

Positive Primary Analysis from the Phase 2 OPTIC Study of Ponatinib (Iclusig®) in Chronic Phase-Chronic Myeloid Leukemia (CP-CML) to be Presented at the 2021 ASCO Annual Meeting

May 20, 2021

- OPTIC trial evaluating response-based dosing regimens of ponatinib in patients with resistant CP-CML met primary endpoint, confirming optimal benefit-risk profile achieved via 45mg/day starting dose reduced to 15mg/day upon response

WILMINGTON, Del.--(BUSINESS WIRE)-- Incyte (Nasdaq:INCY) today announced that data from the primary analysis of the Phase 2 OPTIC (Optimizing Ponatinib Treatment In CML) trial will be presented during an oral session (Abstract #7000) at the 2021 American Society of Clinical Oncology (ASCO) Annual Meeting, held virtually June 4-8, 2021. The OPTIC trial – an ongoing, randomized, open-label study prospectively evaluating response-based dosing regimens of ponatinib (Iclusig®) over a range of three starting doses (45mg, 30mg, 15mg) followed by dose reduction to 15mg with the aim of optimizing efficacy and safety in patients with chronic-phase chronic myeloid leukemia (CP-CML) who are resistant to prior tyrosine kinase inhibitor (TKI) therapy – met its primary endpoint.

The trial, sponsored by Takeda and co-funded by Incyte, evaluated treatment in patients with resistant disease, with and without mutations. The results show that the optimal benefit-risk profile for ponatinib in patients with CP-CML was achieved with a starting dose of 45mg/day, and upon response (achieving $\leq 1\%$ BCR-ABL1^{IS}), dose reduction to 15mg/day. The results also suggest a clinically-manageable safety profile for ponatinib. Data from the OPTIC interim analysis (cutoff date of July 2019), which evaluated 216 patients with a median follow-up of 21 months, were [previously reported](#). The primary analysis (cutoff date of May 2020) evaluated 283 patients with a median follow-up of 32 months. All patients in the OPTIC trial were evaluable for the primary endpoint at the time of this analysis.

"The OPTIC primary analysis reinforces the positive response that is achievable with ponatinib in appropriate patients with CP-CML, and the ability that response-based regimens have to maximize efficacy, while maintaining a manageable safety profile," said Luca Marini, M.D., Regional Vice President, Head of European Medical Affairs, Incyte. "The OPTIC trial provides additional confirmation on the optimization of ponatinib dosing and reinforces its role as a meaningful treatment option for patients."

Key findings from the OPTIC primary analysis include:

- The maximum rates of $\leq 1\%$ BCR-ABL1^{IS} at 12 months, the primary endpoint, were achieved in the 45mg/day starting dose cohort (44.1%), and 73.3% of patients in this cohort maintained response with the dose reduction to 15mg/day. The 30mg/day and 15mg/day starting dose cohorts also demonstrated benefit (29.0% and 23.1% $\leq 1\%$ BCR-ABL1^{IS} at 12 months, respectively), especially in patients with less-resistant disease and with a T315I mutation.
- Positive survival outcomes were estimated in all three arms, with an 89.3% 36-month overall survival (OS) probability anticipated for the 45mg starting dose cohort and 73.3% progression-free survival (PFS) anticipated for the same cohort.
 - This indicates that the dose-reduction strategy did not impact OS regardless of prior second-generation TKI resistance or the presence of BCR-ABL1 mutations.
- Rates of arterial occlusive events (AOEs) observed at the time of primary analysis (6% overall and 9.6% in the 45mg starting dose cohort) suggest a clinically manageable safety profile.
- Safety data include:
 - Among all study participants (N=283), the most common treatment-emergent adverse events (TEAEs) Grade 3 or greater were thrombocytopenia (27%), neutropenia (17%) and anemia (7%).
 - Reported AOE rates were 10%, 5% and 3% for the 45mg, 30mg, 15mg/day starting dose cohorts, respectively. Grade 3 or greater AOE rates were 5%, 5% and 3% for the 45mg, 30mg and 15mg/day starting dose cohorts, respectively.
 - Reported serious AOE rates were 4%, 4% and 3% for the 45mg, 30mg, 15mg/day starting dose cohorts, respectively. There were four deaths related to AEs (two sudden deaths and two pneumonia).

"As a physician, I am pleased by the results of the OPTIC trial evaluating patients with resistant CP-CML, who are in need of additional options to improve outcomes," said Dr. Gianantonio Rosti, M.D., Istituto Romagnolo per lo Studio dei Tumori "Dino Amadori" (IRST S.r.l.) Istituto di Ricovero e Cura a Carattere Scientifico. "It is encouraging to see the positive benefit-risk profile that can be achieved with ponatinib through a response-based dosing regimen, therefore providing efficacy while also managing the risk for arterial occlusive events."

Incyte has an exclusive license from Takeda Pharmaceuticals International AG to commercialize ponatinib in the European Union and 29 other countries, including Switzerland, UK, Norway, Turkey, Israel and Russia. Iclusig is marketed in the U.S. by Millennium Pharmaceuticals, Inc., a wholly owned subsidiary of Takeda Pharmaceutical Company Limited.

About the OPTIC Trial

OPTIC (Optimizing Ponatinib Treatment In CML) is a randomized, dose-ranging Phase 2 trial designed to evaluate three starting doses (15mg, 30mg, 45mg) of 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 ponatinib in these patients. The primary endpoint of the trial is achieving $\leq 1\%$ BCR-ABL1 at 12 months. A total of 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

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.

About Ponatinib (Iclusig®) Tablets

Ponatinib (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.

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.

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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](https://www.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 Company's ongoing clinical development program for ponatinib and the Company's chronic-phase chronic myeloid leukemia program generally, its clinical development pipeline and whether or when ponatinib or any development compounds will be approved or commercially available for use in the United States or elsewhere for chronic myeloid leukemia program generally or any other indication, its presentation plans for the upcoming 2021 American Society of Clinical Oncology (ASCO) Annual Meeting 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 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; 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; the acceptance of the Company's products in the marketplace; market competition; sales, marketing, manufacturing and distribution requirements; greater than expected expenses; 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, 2020, and the quarterly report on Form 10-Q for the quarter ended March 31, 2021. The Company disclaims any intent or obligation to update these forward-looking statements.



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