssen Pharmaceutical Companies of Johnson & Johnson today announced results from the Phase 1b/2 NORSE (NCT03473743) study evaluating BALVERSA® (erdafitinib) in combination with cetrelimab, an anti-programmed cell death protein 1 (PD-1) monoclonal antibody, compared to BALVERSA® monotherapy in patients with locally advanced or metastatic urothelial carcinoma (mUC) with fibroblast growth factor receptor (FGFR)3 or FGFR2 genetic alterations who are ineligible for cisplatin, a current standard of care treatment for mUC. The results were highlighted in an oral presentation at the European Society for Medical Oncology (ESMO) Annual Congress 2021 virtual meeting on Friday, September 17 (Abstract #LBA 27).[1]

Preliminary findings suggest robust clinical activity and depth of response in patients treated with BALVERSA® in combination with cetrelimab.[1] The overall safety of treatment with BALVERSA® in combination with cetrelimab was generally consistent with BALVERSA® monotherapy and aligned with the known safety profile of approved anti–PD-1 therapies.[1]

At the time of analysis, the investigator-assessed objective response rate (ORR) in 19 patients treated with BALVERSA® in combination with cetrelimab was 68 percent (95 percent confidence interval [CI]; 43-87), of which 21 percent (n=4) were complete responses (CR) and 47 percent were partial responses (PR).[1] The disease control rate (DCR) was 90 percent (95 percent CI; 67-99) for evaluable patients using the Response Evaluation Criteria in Solid Tumors Version 1.1* (RECIST v1.1) criteria.[1] The ORR in 18 patients treated with BALVERSA® monotherapy was 33 percent (95 percent CI; 13-59), in which one patient showed a CR and 28 percent (n=5) were partial responses. The DCR was 100 percent (95 percent CI; 82-100).[1]

"PD-1 inhibitors have become treatment options for many types of solid tumors, including bladder cancer. Now, as we learn more about the genetic factors that impact treatment outcomes, we are exploring new treatment approaches that may help patients with specific mutations, including FGFR-alterations and fusions," said Thomas Powles, MRCP, M.D., Professor of Uro-Oncology, Director of Barts Cancer Institute, London and principal study investigator.[†] "With this combination of erdafitinib and cetrelimab, we aim to change the tumor microenvironment to make it more receptive to PD-1 intervention."

Fibroblast growth factor receptors are a family of receptor tyrosine kinases that can be activated by genetic alterations in a variety of tumor types, potentially leading to increased tumor cell growth and survival.[2] Approximately 20 percent of patients diagnosed with mUC have an FGFR genetic alteration.[3,4] A current standard of care for mUC is cisplatin-based chemotherapy, however, more than 50 percent of patients with mUC may be ineligible for cisplatin treatment, underscoring a need for new treatment options.[5] Alternative options for patients with newly diagnosed mUC include different chemotherapy regimens or PD-1 inhibitors, which enhance T-cell immune responses against the tumor cells.[6]

The findings presented at ESMO build upon the growing set of BALVERSA® data. In 2019 the U.S. Food and Drug Administration (FDA) granted accelerated approval to BALVERSA®, with a companion diagnostic, as a once-daily oral FGFR kinase inhibitor for patients with mUC that have susceptible FGFR3 and 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. 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.[7]

The safety profile of BALVERSA® in combination with cetrelimab (n=24) was generally similar to that of BALVERSA® monotherapy (n=24), with the most common treatment-emergent adverse events (AEs) being hyperphosphatemia (BALVERSA® in combination with cetrelimab vs

BALVERSA® monotherapy, 58 percent vs 58 percent), stomatitis (54 percent vs 63 percent), diarrhea (42 percent vs 50 percent), dry mouth (58 percent vs 21 percent), dry skin (38 percent vs 21 percent) and anemia (25 percent vs 25 percent).[1] Grade 3-4 AEs occurred in 12 patients (50 percent) in the BALVERSA® in combination with cetrelimab arm and 9 patients (38 percent) in the BALVERSA® arm.[1] In the BALVERSA® in combination with cetrelimab arm, the most frequent Grade 3-4 AEs were stomatitis (n=3 [12.5 percent]), lipase increased (n=3 [12.5 percent]), and fatigue (n=2 [8.3 percent]); in the BALVERSA® arm, these were anemia (n=3 patients [12.5 percent]) and general physical health deterioration (n=3 [12.5 percent]).[1]

"As the first targeted treatment approved for patients with locally advanced or metastatic bladder cancer and FGFR3 or FGFR2 genetic alterations after platinum-based chemotherapy, we are encouraged by the data that continue to support the safety and efficacy of BALVERSA and its benefit for these patients with high unmet medical need. By investigating two active classes of drugs with BALVERSA and cetrelimab, our aim is to maximize the potential benefits of this combination approach for these patients," said Craig Tendler, M.D., Vice President, Late Development and Global Medical Affairs, Oncology, Janssen Research & Development, LLC. "The continued development of BALVERSA reflects Janssen's ongoing commitment to offer more personalized therapy approaches for patients with bladder cancer, a disease where there is considerable need for more effective treatment using innovative approaches."

*RECIST (version 1.1) refers to Response Evaluation Criteria in Solid Tumors, which is a standard way to measure how well solid tumors respond to treatment and is based on whether tumors shrink, remain the same or increase in size.[8]

About the NORSE Study[9]

NORSE (NCT03473743) is an open-label, Phase 1b/2 multicenter study of BALVERSA® in combination with cetrelimab in patients with locally advanced or metastatic urothelial cancer and FGFR3 or FGFR2 gene alterations. Participants enrolled in Phase 1b may have received any number of lines of prior therapy, and participants enrolled in Phase 2 had no prior systemic therapy for metastatic disease and are ineligible for cisplatin-based chemotherapy, currently the standard of care. Phase 1b established the recommended Phase 2 dose (RP2D) for BALVERSA® in combination with cetrelimab, and Phase 2 evaluates the safety and efficacy of the RP2D. The study is being conducted in three phases: screening phase, treatment phase and follow-up phase. Study evaluations include efficacy, pharmacokinetics, pharmacodynamics, immunogenicity, biomarkers and safety. Enrollment of the Phase 2 part of the NORSE study is currently ongoing.

About Urothelial Carcinoma

Urothelial carcinoma, also known as transitional cell carcinoma, starts in the innermost lining of the bladder.[10] It is the most common and frequent form of bladder cancer, representing more than 90 percent of all bladder cancers.[11] Approximately one in five patients (20 percent) diagnosed with mUC have an FGFR genetic alteration.[4,5] 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.[3] In the U.S. each year, it is estimated that up to 3,000 people with urothelial carcinoma will test positive for FGFR genetic alterations.[8,9,12,13] Fibroblast growth factor receptor 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 6 percent.[14]

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 metastatic urothelial carcinoma (mUC) that has susceptible FGFR3 or FGFR2 genetic alterations and has 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.[7,15]

BALVERSA® is being studied in multiple clinical trials including the Phase 3 THOR (NCT03390504) study evaluating BALVERSA® versus standard of care, consisting of chemotherapy (docetaxel or vinflunine) or anti-PD-1 agent pembrolizumab, in participants with advanced urothelial cancer and selected FGFR aberrations with disease progression following one prior line of therapy; the Phase 2 THOR-2/BLC2003 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 2 RAGNAR (NCT04083976) study assessing BALVERSA® in patients with advanced solid tumors and FGFR genetic alterations.[16,17,18]

In 2008, Janssen 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 Cetrelimab

Cetrelimab is a Janssen discovered and developed investigational programmed cell death receptor-1 (PD-1) monoclonal antibody being studied in the treatment of bladder cancer, prostate cancer, and multiple myeloma as a combination treatment. Cetrelimab is also being evaluated in multiple combination regimens across the Janssen oncology portfolio.

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 – 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®. Monitor for hyperphosphatemia and follow the dose modification guidelines when required *[see Dosage and Administration (2.2, 2.3)]*.

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%), onycholysis (41%), 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*, keratitis†, onycholysis* (10%), and hyperphosphatemia.

*Included within onycholysis. †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, Immunology, Infectious Diseases & Vaccines, Neuroscience, Oncology and Pulmonary Hypertension.

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

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[†]Dr. Powles has been a paid consultant to Janssen; he has not been paid for any media work.

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) and 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 and Janssen Biotech Inc. or any of the other Janssen Pharmaceutical Companies 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 January 3, 2021, including in the sections captioned "Cautionary Note Regarding Forward-Looking Statements" and "Item 1A. Risk Factors," and in the company's most recently filed Quarterly Report on Form 10-Q, and the company's subsequent 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 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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