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MEDIA & INVESTOR RELEASE

Novartis announces first data from REACH3 trial showing Jakavi® (ruxolitinib) significantly improved outcomes in patients with steroid-resistant/dependent chronic GvHD

- *Results of REACH3 trial also demonstrate significant improvements in failure-free survival (FFS) and patient-reported symptoms*[1]

- *Chronic graft-versus-host disease (GvHD) is a life-threatening complication of stem cell transplants and half of patients become steroid refractory/dependent*[2,3]

- *Findings from the study were presented at ASH 2020, and complement previously reported positive results for Jakavi in acute GvHD; data to be submitted to ex-U.S. health authorities*[4]

Basel, December 4, 2020 — Detailed results from the pivotal Phase III REACH3 study demonstrate Jakavi® (ruxolitinib) significantly improved outcomes across a range of efficacy measures in patients with steroid-refractory/dependent chronic graft-versus-host disease (GvHD) compared to best available therapy (BAT)[1]. The results of REACH3, the first successful, randomized Phase III trial in chronic GvHD, were presented today during the 62nd American Society of Hematology Annual Meeting & Exposition (ASH). REACH3 is jointly sponsored by Novartis and Incyte.

“The damaging and sometimes deadly effects of chronic GvHD following stem cell transplant present significant treatment challenges, particularly for the nearly half of patients who do not adequately respond to steroid treatment,” said Dr. Robert Zeiser, University Hospital Freiburg, Department of Haematology, Oncology and Stem Cell Transplantation, Freiburg, Germany. “Based on the compelling REACH3 results, we now have a potential new standard of care for these patients.”

In REACH3, patients treated with Jakavi achieved significantly greater overall response rate (ORR) compared to BAT (49.7% vs. 25.6%; $p<0.0001$[i]) at Week 24, the primary endpoint of the study[1]. Jakavi also demonstrated statistically significant and clinically meaningful improvements in key secondary endpoints:

- Patients receiving Jakavi had a significant improvement of failure-free survival (FFS; defined as time to the earliest recurrence of the underlying disease, the start of new systemic treatment for chronic GvHD, or death) than patients receiving BAT (median FFS not yet reached vs. 5.7 months; hazard ratio, 0.370, 95% CI, 0.268 to 0.510; $p<0.0001$)[1].
- Patients treated with Jakavi also had greater improvements in patient-reported symptoms than those treated with BAT (24.2% vs. 11.0%; $p=0.0011$), as measured by the rate of responders who achieved a reduction of ≥ 7 points of total symptom score (TSS) from baseline of the modified Lee Symptom Score (mLSS)[1].

- Additionally, best overall response (BOR) rate was achieved in 76.4% of patients in the Jakavi arm compared to 60.4% in the BAT arm (odds ratio [OR], 2.17; 95% CI, 1.34-3.52). The median duration of response was 6.24 months in the BAT arm, but was not reached in the Jakavi arm[1].

“These impressive results in chronic GvHD, which complement previous positive findings in the acute form of the disease, clearly define the role Jakavi can play in improving outcomes for patients facing this difficult-to-treat condition,” said David Feltquate, Head Hematology Development Unit, Novartis. “Jakavi is the first treatment to demonstrate efficacy in a large-scale randomized clinical trial in steroid-refractory/dependent chronic GvHD, and with these meaningful data we look forward to advancing discussions with regulatory authorities.”

No new safety signals were observed in REACH3, and adverse events (AEs) attributable to treatment were consistent with the known safety profile of Jakavi. The most common AEs in the Jakavi vs. BAT arms were anemia (29.1% vs. 12.7%), thrombocytopenia (21.2% vs. 14.6%), hypertension (15.8% vs. 12.7%) and pyrexia (15.8% vs. 9.5%). While 37.6% and 16.5% of patients required Jakavi and BAT dose modifications, respectively, the number of patients who discontinued treatment due to AEs was low (16.4% and 7%, respectively). Mortality rates were similar across treatment arms (19% vs. 16% BAT)[1]. Deaths reported as primarily due to chronic GvHD were slightly higher for Jakavi.

GvHD, a common and potentially life-threatening complication that can arise after allogeneic stem cell transplants, is a reaction where the donor’s cells attack the recipient’s normal cells because it sees them as foreign[2]. The two main types of GvHD are acute GvHD, which occurs within 100 days of transplant, and chronic GvHD, which occurs after 100 days of transplant[2]. Around 50 percent of people experience either acute or chronic GvHD, or both, following allogeneic stem cell transplant[3]. Symptoms of chronic GvHD can affect the skin, gastrointestinal tract, liver, mouth, lungs and joints[5]. There is a need for additional treatment options for people who do not respond to initial steroid therapy for GvHD or are considered steroid-refractory[3].

In 2019, the US Food and Drug Administration approved ruxolitinib (marketed by Incyte Corporation in the U.S. as Jakafi®) for the treatment of steroid-refractory acute GvHD in adult and pediatric patients 12 years and older based on results of the single-arm Phase II REACH1 trial[6]. REACH3 (NCT03112603) is a Phase III, randomized, open-label, global multicenter study to evaluate Jakavi compared to BAT in patients with steroid-refractory or steroid-dependent chronic GvHD following allogeneic stem cell transplant[7]. Regulatory filings for steroid-refractory/dependent GvHD in Europe and other ex-US countries based on these data are planned for the first half of 2021.

Visit **https://www.virtualcongress.novartis.com/ash20** for the latest information from Novartis including our bold approach to reimagining care in hematology, and access to our ASH Virtual Congress 2020 symposia and data presentations (for registered participants).

About Jakavi® (ruxolitinib)
Jakavi® (ruxolitinib) is an oral inhibitor of the JAK 1 and JAK 2 tyrosine kinases. Jakavi is approved by the European Commission for the treatment of adult patients with polycythemia vera (PV) who are resistant to or intolerant of hydroxyurea and for the treatment of disease-related splenomegaly or symptoms in adult patients with primary myelofibrosis (MF) (also known as chronic idiopathic MF), post-polycythemia vera MF or post-essential thrombocythemia MF. Jakavi is approved in over 100 countries for patients with MF, including EU countries, Switzerland, Canada, Japan and in more than 85 countries for patients with PV, including EU countries, Switzerland, Japan and Canada. The exact indication for Jakavi varies by country. Additional worldwide regulatory filings are underway in MF and PV.

Novartis licensed ruxolitinib from Incyte Corporation for development and commercialization outside the United States. Ruxolitinib is marketed in the United States by Incyte Corporation

as Jakafi® for patients with PV who have had an inadequate response to or are intolerant of hydroxyurea, for patients with intermediate or high-risk MF, and steroid-refractory acute GvHD in adult and pediatric patients 12 years and older[6].

The recommended starting dose of Jakavi in PV is 10 mg given orally twice daily. The recommended starting dose of Jakavi in MF is 15 mg given orally twice daily for patients with a platelet count between 100,000 cubic millimeters (mm) and 200,000 mm, and 20 mg twice daily for patients with a platelet count of >200,000 mm. Doses may be titrated based on safety and efficacy. There is limited information to recommend a starting dose for MF and PV patients with platelet counts between 50,000/mm and <100,000/mm. The maximum recommended starting dose in these patients is 5 mg twice daily, and patients should be titrated cautiously[6].

Jakavi is a registered trademark of Novartis AG in countries outside the United States. Jakafi is a registered trademark of Incyte Corporation. The safety and efficacy profile of Jakavi has not yet been established outside of its approved indications.

Important Safety Information
Jakavi can cause serious side effects, including a decrease in blood cell count and infections. Complete blood count monitoring is recommended. Dose reduction or interruption may be required in patients with any hepatic impairment or severe renal impairment or in patients developing hematologic adverse reactions such as thrombocytopenia, anemia and neutropenia. Dose reductions are also recommended when Jakavi is co-administered with strong CYP3A4 inhibitors or fluconazole. Use of Jakavi during pregnancy is not recommended, and women should avoid becoming pregnant during Jakavi therapy. Women taking Jakavi should not breast feed. Progressive multifocal leukoencephalopathy (PML) has been reported. Physicians should be alert for neuropsychiatric symptoms suggestive of PML.

Hepatitis B viral load (HBV-DNA titer) increases have been reported in patients with chronic HBV infections. Patients with chronic HBV infection should be treated and monitored according to clinical guidelines. Non-melanoma skin cancer (NMSC) has been reported in Jakavi treated patients. Periodic skin examination is recommended. Very common adverse reactions in MF (>10%) include urinary tract infections, anemia, thrombocytopenia, neutropenia, hypercholesterolemia, dizziness, headache, alanine aminotransferase increased, aspartate aminotransferase increased, bruising and weight gain. Common adverse reactions in MF (1 to 10%) include herpes zoster and flatulence. Uncommon adverse reactions in MF include tuberculosis. Very common adverse reactions in PV (>10%) include anemia, thrombocytopenia, hypercholesterolemia, hypertriglyceridemia, dizziness, alanine aminotransferase increased and aspartate aminotransferase increased. Common adverse reactions in PV (1 to 10%) include urinary tract infections, herpes zoster, weight gain, constipation and hypertension.

Please see full Prescribing Information available at **www.jakavi.com**.

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This press release contains forward-looking statements within the meaning of the United States Private Securities Litigation Reform Act of 1995. Forward-looking statements can generally be identified by words such as “potential,” “can,” “will,” “plan,” “may,” “could,” “would,” “expect,” “anticipate,” “seek,” “look forward,” “believe,” “committed,” “investigational,” “pipeline,” “launch,” or similar terms, or by express or implied discussions regarding potential marketing approvals, new indications or labeling for the investigational or approved products described in this press release, or regarding potential future revenues from such products. You should not place undue reliance on these statements. Such forward-looking statements are based on our current beliefs and expectations regarding future events, and are subject to significant known and unknown risks and uncertainties. Should one or more of these risks or uncertainties materialize, or should underlying assumptions prove incorrect, actual results may vary materially from those set forth in the forward-looking statements. There can be no

guarantee that the investigational or approved products described in this press release will be submitted or approved for sale or for any additional indications or labeling in any market, or at any particular time. Nor can there be any guarantee that such products will be commercially successful in the future. In particular, our expectations regarding such products could be affected by, among other things, the uncertainties inherent in research and development, including clinical trial results and additional analysis of existing clinical data; regulatory actions or delays or government regulation generally; global trends toward health care cost containment, including government, payor and general public pricing and reimbursement pressures and requirements for increased pricing transparency; our ability to obtain or maintain proprietary intellectual property protection; the particular prescribing preferences of physicians and patients; general political, economic and business conditions, including the effects of and efforts to mitigate pandemic diseases such as COVID-19; safety, quality, data integrity or manufacturing issues; potential or actual data security and data privacy breaches, or disruptions of our information technology systems, and other risks and factors referred to in Novartis AG's current Form 20-F on file with the US Securities and Exchange Commission. Novartis is providing the information in this press release as of this date and does not undertake any obligation to update any forward-looking statements contained in this press release as a result of new information, future events or otherwise.

About Novartis

Novartis is reimagining medicine to improve and extend people's lives. As a leading global medicines company, we use innovative science and digital technologies to create transformative treatments in areas of great medical need. In our quest to find new medicines, we consistently rank among the world's top companies investing in research and development. Novartis products reach nearly 800 million people globally and we are finding innovative ways to expand access to our latest treatments. About 110,000 people of more than 140 nationalities work at Novartis around the world. Find out more at https://www.novartis.com.

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i. Descriptive P value given for ORR at the primary analysis as the efficacy boundary was crossed at the interim analysis (ORR, P = 0.0003).

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