Incyte's CDK2 Inhibitor INCB123667 Shows Promising Evidence of Clinical Activity in Patients with Advanced Solid Tumors, Notably Ovarian Cancer

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- *New antitumor response data from a range of doses and regimens unveiled today at Incyte investor event*
- *These results build upon safety and tolerability data presented earlier today during a mini-oral presentation at the European Society of Medical Oncology (ESMO) Congress 2024*
- *Findings support the initiation of a pivotal trial in ovarian cancer, expected to begin in 2025; additional plans to evaluate INCB123667 in combination with other treatments are underway*

WILMINGTON, Del.--(BUSINESS WIRE)--Sep. 14, 2024-- Incyte (Nasdaq:INCY) today announced new early clinical data for INCB123667, a highly selective, potential first-in-class CDK2 inhibitor, in patients with advanced solid tumors. The trial results, presented during a mini-oral presentation at the European Society of Medical Oncology (ESMO) with new, updated data shared during the Company's investor event, highlight the potential of INCB123667 as a differentiated treatment option for cancers with increased Cyclin E1 activity, amplification and/or overexpression in cells predictive of CDK2 dependency.

In the trial, patients with advanced or metastatic solid tumors (n=205) – including ovarian cancer, endometrial cancer, gastrointestinal cancer, HR+/HER2- breast cancer and triple negative breast cancer, among others – received varying doses of INCB123667 ranging from 50mg to 150mg using once-daily (QD) and twice-daily (BID) dosing schedules.

New data from the Phase 1b dose expansion portion of the trial (data cut-off August 26, 2024) presented today during Incyte's investor event, demonstrate single-agent antitumor activity, and decreases in circulating tumor DNA (ctDNA) across a range of doses and regimens, notably in patients with ovarian cancer and endometrial cancer whose tumors overexpress Cyclin E1. The trial is ongoing, and the data will continue to mature.

- Of the 37 evaluable participants with platinum-resistant ovarian cancer treated at three (3) selected dose levels (50mg BID, 100mg QD and 125mg QD) in the expansion portion of the trial, nine participants (24.3%) experienced an overall response (OR; 2 complete responses [CR] and 7 partial responses [PRs]). The highest OR rate of 31.3% (5 responders, including 2 CRs) was found in the 50mg BID cohort (16 evaluable participants). Additionally, a disease control rate (DCR) of 75.7% (28/37) was achieved in patients with ovarian cancer.
- In addition, 4 PRs were reported among patients with endometrial cancer.

"The early-stage clinical activity of INCB123667 represents an exciting and promising breakthrough for patients with ovarian cancer. We believe this novel CDK2 inhibitor has the potential to be a foundational treatment for platinum-resistant ovarian cancer, offering a new and differentiated treatment for patients who currently have limited treatment options," said Pablo Cagnoni M.D., President, Head of Research and Development, Incyte. "We look forward to advancing the development of INCB123667 for the treatment of patients with ovarian cancer both as a single agent and in combination."

The Part 1b data build on results from the dose escalation portion (Part 1a) of the trial evaluating the safety and tolerability of INCB123667 presented during a mini-oral presentation (Mini oral session: Developmental therapeutics) at ESMO.

Results from the Part 1a dose escalation portion of the trial (data cut-off July 15, 2024) include:

- INCB123667 demonstrated a manageable safety profile (n=84). The most common hematologic treatment-related adverse events (TRAEs) were thrombocytopenia (35%, 13% Grade 3), anemia (30%, 7% Grade 3) and neutropenia (26%, 8% Grade 3). The most common non-hematologic TRAEs were nausea (42%), fatigue (23%) and vomiting (17%); all of which were Grade 1 and 2 except one case of Grade 3 vomiting and one case of Grade 3 fatigue.
- Strong selective inhibition of CDK2 was observed resulting in circulating tumor DNA (ctDNA) reduction at all dose levels. During dose escalation, 39 out of 48 patients who had ctDNA measurements at cycle 1, day 1 and cycle 2, day 1 showed reductions in ctDNA.

"Results from this study presented today at ESMO reinforce the idea that the novel and highly selective CDK2 inhibitor INCB123667 may provide a potential new treatment option for cancers with increased Cyclin E1 signaling (CCNE1 amplification and Cyclin E1 overexpression), predictive of CDK2 dependency," said Dr. Matteo Simonelli, Head of Early-Drug Development in Solid Tumors at IRCCS Humanitas Research Hospital. "The data speak to the potential of INCB123667 as an active and selective targeted therapy for different cancer types, particularly ovarian cancer, and I look forward to seeing further results in later stages of development."

The study is ongoing. Plans are underway to initiate a pivotal study in ovarian cancer next year and evaluate INCB123667 in combination with other treatments.

Conference Call and Webcast Information

Incyte will host an in-person analyst and investor event today from 1:00-2:30 p.m. ET (7:00-8:30 p.m. CEST) to discuss key data presentations at ESMO including data from the POD1UM-303 Presidential Symposia and its CDK2 inhibitor program. The CDK2 data will include updated results from a later data cut-off, as well as the data included in the ESMO accepted abstract and mini-oral presentation.

To access the conference call, please dial 877-407-8037 for domestic callers or +1 201-689-8037 for international callers. When prompted, provide the conference identification number, 13748627.

The conference call will also be webcast live and can be accessed at investor.incyte.com.

About the Trial (NCT05238922)

This open-label, dose-escalation and dose-expansion Phase 1 study is evaluating the safety, tolerability, pharmacokinetics, pharmacodynamics and preliminary efficacy of INCB123667 when administered as monotherapy at the recommended dose for expansion (RDE[s]) in participants with selected advanced or metastatic solid tumors. Part 1A (dose escalation) determined the recommended dose of INCB123667 for expansion and the maximum tolerated dose (MTD). Part 1B (cohort dose expansion phase) will further explore antitumor activity of INCB123667 as a monotherapy in six tumor-specific cohorts at the RDEs defined in Part 1A.

For more information about the study, please visit: https://clinicaltrials.gov/study/NCT05238922.

About INCB123667

INCB123667 is a novel, potent and selective oral small molecule inhibitor of CDK2 which has been shown to suppress tumor growth as monotherapy and in combination with standard of care, in Cyclin E amplified tumor models. Cyclin E amplification and overexpression has been reported to be associated with CDK4/6 resistance and poor clinical outcomes in ovarian, gastric, endometrial and breast cancers. INCB123667 has the potential to be a highly targeted and efficacious treatment for advanced solid tumors, including gynecologic tumors, endometrial, uterine, gastric and triple negative breast cancer, among others.

About Incyte

A global biopharmaceutical company on a mission to *Solve On.*, Incyte follows the science to find solutions for patients with unmet medical needs. Through the discovery, development and commercialization of proprietary therapeutics, Incyte has established a portfolio of first-in-class medicines for patients and a strong pipeline of products in Oncology and Inflammation & Autoimmunity. Headquartered in Wilmington, Delaware, Incyte has operations in North America, Europe and Asia.

For additional information on Incyte, please visit Incyte.com or follow us on social media: LinkedIn, X, Instagram, Facebook, YouTube.

Incyte Forward-looking Statements

Except for the historical information set forth herein, the matters set forth in this press release, including statements regarding the presentation of data for Incyte's CDK2 inhibitor (INCB123667), the potential this CDK2 inhibitor offers for patients, and expectations regarding ongoing and future clinical trials contain predictions, estimates, and other forward-looking statements.

These forward-looking statements are based on our current expectations and are subject to risks and uncertainties that may cause actual results to differ materially, including unanticipated developments in and risks related to: unanticipated delays; further research and development and the results of clinical trials possibly being unsuccessful or insufficient to meet applicable regulatory standards or warrant continued development; the ability to enroll sufficient numbers of subjects in clinical trials and the ability to enroll subjects in accordance with planned schedules; determinations made by the FDA and regulatory agencies outside of the United States; the efficacy or safety of our products; the acceptance of our products in the marketplace; market competition; unexpected variations in the demand for our products and the products of our collaboration partners; the effects of announced or unexpected price regulation or limitations on reimbursement or coverage for our products; sales, marketing, manufacturing, and distribution requirements, including our ability to successfully commercialize and build commercial infrastructure for newly approved products and any additional new products that become approved; and other risks detailed from time to time in our reports filed with the U.S. Securities and Exchange Commission, including our annual report on Form 10-K and our quarterly report on Form 10-Q for the quarter ended June 30, 2024. We disclaim any intent or obligation to update these forward-looking statements.

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