Epacadostat in Combination with Pembrolizumab Demonstrates Promising Clinical Activity in Multiple Advanced Cancers

November 3, 2015

Combination of IDO1 inhibitor plus PD-1 antagonist demonstrates responses and disease control in a broad range of tumor types and is generally well-tolerated with low rates of Grade 3 or higher adverse events

WILMINGTON, Del.--(BUSINESS WIRE)--Nov. 3, 2015-- Incyte Corporation (Nasdaq:INCY) announces the first presentation of findings from the ongoing proof-of-concept Phase 1/2 study evaluating epacadostat, Incyte's selective IDO1 inhibitor, in combination with pembrolizumab, an anti-PD-1 therapy. Results evaluating 19 patients for efficacy and 28 patients for safety, indicate a 79 percent (n=15/19) disease control rate (DCR) in evaluable patients with advanced cancers. Responses were observed in all tumor types assessed. In the melanoma group (n=7), four of seven patients treated with the combination of epacadostat and pembrolizumab had an objective response, including 2 complete responses (CRs), with disease control demonstrated in six of the seven patients treated with the combination.

These results (see Appendix) will be published in the Journal for ImmunoTherapy of Cancer on November 4, 2015. Updated study results—including safety data on 56 patients and efficacy data on 47 patients, inclusive of 19 evaluable melanoma patients—will be presented by Dr. Tara Gangadhar as a late-breaking oral presentation (Abstract #142) on Friday, November 6, 2015 from 12:00-12:15 PM EST at the Society for Immunotherapy of Cancer (SITC) 30th Anniversary Annual Meeting & Associated Programs. Following the presentation, the updated data will be made available on www.incyte.com.

"These new data underscore the potential of epacadostat to treat advanced forms of cancer when used in combination with an anti-PD-1 therapy," said Rich Levy, MD, Chief Drug Development Officer of Incyte. "We look forward to further evaluating the clinical benefits of the combination of epacadostat and pembrolizumab, both within the planned Phase 3 melanoma study that is expected to begin in the first half of next year, and in other future clinical programs."

About the Study

The ongoing dose-escalation and dose-expansion study of epacadostat in combination with pembrolizumab includes patients with advanced melanoma, renal cell carcinoma (RCC), transitional cell carcinoma (TCC), non-small cell lung cancer (NSCLC), endometrial adenocarcinoma (EA), or squamous cell carcinoma of the head and neck (SCCHN). Patients previously treated with anti-PD-1 or anti-CTLA-4 therapies were excluded.

Study Results

Overall Response Rates (ORR) and Disease Control Rates (DCR) in Advanced Cancers

Evaluable Patients n (%)	Melanoma n=7	RCC n=5	TCC n=2	NSCLC n=2	EA n=2	SCCHN n=1	Total (n)
ORR (CR + PR)	4 (57)	2 (40)	1 (50)	1 (50)	1 (50)	1 (100)	10 (53)
DCR (CR + PR + SD)	6 (86)	4 (80)	1 (50)	2 (100)	1 (50)	1 (100)	15 (79)

CR = complete response, PR = partial response, SD = stable disease (RECIST 1.1)

Adverse events (AEs) included a DLT (grade 3 rash) observed in 1/8 patients with epacadostat 50 mg BID/pembrolizumab 2 mg/kg; no DLTs were observed with epacadostat 100 mg BID/pembrolizumab 2 mg/kg. The most common (≥20%) all grade AEs were fatigue, diarrhea, rash, arthralgia, and nausea; the majority of these were grade 1 or 2. Grade ≥3 immune-related AEs were mucosal inflammation and rash (n=1 [4%] each).

Correlations between biomarker expression and response are being evaluated, and enrollment in expansion cohorts is ongoing.

These data will be discussed as part of Incyte's previously arranged third quarter 2015 financial results conference call and webcast at 10:00 AM ET on Tuesday, November 3, 2015.

About Epacadostat

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. Epacadostat 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.

Epacadostat has shown proof-of-concept clinical data in patients with unresectable or metastatic melanoma in combination with the CTLA-4 inhibitor ipilimumab, and is currently in four proof-of-concept clinical trials with PD-1 and PD-L1 immune checkpoint inhibitors in a variety of cancer histologies. A Phase 3 study evaluating the combination of epacadostat with pembrolizumab as first-line treatment for patients with advanced or metastatic melanoma is expected to begin in the first half of 2016.

About Incyte

Incyte Corporation is a Wilmington, Delaware-based biopharmaceutical company focused on the discovery, development and commercialization of

proprietary therapeutics, primarily for 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 planned commencement of the Phase 3 trial for epacadostat in combination with pembrolizumab for advanced or metastatic melanoma, the efficacy of such trial and the effect such trial may have on patient outcomes, and the evaluation of epacadostat in other clinical programs, 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 the high degree of risk associated with drug development, results of further research and development, unanticipated delays, other market or economic factors and technological advances, regulatory approval of the transaction 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, 2015. Incyte disclaims any intent or obligation to update these forward-looking statements.

Appendix

Preliminary results from a phase 1/2 study of epacadostat (INCB024360) in combination with pembrolizumab in patients with selected advanced cancers

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Background

Indoleamine 2,3-dioxygenase 1 (IDO1) is a tryptophan-catabolizing enzyme that is expressed in many cancers and induces immune tolerance by suppressing T-cell responses. Epacadostat is a potent, selective oral inhibitor of IDO1. A dose-escalation study of epacadostat with ipilimumab in patients with advanced melanoma showed favorable ORR, disease control rate (DCR), and PFS in immunotherapy-naïve patients.[1] Preliminary data of epacadostat with pembrolizumab in patients with selected advanced cancers are reported.

Methods

This is an ongoing dose-escalation and dose-expansion study of epacadostat with pembrolizumab in patients with Stage IIIB, IV, or recurrent NSCLC, melanoma, transitional cell carcinoma (TCC), RCC, endometrial adenocarcinoma (EA), or SCCHN with a 3+3+3 phase 1 design (NCT02178722). Patients previously treated with anti-PD-1 or anti-CTLA-4 therapies were excluded. Enrollment is complete in the epacadostat 25 mg BID, 50 mg BID, and 100 mg BID cohorts with pembrolizumab 2 mg/kg IV q3 weeks. Expansion cohorts of epacadostat 50 mg BID, 100 mg BID, and 300 mg BID with pembrolizumab 200 mg are enrolling. Safety, tolerability, and investigator-assessed tumor response (RECIST 1.1) were evaluated.

Results

As of August 21, 2015, 54 patients were enrolled. This report includes safety data on 28 patients (melanoma [n=11], RCC [n=5], NSCLC [n=5], TCC [n=3], EA and SCCHN [n=2 each]) and 19 patients evaluable for efficacy as of July 13, 2015. A DLT (grade 3 rash) was observed in 1/8 patients with epacadostat 50 mg BID/pembrolizumab 2 mg/kg; no DLTs were observed with epacadostat 100 mg/pembrolizumab 2 mg/kg. The most common (≥20%) all grade AEs were fatigue, diarrhea, rash, arthralgia, and nausea; the majority of these were grade 1 or 2. Grade ≥3 immune-related AEs were mucosal inflammation and rash (n=1 [4%] each). Reductions in tumor burden were observed in 15/19 evaluable patients. Responses were observed in all tumor types (Table), and all are ongoing. In 7 evaluable melanoma patients, ORR was 57% and DCR was 86%, which included 2 CRs. In 5 evaluable RCC patients, ORR was 40% and DCR was 80%. Based on a PK-PD model for epacadostat, nearly all patients' C_{avg} exceeded the IC_{50}, the range of active drug exposure seen in preclinical models.

Conclusions

Epacadostat with pembrolizumab was generally well tolerated and efficacy data suggest promising clinical activity. Correlations between biomarker expression and response are being evaluated. Enrollment in expansion cohorts is ongoing. Updated data will be presented.

Reference

1) Gibney GT, et al. European Cancer Congress 2015 [abstract 511].

Evaluable patients*, n (%)	Melanoma (n=7)	RCC (n=5)	TCC (n=2)	NSCLC (n=2)	EA (n=2)	SCCHN (n=1)
ORR (CR+PR)	**4 (57)**	**2 (40)**	**1 (50)**	**1 (50)**	**1 (50)**	**1 (100)**
CR	2 (29)	0	0	0	0	0
PR	2 (29)	2 (40)	1 (50)	1 (50)	1 (50)	1 (100)
SD	2 (29)	2 (40)	0	1 (50)	0	0

DCR (CR+PR+SD)	**6 (86)**	**4 (80)**	**1 (50)**	**2 (100)**	**1 (50)**	**1 (100)**
PD	1 (14)	0	1 (50)	0	0	0
Not assessable	0	1 (20)	0	0	1 (50)	0

*Patients with ≥ 1 post-baseline response assessment or discontinued from study or died before response could be assessed.

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