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News Release

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Janssen Announces Erdafitinib Improved Overall Survival Versus Chemotherapy in Patients with Metastatic or Unresectable Urothelial Carcinoma and Selected Fibroblast Growth Factor Receptor Gene Alterations After Prior Anti-PD-(L)1 Treatment

Confirmatory data from Cohort 1 of the Phase 3 THOR study showed greater than four-month improvement in median overall survival in patients treated with erdafitinib versus chemotherapy[1]

BEERSE, Belgium, 5 June 2023 – The Janssen Pharmaceutical Companies of Johnson & Johnson today announced results from an interim analysis of Cohort 1 of the Phase 3 THOR study, evaluating treatment with erdafitinib versus chemotherapy in patients with metastatic or unresectable urothelial carcinoma (UC) and selected fibroblast growth factor receptor (FGFR) gene alterations who had received prior treatment with an anti-programmed death ligand 1 (PD-(L)1) agent.[1] In this cohort, the study met its primary endpoint of overall survival (OS) and reduced the risk of death by 36 percent.[1] These confirmatory data were featured in a Late-Breaking Presentation Session (Abstract #LBA4619) at the 2023 American Society of Clinical Oncology (ASCO) Annual Meeting, taking place in Chicago, from 2–6 June.

"These results represent the first data from a randomised, controlled trial evaluating erdafitinib for the treatment of patients with FGFR-altered urothelial carcinoma, who often experience poor disease outcomes," said Yohann Loriot†, M.D., Ph.D., Institut Gustave Roussy and University of Paris-Saclay, France, and principal study investigator. "The use of

erdafitinib in this setting supports recommendations for FGFR testing in all patients with metastatic urothelial cancer."

THOR (NCT03390504) is a Phase 3 randomised, open-label, multicentre study evaluating the efficacy and safety of erdafitinib.[1] Patients were categorised to one of two cohorts based on the type of prior therapy they had received: prior treatment with an anti-PD-(L)1 agent (Cohort 1) or prior treatment not containing an anti-PD-(L)1 agent (Cohort 2).[1] Patients in Cohort 1 were randomised to receive either erdafitinib or chemotherapy in a 1:1 ratio and patients in Cohort 2 were randomised to receive either erdafitinib or pembrolizumab in a 1:1 ratio.[1] 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.[1]

Results from the interim analysis of Cohort 1 included data inclusive of 266 patients where 136 patients were assigned to erdafitinib and 130 were randomised to chemotherapy.[1] Median follow-up was 15.9 months.[1] At the data cutoff on 15 January 2023, OS in patients who received erdafitinib was 12.1 months compared to 7.8 months in patients who received chemotherapy (Hazard Ratio (HR) 0.64; [95 percent Confidence Interval (CI), 0.47-0.88]; p=0.005).[1] Treatment with erdafitinib also showed an improvement in median PFS compared to chemotherapy of 5.6 months versus 2.7 months (HR 0.58; [95 percent CI, 0.44-0.78]; p=0.0002)[1] and an ORR of 45.6 percent versus 11.5 percent (Relative Risk (RR) 3.94; [95 percent CI, 2.37-6.57]; p<0.001).[1] These data met the predefined criteria for superiority, and the independent data safety monitoring committee recommended that the study be stopped at the interim analysis and that all patients randomised to chemotherapy be offered the opportunity to cross-over to erdafitinib.[1]

Across all subgroups, OS benefit with erdafitinib versus chemotherapy was consistently observed.[1] Subgroups included FGFR alteration type, baseline Eastern Cooperative Oncology Group performance status, lines of prior treatment, visceral metastasis, primary tumour location and type of chemotherapy.[1]

The safety profile of erdafitinib observed in THOR was consistent with the known safety profile of erdafitinib in metastatic urothelial carcinoma (mUC).[1] Serious treatment-related adverse events (TRAEs) were observed in 13.3 percent of patients who received erdafitinib and 24.1 percent of patients randomised to chemotherapy, and grade three or higher

adverse events were observed in 45.9 percent of patients on erdafitinib and 46.4 percent on chemotherapy.[1] 8.1 percent of patients who received erdafitinib and 13.4 percent of patients who received chemotherapy had TRAEs that lead to discontinuation of therapy.[1] TRAEs leading to death were reported in one patient who received erdafitinib and six patients who received chemotherapy.[1]

"Bladder cancer, of which urothelial carcinoma is the most common form, carries a high burden of disease for patients. Europe has the second highest rates of bladder cancer in the world, with over 203,000 patients diagnosed in 2020 alone. Patients with advanced UC, including FGFR-driven tumours who have exhausted standard treatment options, can face a particularly poor prognosis," said Martin Vogel, EMEA Therapeutic Area Lead Oncology, Janssen-Cilag GmbH. "These data demonstrate the potential benefit of targeted therapy in effectively inhibiting the growth of FGFR-altered tumours and provides hope that we can tailor treatment to improve outcomes for these patients."

Final Results from the Phase 2 NORSE Study Evaluating Erdafitinib and Cetrelimab Combination Therapy

Also presented were data from the Phase 2 NORSE study evaluating erdafitinib alone and in combination with cetrelimab, an investigational anti-programmed death receptor-1 (PD-1) monoclonal antibody, as first-line treatment of patients with mUC who were ineligible for cisplatin-based chemotherapy and who had FGFR alterations.[2] Both the combination and monotherapy treatment demonstrated a clinically meaningful response, with an ORR of 54.5 percent (95 percent CI, 38.8-69.6) in the combination arm and of 44.2 percent (95 percent CI, 29.1-60.1) in the monotherapy arm, and was well-tolerated in patients.[2] In the combination arm, six patients achieved a complete response (CR) and one patient in the monotherapy arm achieved a CR.[2] Median PFS in the combination arm was 11.0 months (95 percent CI, 5.45-13.63), versus 5.6 months (95 percent CI, 4.34-7.36) in the monotherapy arm.[2] Grade three or higher TRAEs were observed in 45.5 percent of patients who received erdafitinib and cetrelimab combination therapy and 46.5 percent of patients who received erdafitinib monotherapy.[2]

Results from the Phase 2 RAGNAR Study Evaluating the Efficacy and Safety of Erdafitinib

Additionally, data from the phase 2 RAGNAR study, evaluating the efficacy and safety of erdafitinib in patients with advanced or metastatic solid tumours with prespecified FGFR alterations, regardless of tumour location or histology (tumour-agnostic), were also presented at ASCO this year.[3] Treatment with erdafitinib demonstrated a clinically meaningful response at a median follow-up of 17.9 months, with an ORR of 30 percent (95 percent CI, 24-36). Responses were observed across 16 distinct tumours. Among the 64 responding patients, three percent of patients had a CR and 27 percent of patients had a partial response. Grade three or higher TRAEs were observed in 46 percent of patients who received erdafitinib. Serious TRAEs were observed in 8.3 percent of patients and no deaths due to TRAEs were observed.

"Janssen's ongoing evaluation of erdafitinib reinforces our commitment to improving outcomes for people diagnosed with bladder cancer and to identify therapeutic solutions for late-stage as well as early stage disease," said Kiran Patel, M.D., Vice President, Clinical Development, Solid Tumors, Janssen Research & Development, LLC. "Through ongoing trials, including the Phase 3 THOR study and the Phase 2 NORSE and RAGNAR studies, we continue to add to the growing body of evidence supporting the impact of this important targeted therapy in bladder cancer and with other tumour types with FGFR genetic alterations."

Erdafitinib received accelerated approval from the FDA as a targeted therapy for adult patients with locally advanced or mUC with 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. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.[1,4]

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About THOR

THOR (NCT03390504) is a Phase 3 randomised, open-label, multicenter study evaluating the efficacy and safety of erdafitinib.[5] The study compares erdafitinib with standard of care treatments chemotherapy (investigators choice of docetaxel or vinflunine) or pembrolizumab in patients with metastatic or unresectable UC with selected FGFR genetic alterations that has progressed during or after one or two prior lines of therapy, at least one

of which includes an anti-PD-(L)1 agent (Cohort 1) or one prior treatment not containing an anti-PD-(L)1 agent (Cohort 2).[5] The trial consists of screening, a treatment phase (from randomisation 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 participants death, withdraws consent, lost to follow-up study completion for the respective cohort, whichever comes first).[5] A long-term extension period is planned for after the clinical cutoff date is achieved for the final analysis of each cohort and eligible patients will continue to benefit from the study intervention. The primary endpoint of the study is OS; PFS, ORR, DOR, patient-reported outcomes, safety and PK are secondary endpoints.[5]

About NORSE

NORSE (NCT03473743) is an open-label, Phase 1b/2 study of erdafitinib in combination with cetrelimab in patients with locally advanced or mUC and FGFR3 or FGFR2 gene alterations.[6] 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 erdafitinib in combination with cetrelimab, and Phase 2 evaluates the safety and efficacy of the RP2D.[6] 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.[6]

About RAGNAR

RAGNAR (NCT04083976) is a Phase 2 clinical trial evaluating the safety and efficacy of erdafitinib in patients with advanced solid tumours, regardless of cancer type or tumour location (tumour-agnostic), driven by FGFR1–4 alterations.[7] Patients in the trial have progressed on or after at least one line of systemic therapy and have no alternative standard treatment options.[7] 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 (tumour histologies evaluated include but are not limited to cholangiocarcinoma [bile duct cancer], high- and low-grade glioma [a tumour 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 six to 17 with FGFR alterations.[7]

The primary endpoint of RAGNAR is independent review committee assessed ORR. Key secondary endpoints include investigator-assessed ORR, DOR, disease control rate (DCR), clinical benefit rate, PFS, OS and incidence and severity of adverse events.[7]

About Erdafitinib

Erdafitinib is a once-daily, oral pan-fibroblast growth factor receptor (FGFR) tyrosine kinase inhibitor being evaluated by Janssen Research & Development in Phase 2 and 3 clinical trials in patients with advanced urothelial cancer.[8,9]

In addition to the Phase 3 THOR, Phase 1b/2 NORSE and Phase 2 RAGNAR studies, erdafitinib is being studied in the Phase 2 THOR-2/BLC2003 (NCT04172675) study examining erdafitinib versus investigator choice of intravesical chemotherapy in participants who received Bacillus Calmette-Guérin and recurred with high risk non-muscle-invasive bladder cancer.[10]

In 2008, Janssen Pharmaceutica NV entered into an exclusive worldwide license and collaboration agreement with Astex Therapeutics Limited to develop and commercialise erdafitinib.[11]

About Cetrelimab

Administered intravenously, cetrelimab is an investigational programmed cell death receptor-1 (PD-1) monoclonal antibody[12] being studied to treat bladder cancer, prostate cancer, melanoma, and multiple myeloma as part of a combination treatment. Cetrelimab is also being evaluated in multiple other combination regimens across the Janssen portfolio.[13]

About Urothelial Carcinoma

Urothelial carcinoma (UC), also known as transitional cell carcinoma, starts in the innermost lining of the bladder.[14] It is the most common and frequent form of bladder cancer, representing more than 90 percent of all bladder cancers.[15] Up to one in five patients (20 percent) diagnosed with mUC have a fibroblast growth factor receptor (FGFR) genetic alteration.[9] FGFRs are a family of receptor tyrosine kinases that can be activated by genetic

alterations in a variety of tumour types, and these alterations may lead to increased tumour cell growth and survival.[16] FGFRs play a key role in several biological processes including tissue repair, inflammatory response and metabolism.[17] 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 tumour cell growth and survival.[18] Patients with advanced UC, including FGFR-driven tumours, who have exhausted standard treatment options typically face a poor prognosis.[19] The five-year survival rate for patients with metastatic bladder cancer that has spread to distant parts of the body is currently 8 percent.[20]

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.

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[†]Dr. Loriot has served as a paid consultant to the Janssen Pharmaceutical Companies; 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 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 materialise, actual results could vary materially from the expectations and projections of Janssen Pharmaceutica NV, Janssen-Cilag GmBH, Janssen Research & Development, LLC, 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 behaviour 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 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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