**News Release**

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# Janssen Presents Initial Results from the Phase 2 RAGNAR Study of BALVERSA® (erdafitinib) in Patients with Advanced Solid Tumors with FGFR Alterations

*Data from RAGNAR, the largest tumor-agnostic study reported for a targeted therapy and the first to evaluate FGFR-driven malignancies, featured in oral presentation at the 2022 ASCO Annual Meeting*

**June 7, 2022 (CHICAGO) –** The Janssen Pharmaceutical Companies of Johnson & Johnson today announced initial results from the pivotal Phase 2 RAGNAR study evaluating the investigational use of BALVERSA® (erdafitinib), a fibroblast growth factor receptor (FGFR) kinase inhibitor, in patients with advanced solid tumors with prespecified FGFR alterations. At a planned interim analysis (IA), responses were observed across a variety of FGFR-driven solid tumors for patients who had exhausted standard treatment options prior to being treated with BALVERSA®.[1] These results will be featured in an oral presentation (Abstract #3007) today at the 2022 American Society of Clinical Oncology Annual Meeting.

RAGNAR (NCT04083976) is a Phase 2 clinical study designed to evaluate the efficacy and safety of BALVERSA® in patients with advanced or metastatic solid tumors and prespecified FGFR gene alterations, regardless of tumor location or histology (tumor-agnostic). The IA was based on 178 patients with 32 distinct solid tumor histologies.[1] Patients in the study were prospectively identified by local molecular testing or central next-generation

sequencing (NGS); the most common tumor types were cholangiocarcinoma (bile duct cancer) (n=31), high-grade glioma (tumor of the brain or spinal cord) (n=29), breast cancer (n=14), pancreatic cancer (n=13) and squamous non-small cell lung cancer (n=11).[1] The study also included tumors that occur less frequently in the real world such as salivary gland and parathyroid carcinomas (rare endocrine malignancies), as well as tumors of unknown primary origin.[1] Study participants were heavily pretreated, with 74.7 percent (n=133) having received two or more prior lines of therapy.[1]

The primary endpoint of the RAGNAR study is the overall response rate (ORR) as assessed by an independent review committee (IRC). At the IA data cutoff, IRC assessed an ORR of 29.2 percent (95 percent confidence interval [CI], 22.7-36.5) and a disease control rate (DCR) of 72.5 percent (95 percent CI, 65.3-78.9) for the overall tumor-agnostic patient population.[1] Investigators observed responses in 14 distinct tumor types. This included responses in hard-to-treat malignancies such as salivary gland cancer (100 percent ORR; treated n=5, responders n=5), pancreatic cancer (31 percent ORR; treated n=13, responders n=4) and glioblastoma (21 percent ORR; treated n=29, responders=6).[1] Investigators also observed an overall 7.1-month median duration of response (DOR) (95 percent CI, 5.5-9.3). At the data cutoff, 51.1 percent (n=24) of patients who had responded to treatment continued to show a response.[1] The primary analysis for all patients treated in this RAGNAR cohort, known as the broad panel cohort, is anticipated later this year.

The safety profile of BALVERSA® observed in RAGNAR was consistent with the known safety profile of BALVERSA® in metastatic urothelial carcinoma (mUC). Across tumor types, 44.9 percent of patients experienced adverse events of grade three or above.[1] Adverse events were manageable with supportive care and treatment interruptions or reductions, when necessary.[1] The discontinuation rate due to drug-related adverse events was 7.3 percent.[1]

"Diagnostic advances in the identification of FGFR gene alterations have opened the door to targeted, tumor-agnostic treatment approaches for patients," said Yohann Loriot, M.D., Ph.D., Institut Gustave Roussy and University of Paris-Saclay, and principal study investigator.‡ "Results from the RAGNAR study show that, through the targeted inhibition of FGFR receptors, we may be able to tailor treatment for patients with advanced FGFR-driven cancers, regardless of tumor location or histology."

In 2019, BALVERSA® was granted accelerated approval by the U.S. Food and Drug Administration (FDA) as a targeted therapy for adult patients with locally advanced or mUC with susceptible FGFR2 or FGFR3 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.[2]

"Janssen is committed to advancing precision medicine approaches for the treatment of patients with biomarker-driven cancers, an area of clear unmet need," said Kiran Patel, M.D., Vice President, Clinical Development, Solid Tumors, Janssen Research & Development, LLC. "RAGNAR, Janssen's first tumor-agnostic study, demonstrates our commitment to understand the biology of disease, identify new treatment pathways and improve patient outcomes. We look forward to progressing the development of BALVERSA for these patients and sharing additional updates on this program in the future."

**About FGFR Alterations**

Fibroblast growth factor receptors are a family of receptor tyrosine kinases that help cells grow, survive and multiply; FGFRs play a key role in several biological processes including tissue repair, inflammatory response and metabolism.[3,4,5] Fusions or mutations in the genes that control FGFR (known as FGFR1–4 alterations) may lead to the development and progression of certain cancers by increasing tumor cell growth and survival.[5] Patients with advanced, FGFR-driven solid tumors who have exhausted standard treatment options typically face a poor prognosis.

**About the RAGNAR Study**

RAGNAR (NCT04083976) is a Phase 2 clinical trial evaluating the safety and efficacy of BALVERSA® in patients with advanced solid tumors, regardless of cancer type or tumor location (tumor-agnostic), driven by FGFR1–4 alterations. Patients in the trial have progressed on or after at least one line of systemic therapy and have no alternative standard treatment options. Following screening by local molecular testing or central NGS, patients are enrolled in four separate cohorts: a broad panel cohort of patients with pathogenic FGFR mutations or gene fusions (tumor histologies evaluated include but are not limited to cholangiocarcinoma [bile duct cancer], high- and low-grade glioma [a tumor type occurring in the brain or spinal cord], breast, pancreatic, squamous and non-squamous non-small cell lung cancer, colorectal, endometrial, esophageal, salivary gland, ovarian, duodenal [cancer occurring in the first part of the small intestine], thyroid and cancer of

unknown primary origin); an exploratory cohort of patients with other FGFR mutations; a cholangiocarcinoma expansion cohort; and a pediatric cohort of patients ages 6 to 17 with FGFR alterations.[1]

The primary endpoint of RAGNAR is IRC-assessed ORR. Key secondary endpoints include investigator-assessed ORR, DOR, DCR, clinical benefit rate, progression free survival, overall survival and incidence and severity of adverse events.

**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 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.[2,6]

In addition to RAGNAR, BALVERSA® is being studied in 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 or two prior lines of therapy; and the randomized Phase 2 THOR-2 (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.[7,8]

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.

**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%), 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, & 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, Janssen Biotech, Inc. and Janssen Pharmaceutica NV are part of the Janssen Pharmaceutical Companies of Johnson & Johnson.

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‡Dr. Loriot has served as a 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). 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 Pharmaceutica N.V., 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 2, 2022, 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 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] Loriot et al. Tumor agnostic efficacy and safety of erdafitinib in patients (pts) with advanced solid tumors with prespecified fibroblast growth factor receptor alterations (FGFRalt) in RAGNAR: interim analysis (IA) results. ASCO 2022.

[2] BALVERSA Prescribing Information.

[3] Xie Y, Su N, Yang J, et al. FGF/FGFR signaling in health and disease. Signal Transduct Target Ther. 2020;5(1):181.

[4] Katoh M. Fibroblast growth factor receptors as treatment targets in clinical oncology. Nat Rev Clin Oncol. 2019;16(2):105-122.

[5] 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.

[6] 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 June 2022.

[7] Clinicaltrials.gov. A Study of Erdafitinib Compared With Vinflunine or Docetaxel or Pembrolizumab in Participants With Advanced Urothelial Cancer and Selected Fibroblast Growth Factor Receptor (FGFR) Gene Aberrations. https://clinicaltrials.gov/ct2/show/NCT03390504. Accessed June 2022.

[8] Clinicaltrials.gov. A Study of Erdafitinib Versus Investigator Choice of Intravesical Chemotherapy in Participants Who Received Bacillus Calmette-Guérin (BCG) and Recurred With High Risk Non-Muscle-Invasive Bladder Cancer (NMIBC). https://www.clinicaltrials.gov/ct2/show/NCT04172675?term=NCT04172675&draw=2&rank=1. Accessed June 2022.