Incyte Announces Full Results from Proof-of-Concept Phase II RECAP Trial of Jakafi® (ruxolitinib) in Combination with Capecitabine in Patients with Metastatic Pancreatic Cancer

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- *Overall survival favored ruxolitinib plus capecitabine versus capecitabine alone in pre-specified subgroup of patients with elevated CRP, an established marker of systemic inflammation and poor prognosis in cancer*
- *These data support targeting onco-inflammation through the JAK-STAT pathway and form the basis of an expanded clinical development program evaluating ruxolitinib in pancreatic cancer and other solid tumor types*

Incyte to host a webcast for investors featuring key results from this trial on Monday, June 2, at 6:45 p.m. CDT

CHICAGO--(BUSINESS WIRE)--Jun. 2, 2014-- Incyte Corporation (Nasdaq: INCY) today announced full results from RECAP, a Phase II trial of ruxolitinib, a JAK1/JAK2 inhibitor, in combination with capecitabine in second-line metastatic pancreatic cancer. The findings from this proof-of-concept trial showed that ruxolitinib plus capecitabine prolonged survival over capecitabine alone in patients with elevated C-reactive protein (CRP), a well-established marker of systemic inflammation (hazard ratio = 0.47; 95% CI, 0.26-0.85; *P*=0.01 (2-sided)). Patients in this subgroup treated with ruxolitinib plus capecitabine also achieved improvements in other efficacy measures including objective response rate, clinical benefit response, and weight gain. These data were presented at the 50th Annual Meeting of the American Society of Clinical Oncology (ASCO) in Chicago.

Systemic inflammation is commonly observed in patients with advanced malignancies and has been associated with poor survival.[1,2] The majority of patients with pancreatic cancer exhibit evidence of systemic inflammation, which can be associated with weight loss, decreased muscle mass, and poor performance status.[3] Elevated CRP, a well characterized, sensitive, and readily measurable marker of systemic inflammation, has negative prognostic significance in many human cancers, including pancreatic cancer.[4,5,6,7]

“Ruxolitinib in combination with capecitabine was generally well tolerated and exhibited greater clinical activity compared to capecitabine alone in patients with second-line metastatic pancreatic cancer and elevated CRP,” said Herbert Hurwitz, M.D., Professor of Medicine, Duke University School of Medicine, principal investigator of RECAP who presented the study findings. “Local and systemic inflammation adversely affect patient outcomes in pancreatic cancer and many other malignancies. The findings are very encouraging, especially given the limited treatment options for these patients.”

The RECAP study enrolled 127 patients: 64 randomized to receive ruxolitinib plus capecitabine and 63 to capecitabine alone. In the intent-to-treat population, the hazard ratio for overall survival was 0.79 (95% CI, 0.53–1.18; *P*=0.25 (2-sided)). When patients with elevated CRP levels were evaluated (n=60), a pre-specified subgroup based on median CRP at study entry (13 mg/L), the hazard ratio for overall survival was 0.47 (95% CI: 0.26–0.85; *P*=0.01 (2-sided)). In this subgroup, the probability of survival in the ruxolitinib plus capecitabine group versus the capecitabine alone group at three, six, and 12 months was 48 percent, 42 percent, and 11 percent versus 29 percent, 11 percent, and 0 percent, respectively; the median time to death was 83 days in the ruxolitinib plus capecitabine group versus 55 days in the capecitabine alone group with greater differences between the treatment arms emerging after the median time to death. A post hoc analysis of overall survival was also conducted using the modified Glasgow Prognostic Score (mGPS), a well-characterized and prognostically relevant measure of inflammation in cancer.[8] Among patients in the higher risk categories (mGPS = 1 or 2 corresponding to patients with CRP >10 mg/L), overall survival favored the ruxolitinib-capecitabine combination over capecitabine alone (HR = 0.60; 95% CI, 0.35-1.03; *P*=0.063 (2-sided)).

Similar trends were observed in progression-free survival. The hazard ratio was 0.75 (95% CI: 0.51–1.10; *P*=0.14 (2-sided)) in favor of ruxolitinib plus capecitabine in the intent-to-treat population, and 0.62 (95% CI: 0.35–1.10; *P*=0.10 (2-sided)) in the subgroup of patients with CRP > 13 mg/L. Benefits with ruxolitinib plus capecitabine treatment were also observed in objective response rate, clinical benefit response (a composite of improvement in pain intensity, Karnofsky performance status, analgesia, and weight), and weight gain.

Treatment with ruxolitinib plus capecitabine was generally well tolerated. Grade ≥3 anemia occurred more frequently in patients treated with ruxolitinib plus capecitabine (15.3%) compared with those who received placebo plus capecitabine (1.7%). Grade ≥3 neutropenia and thrombocytopenia were uncommon in ruxolitinib-treated patients. Grade 3 or 4 non-hematologic adverse events that occurred more frequently with ruxolitinib plus capecitabine compared with placebo plus capecitabine included pulmonary embolism (11.9% vs 5.0%), stomatitis (6.8% vs 0%), and pneumonia (8.5% vs 1.7%). Differences in exposure between treatment groups (mean of 99.6 days for ruxolitinib plus capecitabine vs 67.4 days for capecitabine alone) may have contributed to the differences in the rates of adverse events.

“RECAP provides the first evidence that targeting onco-inflammation through the JAK-STAT pathway with ruxolitinib may improve survival in patients with elevated CRP,” said Hervé Hoppenot, President and Chief Executive Officer, Incyte. “We have initiated a pivotal Phase III clinical program in patients with mGPS of 1 or 2 to confirm these findings in pancreatic cancer. We are also investigating the utility of ruxolitinib in other tumor types in which onco-inflammation plays a key role.”

The slides used during the presentation can be accessed at 2014 ASCO - RECAP Presentation.

Incyte’s Phase III program in pancreatic cancer includes two double-blind, placebo-controlled trials focusing on patients with mGPS of 1 or 2 which is also defined as CRP >10 mg/L: JANUS 1 (NCT02117479) and JANUS 2 (NCT02119663). Clinical trials evaluating ruxolitinib activity using mGPS-based patient selection criteria are ongoing in other solid tumors (colorectal cancer (NCT02119676), non-small cell lung cancer (NCT02119650), and breast cancer (NCT02120417)).

About the RECAP Trial

The **R**uxolitinib **E**fficacy and safety in combination with **CA**pecitabine for subjects with recurrent or treatment refractory metastatic **P**ancreatic cancer (RECAP) trial was a Phase II, randomized, double-blind, placebo-controlled, proof-of-concept trial that investigated ruxolitinib in combination with capecitabine compared to capecitabine alone as treatment for metastatic pancreatic cancer. The trial was designed, in part, to characterize patients with metastatic pancreatic cancer who may benefit from JAK pathway inhibition with ruxolitinib therapy.

An open-label, run-in period was included to assess the safety of ruxolitinib plus capecitabine in a cohort of nine patients. After completion of this run-in period, the randomized, double-blind portion of the study was conducted. One hundred twenty seven patients were randomized to one of two treatment arms: ruxolitinib 15 mg twice daily plus capecitabine 2000 mg/m^2, as 1000 mg/m^2 twice daily (n=64) or placebo plus capecitabine 2000 mg/m^2, as 1000 mg/m^2 twice daily (n=63). Oral ruxolitinib or placebo was self-administered every day of each 21-day cycle. Capecitabine was self-administered for the initial 14 days of each cycle. The primary endpoint of RECAP was overall survival measured from the time of randomization to the occurrence of death or discontinuation.

About Ruxolitinib

Ruxolitinib is an oral, selective inhibitor of Janus kinases 1 and 2 (JAK1 and JAK2). In the United States, ruxolitinib, brand name Jakafi®, is indicated for treatment of patients with intermediate or high-risk myelofibrosis (MF), including primary MF, post-polycythemia vera MF and post-essential thrombocythemia MF. Jakafi is marketed by Incyte in the United States and by Novartis as Jakavi® (ruxolitinib) outside the United States.

Important Safety Information

Jakafi can cause serious side effects including:

Low blood counts: Jakafi may cause your platelet, red blood cell, or white blood cell counts to be lowered. If you develop bleeding, stop taking Jakafi and call your healthcare provider. Your healthcare provider will perform blood tests to check your blood counts before you start Jakafi and regularly during your treatment. Your healthcare provider may change your dose of Jakafi or stop your treatment based on the results of your blood tests. Tell your healthcare provider right away if you experience unusual bleeding, bruising, fatigue, shortness of breath, or a fever.

Infection: You may be at risk for developing a serious infection while taking Jakafi. Tell your healthcare provider if you develop symptoms such as chills, nausea, vomiting, aches, weakness, fever, or painful skin rash or blisters.

The most common side effects of Jakafi include dizziness and headache.

These are not all the possible side effects of Jakafi. Ask your healthcare provider or pharmacist for more information. Tell your healthcare provider about any side effect that bothers you or that does not go away.

Before taking Jakafi, tell your healthcare provider about all the medications, vitamins, and herbal supplements you are taking and all your medical conditions, including if you have an infection, have or had liver or kidney problems, are on dialysis, or have any other medical condition. Do not drink grapefruit juice while taking Jakafi.

Women should not take Jakafi while pregnant or planning to become pregnant, or if breast-feeding.

Please see the Full Prescribing Information available at www.jakafi.com, which includes a more complete discussion of the risks associated with Jakafi.

About the Webcast

Incyte will host an investor meeting, which will be webcast live at 6:45 p.m. CDT on June 2, 2014, and can be accessed at www.incyte.com under Investor Relations, Events and Webcasts. A replay of the event will be available for 60 days.

About Incyte

Incyte Corporation is a Wilmington, Delaware-based biopharmaceutical company focused on the discovery, development and commercialization of proprietary small molecule drugs, primarily in oncology. For additional information on Incyte, please visit the Company's website at www.incyte.com.

Forward-Looking Statements

Except for the historical information set forth herein, the matters set forth in this press release, including without limitation statements with respect to the potential efficacy, safety and therapeutic value of, and Incyte's plans for, ruxolitinib in pancreatic cancer and other solid tumors, including that ruxolitinib may improve survival in patients with elevated CRP, contain predictions and estimates and are forward-looking statements within the meaning of the "safe harbor" provisions of the Private Securities Litigation Reform Act of 1995. These forward-looking statements are based on Incyte'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 the efficacy or safety of ruxolitinib, the results of further research and development, the high degree of risk and uncertainty associated with drug development, clinical trials and regulatory approval processes, other market or economic factors, competitive and technological advances, and other risks detailed from time to time in Incyte's filings with the Securities and Exchange Commission, including its Quarterly Report on Form 10-Q for the quarter ended March 31, 2014. Incyte disclaims any intent or obligation to update these forward-looking statements.

References

[1] Hanahan D, Coussens LM. *Cancer Cell*. 2012;21:309-22.

[2] Seruga B, et al. *Nat Rev Cancer*. 2008;8:887–99.

[3] Fearon KC, et al. *World J Surg*. 1999;23:584-8.

[4] McMillan DC, et al. *Nutr Cancer*. 2001;41:64-9.

[5]Al Murri, et al. *Br J Cancer*. 2006;94:227-30.

[6] Proctor MJ, et al. *Br J Cancer*. 2010;103:870-6.

[7] McMillan DC. *Cancer Treat Rev.* 2013;39:534-40.
[8] McMillan DC, et al. *Int J Colorectal Dis.* 2007;22:881-6.

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