Incyte's Novel Mutant CALR Antibody Unveiled at ASH 2022 Plenary Scientific Session

December 11, 2022

- *- INCA033989, a new anti-mutant calreticulin (CALR)-targeted monoclonal antibody, represents important research milestone in myelofibrosis (MF) and essential thrombocythemia (ET)*
- *- INCA033989 abstract selected as one of only six ASH plenary presentations*
- *- INCA033989 clinical trials to begin in 2023*
- *- Research highlights Incyte's discovery capabilities and progress of its LIMBER program evaluating new targets and combinations for patients with myeloproliferative neoplasms (MPNs) and graft-versus-host disease (GVHD)*

WILMINGTON, Del.--(BUSINESS WIRE)--Dec. 11, 2022-- Incyte (Nasdaq:INCY) today announced new research detailing the development and mechanism of action of INCA033989, an Incyte-discovered, investigational novel anti-mutant calreticulin (CALR)-targeted monoclonal antibody. Pre-clinical data indicate that INCA033989 can alter disease course by reducing mutant CALR allele burden and thus may be an efficacious and safe treatment in patients with myelofibrosis (MF) and essential thrombocythemia (ET). This research was featured in the Plenary Scientific Session (Abstract #6. Session: Hematology Disease Topics & Pathways: Research, Diseases, Therapies, Myeloid Malignancies) at the 64th American Society of Hematology (ASH) Annual Meeting, held December 10-13, 2022, in New Orleans and virtually[1].

"As a pioneer in the field of myeloproliferative neoplasms (MPNs), having brought the first FDA-approved treatment to patients, we are excited to have the opportunity to share details of our latest research," said Dash Dhanak, Ph.D., Executive Vice President and Chief Scientific Officer, Incyte. "We continue to apply our deep understanding of the complex biology of MPNs to expand treatment options for patients and the work on INCA033989 presented today reflects our progress toward this goal. We look forward to continuing to advance the development of this potential new treatment and to initiating clinical trials for INCA033989 next year."

CALR mutations are responsible for disease development in approximately 25-35%[2,3] of patients with MF and ET – two common types of MPNs. INCA033989 binds with high affinity to mutant CALR and inhibits oncogenesis, the process of cells becoming cancerous, in cells expressing this oncoprotein. As described in our presentation, INCA033989 potently antagonizes CALR oncogenic function, resulting in selective inhibition of JAK/STAT signaling only in CALR-mutated cells with no effect on normal, non-oncogenic cells. This selectivity of action with INCA033989 results in the specific killing of tumor cells harboring the mutation and is suggestive of the potential to alter the course of disease in patients with CALR-mutant MF and ET.

"Diseases like myelofibrosis and essential thrombocythemia are often difficult to understand and treat, and unique approaches are necessary to develop effective and safe therapies," said Srdan Verstovsek, M.D., Ph.D., Professor of Medicine, Department of Leukemia, University of Texas MD Anderson Cancer Center. "As a leader in the field, Incyte is uniquely positioned to develop novel medicines for these rare blood cancers, and this research provides strong rationale for the continued investigation and clinical advancement of INCA033989 – a novel treatment approach that targets CALR mutations."

More information regarding the congress and the more than 50 abstracts from Incyte's oncology portfolio being featured at the meeting is available on the ASH website: https://www.hematology.org/meetings/annual-meeting.

About Myeloproliferative Neoplasms

Myeloproliferative neoplasms (MPNs) are a closely related group of blood cancers in which the bone marrow functions abnormally. The bone marrow is where the body's blood cells are made. MPNs are progressive blood cancers that can strike anyone at any age, but they are more common in older adults. Estimates of the prevalence of MPNs vary, but analysis of claims data suggests there may be as many as 200,000 people in the U.S. living with the most prevalent MPNs: myelofibrosis, polycythemia vera or essential thrombocythemia[4].

About LIMBER

Incyte is a leader in the discovery and development of therapies for patients with myeloproliferative neoplasms (MPNs) and graft-versus-host disease (GVHD). The Leadership In MPNs and GVHD BEyond Ruxolitinib (LIMBER) program is designed to evaluate multiple monotherapy and combination strategies to improve and expand treatments for patients with MPNs and GVHD. The program currently has three key areas of focus: development of a new, once-daily formulation of ruxolitinib; ruxolitinib-based combinations with new targets such as PI3Kδ, BET and ALK2; and new therapeutic options such as mutant CALR.

About Incyte

Incyte is a Wilmington, Delaware-based, global biopharmaceutical company focused on finding solutions for serious unmet medical needs through the discovery, development and commercialization of proprietary therapeutics. For additional information on Incyte, please visit Incyte.com and follow @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 from Incyte's clinical development pipeline, whether or when any development compounds or combinations will be approved or commercially available for use in humans anywhere in the world outside of the already approved indications in specific regions 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; the effects of the COVID-19 pandemic and measures to address the pandemic on Incyte and its partners' clinical trials, supply chain, other third-party providers and development and discovery operations; determinations made by the U.S. FDA and other regulatory authorities outside of the United States; 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 Incyte's reports filed with the Securities and Exchange Commission, including its annual report and its quarterly report on Form 10-Q for the quarter ended September 30, 2022. Incyte disclaims any intent or obligation to update these forward-looking statements.

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[1] Reis E, et al. Discovery of INCA033989, a Monoclonal Antibody That Selectively Antagonizes Mutant Calreticulin Oncogenic Function in Myeloproliferative Neoplasms. Presented at the 64 ASH Annual Meeting, December 10-13, 2022.

[2] Nagalia et al. Somatic CALR mutations in myeloproliferative neoplasms with nonmutated JAK2. *N Engl J Med 2013*; 369:2391-2405.

[3] Klampfl T et al. Somatic Mutations of Calreticulin in Myeloproliferative Neoplasms. *N Engl J Med* 2013; 369:2379-2390.

[4] Data on file.

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