Incyte Announces New Positive Data at EHA 2026 Showed INCA033989 Achieved Rapid, Robust and Sustained Clinical and Molecular Responses and Was Well Tolerated in Patients with Myelofibrosis and Essential Thrombocythemia

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- *In myelofibrosis (MF), INCA033989 delivered rapid and durable clinical benefits including meaningful spleen volume reductions, symptom improvement and anemia responses, both as a monotherapy and in combination with ruxolitinib*
- *In essential thrombocythemia (ET), 87% of patients achieved a hematologic response, including 70% complete responses; responses were rapid (median ~2 weeks to a durable complete hematologic response) and durable (median response duration of 23 weeks)*
- *Across MF and ET, INCA033989 consistently reduced mutant CALR (mutCALR) variant allele frequency (VAF) in most evaluable patients, with reductions correlating with clinical responses and supporting its potential for disease modification*
- *First-in-class mutCALR-targeted antibody shows potential to modify disease biology in both MF and ET*
- *INCA033989 demonstrated a favorable and manageable safety profile with no dose-limiting toxicities, with most patients with MF and ET continuing treatment*

WILMINGTON, Del.--(BUSINESS WIRE)--Jun. 13, 2026-- Incyte (Nasdaq:INCY) today announced updated 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, in patients with mutCALR-expressing myeloproliferative neoplasms (MPNs). INCA033989 demonstrated rapid, clinically meaningful responses and consistent molecular activity across both myelofibrosis (MF) and essential thrombocythemia (ET), with convergent evidence supporting the potential for disease modification.

These findings are being presented in oral and poster presentations at the European Hematology Association (EHA) 2026 Congress in Stockholm, Sweden (Session: Myeloproliferative neoplasms – Clinical, Presentation numbers: S216, PS1983, PF884).

“The data presented at EHA 2026 demonstrate clinically meaningful and consistent responses with INCA033989 across both myelofibrosis and essential thrombocythemia,” said Pablo J. Cagnoni, M.D., President of Incyte and Global Head of Research and Development. “What distinguishes INCA033989 is its potential to deliver disease control while targeting the biology that drives it. We remain on track to initiate our pivotal ET study by mid-2026 and are actively engaging regulators on a pivotal MF program.”

Results in Patients with Myelofibrosis (MF)

The safety, tolerability, and efficacy of INCA033989 in Type 1 and non-Type 1 patients with MF harboring a CALR mutation is being evaluated in two ongoing Phase 1 studies. Results demonstrate that INCA033989 delivers broad, clinically meaningful improvements across spleen volume, symptom burden and anemia in patients with MF. As a monotherapy and in combination with ruxolitinib, INCA033989 had a manageable safety profile and the majority of patients remained on treatment – no dose-limiting toxicities were observed, and a maximum tolerated dose was not reached.

Monotherapy: INCA033989 was evaluated as monotherapy in patients who were resistant, refractory or intolerant to JAK inhibitor treatment after ≥12 weeks (JAK R/R/I), or ineligible to JAK inhibitor therapy. The dose escalation cohort evaluated INCA033989 from 24-3500 mg, and the dose expansion cohort evaluated 250 mg and 2000 mg.

INCA033989 monotherapy demonstrated durable clinical benefit, with clinically meaningful improvements across spleen volume, symptoms and anemia across both JAK R/R/I and JAK ineligible patients.

- **Spleen Volume Reduction (SVR):** Rapid and robust spleen volume reductions were observed in patients, with 55% (38/69) and 39% (27/69) of patients achieving the best SVR25 and SVR35 reduction, respectively. At Week 24, 27% (17/62) patients achieved SVR35, including 47% (8/17) JAK ineligible and 20% (9/45) JAK R/R/I. Robust responses were observed in JAK ineligible patients regardless of mutation type (60% [6/10] Type-1 vs. 29% [2/7] non-Type 1). In JAK R/R/I patients, clinically meaningful reductions were observed in 31% (8/26) of Type-1 patients across all evaluated doses at Week 24, and 33% (1/3) of non-Type-1 patients evaluated at 2500 mg, the highest evaluated dose.
- **Symptom Improvement:** Improvements in symptoms were also observed in the majority of patients, with 53% of patients achieving at least a 50% best TSS reduction (TSS50). At Week 24, 32% of patients achieved TSS50, including 29% and 33% of JAK ineligible and JAK R/R/I patients, respectively.
- **Anemia:** Rapid and durable anemia improvements were observed in most patients, with anemia response occurring in 60% of evaluable anemic patients, and 52% of patients achieved a major anemia response. Improvements in anemia were observed across patients regardless of prior JAK exposure, including 63% of JAK R/R/I patients and 55% of JAK ineligible patients.
- **Molecular:** Consistent reductions in variant allele frequency (VAF) were observed across most patients, regardless of prior JAK exposure and mutation type, with 89% of patients achieving a reduction in whole blood mutCALR VAF (Type 1: 90%, Non-Type 1: 88%), and 81% of patients achieving a ≥25% reduction in mutCALR peripheral blood mononuclear cells (PBMC) from baseline (Type 1: 62%, Non-Type 1: 38%).

INCA033989 was generally well-tolerated, with 84% (70/83) of patients remaining on therapy at the time of the data cut off. Treatment emergent adverse events (TEAEs) occurred in 92% (76) of patients, with 27% (22) of patients experiencing Grade ≥3 TEAEs, the most frequent of which were cytopenias. No dose-limiting toxicities were observed, and discontinuations due to TEAEs were limited (n=2).

Combination therapy: INCA033989 (dose range: 70 to 2,500 mg) was evaluated in combination with ruxolitinib in patients with MF who experience a suboptimal response to ruxolitinib monotherapy. INCA033989 demonstrated additive, multi-domain clinical activity in patients when administered in combination with ruxolitinib.

- **SVR:** At Week 24, 55% (11/20) and 30% (6/20) of patients achieved SVR25 and SVR35, respectively.
- **Symptom Improvement:** 31% (5/16) of patients achieved TSS50 at Week 24.
- **Anemia:** Anemia response occurred in 35% (6/17) of evaluable anemic patients.

INCA033989 in combination with ruxolitinib was generally well-tolerated, with 76% (16) of patients remaining on treatment at the time of the data cut off. In the combination arm (n=21), all patients experienced TEAEs. Grade ≥3 TEAEs were reported in 67% (14) of patients, most commonly anemia (33%).

Translational data

- Clinical response occurred regardless of mutational complexity with SVR, anemia and molecular responses observed in patients with and without high molecular risk (HMR) mutations.
- 93% of patients with HMR had a reduction in whole blood mutCALR VAF, as did 88% of those without HMR mutations.
- A reduction in mutCALR-positive hematopoietic stem and progenitor cells (HSPCs) was also seen, indicating activity at the level of disease-initiating cells.

"Patients with CALR-mutated MF have distinct disease biology and often respond poorly to available therapies, underscoring the need for treatments targeting the underlying driver of disease," said Claire Harrison, M.D., Professor of MPNs and Deputy Chief Medical Officer, Guy's and St. Thomas' NHS Foundation Trust. "What stands out in these data is that INCA033989 produced rapid and robust spleen, symptom and anemia responses, alongside reductions in mutCALR allele burden regardless of HMR mutations, pointing to activity at the level of the disease-initiating clone."

Results in Patients with Essential Thrombocythemia

In patients with ET, INCA033989 demonstrated rapid, deep and durable hematologic and molecular responses across both Type 1 and non-Type 1 CALR patients, supporting potential for disease modification in a population resistant or intolerant to prior cytoreductive therapy.

Hematologic Response:

- Across doses, 70% (80/114) of patients achieved a complete hematologic response (CHR, platelet count ≤400 × 109/L and leukocytes <10 × 109/L) and 87% achieved complete or partial hematologic response (CHR/PHR, platelet count ≤600 × 109/L and leukocytes <10 × 109/L).
- 81% of patients with Type 1 mutCALR achieved a durable (≥12 weeks) CHR at 750 mg and above; and 50% of patients with non–Type 1 mutCALR achieved a durable CHR/PHR at 2500 mg. The median time to onset of durable CHR was 2.1 weeks.

Molecular Response and Disease Biology:

- ≥25% reduction in mutCALR VAF correlated with durable CHR (nominal P<0.0001, n=103).
- Of the patients who achieved a CHR and had ≥1 post-baseline VAF assessment, 73% achieved ≥25% reduction in VAF.
- Durable molecular response was observed in both Type 1 and non–Type 1 mutCALR.
- A reduction in mutCALR megakaryocytes was seen in both Type 1 and non-Type 1 patients treated with INCA033989

INCA033989 was well tolerated with 95% of patients remaining on treatment. The median duration of INCA033989 exposure was 8.1 months (range from 0.59 to 27.0 months). A low incidence of Grade ≥3 adverse events was observed (19%); the most common were neutropenia (4.4%) and lipase increase (3.5%). Grade ≥3 cytopenia TEAEs occurred in 6% (7/114) of patients; no Grade ≥3 thrombocytopenia TEAEs were observed.

"In patients with ET who were resistant to or intolerant of prior cytoreductive therapy, INCA033989 resulted in rapid and durable normalization of platelet counts with accompanying molecular responses, with the majority of patients achieving a CHR," 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. "As there are currently no mutation-specific treatments available for patients with ET, this approach is critically important for this high-risk patient population. These results provide a strong foundation for advancing INCA033989 into a registrational Phase 3 study."

In November of 2025, INCA033989 was granted Breakthrough Therapy designation by the U.S. Food and Drug Administration (FDA) for the treatment of patients with ET harboring a Type 1 CALR mutation who are resistant or intolerant to at least one cytoreductive therapy. A Phase 3 study of INCA033989 in mutCALR positive patients with ET who are resistant or intolerant to at least one prior cytoreductive therapy (EXCALIBUR-ET2, NCT07623200) is being initiated in mid-2026.

More information regarding the EHA 2026 Congress can be found on the EHA website: https://ehaweb.org/connect-network/eha2026-congress.

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.[4] In MF, it is estimated that 70-83% of CALR mutations in the U.S. are identified as Type 1, with 15-30% identified as non-Type 1.[4,5] There are currently no targeted therapies for CALR mutations.

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. INCA033989 received Breakthrough Therapy designation by the U.S. Food and Drug Administration (FDA) for the treatment of patients with ET harboring a Type 1 CALR mutation who are resistant or intolerant to at least one cytoreductive therapy. A Phase 3 study of INCA033989 in patients with ET with a Type 1 or non-Type 1 CALR mutation who are resistant or intolerant to at least one cytoreductive therapy is being initiated (EXCALIBUR-ET2, NCT07623200).

About the INCA33989-101 & INCA33989-102 Trials

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 essential thrombocythemia (ET) and myelofibrosis (MF).

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 Incyte®

Incyte is redefining what's possible in biopharmaceutical innovation. Through deep scientific expertise and a relentless focus on patients, we have built an established portfolio of first-in-class medicines and an extensive portfolio of next-generation medicines across our key franchises: Hematology, Oncology and Inflammation & Autoimmunity.

To learn more, visit Incyte.com and Investor.Incyte.com. Follow us on social media: LinkedIn, X and Instagram.

Forward-Looking Statements

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995 and other federal securities laws, including statements regarding the presentation of data for INCA033989; the potential for disease modification and the potential to benefit patients offered by INCA033989; expectations regarding ongoing and future clinical trials, including the timing of such trials; and Incyte's aspirations and goals as set forth under the heading "About Incyte."

Actual results may differ materially from those indicated in the forward-looking statements as a result of various important factors, including the sufficiency of clinical trial data 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; actions of regulatory agencies, which may affect the initiation, timing and progress of clinical trials and marketing approval; the efficacy or safety of Incyte's products; Incyte's ability to achieve commercial success for its products, once approved; Incyte's ability to obtain and maintain protection of intellectual property for its products and technology; Incyte's reliance on third parties and partners; the acceptance of Incyte's products in the marketplace; market competition, sales, marketing, manufacturing and distribution requirements; greater than expected expenses, including expenses relating to litigation or strategic activities; and those risks and uncertainties discussed in greater detail in Incyte's reports filed with the U.S. Securities and Exchange Commission, including its annual report on Form 10-K for the year ended December 31, 2025, and its quarterly report on Form 10-Q for the quarter ended March 31, 2026. 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)

[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%200www.ncbi.nlm.nih.gov)

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[5] Guglielmelli, P., Maccari, C., Sordi, B. et al. Phenotypic correlations of CALR mutation variant allele frequency in patients with myelofibrosis. *Blood Cancer J.* 13, 21 (2023). Link to source (https://doi.org/10.1038/s41408-023-00786-x)

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