

Incyte Reaches Agreement with the FDA on a Special Protocol Assessment for the Phase III Clinical Trial of INCB18424 in Polycythemia Vera

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Global Phase III RESPONSE Clinical Trial to Begin in October

WILMINGTON, Del., Sep 13, 2010 (BUSINESS WIRE) -- **Incyte Corporation (Nasdaq:INCY)** announced today that it has reached agreement with the U.S. Food and Drug Administration (FDA) regarding a Special Protocol Assessment (SPA) for the design of a pivotal Phase III trial for its JAK1 and JAK2 inhibitor, INCB18424 in patients with polycythemia vera (PV), a blood cancer that belongs to a group of diseases known as myeloproliferative neoplasms (MPNs). Two Phase III trials of INCB18424 in myelofibrosis, also an MPN, COMFORT-I and COMFORT-II, are already fully enrolled and are expected to be completed later this year.

RESPONSE (Randomized, open label, multicenter phase III study of Efficacy and Safety in Polycythemia vera subjects who are resistant to or intolerant of hydroxyurea: JAK inhibitor INCB18424 tablets versus best available care) is a global study conducted by Incyte in the US and Novartis in rest of world and is expected to enroll approximately 300 patients with PV who are resistant to or intolerant of hydroxyurea (HU). RESPONSE will compare the efficacy and safety of INCB18424 to the physician's choice of best available therapy. Patient enrollment in the US is expected to begin in October (<http://www.responsetrial.com>).

"Securing the SPA for INCB18424 in PV establishes the requirements we must meet to obtain approval in this second indication and supports our objective to expand beyond myelofibrosis," stated Paul A. Friedman, M.D., Incyte's President and CEO. "The encouraging results from the ongoing Phase II PV trial, combined with the data we anticipate achieving from RESPONSE, have the potential to clearly establish the long-term safety and efficacy of INCB18424 and optimally position the compound for use in these underserved patients."

Srdan Verstovsek, M.D., Ph.D., Associate Professor, Leukemia Department, Myeloproliferative Disorders Program Leader, University of Texas M.D. Anderson Cancer Center, and the US principal investigator for RESPONSE, stated, "Patients with advanced PV represent a particularly high-risk group with few therapeutic options for long-term care. These patients would benefit from new chronic therapies that safely and effectively address the aberrant hematological measures, enlarged spleens and significant disease-related symptoms that so negatively impact their lives. In previous trials, INCB18424 has been well tolerated in patients with advanced PV, and much sicker patients with myelofibrosis for as long as 30 months. In the Phase II trial involving 34 PV patients who were HU resistant or HU intolerant, INCB18424 provided rapid and durable activity in these patients. We look forward to evaluating INCB18424 in this Phase III trial designed in agreement with FDA."

RESPONSE Trial

Design

RESPONSE is a global, randomized, open-label, multi-center Phase III trial that will compare the efficacy and safety of the oral JAK1 and JAK2 inhibitor INCB18424 to best available therapy in approximately 300 patients with PV. To be eligible for the study, patients must be resistant to or intolerant of HU, require phlebotomy based on inadequate hematocrit control at least once every three months, possess an elevated white blood cell count and/or platelet count and exhibit a palpated spleen length of 5 cm or greater.

Primary efficacy endpoint

The proportion of patients treated with INCB18424 versus best available therapy achieving a response at week 32, with response defined as having achieved both of the following:

- the absence of phlebotomy and
- a greater-than or equal to 35% reduction in spleen volume as assessed by imaging

Key secondary efficacy endpoints

- Proportion of patients treated with INCB18424 versus best available therapy who both achieve the week 32 primary response endpoint and maintain response for 48 weeks from the time that response was initially documented
- Proportion of patients treated with INCB18424 versus best available therapy achieving complete hematologic remission at week 32

Duration of trial

The randomized, controlled period of the trial is 32 weeks. Data are scheduled to be analyzed when the last patient remaining in the study has completed week 80 (i.e. 48 weeks following the primary endpoint at week 32) to enable the assessment of response durability. Patients receiving benefit from INCB18424 at week 80 will be eligible to continue to receive INCB18424 in a separate open-label extension study.

Best available therapy

Therapy will be selected by the investigator on a patient-by-patient basis among the following six options: interferon/pegylated interferon, pipobroman, anagrelide, immunomodulators (imids such as lenalidomide and thalidomide), HU (at a tolerated dose if, in the opinion of the investigator, the patient is likely to receive benefit), and observation only (i.e. absence of treatment apart from aspirin and phlebotomy when the subject is eligible). The dose and

administration schedule of initial best available therapy may be changed at any time, however the initial therapy may only be changed if specific treatment discontinuation or disease progression criteria are met.

Cross-over from best available therapy to INCB18424

Patients randomized to best available therapy, who fail to meet the primary endpoint at week 32 or whose response ends subsequent to week 32, may be eligible to cross over to receive INCB18424.

Current Approach to Treating PV

The current therapeutic approach in PV focuses on lowering the risk for thrombotic events without exposing patients to increased risk of leukemic transformation¹. While phlebotomy and low dose aspirin are accepted as the standard of care for initial therapy, cytoreductive therapy is recommended to aid in the control of erythrocytosis in the presence of poor tolerance to phlebotomy, symptomatic or progressive splenomegaly, or evidence of high thrombotic risk². Though not FDA approved for use in PV, HU is the most frequently used myelosuppressive agent for initial cytoreductive therapy². HU treatment is associated with cytopenias and often unsatisfactory hematological control over time, aphthous and leg ulcers, multiple other toxicities, and risk of leukemia estimated at up to 10% at the 13th year^{3,4}. Therapeutic options beyond HU are limited, and as a consequence, it is estimated that up to 20% of patients may continue on HU even though response is less than satisfactory⁴.

About Special Protocol Assessment

The SPA is a process that allows for official FDA evaluation of the clinical protocols of a Phase III clinical trial intended to form the primary basis for an efficacy claim and provides trial sponsors with a written agreement that the design and analysis of the trial are adequate to support a New Drug Application (NDA) if the trial is performed according to the SPA. Final marketing approval depends on the results of efficacy, the adverse event profile and on an evaluation of the benefit/risk of treatment demonstrated in the Phase III trial. The SPA agreement may only be changed through a written agreement between the sponsor and the FDA, or if the FDA becomes aware of a substantial scientific issue essential to product efficacy or safety. For more information on Special Protocol Assessment, please visit the FDA web site at <http://www.FDA.gov>.

About PV and INCB18424

PV is characterized by the overproduction of red blood cells which increases blood viscosity and leads to elevated thromboembolic risk. Increased levels of white blood cells and platelets are also common. In advanced disease, patients frequently exhibit spleen enlargement and debilitating symptoms including pruritus, night sweats, fatigue, and muscle and bone pain. In the Phase II trial, as presented at the American Society of Hematology Annual Meeting, December 2009, clinical benefits associated with INCB18424 treatment in the 34 PV patients enrolled in the study included hematocrit control without the need for phlebotomy, normalization of white blood cell and platelet counts, and rapid and durable reductions in enlarged spleens and symptoms, particularly pruritus. INCB18424 was generally well tolerated in these patients, and the most common adverse events observed involved low blood cell counts which, in the majority of patients, were reversed by dose reduction.

About the Incyte Novartis Alliance

In November 2009, Incyte and Novartis announced a major collaboration and license agreement for two hematology-oncology programs in which Incyte retained exclusive rights to develop and commercialize INCB18424 in the US and Novartis received exclusive rights to develop and commercialize INCB18424 for territories outside the US. Novartis also received worldwide rights for Incyte's cMET inhibitor, INCB28060.

About Incyte

Incyte Corporation is a Wilmington, Delaware-based drug discovery and development company focused on developing proprietary small molecule drugs for oncology and inflammation. Incyte's most advanced compound, INCB18424, is in Phase III development for myelofibrosis. For additional information on Incyte, visit the Company's web site at <http://www.incyte.com>.

Forward Looking Statements

Except for the historical information contained herein, the matters set forth in this press release, including statements with respect to the anticipated completion of COMFORT-I and COMFORT-II in patients with myelofibrosis, the expected number of patients and time to begin enrollment of patients in RESPONSE, the anticipated data from RESPONSE combined with the results from the ongoing Phase II PV trial having the potential to establish the long-term safety and efficacy of INCB18424 within the segment of advanced PV patients and optimally positioning the compound for use in these patients, and the anticipated schedule for analysis of data from RESPONSE, are all 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 subject to risks and uncertainties that may cause actual results to differ materially, including the high degree of risk and uncertainty associated with drug development and clinical trials, the uncertainty associated with the regulatory approval processes, uncertainty regarding the timing of commencement of RESPONSE, the ability to enroll a sufficient number of patients for RESPONSE in a timely manner or at all, unanticipated developments in the efficacy or safety of INCB18424, 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 June 30, 2010. Incyte disclaims any intent or obligation to update these forward-looking statements.

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1. Finazzi G, Barbui T. (2008) Evidence and expertise in the management of polycythemia vera and essential thrombocythemia. *Leukemia*.; 22:1494-1502.

2. Finazzi G, Barbui T. (2007) How I treat patients with polycythemia vera. *Blood*.;109:5104- 5111.

3. Tefferi A. (2003) Polycythemia vera: a comprehensive review and clinical recommendations. *Mayo Clin Proc*.;78:174-94.

4. Najean Y, Rain JD. (1997) Treatment of polycythemia vera: The use of hydroxyurea and pipobroman in 292 patients under the age of 65 years. Blood.;90:3370-3377.

SOURCE: Incyte Corporation

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