Incyte's First-in-Class mutCALR-Targeted Monoclonal Antibody, INCA033989, Granted Breakthrough Therapy Designation by U.S. FDA

December 7, 2025

- *The Company plans to initiate a Phase 3 program evaluating INCA033989 in essential thrombocythemia (ET) patients with all types of CALR mutations in mid-2026, following alignment with regulators*
- *Updated safety and efficacy data for INCA033989 in ET, and new data in myelofibrosis (MF), will be presented at the upcoming 2025 ASH Annual Meeting*

WILMINGTON, Del.--(BUSINESS WIRE)--Dec. 7, 2025-- Incyte (Nasdaq:INCY) today announced that the U.S. Food and Drug Administration (FDA) has granted Breakthrough Therapy designation to INCA033989, a first-in-class mutant calreticulin (mutCALR)-targeted monoclonal antibody, for the treatment of patients with essential thrombocythemia (ET) harboring a Type 1 CALR mutation who are resistant or intolerant to at least one cytoreductive therapy.

ET is a chronic myeloproliferative neoplasm (MPN) characterized by persistently elevated platelet counts due to abnormal blood cell production in the bone marrow. CALR mutations are the second most common oncogenic driver mutation and are observed in 25% of patients with ET. A 52-bp deletion, also known as a Type 1 mutation, occurs in 55% of patients with a CALR mutation, and is associated with the highest risk of transformation to myelofibrosis (MF) among all ET patients.

"Incyte has long been committed to improving outcomes for patients with MPNs, and this Breakthrough Therapy designation underscores the potential of INCA033989 to be a novel therapy that could significantly transform the treatment of ET patients, who today have limited treatment options," said Pablo J. Cagnoni, M.D., President and Head of Research and Development, Incyte. "The designation allows us to expedite the development pathway for INCA033989 in patients with Type 1 mutations. Looking ahead, we plan to initiate a Phase 3 program evaluating INCA033989 in ET patients with all types of CALR mutations in mid-2026, following alignment with regulators in the first half of next year."

The FDA Breakthrough Therapy Designation was supported by the early Phase 1 data evaluating INCA033989 in ET patients with a Type 1 CALR mutation available at the time of submission.

The preliminary Phase 1 data were presented earlier this year at the 2025 European Hematology Association (EHA) Congress. In the study, INCA033989 was well-tolerated and demonstrated rapid and durable normalization of platelet counts across evaluated doses, with greater responses seen at higher doses across both mutation types. Updated results from the Phase 1 dose escalation and expansion trial are planned for presentation at the 2025 ASH Annual Meeting in Orlando (Session 634; Publication #1024; December 8, 4:30-6:00 p.m. ET).

Incyte plans to develop INCA033989 for patients with Type 1 and non-Type 1 CALR mutations and, following discussions with regulatory agencies, plans to initiate a registrational program evaluating patients with ET with a Type 1 or non-Type 1 CALR mutation who are resistant or intolerant to at least one cytoreductive therapy in the first half of next year.

About Essential Thrombocythemia
Essential thrombocythemia (ET) is a chronic myeloproliferative neoplasm (MPN) characterized by persistently elevated platelet counts due to abnormal blood cell production in the bone marrow. People living with ET are at increased risk for blood clots and bleeding and a proportion of patients may progress over time to myelofibrosis or acute leukemia.

About 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] In Essential thrombocythemia (ET) and myelofibrosis (MF), CALR mutations occur in ~25-35% of patients.[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 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 INCA033989 studies, 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: 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-K for the quarter ended September 30, 2025. Incyte disclaims any intent or obligation to update these forward-looking statements.

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[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)

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

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