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Incyte Announces Positive CHMP Opinion for Ruxolitinib (Jakavi®) for the Treatment of Acute and Chronic Graft-Versus-Host Disease

- The positive opinion from the CHMP is based on data from the Phase 3 REACH2 and REACH3 trials, which demonstrated that ruxolitinib (Jakavi®) improved response rates and failure-free survival compared to best available therapy, which provides a promising opportunity for patients living with graft-versus-host disease (GvHD)1,2
- Graft-versus-host disease (GVHD) is a life-threatening complication of stem cell transplants, with no established standard of care in Europe for patients who do not adequately respond to first-line steroid treatment3,4
- Nearly half of patients experience acute or chronic GVHD following allogeneic transplants 3,4

WILMINGTON, Del.--(BUSINESS WIRE)-- Incyte (Nasdaq:INCY) today announced that the European Medicines Agency's Committee for Medicinal Products for Human Use (CHMP) has issued a positive opinion recommending approval of ruxolitinib (Jakavi®) for the treatment of patients aged 12 years and older with acute graft-versus-host disease or chronic graft-versus-host disease (GVHD) and who have inadequate response to corticosteroids or other systemic therapies. If approved, ruxolitinib will be the first JAK1/2 inhibitor available for patients with GVHD in Europe.4 Ruxolitinib is marketed as Jakavi by Novartis in Europe and as Jakafi® by Incyte in the U.S.

"We are pleased that the CHMP has recommended approval of ruxolitinib for the treatment of acute or chronic GVHD in Europe," said Peter Langmuir, M.D., Group Vice President, Oncology Targeted Therapies, Incyte. "With this positive opinion, patients living with these life-threatening complications who do not respond to first-line steroids therapies are one step closer to having a new potential standard of care."

The CHMP positive opinion was based on data from the Phase 3 REACH2 and REACH3 clinical studies, in which ruxolitinib demonstrated superiority versus best available therapy (BAT) in patients with steroid-refractory and steroid-dependent acute and chronic GVHD, respectively.

Results from the REACH2 trial showed an overall response rate (ORR) at Day 28 was superior in the ruxolitinib arm at 62.3% vs. 39.4% in the BAT arm (odds ratio [OR], 2.64; p<0.001) in patients with steroid refractory/dependent acute GVHD; and in those patients who maintained response at Day 56, the ORR in the Jakavi arm was 40% vs. 22% in the BAT arm (p<0.001). In REACH3, treatment with ruxolitinib led to significant improvements in ORR compared to BAT (49.7% vs. 25.6%; OR, 2.99; P<0.0001) in patients with steroid refractory/dependent chronic GVHD at week 24, the primary endpoint of the study, regardless of the individual organs involved at baseline. Also, best overall response (BOR) rate at any time up to week 24 was achieved in 76.4% of patients in the ruxolitinib arm compared to 60.4% in the BAT arm (OR, 2.17; 95% CI, 1.34-3.52). Results from the two studies were published in the April 22, 2020 (**REACH2**), and July 15, 2021 (**REACH3**) issues of The New England Journal of Medicine.1,2

GVHD is a condition that can occur after an allogeneic stem cell transplant (the transfer of stem cells from a donor) where the donated cells initiate an immune response and attack the transplant recipient's organs, leading to significant morbidity and mortality. There are two major forms of GVHD: acute, which generally occurs within 100 days of transplant, and chronic, which generally occurs more than 100 days after transplant.2 GVHD can affect multiple organ systems including the skin, gastrointestinal (digestive) tract and liver.

"For many hematologic diseases allogeneic transplant is the only treatment with the potential to be curative; however, half will go on to develop acute or chronic GVHD," said Dr. Robert Zeiser, University Hospital Freiburg, Department of Haematology, Oncology and Stem Cell Transplantation, Freiburg, Germany. "It is encouraging that we may soon have a new standard of care for patients with this often debilitating condition who do not adequately respond to first-line corticosteroids."

The CHMP opinion to recommend the use of ruxolitinib in acute and chronic GVHD is now being reviewed by the European Commission, which has the authority to grant marketing authorization for medicinal products in the European Union. The EC will review the CHMP recommendations and is expected to make a final decision within approximately 2 months.

In 2019, Jakafi® (ruxolitinib) was approved by the U.S. Food and Drug Administration (FDA) for the treatment of steroid-refractory acute GVHD in adult and pediatric patients 12 years and older, based on the positive results of the Phase 2 REACH1 trial.5 Additionally, in 2021, Jakafi was approved by the FDA for treatment of chronic GVHD after failure of one or two lines of systemic therapy in adult and pediatric patients 12 years and older, based on the positive results of the Phase 3 REACH3 trial.5

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.5

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.

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 whether and when ruxolitinib (Jakavi®) will be approved in Europe for treatment of acute and chronic GVHD, statements regarding the Company's ongoing clinical development program for ruxolitinib, the REACH program, and the Company's GVHD program generally, contain predictions, estimates and other forward-looking statements.

These forward-looking statements are based on the Company'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 and the ability to enroll subjects in accordance with planned schedules; the effects of the COVID-19 pandemic and measures to address the pandemic on the Company's clinical trials, supply chain and other third-party providers and development and discovery operations; the Company's dependence on its relationships with its collaboration partners; the efficacy or safety of the Company's products and the products of the Company's collaboration partners; the acceptance of the Company's products and the products of the Company's collaboration partners in the marketplace; market competition; sales, marketing, manufacturing and distribution requirements; greater than expected expenses; expenses relating to litigation or strategic activities; and other risks detailed from time to time in the Company's reports filed with the Securities and Exchange Commission, including its annual report on Form 10-K for the year ended December 31, 2021. The Company disclaims any intent or obligation to update these forward-looking statements.

1 Zeiser R, et al. Ruxolitinib for Glucocorticoid-Refractory Chronic Graft-versus-Host Disease (REACH3). New England Journal of Medicine; July 2021.
2 Zeiser, R, et al. Ruxolitinib for Glucocorticoid-Refractory Acute Graft-versus-Host Disease (REACH2). New England Journal of Medicine. April 2020.
3 Leukemia and Lymphoma Society. Graft-Versus-Host Disease Overview. 2021. Available at: **https://www.lls.org/treatment/types-treatment/stem-cell-transplantation/graft-versus-host-disease**
4 Jaglowski SM, et al. Graft-versus-Host Disease: Why Haven't We Made More Progress? Curr Opin Hematol. 2014;21(2):141-147
5 Jakafi (ruxolitinib) tablets: Prescribing Information. U.S. Food and Drug Administration.

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