Incyte Announces Phase 1 Results for its TGFβR2×PD-1 Bispecific Antibody in Advanced Colorectal Cancer and KRAS G12D Inhibitor in Advanced Pancreatic Ductal Adenocarcinoma

October 19, 2025

- *Data presented at ESMO 2025 show INCA33890, a TGFβR2×PD-1 bispecific antibody, has the potential to be an effective treatment in microsatellite stable (MSS) colorectal cancer*
- *Planned initiation of registrational program for INCA33890 in MSS colorectal cancer in 2026*
- *Maturing data for INCB161734, a KRAS G12D inhibitor, shows a favorable safety profile and evidence of clinical benefit in heavily pre-treated pancreatic ductal adenocarcinoma (PDAC) patients*
- *Incyte will expand on the results from the oral presentations at an in-person and webcasted event on Sunday, October 19, 2025, from 1:30 – 3:00 p.m. EDT (7:30 – 9:00 p.m. CEST)*

WILMINGTON, Del.--(BUSINESS WIRE)--Oct. 19, 2025-- Incyte (Nasdaq:INCY) announced the first clinical data evaluating its TGFβR2×PD-1 bispecific antibody (INCA33890) for patients with microsatellite stable (MSS) colorectal cancer; and its potent, selective and orally bioavailable KRAS G12D inhibitor (INCB161734) for patients with KRAS G12D mutations, specifically pancreatic ductal adenocarcinoma (PDAC). The data were featured in two oral sessions (Investigational immunotherapy; Abstract #1522MO and Developmental therapeutics; Abstract #916O, respectively) at the European Society of Medical Oncology (ESMO) Congress 2025.

“The proof-of-concept data highlight the potential of INCA33890 and INCB161734 to address significant medical needs in patients with advanced solid tumors, including MSS colorectal cancer and PDAC,” said Pablo J. Cagnoni, M.D., President and Head of Research and Development, Incyte. “These results, including the favorable safety profiles as monotherapies, support continued clinical development. We look forward to exploring the development of these two novel targeted therapies in combination with current standard of care as frontline treatments.”

INCA33890 (TGFβR2×PD-1)

In an October 17, 2025, mini oral session at ESMO, data were presented from the monotherapy arm (Part 1) of the INCA33890 Phase 1 trial, which included patients with advanced or metastatic solid tumors – including MSS colorectal cancer, ovarian cancer (OC), squamous cell carcinoma of the head and neck (SCCHN), non-small cell lung cancer (NSCLC), gastric/gastroesophageal junction cancer (GC/GEJ) and PDAC – who experienced disease progression after receiving available therapies or were intolerant to, ineligible for or declined standard treatments, including immune checkpoint inhibitors. These patients received doses of INCA33890 ranging from 100 mg to 1,500 mg every two weeks (Q2W) to 900 mg intravenously (IV) every four weeks (Q4W) in continuous 28-day cycles. INCA33890 300 mg, 600 mg and 900 mg Q2W were selected as the recommended doses for expansion (RDE).

Initial data (cut-off July 25, 2025) showed promising clinical efficacy with INCA33890 treatment. This trial is ongoing, and the data will continue to mature. Of note:

- INCA33890 demonstrated a manageable safety profile across all enrolled patients (n=260) – the occurrence and severity of immune related adverse reactions was similar to approved immune checkpoint inhibitors. The most common treatment-related adverse events (TRAEs) among individuals treated with INCA33890 across RDE (n=239) were fatigue (13.8%), pruritus (8.8%) and infusion-related reactions (8.4%).
- Among patients with metastatic MSS colorectal cancer treated with INCA33890 at RDE (n=105), the vast majority (93.3%) had received more than two prior treatment regimens and 71.4% had active liver metastases at the time of treatment.
    - Within this cohort, 16 patients treated with INCA33890 responded (14 confirmed), with 15.2% achieving an objective response rate (ORR) and a median duration of therapy of 7.3 months.
    - The ORR among metastatic MSS colorectal cancer patients treated with INCA33890 was similar across RDE. Deep tumor responses were observed among patients with liver metastasis (n=9) – 12.0% achieved an ORR with a disease control rate (DCR) of 20.0%. Additionally, seven patients with no liver metastases treated with INCA33890 responded, achieving an ORR of 23.3% and DCR of 50.0%.

“Increased TGFβR2 expression is associated with poor prognosis in multiple solid tumor types, including colorectal cancer, which is third most common cancer and the second leading cause of cancer-related mortality worldwide,” said Elena Garralda, M.D., Ph. D., Trial Investigator and Director of Early Drug Development at the Vall d'Hebron Institute of Oncology. “The efficacy data presented at ESMO in MSS colorectal cancer, coupled with tolerable safety profile, provide proof of concept for this differentiated approach of on-target inhibition of the TGF-β pathway. I look forward to seeing further development of this promising drug.”

Evaluation of INCA33890 900 mg Q2W in combination with standard of care (SoC) treatments in patients with MSS colorectal cancer is ongoing. Dose escalation has been completed across combination therapy cohorts and no DLTs were identified. Incyte plans to initiate a registrational program for INCA33890 in MSS colorectal cancer in 2026.

INCB161734 (KRAS G12D)

In an October 19, 2025, proffered paper session, data were presented from the monotherapy arm (Part 1) of the INCB161734 Phase 1 trial in patients with select advanced or metastatic solid tumors and documented KRAS G12D mutation – including PDAC, colorectal cancer, NSCLC, OC and other solid tumors – who received varying doses of INCB161734 ranging from 200 mg to 1,600 mg daily. The dose escalation portion of the study is complete – two doses, 600 mg daily and 1,200 mg daily, were selected for expansion.

Preliminary data (cut-off August 1, 2025) demonstrated evidence of clinical benefit in advanced or metastatic PDAC patients treated with INCB161734 (n=83). This trial is ongoing, and the data will continue to mature. Specifically:

- INCB161734 demonstrated a manageable safety profile across all treated patients (n=136). No DLTs were reported in dose escalation, and the maximum tolerated dose (MTD) was not reached. No fatal adverse events (AEs) were considered related to treatment. The most common TRAEs across tumor types, nausea (58.1%), diarrhea (50.7%), vomiting (45.6%) and fatigue (17.4%), were mostly Grade 1.
- PDAC patients receiving 600 mg (n=25) and 1,200 mg (n=29) INCB161734 daily demonstrated objective response rates (ORR; 20% and 34%) and high DCRs (64% and 86%). The study is ongoing for the majority of patients; data on durability of response is expected in the first half of 2026.

“PDAC is a highly aggressive cancer, and patients with G12D-mutated PDAC currently have an average five-year survival rate of less than ten percent,” said Dr. Jayesh Desai, Tiral Investigator, Medical Oncologist and Associate Director of Clinical Research at the Peter MacCallum Cancer Centre. “It is encouraging to see promising antitumor activity and strong molecular response with INCB161734 monotherapy in this heavily pretreated patient population, and I believe these data speak to the potential of INCB161734 to be an impactful, selective targeted therapy for PDAC.”

Evaluation of the data for INCB161734 in patients with PDAC is ongoing with results expected in 2026. Based on the findings, the company will conduct a comprehensive review of the data to inform next steps for the program, including discussions with regulatory authorities.

More information regarding the 2025 ESMO Congress and the data from Incyte’s oncology portfolio being featured at the meeting can be found on the ESMO website: https://www.esmo.org/meeting-calendar/esmo-congress-2025.

Analyst Event and Webcast
The data from the ESMO oral presentations and additional results from INCA33890 in patients with MSS colorectal cancer and INCB161734 in patients with PDAC will also be discussed at an in-person analyst and investor event on Sunday, October 19, 2025, from 1:30 – 3:00 p.m. ET (7:30 – 9:00 p.m. CEST) at ESMO.

The event will be webcasted and can be accessed via the Events and Presentations tab of the Investor section of Incyte.com and it will be available for replay for 30 days.

More information regarding the 2025 ESMO Congress can be found at: https://www.esmo.org/meeting-calendar/esmo-congress-2025.

About INCA33890
INCA33890 is an investigational, TGFβR2×PD-1 bispecific antibody, developed in collaboration with Merus using their Biclonics® antibody platform, engineered to block TGF-β–mediated signaling in T cells co-expressing TGF-β and PD-1. TGFβ is known to promote cancer immune evasion and predicts poor response to PD-(L)1 targeted therapies. INCA33890 aims to spare tissues where TGF-β signaling is important for normal function, avoiding the known toxicity of a broad blocking of the TGF-β pathway. INCA33890 offers a promising targeted treatment strategy for patients with advanced or metastatic solid tumors, including microsatellite stable colorectal cancer.[1,2,3,4]

The open-label, multicenter Phase 1 study (NCT05836324) is evaluating the safety, tolerability, dose-limiting toxicities (DLTs), pharmacokinetics (PK), pharmacodynamics (PD) and preliminary efficacy of INCA33890 when administered as a monotherapy and in combination with other standard-of-care treatments (i.e., bevacizumab, bevacizumab and FOLFIRI, bevacizumab and FOLFOX, and cetuximab) in adults (≥18 years old) with advanced or metastatic solid tumors.

The study includes Part 1 evaluating INCA33890 as a monotherapy with Part 1A (dose escalation) and Part 1B (dose expansion). Inclusion criteria for Part 1 requires patients to have experienced disease progression after receiving available therapies or that they were intolerant to, ineligible for or declined standard treatment. Part 2 will evaluate INCA33890 administered in combination with other protocol-defined treatment(s) based on cohort assignment and also includes dose escalation (Part 2A) and dose expansion (Part 2B).

Primary endpoints include evaluating DLTs up to 28 days and safety/tolerability. Key secondary endpoints focus on preliminary efficacy (i.e., objective response rate [ORR], disease control rate [DCR], duration of response [DOR]) up to two years and PK parameters.

For more information about the study, please visit: https://clinicaltrials.gov/study/NCT05836324.

About INCB161734
INCB161734 is an investigational novel, selective and orally bioavailable small molecule inhibitor targeting G12D-mutated KRAS. KRAS is one of the most frequently altered driver oncogenes in solid tumors. The G12D mutation, which represents approximately 40% of oncogenic KRAS mutations in patients with PDAC, is associated with aggressive tumor phenotypes and poor clinical outcomes.

The open-label, dose-escalation and dose-expansion Phase 1 study (NCT06179160) is evaluating the safety, tolerability, pharmacokinetics, pharmacodynamics and preliminary efficacy of INCB161734 when administered as monotherapy and in combination with other anticancer therapies in patients with advanced or metastatic solid tumors harboring the KRAS G12D mutation. The study includes Part 1 evaluating INCB161734 as a monotherapy, with Part 1A (dose escalation), Part 1B (cohort dose expansion), Part 1C (pharmacodynamics) and Part 1D (food-effect). Part 2 will evaluate INCA161734 administered in combination with other protocol-defined treatment(s) based on cohort assignment and also includes dose escalation (Part 2A) and dose expansion (Part 2B).

Primary endpoints include DLTs and TEAEs. Key secondary endpoints include objective ORR, DCR, DOR and PK parameters.

For more information about the study, please visit: https://www.clinicaltrials.gov/study/NCT06179160.

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.

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 from Incyte's clinical development pipeline, the potential offered by INCA33890 and INCB161734, whether or when any development compounds or combinations will be approved or commercially available for use in humans anywhere in the world, and Incyte's goal of improving the lives of patients, contain predictions, estimates and other forward-looking statements.

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: 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; determinations made by the FDA, EMA, and other regulatory authorities; the efficacy or safety of Incyte and its partners' products; the acceptance of Incyte and its partners' products in the marketplace; market competition; sales, marketing, manufacturing and distribution requirements; 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, 2025. Incyte disclaims any intent or obligation to update these forward-looking statements.

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[1]Deng Z, et al. *Signal Transduct Target Ther*. 2024;9:61.

[2]Mariathasan S, et al. *Nature*. 2018;554:544-548.

[3]Donkor MK, et al. *Immunity*. 2011;35:123-34.

[4]Gulley JL, et al. *Mol Oncol*. 2022;16:2117-2134.

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