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MEDIA UPDATE

Novartis announces NEJM publication of positive Phase III REACH3 data for Jakavi in chronic GvHD

- *REACH3 data show Jakavi significantly improved overall response rate (ORR) at week 24 (49.7% vs. 25.6%) with a higher best overall response rate (76.4% vs. 60.4%) vs. best available therapy, among steroid-refractory/dependent chronic graft-versus-host disease (GvHD) patients*[1]

- *Additional new subgroup analysis demonstrated higher ORR for Jakavi-treated patients regardless of the individual organs involved at baseline*[1]

- *Chronic GvHD, a life-threatening disease and long-term complication of stem cell transplants, can affect multiple organs; half of patients become refractory to or dependent on first-line steroids*[2-5]

- *Regulatory submissions outside the US for acute and chronic GvHD are underway*

Basel, July 14, 2021 — Novartis today announced that *The New England Journal of Medicine* (NEJM) published positive results from the Phase III REACH3 trial demonstrating Jakavi® (ruxolitinib) significantly improved outcomes in patients with steroid-refractory/dependent chronic graft-versus-host disease (GvHD) compared to best available therapy (BAT)[1]. The study's main findings, which had been previously presented at the 62nd American Society of Hematology (ASH) Annual Meeting, were published along with new subgroup analyses showing favorable overall response rate (ORR) at week 24 for Jakavi across all major subgroups, including baseline individual organ involvement[1]. REACH3 is jointly sponsored by Novartis and Incyte.

"Patients with chronic GvHD can experience severe and life-threatening symptoms in different organs around the body, which makes the disease more difficult to treat and increases the risk of poor outcomes," said Dr. Robert Zeiser, University Hospital Freiburg, Department of Haematology, Oncology and Stem Cell Transplantation, Freiburg, Germany. "With these new results from REACH3, we can see more clearly the potential benefits of what may become a new standard of care for chronic GvHD patients who have not adequately responded to first-line steroids."

The study found that treatment with Jakavi led to significant improvements in ORR at week 24 (49.7% vs. 25.6%; odds ratio [OR], 2.99; P<0.001[i]), which was the trial's primary endpoint[1]. Also, best overall response (BOR) rate at any time up to week 24 was achieved in 76.4% of patients in the Jakavi arm compared to 60.4% in the BAT arm (OR, 2.17; 95% CI, 1.34-3.52)[1]. Jakavi also demonstrated statistically significant and clinically meaningful improvements in key secondary endpoints[1]:

- Patients on Jakavi achieved longer failure-free survival (FFS) than patients receiving BAT (median FFS not yet reached vs. 5.7 months; hazard ratio, 0.37; 95% CI, 0.27 to 0.51; P<0.001).
- Jakavi-treated patients also had greater improvements in self-reported symptoms compared to BAT[1] (24.2% vs. 11.0%; OR, 2.62; P=0.001)[ii].

In addition, a new subgroup analysis included in the publication found that patients on Jakavi had better outcomes regardless of the individual organs affected at baseline[1].

“These new Jakavi data underscore its potential benefits and the importance of making it available to patients at risk for an all-too-common and life-threatening complication of stem cell transplants,” said Susanne Schaffert, PhD, President, Novartis Oncology. “We are pleased that regulatory submissions are underway and will continue to work toward wide accessibility of this important new medicine for GvHD.”

No new safety signals were observed in REACH3, and adverse events (AEs) attributable to treatment were consistent with the mechanism of action and the known safety profile of Jakavi[1]. The most common AEs of grade 3 or higher in the Jakavi vs. BAT arms were thrombocytopenia (15.2% vs. 10.1%), anemia (12.7% vs. 7.6%), neutropenia (8.5% vs. 3.8%) and pneumonia (8.5% vs. 9.5%). While 37.6% and 16.5% of patients required Jakavi and BAT dose modifications due to AEs, respectively, the number of patients who discontinued treatment due to AEs was low (16.4% Jakavi vs. 7% BAT)[1]. Mortality rates were similar across treatment arms (18.8% Jakavi vs. 16.5% BAT)[1]. Deaths reported as primarily due to chronic GvHD were slightly higher for Jakavi[1].

In 2019, the US Food and Drug Administration (FDA) approved ruxolitinib (marketed by Incyte Corporation in the US 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]. The Incyte filing in the US for Jakafi in steroid-refractory chronic GvHD is currently undergoing review by the FDA. Outside the US, Novartis regulatory submissions for acute and chronic GvHD are underway worldwide.

The NEJM publication of the REACH3 results is available online at www.NEJM.org.

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 refractory 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[7].

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**.

Disclaimer
This media update 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,” “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 media update, 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 media update 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 media update as of this date and does not undertake any obligation to update any forward-looking statements contained in this media update 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, 50.5% with ruxolitinib and 26.3% with control therapy; P<0.001).
ii. 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).

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