

Incyte Announces Preliminary Results of a Phase I/II Study of Combination Immunotherapy in Patients with Melanoma

June 2, 2014

- *Clinical data suggest anti-tumor synergy between Incyte's IDO1 inhibitor INCB24360 and ipilimumab described in an ASCO poster highlights session*
- *Among immunotherapy-naïve patients receiving INCB24360 combined with ipilimumab, 42 percent had an objective response and 75 percent achieved disease control*
- *IDO1 inhibitor-based combination therapy represents a promising and potentially synergistic approach to immuno-oncology*

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 that preliminary results from an ongoing Phase I/II study of INCB24360, its oral indoleamine 2,3-dioxygenase 1 (IDO1) inhibitor, combined with ipilimumab in patients with unresectable or metastatic melanoma were presented at the 50th Annual Meeting of the American Society of Clinical Oncology (ASCO), May 30 to June 3, 2014, in Chicago. The poster reported initial findings showing that the combination was generally well tolerated and produced evidence of clinical response.

In the study, 42 percent (5/12) of immunotherapy-naïve patients who received ipilimumab with INCB24360 at 25 mg or 50 mg twice-daily demonstrated an objective response (complete response + partial response) and 75 percent (9/12) achieved disease control (complete response + partial response + stable disease) as assessed using immune-related response criteria (irRC). One patient with pulmonary metastases treated with ipilimumab and INCB24360 50 mg twice-daily experienced a complete response. Immune-related adverse events observed in these cohorts were generally mild-to-moderate (Grade 1 or Grade 2). Grade 3 or 4 immune related adverse events were qualitatively similar to ipilimumab monotherapy and were generally manageable and reversible.

"In addition to seeing disease control among the 12 immunotherapy-naïve patients, many of these patients also experienced substantial reduction in tumor burden," said Geoffrey T. Gibney, M.D., Moffitt Cancer Center, who presented the study findings. "These preliminary data suggest INCB24360 may improve patient outcomes with manageable toxicity when combined with ipilimumab."

"Immune-targeted combination therapy represents one of the most promising approaches in oncology and our preclinical data suggested that combination of an IDO1 inhibitor with checkpoint inhibitors could have significant anti-tumor synergy," said Hervé Hoppenot, President and Chief Executive Officer, Incyte. "The synergistic activity observed between INCB24360 and ipilimumab increases our confidence in the value of investigating other immunotherapy combinations with INCB24360 in multiple tumor types."

The poster for this presentation can be accessed at [2014 ASCO - INCB24360 poster](#).

About the Study

The ASCO presentation described results from the open-label, dose escalation portion of the ongoing Phase I/II study evaluating the combination of a standard regimen of ipilimumab with oral INCB24360. Study endpoints included safety and tolerability, objective response rate (assessed using irRC and RECIST 1.1 criteria every nine weeks), duration of response, overall and progression-free survival, and IDO1 inhibition.

Additional Safety and Efficacy Findings

Initially, seven patients were enrolled in a cohort receiving ipilimumab with INCB24360 300 mg twice-daily. Five of these patients developed clinically significant (Grade 3 or 4) alanine aminotransferase (ALT) elevations and enrollment was stopped. The ALT elevations observed in the patients receiving the 300 mg dose were reversible with corticosteroids and treatment discontinuation. Although all patients in the 300 mg twice-daily cohort were discontinued before response could be fully evaluated, six of the seven patients were alive after one year, including three who have not received subsequent checkpoint inhibitor immunotherapy. The study was amended to evaluate lower doses of INCB24360.

Seventeen patients were enrolled in the INCB24360 25 mg twice-daily and 50 mg twice-daily cohorts. During the dose limiting toxicity (DLT) observation periods, one patient in the 25 mg cohort who had extensive liver metastases prior to entering the trial experienced a DLT (Grade 3 AST elevation), and two patients in the 50 mg cohort experienced a DLT (Grade 3 diarrhea and Grade 3 ALT elevation). In both cohorts, immune-related treatment-emergent adverse events were generally Grade 1 or Grade 2 and manageable with continued dosing or temporary dose interruption.

Twelve patients who were treatment-naïve for advanced or metastatic disease were enrolled in the INCB24360 25 mg twice-daily and 50 mg twice-daily cohorts. Eight of these immunotherapy-naïve patients experienced a reduction in tumor burden, and most reductions were durable with continued therapy. As of the data cutoff, the majority of immunotherapy-naïve patients are continuing on study therapy or have experienced a prolonged period without the need for subsequent therapy.

Of the five patients who received prior immunotherapy for advanced or metastatic disease, two (40 percent) achieved stable disease by irRC.

Duration of disease control ranged from 60 to more than 379 days (ongoing).

Pharmacodynamic effects with INCB24360 25 mg BID and 50 mg BID were similar to those that were sufficient in preclinical models to achieve maximal therapeutic effect. IDO1 inhibition in this study was consistent with that observed in the phase I open-label study,¹ suggesting that there was no pharmacodynamic interaction with ipilimumab.

About INCB24360

Indoleamine 2,3-dioxygenase 1 (IDO1) is an immunosuppressive enzyme that has been shown to induce regulatory T cell generation and activation, and allow tumors to escape immune surveillance. INCB24360 is an orally bioavailable small molecule inhibitor of IDO1 that has nanomolar potency in both biochemical and cellular assays and has demonstrated potent activity in enhancing T lymphocyte, dendritic cell and natural killer cell responses *in vitro*, with a high degree of selectivity. INCB24360 has been shown to be active in mouse models of cancer as a single agent and in combination with cytotoxic and immunotherapy agents, and its ability to reduce tumor growth is dependent on a functional immune system – consistent with its proposed mechanism of action. A Phase I dose-escalation trial demonstrated that INCB24360 results in greater than 90 percent inhibition of IDO1 activity at generally well-tolerated doses.

In addition to the Phase I/II study in metastatic melanoma in combination with ipilimumab (www.clinicaltrials.gov Identifier: NCT01604889), described in the ASCO presentation, Incyte has also established three clinical research agreements to study INCB24360 in combination with the investigational anti-PD-1 immunotherapy checkpoint inhibitor MK-3475 (Merck), the investigational anti-PD-L1 immune checkpoint inhibitor MEDI 4736 (MedImmune), and the investigational anti-PD-1 immune checkpoint inhibitor nivolumab (Bristol-Myers Squibb).

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, INCB24360, including that INCB24360 may improve patient outcomes with manageable toxicity when combined with ipilimumab, 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 INCB24360, 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.

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Reference

1. Beatty GL, et al. Phase I study of the safety, pharmacokinetics, and pharmacodynamics of the oral inhibitor of indoleamine 2,3-dioxygenase (IDO1) INCB024360 in patients with advanced malignancies. Presented at: 2013 Annual Meeting of the American Society of Clinical Oncology; May 31-June 4, 2013; Chicago, IL.



Source: Incyte Corporation

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