Incyte Announces Data from Two LIMBER Studies Evaluating Combination Treatments in Patients with Myelofibrosis (MF) Presented at ASH 2022

December 10, 2022

- Phase 2 data demonstrate that the addition of parsaclisib to ruxolitinib (Jakafi®) resulted in spleen volume reduction and improvement in symptom burden in patients with myelofibrosis (MF)

- Initial results of a Phase 1/2 study evaluating the safety and tolerability of INCB00928, an ALK2 inhibitor, show INCB00928 improves anemia in patients with MF both as monotherapy and in combination with ruxolitinib

- These studies are part of our LIMBER program evaluating ruxolitinib combinations and potential new targets for appropriate patients with myeloproliferative neoplasms (MPNs)

WILMINGTON, Del.--(BUSINESS WIRE)--Dec. 10, 2022-- Incyte (Nasdaq:INCY) today announced new data from two of its LIMBER (Leadership In MPNs and GVHD BEyond Ruxolitinib) trials evaluating monotherapy and combination strategies using ruxolitinib (Jakafi®) with parsaclisib, its investigational phosphatidylinositol 3-kinase delta (PI3Kδ) inhibitor, and INCB00928 (zilurgisertib), its activin receptor-like kinase (ALK2) inhibitor, in patients with myelofibrosis (MF). These Phase 2 and Phase 1/2 trials (Abstract #236 and Abstract #1714, respectively) were presented at the 64th American Society of Hematology (ASH) Annual Meeting, held December 10-13, 2022, in New Orleans and virtually[1,2].

“Despite the significant advances we have made in the treatment of myeloproliferative neoplasms (MPNs) like MF, a need for additional options remains for those who have an inadequate response to or are unable to tolerate current therapies,” said Peter Langmuir, M.D., Vice President, Oncology Drug Development, Incyte. “The parsaclisib and ruxolitinib data presented at ASH demonstrate the clinical potential of the combination to improve upon the standard of care and continue to support the safety profile. We look forward to building on these results through our Phase 3 LIMBER-304 and LIMBER-313 trials evaluating parsaclisib as an add-on to ruxolitinib and in the frontline setting, both of which are currently underway.”

Final results from the Phase 2 trial (Abstract #236; NCT02718300) evaluating the efficacy and safety of add-on parsaclisib to ruxolitinib for patients with MF who had a suboptimal response to ruxolitinib resulted in additional spleen volume reduction and improvement in symptom burden with add-on parsaclisib. Patients in the trial received parsaclisib daily for eight weeks in combination with stable dose ruxolitinib and then daily or weekly thereafter. Patients who received an all daily parsaclisib dosing schedule appeared to have a more durable efficacy profile compared with daily followed by weekly dosing of parsaclisib. Specifically:

- At 12 weeks of treatment, 59.5% (25), 21.4% (9) and 4.8% (2) of patients who received all daily dosing experienced ≥10%, ≥25% and ≥35% reduction in spleen volume, respectively.
    - Comparatively, 28.1% (9), 3.1% (1) and 0% of patients who received daily followed by weekly dosing experienced ≥10%, ≥25% and ≥35% reduction in spleen volume, respectively.
- At 24 weeks of treatment the reduction was maintained, with 50% (21), 28.6% (12) and 7.1% (3) patients who received all daily dosing experiencing ≥10%, ≥25% and ≥35% reduction in spleen volume, respectively.
    - Comparatively, 12.5% (4), 12.5% (4) and 3.1% (1) of patients who received daily followed by weekly dosing experienced ≥10%, ≥25% and ≥35% reduction in spleen volume, respectively.
- Addition of parsaclisib to ruxolitinib was generally well-tolerated, with limited grade 3 or 4 adverse events and treatment-emergent adverse event (TEAE)-related discontinuations. TEAEs common to PI3Kδ inhibitors in lymphoma (e.g., hepatotoxicity, rash, colitis) were infrequent or absent with the addition of parsaclisib.
    - Serious TEAEs occurring in ≥2 patients overall included pneumonia (n=6; 2 daily/weekly, 1 all daily), fall (n=3; 2 daily/weekly, 1 all daily) and pyrexia (n=2; 1 daily/weekly, 1 all daily).
    - Overall, 9 patients (5 daily/weekly, 4 all daily) had a TEAE leading to parsaclisib discontinuation, and 4 patients (2 daily/weekly, 2 all daily) had a TEAE leading to ruxolitinib discontinuation.

“MF is a rare, chronic blood cancer, and despite the advancements made in treatment, additional options are needed,” said Abdulraheem Yacoub, Associate Professor, Hematologic Malignancies and Cellular Therapeutics, University of Kansas Cancer Center. “I am encouraged by these findings and the potential of parsaclisib and ruxolitinib to be an efficacious combination therapy to help improve outcomes for certain patients living with MF.”

Additionally, data from a Phase 1/2 open-label, dose escalation and expansion study (Abstract #1714; NCT04455841) assessing the safety and tolerability of INCB00928 (zilurgisertib), a potent and selective ALK2 inhibitor, as monotherapy or in combination with ruxolitinib in patients with anemia due to MF were presented at ASH. Anemia occurs in more than one-third of patients at MF diagnosis and can be exacerbated during treatment[3,4]. Initial results of the study observed reduction in post-dose hepcidin levels at all dose levels and observed improvements in anemia among patients treated in both the monotherapy and combination cohorts, which suggest the potential for therapeutic activity. The data also support once-daily dosing of INCB00928 and continued dose escalation to achieve optimal exposure. Treatment with INCB00928 monotherapy and in combination with ruxolitinib resulted in predominantly grade 1/2 TEAEs and no dose-limiting toxicities (DLTs). Few grade ≥3 TEAEs were observed, including thrombocytopenia in two patients with baseline grade 2 thrombocytopenia, and neutropenia in one patient with baseline grade 2 neutropenia. No TEAEs led to study drug discontinuation.

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[5].

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 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[6].

Jakafi is marketed by Incyte in the United States and by Novartis as Jakavi® (ruxolitinib) outside the United States. Jakafi is a registered trademark of Incyte Corporation. Jakavi is a registered trademark of Novartis AG in countries outside the United States.

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

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] Yacoub A, et al. Efficacy and Safety of Add-on Parsaclisib to Ruxolitinib Therapy in Myelofibrosis Patients With Suboptimal Response to Ruxolitinib: Final Results From a Phase 2 Study. Presented at the 64th ASH Annual Meeting, December 10-13, 2022.

[2] Mohan S, et al. A Phase ½ Study of INCB000928 As Monotherapy or Combined with Ruxolitinib (RUX) in Patients (Pts) with Anemia Due to Myelofibrosis (MF). Presented at the 64th ASH Annual Meeting, December 10-13, 2022.

[3] Tefferi A, et al. Mayo Clin Proc. 2012;87(1):25-33.

[4] Naymagon L, Mascarenhas J. Hemasphere. 2017;1(1):doi: 10.1097/HS1099.0000000000000001.

[5] MPN Research Foundation. "MPN Landmark Survey." Available at: https://www.mpnlandmarksurvey.com/pdf/mpn-landmark-survey-summary.pdf. Accessed February 2019.

[6] Jakafi (ruxolitinib) tablets: Prescribing Information. U.S. Food and Drug Administration.

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