

Incyte Announces New Positive Data for INCA033989, its First-In-Class mutCALR-Targeted Monoclonal Antibody, in Patients with Myelofibrosis Presented at ASH 2025

December 7, 2025

- *Rapid and robust reductions in spleen volume and symptoms, and improvements in anemia were observed with INCA033989 as monotherapy and in combination with ruxolitinib (Jakafi®) in patients with myelofibrosis (MF) harboring a CALR mutation (mutCALR)*
- *Results demonstrate a favorable safety profile for INCA033989 as a monotherapy and in combination with ruxolitinib – no dose limiting toxicities were reported and a maximum tolerated dose was not reached*
- *A reduction in peripheral blood mutCALR variant allele frequency (VAF) from baseline was observed in MF patients in the INCA033989 monotherapy arm with ≥ 1 post-baseline VAF measurement*
- *Exploratory analyses from the clinical studies of INCA033989 demonstrate the potential for disease-modifying activity in MF patients with a CALR mutation*
- *Incyte will host an investor event and webcast highlighting these data today, Sunday, December 7, 2025, from 11:00 a.m.-12:30 p.m. ET*

WILMINGTON, Del.--(BUSINESS WIRE)--Dec. 7, 2025-- Incyte (Nasdaq:INCY) today announced new clinical data from two Phase 1 studies evaluating the safety, tolerability and efficacy of INCA033989, a first-in-class mutant calreticulin (mutCALR)-targeted monoclonal antibody, for patients with mutCALR-expressing myeloproliferative neoplasms (MPNs). These preliminary results are from the dose escalation portion of the studies evaluating INCA033989 as a monotherapy in patients with myelofibrosis (MF) harboring a CALR mutation who are resistant, intolerant to or ineligible for JAK inhibitor treatment, and INCA033989 in combination with ruxolitinib (Jakafi®) in patients who experienced a suboptimal response to ruxolitinib monotherapy. These data are being featured in oral presentations (Session 634, Publication #484; Session 631, Publication #71) at the 2025 American Society of Hematology (ASH) Annual Meeting in Orlando.

"These positive study results reinforce our confidence in INCA033989's transformative potential, both as a targeted monotherapy and combination therapy for MF, building on the positive results previously reported in essential thrombocythemia (ET)," said Pablo J. Cagnoni, M.D., President and Head of Research and Development, Incyte. "Our goal is to bring new targeted treatment options to patients across the MPN disease spectrum. In line with this commitment, we plan to initiate a registrational program evaluating INCA033989 for the treatment of patients with MF in 2026."

The preliminary analysis (data cut off September 25, 2025) evaluated the safety and efficacy of INCA033989 in patients with MF as measured by spleen volume reduction $\geq 25\%$ (SVR25) and $\geq 35\%$ (SVR35), change in MPN-Symptom Assessment Form (SAF), total symptom score (TSS), anemia response and mutCALR variant allele frequency (VAF) reduction.

In the monotherapy arm of the trials, patients with MF treated with INCA033989 (dose range 24 to 2,500 mg) experienced rapid and robust spleen and anemia responses and symptom improvements. Specifically:

- At Week 24, 41.7% (15/36) of all evaluable MF patients achieved SVR25, and 33.3% (12/36) achieved SVR35. Among MF patients not previously treated with a JAK inhibitor, 71.4% (5/7) achieved SVR25 and 57.1% (4/7) achieved SVR35. Among those resistant or intolerant to JAK inhibitor treatment, 34.5% (10/29) and 27.6% (8/29) achieved SVR25 and SVR35 at Week 24, respectively.
- Anemia response occurred in more than half (56%; 14/25) of evaluable anemic MF patients, with 40% (10/25) of patients achieving a major response with INCA033989 treatment.
- Nearly all MF patients treated with INCA033989 (93.3%; 42/45) experienced improved symptoms, with 60% (27/45) achieving a $\geq 50\%$ reduction in TSS (TSS50) as best response. At Week 24, 39.4% (13/33) of patients achieved a TSS50.
- Most patients (89.4%; 42/47) with ≥ 1 post-baseline VAF measurement experienced a reduction in mutCALR VAF, and 10.6% (5/47) achieved a $\geq 25\%$ best reduction in VAF.
- Most patients (76.5%; 39/51) in the studies had co-occurring mutations. Of those, 40.5% (15/37) of response eligible patients achieved SVR35 or an anemia response. Single-cell analyses in MF patients with high clonal complexity, including high-risk mutations, showed consistent reductions in all CALR-mutant clones, regardless of the presence of co-occurring variants.

Similarly, in the INCA033989 (dose range 70 to 2,500 mg) and ruxolitinib combination arm of the trials, most MF patients experienced spleen volume reductions and symptom improvements:

- At Week 24, half (50%; 6/12) of all evaluable MF patients achieved SVR25 and 25% (3/12) achieved SVR35.
- Among the 14 evaluable patients, 86% had stable anemia and one (1) patient with non-transfusion dependent anemia had a major anemia response.
- The majority of MF patients (81.3%; 13/16) treated with INCA033989 in combination with ruxolitinib experienced symptom improvement, and 33.3% (3/9) achieved TSS50 at Week 24.

Additionally, exploratory analyses in a subset of MF patients from the studies showed that INCA033989 reduced circulating mutCALR-positive hematopoietic stem and progenitor cells (HSPC) and mutCALR-positive platelet producing cells called megakaryocytes (MK) in the bone marrow, and improved marrow architecture, as measured by increased wild type (mutCALR-negative) MK. Among evaluable anemic MF patients (n=12), erythroid progenitor cells (CD71+ by IHC) in the bone marrow increased, correlating with hemoglobin increase and clinical anemia response. Together, these findings demonstrate the disease-modifying activity of INCA033989 in patients with mutCALR-expressing MF.

INCA033989 was well-tolerated, both as a monotherapy and in combination with ruxolitinib, in patients with MF who were resistant or intolerant to prior JAK inhibitor therapy or ineligible for JAK inhibitor treatment, with no dose-limiting toxicities observed.

- In the monotherapy arm (n=52), 86.5% (45) of patients were still receiving treatment and 13.5% (7) discontinued treatment. Only two (2) patients discontinued treatment due to treatment-emergent adverse events (TEAEs). Two (2) dose and three (3) infusion interruptions due to TEAEs were reported, and a maximum tolerated dose was not reached (dose range 24 to 2,500 mg). Fifty (50) patients across the monotherapy dose cohorts reported a TEAE, 30 of which were deemed treatment related.
 - The most common TEAEs (>20%) were anemia, fatigue, thrombocytopenia, arthralgia, AST elevations, cough, diarrhea, headache, leukopenia, nausea and pruritis – nearly all were Grade 1. Sixteen (16) patients had Grade ≥3 TEAEs, with neutropenia being the most frequent (9.6%).
- In the combination therapy arm (n=20), 85.0% (17) patients were still receiving treatment and 15.0% (3) discontinued treatment. Only two patients discontinued treatment due to TEAEs. One (1) dose and one (1) infusion interruption due to TEAEs were reported, and a maximum tolerated dose was not reached (dose range 70 to 2,500 mg). Twenty (20) patients across the combination therapy dose cohorts reported a TEAE, 13 of which were deemed treatment related.
 - The most common TEAEs (>20%) were anemia, thrombocytopenia, ALT increase, diarrhea and fatigue. Eleven (11) patients experienced Grade ≥3 TEAEs, with anemia (30%) being the most frequent.

“Widely regarded as the most aggressive type of MPN – a group of rare, chronic blood cancers – MF is characterized by bone marrow fibrosis, anemia and splenomegaly, which can lead to debilitating symptoms and increased mortality,” said John Mascarenhas, M.D., Professor of Medicine at the Icahn School of Medicine at Mt. Sinai and Director, Center of Excellence for Blood Cancers and Myeloid Disorders, The Tisch Cancer Institute. “The Phase 1 data evaluating INCA033989 alone and in combination with ruxolitinib offer compelling proof-of-concept for a differentiated, targeted treatment approach in MF. The early signals observed suggest the potential to meaningfully influence the MF disease course, and I look forward to seeing this therapy advance in future clinical studies.”

More information regarding Incyte’s presentations at the 2025 ASH Annual Meeting can be found on the ASH website: <https://www.hematology.org/meetings/annual-meeting/schedule-and-program/programs>.

In addition to MF, INCA033989 is also being evaluated in Phase 1 studies for the treatment of patients with essential thrombocythemia (ET). The U.S. Food and Drug Administration (FDA) recently granted Breakthrough Therapy designation to INCA033989 for the treatment of patients with ET harboring a Type 1 CALR mutation who are resistant or intolerant to at least one cytoreductive therapy. The company plans to initiate a registrational program evaluating INCA033989 for the treatment of patients with ET harboring a Type 1 or non-Type 1 CALR mutation who are resistant or intolerant to at least one cytoreductive therapy in 2026.

Incyte Conference Call and Webcast

Incyte will host an investor event and webcast on Sunday, December 7, 2025, from 11:00 – 12:30 p.m. ET to discuss key mutCALR data presented at ASH.

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.

About Myeloproliferative Neoplasms (MPNs) and Mutations in Calreticulin (mutCALR)

Calreticulin (CALR) is a protein involved in the regulation of cellular calcium levels and normal protein folding. Somatic, or non-inherited, DNA mutations in the CALR gene (mutCALR) can result in abnormal protein function and lead to the development of myeloproliferative neoplasms (MPNs),¹ a closely related group of clonal blood cancers in which the bone marrow functions abnormally, overproducing blood cells.^{2,3} Among two types of MPNs, essential thrombocythemia (ET) and myelofibrosis (MF), mutCALR drives 25-35% of all cases.^{1,2}

Incyte is at the forefront of developing novel therapies for patients with mutCALR ET or MF that target only malignant cells, sparing normal cells, including INCA033989, a first-in-class, mutCALR-specific therapy.

About the INCA033989 Trial Program

The clinical trial program for INCA033989 includes two multicenter, open-label Phase 1 studies, INCA33989-101 (NCT05936359) and INCA33989-102 (NCT06034002). The studies are evaluating the safety, tolerability and efficacy of INCA033989 in ~455 adult (≥18 years old) patients with mutCALR-expressing myeloproliferative neoplasms (MPNs), including myelofibrosis (MF) and essential thrombocythemia (ET).

The primary endpoint of the studies is measured by the number of participants with dose limiting toxicities (DLTs), treatment-emergent adverse events (TEAEs) and the number of participants with TEAEs leading to dose modification or discontinuation. Secondary endpoints include response rates, mean change of ET total symptom score, percentage of MF patients achieving spleen volume reduction, MF patient anemia response, mean change in disease-related allele burden and various pharmacokinetics measures.

For more information on the studies, please visit: <https://clinicaltrials.gov/study/NCT05936359> and <https://clinicaltrials.gov/study/NCT06034002>.

About Jakafi® (ruxolitinib)

Jakafi® (ruxolitinib) is a JAK1/JAK2 inhibitor approved by the U.S. FDA for treatment of polycythemia vera (PV) in adults who have had an inadequate response to or are intolerant of hydroxyurea; intermediate or high-risk myelofibrosis (MF), including primary MF, post-polycythemia vera MF and

post-essential thrombocythemia MF in adults; steroid-refractory acute GVHD in adult and pediatric patients 12 years and older; and chronic GVHD after failure of one or two lines of systemic therapy in adult and pediatric patients 12 years and older.

Jakafi is a registered trademark of Incyte.

Important Safety Information

Jakafi can cause serious side effects, including:

Low blood counts: Jakafi® (ruxolitinib) may cause low platelet, red blood cell, and white blood cell counts. If you develop bleeding, stop taking Jakafi and call your healthcare provider. Your healthcare provider will do a blood test to check your blood counts before you start Jakafi and regularly during your treatment. Your healthcare provider may change your dose of Jakafi or stop your treatment based on the results of your blood tests. Tell your healthcare provider right away if you develop or have worsening symptoms such as unusual bleeding, bruising, tiredness, shortness of breath, or a fever.

Infection: You may be at risk for developing a serious infection during treatment with Jakafi. Tell your healthcare provider if you develop any of the following symptoms of infection: chills, nausea, vomiting, aches, weakness, fever, painful skin rash or blisters.

Cancer: Some people have had certain types of non-melanoma skin cancers during treatment with Jakafi. Your healthcare provider will regularly check your skin during your treatment with Jakafi. Tell your healthcare provider if you develop any new or changing skin lesions during treatment with Jakafi.

Increases in cholesterol: You may have changes in your blood cholesterol levels during treatment with Jakafi. Your healthcare provider will do blood tests to check your cholesterol levels about every 8 to 12 weeks after you start taking Jakafi, and as needed.

Increased risk of major cardiovascular events such as heart attack, stroke or death in people who have cardiovascular risk factors and who are current or past smokers while using another JAK inhibitor to treat rheumatoid arthritis: Get emergency help right away if you have any symptoms of a heart attack or stroke while taking Jakafi, including: discomfort in the center of your chest that lasts for more than a few minutes, or that goes away and comes back, severe tightness, pain, pressure, or heaviness in your chest, throat, neck, or jaw, pain or discomfort in your arms, back, neck, jaw, or stomach, shortness of breath with or without chest discomfort, breaking out in a cold sweat, nausea or vomiting, feeling lightheaded, weakness in one part or on one side of your body, slurred speech.

Increased risk of blood clots: Blood clots in the veins of your legs (deep vein thrombosis, DVT) or lungs (pulmonary embolism, PE) have happened in people taking another JAK inhibitor for rheumatoid arthritis and may be life-threatening. Tell your healthcare provider right away if you have any signs and symptoms of blood clots during treatment with Jakafi, including: swelling, pain, or tenderness in one or both legs, sudden, unexplained chest or upper back pain, shortness of breath or difficulty breathing.

Possible increased risk of new (secondary) cancers: People who take another JAK inhibitor for rheumatoid arthritis have an increased risk of new (secondary) cancers, including lymphoma and other cancers. People who smoke or who smoked in the past have an added risk of new cancers.

The most common side effects of Jakafi include: for certain types of myelofibrosis (MF) and polycythemia vera (PV) – low platelet or red blood cell counts, bruising, dizziness, headache, and diarrhea; for acute GVHD – low platelet counts, low red or white blood cell counts, infections, and swelling; and for chronic GVHD – low red blood cell or platelet counts and infections including viral infections.

These are not all the possible side effects of Jakafi. Ask your pharmacist or healthcare provider for more information. Call your doctor for medical advice about side effects.

Before taking Jakafi, tell your healthcare provider about: all the medications, vitamins, and herbal supplements you are taking and all your medical conditions, including if you have an infection, have or had low white or red blood cell counts, have or had tuberculosis (TB) or have been in close contact with someone who has TB, had shingles (herpes zoster), have or had hepatitis B, have or had liver or kidney problems, are on dialysis, have high cholesterol or triglycerides, had cancer, are a current or past smoker, had a blood clot, heart attack, other heart problems or stroke, or have any other medical condition. Take Jakafi exactly as your healthcare provider tells you. Do not change your dose or stop taking Jakafi without first talking to your healthcare provider.

Women should not take Jakafi while pregnant or planning to become pregnant. Do not breastfeed during treatment with Jakafi and for 2 weeks after the final dose.

Please see the [Full Prescribing Information](#), which includes a more complete discussion of the risks associated with Jakafi.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.

You may also report side effects to Incyte Medical Information at 1-855-463-3463.

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 anti-mutCALR monoclonal antibody (INCA033989), the potential this monoclonal antibody 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 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: 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; the timing of clinical trials, including initiation and completion; determinations made by the FDA, EMA and other regulatory agencies; Incyte's dependence on its relationships with and changes in the plans of its collaboration partners; the efficacy or safety of Incyte's products and the products of Incyte's collaboration partners; the acceptance of Incyte's products and the products of Incyte's collaboration partners in the marketplace; market competition; unexpected variations in the demand for Incyte's products and the products of Incyte's collaboration partners; the effects of announced or unexpected price regulation or limitations on reimbursement or coverage for Incyte's products and the products of Incyte's collaboration partners; sales, marketing, manufacturing and distribution requirements, including Incyte's and its collaboration partners' ability to successfully commercialize and build commercial infrastructure for newly approved products and any additional products that become approved; greater than expected expenses, including expenses relating to litigation or strategic activities; variations in foreign currency exchange rates; and other risks detailed in Incyte's reports filed with the Securities and Exchange Commission, including its annual report on form 10-K and our quarterly report on Form 10-Q for the quarter ended September 30, 2025. Incyte disclaims any intent or obligation to update these forward-looking statements.

¹ Raghavan, M., Wijeyesakere S.J., Peters L.R., Del Cid N. (2013) Calreticulin in the immune system: ins and outs. *Trends in Immunology*, 34(1):13-21. Link to source ([https://www.cell.com/trends/immunology/abstract/S1471-4906\(12\)00131-7?_returnURL=https%3A%2F%2Flinkinghub.elsevier.com%2Fretrieve%2Fpii%2FS1471490612001317%3Fshowall%3Dtrue](https://www.cell.com/trends/immunology/abstract/S1471-4906(12)00131-7?_returnURL=https%3A%2F%2Flinkinghub.elsevier.com%2Fretrieve%2Fpii%2FS1471490612001317%3Fshowall%3Dtrue))

² Nangalia J. Massie C.E., Baxter E.J., Nice F.L., et al. (2013) Somatic CALR mutations in myeloproliferative neoplasms with nonmutated JAK2. *New England Journal of Medicine*, 369(25):2391-2405. Link to source (https://www.nejm.org/doi/10.1056/NEJMoa1312542?url_ver=Z39.88-2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub%20%20www.ncbi.nlm.nih.gov)

³ Klampfl T., Gisslinger, H., Harutyunyan A.S., et al. (2013) Somatic mutations of calreticulin in myeloproliferative neoplasms. *New England Journal of Medicine*, 369(25):2379-2390. Link to source (https://www.nejm.org/doi/10.1056/NEJMoa1311347?url_ver=Z39.88-2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub%20%20www.ncbi.nlm.nih.gov)

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