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For Immediate Release

European Commission approves BALVERSA®▼ (erdafitinib) for adult patients with unresectable or metastatic urothelial carcinoma

First pan FGFR kinase inhibitor to be approved in the European Economic Area, for adults with unresectable or metastatic urothelial carcinoma and susceptible FGFR3 alterations

Approval based on THOR results, showing 36 percent reduction in risk of death with erdafitinib versus chemotherapy[1]

BEERSE, BELGIUM (23 August 2024) – Janssen-Cilag International NV, a Johnson & Johnson company, today announced that the European Commission (EC) has approved BALVERSA®▼(erdafitinib) as a once-daily oral monotherapy for the treatment of adult patients with unresectable or metastatic urothelial carcinoma (mUC), harbouring susceptible fibroblast growth factor receptor 3 (FGFR3) genetic alterations who have previously received at least one line of therapy containing a programmed death receptor-1 (PD-1) or programmed death-ligand 1 (PD-L1) inhibitor in the unresectable or metastatic treatment setting.[2]

“Bladder cancer is one of Europe’s most common cancers and the need for innovative treatment options for people living with unresectable or metastatic urothelial carcinoma remains high,” said Yohann Loriot, M.D., Ph.D., Institut Gustave Roussy and University of Paris-Saclay, France.* “Erdafitinib is a novel, targeted therapy that has been shown to significantly improve overall and progression-free survival for patients with FGFR3 alterations, who, until now, have had limited options available.”

Europe has the highest rate of bladder cancer compared to all continents globally, with nearly a quarter of a million people diagnosed in 2022,[3] representing a 10 percent increase from 2020.[4] Urothelial carcinoma (UC) is the most common form of bladder cancer,[5] and up to 20 percent of patients with mUC have FGFR alterations.[6] Prognosis remains particularly poor for patients with mUC, with only eight percent of people diagnosed at a late metastatic stage surviving for five years.[7,8]

"This important milestone emphasises the vital role of targeted therapies in addressing the unique genetic and disease characteristics of patients living with urothelial cancer, and reinforces our dedication to advancing cutting-edge, precision treatments in oncology,” said Henar Hevia, Ph.D., Senior Director, EMEA Therapeutic Area Lead, Oncology, Johnson & Johnson Innovative Medicine. “The approval of erdafitinib as a precision therapy further highlights the importance of FGFR testing for all patients with metastatic urothelial cancer, and the need for a multi-disciplinary team approach to optimise outcomes for each patient.”

Erdafitinib received EC approval based on results from Cohort 1 of the Phase 3 THOR study (NCT03390504), evaluating the efficacy and safety of erdafitinib (n=136) versus chemotherapy (n=130) in patients with advanced or mUC with select FGFR alterations who have progressed on or after one or two prior treatments, at least one of which includes an anti-PD-(L)1 agent.[1,9]

In June 2023, based on the recommendation of the independent data safety monitoring committee, the THOR study was stopped following the interim efficacy analysis and all patients randomised to chemotherapy (docetaxel or vinflunine) were offered the opportunity to receive erdafitinib as crossover therapy.[1] The results demonstrate that a median overall survival (OS) of over one year was achieved in patients receiving erdafitinib at the data cut-off, marking a significant improvement as compared to those in the chemotherapy arm (12.1 months vs. 7.8 months; hazard ratio [HR]=0.64; 95 percent confidence interval [CI]**, 0.44-0.93; P=0.0050).[2] Treatment with erdafitinib also showed an improvement in median progression-free survival (PFS) compared to chemotherapy of 5.6 months versus 2.7 months (HR=0.58; 95 percent CI**, 0.41-0.82; P=0.0002) and confirmed overall response rate (ORR) of 35.3 percent versus 8.5 percent.[2]

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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.[1] Grade 3 or higher adverse events (TRAEs) were observed in 45.9 percent of patients on erdafitinib and 46.4 percent on chemotherapy.[1] Amongst patients who received erdafitinib, 8.1 percent had TRAEs that led to discontinuation of therapy, versus 13.4 percent of patients who received chemotherapy.[1] TRAEs leading to death were reported in one patient who received erdafitinib and six patients who received chemotherapy.[1]

“The EC approval of erdafitinib reflects our unwavering commitment to transforming outcomes for people living with unresectable or metastatic urothelial carcinoma,” said Kiran Patel, M.D., Vice President, Clinical Development, Solid Tumours, Johnson & Johnson Innovative Medicine. “We look forward to continuing our research and development efforts to bring new hope and improved outcomes to more patients in the future.”

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About the THOR Study
THOR (NCT03390504) is a Phase 3 randomised, open-label, multicentre study evaluating the efficacy and safety of erdafitinib. All patients included in the study had metastatic or unresectable UC,[9] with selected FGFR genetic alterations and showed disease progression during or after one or two prior lines of treatment.[9] The study compared erdafitinib in two cohorts; erdafitinib versus standard of care chemotherapy (investigators choice of docetaxel or vinflunine) after at least one line of treatment including an anti-PD-(L)1 agent (Cohort 1);[9] and erdafitinib compared to pembrolizumab after one prior treatment not containing an anti-PD-(L)1 agent (Cohort 2).[9] The trial consists of a screening step, 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, withdrawal of consent, lost to follow-up, study completion for the respective cohort, whichever comes first).[9] A long-term extension period is already operational following the clinical cut-off date of the final analysis of each cohort and eligible patients are continuing to benefit from the study intervention.[9] The primary endpoint of the study is OS, with secondary endpoints being PFS, ORR, duration of response (DOR), patient-reported outcomes, safety and pharmacokinetics (PK).[9]

Results from Cohort 1 were presented at the 2023 American Society of Clinical Oncology (ASCO) Annual Meeting,[1] with findings from Cohort 2 presented at the 2023 European Society of Medical Oncology (ESMO) congress.[10]

About Erdafitinib
Erdafitinib is a pan-fibroblast growth factor receptor (FGFR) tyrosine kinase inhibitor approved for the treatment of adult patients with unresectable or metastatic urothelial carcinoma (UC), harbouring susceptible FGFR3 genetic alterations who have previously received at least one line of therapy containing a PD-1 or PD-L1 inhibitor in the unresectable or metastatic treatment setting.[2,11]

Erdafitinib is also being evaluated in the Phase 1 study/BLC1003 (NCT05316155)[12] in patients with non-muscle invasive or muscle invasive bladder cancer with selected FGFR alterations, given via an intravesical targeted releasing system (TAR-210).[12] In addition, the Phase 3 MoonRISe-1 /BLC3004 (NCT06319820) study is evaluating TAR-210 versus single agent intravesical chemotherapy in participants with intermediate risk non-muscle invasive bladder cancer.[13]

In addition to the EC approval, in January 2024 Johnson & Johnson obtained U.S. Food and Drug Administration (FDA) full approval of erdafitinib for the treatment of adult patients with locally advanced or mUC with susceptible FGFR3 genetic alterations, whose disease has progressed on or after at least one line of prior systemic therapy, based upon Cohort 1 of the Phase 3 THOR study.[14]

In 2008, Janssen Pharmaceutica NV entered into an exclusive worldwide licence and collaboration agreement with Astex Pharmaceuticals to develop and commercialise erdafitinib.[15]

For a full list of adverse events and information on dosage and administration, contraindications and other precautions when using erdafitinib, please refer to the Summary of Product Characteristics.[2]

▼ In line with EMA regulations for new medicines, erdafitinib is subject to additional monitoring.

About Urothelial Carcinoma
Urothelial carcinoma (UC) starts in the innermost lining of the bladder.[16] Almost all bladder cancers – more than 90 percent – are UCs.[17] Up to one in five patients (20 percent) diagnosed with mUC have a fibroblast growth factor receptor

(FGFR) genetic alteration.[8] 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.[18] FGFRs play a key role in several biological processes, including tissue repair, inflammatory response and metabolism.[19] 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.[20] Patients with advanced UC, including FGFR-driven tumours, face a poor prognosis and the need for innovative therapies remains high.[21] The five-year survival rate for patients with metastatic bladder cancer that has spread to distant parts of the body is currently 8 percent.[22]

About FGFR Testing
Testing for somatic mutations and fusions in FGFR genes can identify patients with urothelial carcinoma who may be eligible for treatment with FGFR-targeted therapies such as erdafitinib.[23] Identification of actionable FGFR alterations may allow for utilisation of biomarker-guided therapy.[24] FGFR testing to detect gene mutations and fusions can be performed using validated laboratory developed tests involving polymerase chain reaction (PCR) and next-generation sequencing (NGS) techniques as recommended in the ESMO 2024 and EAU 2024 guidelines.[24,25,26] These guidelines recommend early molecular/genomic testing, ideally at diagnosis of advanced bladder cancer, to facilitate treatment decision-making and prevent delays in administering later lines of therapy.[26,27]

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 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.

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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. 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-Cilag International NV, Janssen Pharmaceutica NV 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 December 31, 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 http://www.sec.gov/, http://www.jnj.com/ or on request from Johnson & Johnson. None of Janssen-Cilag International NV, Janssen Pharmaceutica NV nor Johnson & Johnson undertake to update any forward-looking statement as a result of new information or future events or developments.

*Professor Loriot has provided consulting, advisory, and speaking services to Johnson & Johnson; they have not been paid for any media work.

**Repeated confidence intervals are provided.

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