Interim Data from the Open Label Phase 2 OPTIC Study of Iclusig® (ponatinib) for Chronic Phase-CML Presented at the ASCO and EHA Virtual Meetings

May 29, 2020

***-** Data from the interim analysis of the Phase 2 OPTIC trial show that response-based dosing regimens of Iclusig can optimize benefit-risk profile in patients with resistant or intolerant chronic phase-chronic myeloid leukemia (CML)*

WILMINGTON, Del.--(BUSINESS WIRE)--May 29, 2020-- Incyte (Nasdaq:INCY) today announced that data from the interim analysis of the Phase 2 OPTIC (**O**ptimizing **P**onatinib **T**reatment **I**n **C**ML) trial, which was sponsored by Takeda and co-funded by Incyte, will be presented during an oral session at the upcoming 2020 American Society of Clinical Oncology Virtual Meeting (ASCO20; May 29 – May 31) (Abstract #7502)[1]; and at the virtual 25thCongress of the European Hematology Association (EHA25; June 11 – 14) (Abstract #S172)[2].

The OPTIC trial is an ongoing randomized, open-label study prospectively evaluating response-based dosing regimens of Iclusig® (ponatinib) over a range of three starting doses (45 mg, 30 mg, 15 mg) with the aim of optimizing its efficacy and safety in patients with chronic-phase chronic myeloid leukemia (CP-CML), who are resistant or intolerant to prior tyrosine kinase inhibitor (TKI) therapy. With a median follow up of approximately 21 months, data from the interim analysis of the OPTIC trial show that the optimal benefit-risk profile for Iclusig in patients with CP-CML is achieved with a daily starting dose of 45 mg followed by a dose reduction to 15 mg upon achieving ≤1% BCR-ABL1. This dosing regimen resulted in an adjudicated arterial occlusive event (AOE) rate of 5.3%.

“As a physician, my focus is on treating CP-CML patients in a manner that will provide the best possible outcome by achieving desirable efficacy, while maintaining a manageable safety profile,” said Dr. Gianantonio Rosti, M.D., Institute of Haematology and Oncology, St Orsola University Hospital, Bologne. “I believe that patient selection, good management of comorbidities, close monitoring and appropriate dose adjustments are key factors in the management of CP-CML. I am encouraged by these data on the benefit-risk profile that is emerging from the interim OPTIC data of the Iclusig regimen starting at 45 mg, followed by a dose reduction to 15 mg.”

“The interim data from OPTIC provide important additional context around the safety profile of Iclusig in appropriate patients with CP-CML.” said Luca Marini, M.D., Regional VP, Head of European Medical Affairs, Incyte. “We believe that they may offer additional guidance to healthcare providers on how to optimize treatment with the goal of maintaining efficacy while reducing the risk of arterial occlusive events.”

Key findings from the OPTIC interim analysis (IA; cutoff date of July 2019) include:

- With median follow-up time of approximately 21 months, 77% (n/N=216/282) of patients in the OPTIC trial were evaluable for the primary endpoint.
- The OPTIC IA shows benefit of ponatinib in all three starting doses in a largely resistant population where the majority of patients (>60%) demonstrated less than a complete hematologic response (CHR) to immediate prior therapy.
- The maximum rates of ≤1% BCR-ABL1^{IS} at 12 months were achieved in the 45 mg/day starting dose cohort (38.7%), and responses were maintained with the dose reduction to 15 mg/day.
- With the protocol-mandated dose reduction for response in the higher dose cohorts, 75% patients in 45 mg cohort and 88% patients in 30 mg cohort were able to maintain ≤1% BCR-ABL1^{IS} response for as long as up to two years.
- Safety data as of the IA cutoff date include:
    - Among all patients (N=282), the most common treatment-emergent adverse events (TEAEs) of any grade (occurring in ≥10% of all patients) were thrombocytopenia (39.4%), neutropenia (25.2%), hypertension (24.1%), anemia (17.4%), headache (17.0%), increased lipase (16.0%), arthralgia (14.2%), constipation (12.4%), platelet count decrease (10.6%) and ALT increase (10.3%).
    - There was a dose-dependent trend in arterial occlusive event (AOE) rates:
        - Pre-adjudicated AOEs were reported in (45 mg, 30 mg, 15 mg/day starting dose cohorts) 8.5% (n/N = 8/94), 4.3% (n/N = 4/94), and 2.1% (n/N = 2/94).
        - Prospective adjudication of AOEs by independent experts resulted in (45 mg, 30 mg, 15 mg/day starting dose cohorts) 5.3% (n/N = 5/94), 4.3% (n/N = 4/94), and 1.1% (n/N = 1/94).
    - At the IA, there were no AOE-related deaths reported.
- The complete primary analysis of the OPTIC trial will be conducted after all patients have at least 12 months of follow-up and will be presented at a later date.

Incyte has an exclusive license from Takeda Pharmaceuticals International AG to commercialize Iclusig in the European Union and 29 other countries, including Switzerland, UK, Norway, Turkey, Israel and Russia. Iclusig is marketed by Takeda Pharmaceuticals International AG in the U.S.

About the OPTIC Trial

OPTIC (**O**ptimizing **P**onatinib **T**reatment **I**n **C**ML) is a randomized, dose-ranging Phase 2 trial designed to evaluate three starting doses (15 mg, 30 mg, 45 mg) of Iclusig® (ponatinib) in patients with resistant chronic-phase chronic myeloid leukemia (CP-CML) or who had documented history of presence of T315I mutation after receiving any number of prior tyrosine kinase inhibitors (TKIs). Dose reduction at response occurred per study protocol. The trial is expected to inform the optimal use of Iclusig in these patients. The primary endpoint of the trial is achieving ≤1% BCR-ABL1 at 12

months. Approximately 283 patients were enrolled at clinical sites around the world. Dose reduction at response occurred per study protocol.

For more information about the OPTIC study, please visit: https://clinicaltrials.gov/ct2/show/NCT02467270.

About CML and Ph+ ALL

CML – a rare malignancy – is one of four main types of leukemia; it is a result of a genetic mutation that takes place in early, immature versions of myeloid cells, which form red blood cells, platelets and most types of white blood cells. Subsequently, an abnormal gene called BCR-ABL1 forms, turning the damaged cell into a CML cell. CML typically progresses slowly, but it can change into a fast-growing acute leukemia that is hard to treat.

Ph+ ALL is a rare form of ALL that accounts for one quarter of adult ALL cases. and is characterized by the presence of an abnormal gene, known as the Philadelphia chromosome. In patients who are Philadelphia chromosome positive (Ph+), an abnormal chromosome is formed when pieces of chromosomes 9 and 22 switch with each other. This forms a longer chromosome 9 and a shorter chromosome 22, which leads to the development of BCR-ABL1 and is associated with Ph+ ALL.

About Iclusig® (ponatinib) Tablets

Iclusig targets not only native BCR-ABL but also its isoforms that carry mutations that confer resistance to treatment, including the T315I mutation, which has been associated with resistance to other approved TKIs.

Iclusig is approved in the U.S., EU, UK, Australia, Switzerland, Israel and Canada.

In the EU, Iclusig is approved for the treatment of adult patients with chronic phase, accelerated phase or blast phase chronic myeloid leukemia (CML) who are resistant to dasatinib or nilotinib; who are intolerant to dasatinib or nilotinib and for whom subsequent treatment with imatinib is not clinically appropriate; or who have the T315I mutation, or the treatment of adult patients with Philadelphia-chromosome positive acute lymphoblastic leukemia (Ph+ ALL) who are resistant to dasatinib; who are intolerant to dasatinib and for whom subsequent treatment with imatinib is not clinically appropriate; or who have the T315I mutation.

Click here to view the Iclusig EU Summary of Medicinal Product Characteristics.

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 the presentation of data from the OPTIC trial, and whether or when ponatinib might be approved or commercially available for use in humans anywhere in the world outside of the already approved indications in specific regions, its presentation plans for the upcoming ASCO and EHA meetings and its goal of improving the lives of patients, 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; determinations made by the FDA; 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 Form 10-K for the year ended March 31, 2020. The Company disclaims any intent or obligation to update these forward-looking statements.

References

1. Cortes, J. Interim Analysis (IA) of OPTIC: A Dose-Ranging Study of Three Ponatinib (PON) Starting Doses. Abstract #7502. 2020 American Society of Clinical Oncology Virtual Meeting (ASCO20; May 29 – May 31, 2020).
2. Cortes, J. Interim Analysis from the OPTIC Trial, a Dose-Ranging Study of 3 Starting Doses of Ponatinib. Abstract #S172. 25thCongress of the European Hematology Association (EHA25; June 11 – 14, 2020).

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