Incyte Announces Positive CHMP Opinion for Capmatinib (Tabrecta®) for the Treatment of METex14 Advanced Non-Small Cell Lung Cancer

April 22, 2022

- *The positive opinion from the CHMP is based on Phase 2 GEOMETRY mono-1 study showing an overall response rate (ORR) of 51.6% in a cohort evaluating second-line patients only and 44% in all previously-treated patients with advanced non-small cell lung cancer (NSCLC) harboring alterations leading to MET exon 14 (METex14) skipping[1]*
- *METex14 skipping is a recognized oncogenic driver[2] occurring in 3-4% of NSCLC cases[3]; therapies targeting difficult-to-treat mutations may provide new options for patients*
- *Tabrecta was discovered by Incyte scientists, and Novartis has exclusive worldwide development and commercialization rights*

WILMINGTON, Del.--(BUSINESS WIRE)--Apr. 22, 2022-- Incyte (Nasdaq:INCY) today announced that the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency's (EMA) has issued a positive opinion that recommends granting marketing authorization for capmatinib (Tabrecta®) as a monotherapy for the treatment of adults with advanced non-small cell lung cancer (NSCLC) harboring alterations leading to mesenchymalepithelial-transition factor gene (MET) exon 14 (METex14) skipping who require systemic therapy following prior treatment with immunotherapy and/or platinum-based chemotherapy.

"We are pleased by the positive CHMP opinion recommending capmatinib as a treatment for certain patients with METex14 advanced non-small cell lung cancer and encouraged by what this Incyte-discovered product could mean for patients in Europe," said Peter Langmuir, M.D., Group Vice President, Oncology Targeted Therapies, Incyte. "Now patients in Europe who have advanced NSCLC with alterations leading to METex14 skipping are closer to having another therapeutic option that may target the recognized oncogenic driver of their cancer."

The CHMP opinion is based on data the Phase 2 GEOMETRY mono-1 study that demonstrated positive overall response rates (ORR) among adult patients with advanced NSCLC whose tumors have alterations leading to METex14 skipping[1]. Based on data presented at the 2021 American Society of Clinical Oncology (ASCO) Annual Meeting, in the 31 patients who received Tabrecta as second-line therapy in the METex14 skipping pretreated population, a confirmed ORR of 51.6% (95% CI, 33.1-69.8)was achieved, and the ORR across all 100 previously-treated patients, which included patients who received one or two prior lines of systemic therapy, was 44.0% (95% CI, 34.1-54.3)[1]. The most common treatment-related adverse events (AEs) (incidence ≥20%) were peripheral oedema, nausea, fatigue, vomiting, dyspnea, decreased appetite and back pain[1].

"Patients with alterations leading to METex14 skipping have an urgent need for treatment options, as this form of lung cancer is aggressive, often diagnosed in an advanced stage and frequently comes with a poor prognosis," said Juergen Wolf, MD, from the Center for Integrated Oncology, University Hospital Cologne, Germany, and lead investigator of the GEOMETRY mono-1 trial. "The positive CHMP opinion for Tabrecta brings an option to for a treatment specific to their tumor. If approved by the European Commission, new targeted therapies like Tabrecta—supported by early and broad molecular testing of patients' tumors—can better guide treatment decisions and ensure patients receive the appropriate therapy for their cancer."

In the European Union, there are an estimated 291,000 patients with locally advanced or metastatic NSCLC[4]. METex14 skipping, a recognized oncogenic driver[2], occurs in approximately 3-4% of NSCLC cases[3].

Novartis has exclusive worldwide development and commercialization rights to Tabrecta. Incyte is eligible for a total of over $500 million in milestones as well as royalties of between 12-14% on global net sales by Novartis.

About GEOMETRY mono-1
The Novartis-sponsored GEOMETRY mono-1 trial is a Phase 2, multi-center, non-randomized, open-label, multi-cohort study in adult patients with EGFR wild-type, ALK-negative rearrangement, advanced NSCLC with alterations that lead to MET exon-14 skipping who received 400 mg of capmatinib orally twice daily[1].

Patients were assigned to cohorts on the basis of MET status and previous lines of therapy. The primary endpoint was overall response rate (ORR) based on the Blinded Independent Review Committee (BIRC) assessment per RECIST v1.1. The key secondary endpoint was duration of response (DOR) evaluated by BIRC[1].

Mature data from the trial, including from an expansion cohort analysis, showed Tabrecta demonstrated a median duration of response of 9.7 months (95% CI, 5.6-13.0) in all previously-treated patients (n=100)[1]. In addition, Tabrecta demonstrated a median overall survival of 13.6 months (95% CI, 8.6-22.2) in previously-treated patients (n=69)[1]. The median progression-free survival was 5.5 months (95% CI, 4.2-8.1) for all previously-treated patients (n=100) and 6.9 months (95% CI, 4.2-13.3) for patients who received Tabrecta as second-line therapy (n=31)[1]. The Disease Control Rate across all previously-treated patients was 82.0% (95% CI, 73.1-89.0)[1]. The expansion cohort analysis enrolled 160 patients with MET alterations and included previously-treated cohorts (n=100) who had been treated with one or two prior lines of systemic therapy for advanced disease, as well as treatment-naive cohorts (n=60)[1].

Overall, Tabrecta demonstrated a manageable safety profile and there were no new safety signals or unexpected safety findings[1]. The most common treatment-related adverse events (AEs) (incidence ≥20%) were peripheral oedema, nausea, fatigue, vomiting, dyspnea, decreased appetite and back pain[1].

About Tabrecta® (capmatinib)
Tabrecta is approved in several countries including the U.S., Japan and Switzerland. It is the number one prescribed targeted therapy for patients with advanced NSCLC with alterations leading to METex14 skipping globally[5].

Tabrecta is a kinase inhibitor that targets MET. Tabrecta was discovered by Incyte and licensed to Novartis in 2009. Under the agreement, Incyte granted Novartis worldwide exclusive development and commercialization rights to capmatinib and certain back-up compounds in all indications.

About MET exon 14 skipping
MET (mesenchymal-epithelial transition), a receptor tyrosine kinase coded by the *MET* gene, normally plays an important role in cell signaling, proliferation and survival[2]. Many cancers are associated with abnormal signaling through the MET receptor pathway, caused by multiple mechanisms including point mutations, insertions, and deletions that lead to skipping of exon 14. MET exon 14 (METex14) skipping is an oncogenic alteration in NSCLC that can result in overstimulation of the MET pathway[2].

Patients with alterations that lead to METex14 skipping often have a poor prognosis due to the aggressiveness of the cancer and limited treatment options[6-8].

About Incyte
Incyte is a Wilmington, Delaware-based, global biopharmaceutical company focused on finding solutions for serious unmet medical needs through the discovery, development and commercialization of proprietary therapeutics. For additional information on Incyte, please visit Incyte.com and follow @Incyte.

Forward-Looking Statements
Except for the historical information set forth herein, the matters set forth in this press release, including statements regarding whether and when capmatinib might be approved for use in Europe and/or provide a successful treatment option for patients with NSCLC, the Company's ongoing clinical development program for capmatinib, the GEOMETRY program and the Company's NSCLC program generally contain predictions, estimates and other forward-looking statements.

These forward-looking statements are based on the Company's current expectations and subject to risks and uncertainties that may cause actual results to differ materially, including unanticipated developments in and risks related to: unanticipated delays; further research and development and the results of clinical trials possibly being unsuccessful or insufficient to meet applicable regulatory standards or warrant continued development; the ability to enroll sufficient numbers of subjects in clinical trials and the ability to enroll subjects in accordance with planned schedules; the effects of the COVID-19 pandemic and measures to address the pandemic on the Company's clinical trials, supply chain and other third-party providers and development and discovery operations; the Company's dependence on its relationships with its collaboration partners; the efficacy or safety of the Company's products and the products of the Company's collaboration partners; the acceptance of the Company's products and the products of the Company's collaboration partners in the marketplace; market competition; sales, marketing, manufacturing and distribution requirements; greater than expected expenses; expenses relating to litigation or strategic activities; and other risks detailed from time to time in the Company's reports filed with the Securities and Exchange Commission, including its annual report for the year ended December 31, 2021. The Company disclaims any intent or obligation to update these forward-looking statements.

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[3] Salgia R. MET in lung cancer: biomarker selection based on scientific rationale. *Mol Cancer Ther*. 2017;16(4):555-565.

[4] Data on file.

[5] Data on file

[6] Tong JH, et al. MET amplification and exon 14 splice site mutation define unique molecular subgroups of non-small cell lung carcinoma with poor prognosis. *Clin Cancer Res*. 2016;22:3048-3056.

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