Phase III studies of Jakafi™ (ruxolitinib) published in The New England Journal of Medicine Demonstrate Significant Clinical Benefit for Patients with Myelofibrosis

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- *Results from the COMFORT-I and COMFORT-II Phase III trials show Jakafi significantly reduced spleen volume and debilitating symptoms associated with myelofibrosis (MF), a life-threatening blood cancer*
- *Updated analysis from COMFORT-I suggests Jakafi may provide an overall survival benefit as compared to placebo*

WILMINGTON, Del.--(BUSINESS WIRE)--Feb. 29, 2012-- The *New England Journal of Medicine (NEJM)* today published results from two Phase III studies (COMFORT-I and COMFORT-II) of Jakafi™ (ruxolitinib), a JAK1 and JAK2 inhibitor recently approved by the Food and Drug Administration (FDA) for the treatment of intermediate or high-risk myelofibrosis (MF). These data, which were included in the New Drug Application for Jakafi submitted by Incyte Corporation (Nasdaq:INCY), showed that the treatment significantly reduced spleen volume and improved symptoms of MF. Additionally, in an updated analysis of COMFORT-I, treatment with Jakafi was associated with improved overall survival compared to placebo.[1,2]

MF is a life-threatening blood cancer characterized by an enlarged spleen and progressive, debilitating symptoms* such as fatigue, severe itching (pruritus), night sweats, bone pain, early satiety (a feeling of fullness), and weight loss that can lead to impaired quality of life.[3]

“Given the life-threatening nature and disease burden of myelofibrosis, it’s gratifying to see a treatment that may provide an overall survival benefit as well as reduce the splenomegaly and symptoms that impact so many of these patients. Importantly, patients receiving ruxolitinib experienced these benefits regardless of their JAK2V617F mutation status,” stated Srdan Verstovsek, M.D., Ph.D., Associate Professor, Department of Leukemia, Division of Cancer Medicine, The University of Texas MD Anderson Cancer Center and the principal investigator of the COMFORT-I pivotal trial.

Dr. Verstovsek added, “Another key finding from the Phase III trials is that patients receiving placebo or best available therapy continued to see their spleens increase in size and their symptoms worsen, further supporting the therapeutic benefit of ruxolitinib.”

In COMFORT-I, a Phase III double-blind, placebo-controlled trial of 309 patients, 41.9% of patients receiving ruxolitinib achieved the primary endpoint of at least a 35% reduction in spleen volume reduction roughly equivalent to a reduction in palpable spleen size by 50% at week 24 compared with 0.7% of patients in the placebo group ($p<0.001$). The reductions in spleen volume observed with ruxolitinib therapy were durable, with 67% of responding patients maintaining this response for at least 48 weeks. Almost all patients treated with ruxolitinib had some reduction in spleen volume, whereas the majority of patients receiving placebo had spleen growth.

Significantly more patients in the group receiving ruxolitinib than in the placebo group experienced at least a 50% improvement in Total Symptom Score (which comprises scores for night sweats, itching, abdominal discomfort, pain under the ribs on the left side, early feeling of fullness, and muscle/bone pain) at week 24 (45.9% vs 5.3%; $p<0.001$). The majority of responses occurred within the first 4 weeks of treatment. Most patients treated with ruxolitinib had some improvement in Total Symptom Score, while the majority of patients receiving placebo experienced worsening of their symptoms.

A survival analysis conducted at the time of a planned safety data cutoff with 4 additional months of follow-up suggests a survival advantage for ruxolitinib over placebo with 13 (8.4%) deaths in the ruxolitinib and 24 (15.6%) in the placebo group (median follow-up, 51 weeks; HR, 0.50; 95% CI, 0.25-0.98; $p=0.04$). Median survival has not yet been reached.

The clinical benefits of ruxolitinib therapy were also observed in other patient-reported outcomes, including the Patient Global Impression of Change. At week 24, 67% of patients treated with ruxolitinib rated their overall condition as much improved or very much improved, whereas most placebo-treated patients rated it as unchanged or worse.

Anemia and thrombocytopenia were the most common adverse events, but rarely led to discontinuation (1 patient in each treatment group for each event). Non-hematologic adverse events that occurred more frequently in the ruxolitinib group were bruising, dizziness, and headache. Adverse events that occurred after interruption or discontinuation of ruxolitinib treatment showed no pattern of a withdrawal effect; rather, and as expected, myelofibrosis symptoms gradually returned to baseline levels over approximately one week after stopping therapy.

In the COMFORT-II trial, an open label trial comparing ruxolitinib to best available therapy, conducted by Novartis, Incyte’s collaboration partner outside of the U.S., ruxolitinib produced a volumetric spleen size reduction of 35% or greater in 28.5% of myelofibrosis patients compared to 0% of patients in the best available therapy (BAT) arm at 48 weeks ($p<0.001$). At week 24, 32% of patients treated with ruxolitinib demonstrated a 35% or greater volumetric spleen size reduction compared to 0% of patients treated with BAT ($p<0.001$) for the key secondary endpoint. Additionally, ruxolitinib was associated with improvements in myelofibrosis symptoms at each evaluation as compared to BAT.

Consistent ruxolitinib therapy during COMFORT-II also provided a marked and durable improvement in overall quality of life measures, functioning and symptoms, including appetite loss, dyspnea, fatigue, insomnia and pain, by week 48, compared to a worsening of symptoms in BAT-treated patients. In the group treated with ruxolitinib, the most common adverse events were anemia and thrombocytopenia. The most frequently reported serious adverse event (SAE) was anemia for both arms (ruxolitinib, 5%; BAT, 4%). Pneumonia was the only SAE reported in ≥5% of patients in either arm (ruxolitinib, 1%; BAT, 5%).

* *Symptoms studied in COMFORT-I were abdominal discomfort, pain under the left ribs, night sweats, itching, bone/muscle pain, and early satiety.*

About the COMFORT-I Trial

The COMFORT-I study is a randomized, double-blind placebo-controlled trial that enrolled 309 patients with primary myelofibrosis (MF),

post-polycythemia vera myelofibrosis (PPV-MF) or post-essential thrombocythemia myelofibrosis (PET-MF) in 89 study locations in the United States, Australia, and Canada. The primary endpoint was the proportion of patients with ≥35% spleen volume reduction at 24 weeks assessed by magnetic resonance imaging or computed tomography. Secondary endpoints included durability of spleen volume response, changes in myelofibrosis-related symptoms (assessed by Total Symptom Score using the modified Myelofibrosis Symptom Assessment Form v2.0 diary), and overall survival.

Patients with intermediate-2 or high-risk myelofibrosis were randomized to twice-daily oral ruxolitinib (n=155) or placebo (n=154). The starting dose of ruxolitinib was based on baseline platelet count.

The median follow-up was 32 weeks at the time of the prospectively defined data cutoff. For the analysis of overall survival, additional data were collected for a planned 4-month safety update, with a median follow-up of 51 weeks. Patients continue to receive ruxolitinib therapy beyond week 48 to determine longer-term outcomes of efficacy and safety. COMFORT-I was not designed or powered to demonstrate a statistically significant difference in overall survival within the timeframe of the study endpoint.

See Important Safety Information below. The prescribing information for Jakafi can be found at: (http://www.incyte.com/products/uspi_jakafi.pdf).

About the COMFORT-II Trial

COMFORT-II is a randomized, open-label Phase III trial of ruxolitinib versus BAT that enrolled 219 patients with primary MF, PPV-MF or PET-MF in 56 study locations in Europe. Two-thirds of the patients enrolled received ruxolitinib (starting dose 15 or 20 mg twice daily) and one-third received the investigator-selected BAT.

The primary endpoint for COMFORT-II was the proportion of patients achieving a reduction in spleen volume of 35% or more from baseline at week 48 as measured by MRI (or CT scan in applicable patients). Patients continue to receive ruxolitinib therapy beyond week 48 to determine longer-term outcomes of efficacy and safety.

COMFORT-II was not designed or powered to demonstrate a statistically significant difference in overall survival within the timeframe of the study endpoint. Additionally, the survival analysis in COMFORT-II was confounded by the small number of patients randomized to BAT, the significant early crossover of patients from BAT to ruxolitinib, and limited follow-up data on survival in a large proportion of patients.

COMFORT-II was conducted by Novartis in Europe.

Indication, Usage and Dosing

Jakafi is indicated for treatment of patients with intermediate or high-risk myelofibrosis, including primary MF, post-polycythemia vera MF and post-essential thrombocythemia MF. Intermediate and high-risk MF patients include anyone over the age of 65 or who have or have had any of the following: anemia, constitutional symptoms, elevated white blood cell or blast counts or platelet counts less than 100 X 10^9/L.[4,5]

The recommended starting dose is based on the patient's platelet count. Dosage should be adjusted based on safety and efficacy. A blood cell count must be performed before initiating therapy with Jakafi and complete blood counts should be monitored every 2-4 weeks until doses are stabilized.

For more information and complete prescribing information, visit www.Jakafi.com.

Important Safety Information

Treatment with Jakafi can cause hematologic adverse reactions, including thrombocytopenia, anemia and neutropenia, which are each dose-related effects, with the most frequent being thrombocytopenia and anemia. A complete blood count must be performed before initiating therapy with Jakafi. Complete blood counts should be monitored as clinically indicated and dosing adjusted as required. The three most frequent non-hematologic adverse reactions were bruising, dizziness and headache. Patients with platelet counts less than 200 X 10^9/L at the start of therapy are more likely to develop thrombocytopenia during treatment. Thrombocytopenia was generally reversible and was usually managed by reducing the dose or temporarily withholding Jakafi. If clinically indicated, platelet transfusions may be administered. Patients developing anemia may require blood transfusions. Dose modifications of Jakafi for patients developing anemia may also be considered. Neutropenia (ANC <0.5 X 10^9/L) was generally reversible and was managed by temporarily withholding Jakafi. Patients should be assessed for the risk of developing serious bacterial, mycobacterial, fungal and viral infections. Active serious infections should have resolved before starting Jakafi. Physicians should carefully observe patients receiving Jakafi for signs and symptoms of infection (including herpes zoster) and initiate appropriate treatment promptly. A dose modification is recommended when administering Jakafi with strong CYP3A4 inhibitors or in patients with renal or hepatic impairment [see Dosage and Administration]. Patients should be closely monitored and the dose titrated based on safety and efficacy. There are no adequate and well-controlled studies of Jakafi in pregnant women. Use of Jakafi during pregnancy is not recommended and should only be used if the potential benefit justifies the potential risk to the fetus. Women taking Jakafi should not breast-feed. Discontinue nursing or discontinue the drug, taking into account the importance of the drug to the mother.

About Myelofibrosis

Myelofibrosis (MF) is a life-threatening blood cancer that belongs to a group of diseases referred to as myeloproliferative neoplasms (or MPNs). MF has a poor prognosis and limited treatment options.[4] While the exact prevalence of MF is uncertain, and estimates vary widely, based on extensive market research, Incyte believes MF affects about 16,000 to 18,500 people in the U.S.[6] The enlarged spleen and debilitating symptoms of MF are linked to dysregulated signaling in the Janus kinase (JAK) pathway. This dysregulation may be caused by various mechanisms and mutations, such as the JAK2V617F mutation.[7,8]

About the Incyte-Novartis Collaboration

In 2009, Incyte entered into a worldwide collaboration and license agreement with Novartis. Incyte retained exclusive rights for the development and commercialization of ruxolitinib (INCB424) in the United States. Novartis received exclusive rights to the development and potential commercialization of ruxolitinib in all hematology-oncology indications outside of the United States.

About Incyte

Incyte Corporation is a Wilmington, Delaware-based biopharmaceutical company focused on the discovery, development and commercialization of proprietary small molecule drugs for oncology and inflammation. For additional information on Incyte, please visit the Company's web site 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 Jakafi™(ruxolitinib), including the potential efficacy and therapeutic and commercial value of Jakafi and that treatment that may provide an overall survival benefit compared to placebo, contain predictions, estimates and other forward-looking statements.

These forward-looking statements are 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 Jakafi, the acceptance of Jakafi in the marketplace, risks related to market competition, the results of further research and development, risks and uncertainties associated with sales, marketing and distribution requirements, and other risks detailed from time to time in Incyte's reports filed with the Securities and Exchange Commission, including our Form 10-K for the year ended December 31, 2011.

Incyte disclaims any intent or obligation to update these forward-looking statements.

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