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Novartis announces data show majority of patients with polycythemia vera treated with Jakavi® achieved long-term disease control

- *Preplanned analysis at 18 months demonstrate 80% of PV patients treated with Jakavi® (ruxolitinib) experienced a durable response for at least one year[1]*
- *In the study, 83% of patients in the Jakavi arm remained on treatment; findings reinforce the long-term safety profile of Jakavi[1]*
- *Jakavi, the only targeted therapy approved for PV in the EU, addresses an unmet need as 1 in 4 patients with PV is resistant to/intolerant of current treatments[2]*

Basel, June 13, 2015 – Novartis today announced long-term safety and efficacy results from the pivotal Phase III RESPONSE study evaluating Jakavi® (ruxolitinib) for the treatment of patients with polycythemia vera (PV) who are resistant to or intolerant of hydroxyurea. A preplanned analysis of the study at 18 months demonstrated that 80% of patients with inadequately controlled PV treated with Jakavi experienced a durable response of sustaining hematocrit less than 45% without the use of phlebotomy and reducing spleen size, two key measures of disease control, for at least one year[1]. Findings were presented at the 20th Congress of the European Hematology Association (EHA) in Vienna, Austria.

"Polycythemia vera can lead to serious complications if inadequately controlled, and these data demonstrate the ability of Jakavi to provide a durable and comprehensive clinical benefit in this patient population," said lead study investigator Jean-Jacques Kiladjian, MD, PhD, Hôpital Saint-Louis et Université Paris Diderot. "There is currently a significant unmet need for patients with polycythemia vera who are unable to tolerate or control their disease on other treatments. For these patients, Jakavi represents a valuable new option as confirmed by results from the long-term Phase III study."

PV is a rare and incurable blood cancer associated with an overproduction of blood cells that can cause serious cardiovascular complications, such as blood clots, stroke and heart attack[3]. Approximately 25% of patients with PV develop resistance (inadequate response) to or intolerance (unacceptable side effects) of hydroxyurea and are considered to have inadequately controlled disease[2]. This is typically defined as hematocrit levels greater than 45%, elevated white blood cell count and/or platelet count, and may be accompanied by debilitating symptoms and/or an enlarged spleen[2,4,5].

In the Phase III study, 83% of patients with PV randomized to Jakavi were still receiving treatment at 18 months (median exposure of 111 weeks) compared to 0 patients on the best available treatment arm. Results also show that Jakavi-treated patients who achieved hematocrit control without phlebotomy had an 89% probability of maintaining their response for 18 months from the time of their initial response and all patients who had an initial spleen response maintained their reduction in spleen size. Of the patients on the Jakavi arm at week 32, 90% of patients did not have a phlebotomy between weeks 32 and 80. In addition, patients treated with Jakavi who achieved complete hematologic remission at week 32 had a 69% probability of maintaining their response for at least 18 months from the time of their initial response[1]. A separate analysis of the

study at 18 months demonstrated treatment with Jakavi also led to sustained control of white blood cell and platelet levels, important PV hematologic parameters, with the largest reductions for patients with the most elevated values at baseline[6].

“Until the recent European Commission approval of Jakavi for the treatment of adult patients with polycythemia vera, there were limited alternative treatments available for these patients,” said Bruno Strigini, President, Novartis Oncology. “These long-term data not only reinforce the robust evidence we have surrounding Jakavi in polycythemia vera, but also our commitment to bringing new and innovative therapies to people with blood cancers.”

Overall, Jakavi was well tolerated. In the Jakavi-treatment arm, the rate for Grade 3 or 4 anemia and thrombocytopenia was 0.9 and 2.6 events per 100 patient-year exposure, respectively, and did not increase from the week 48 analysis. The most common non-hematologic adverse events (AEs) in the Jakavi arm were headache, diarrhea, pruritus and fatigue, which were mainly Grade 1 or 2. Treatment discontinuation due to AEs remained low in the Jakavi arm (4.5%)[1].

About the Pivotal Clinical Trial
RESPONSE is a global, randomized, open-label trial conducted at more than 90 trial sites. 222 patients with PV resistant to or intolerant of hydroxyurea were randomized 1:1 to receive either Jakavi (starting dose of 10 mg twice daily) or best available therapy, which was defined as investigator-selected monotherapy or observation only. The Jakavi dose was adjusted as needed throughout the trial. In the Jakavi arm, patients had a PV diagnosis for a median of 8.2 years and had previously received hydroxyurea for a median of approximately three years. Most patients (>80%) had received at least two phlebotomies in the last 24 weeks prior to screening. Patients were classified as intolerant or resistant to hydroxyurea based on the modified European LeukemiaNet (ELN) defined criteria[1].

The primary endpoint of the trial was the proportion of patients whose hematocrit was controlled without phlebotomy eligibility from week 8 through 32 (with no more than one phlebotomy eligibility between randomization and week 8) and whose spleen volume was reduced by 35% or more from baseline as assessed by imaging at week 32. Patients in the trial who were deemed to be eligible for phlebotomy had hematocrit that was greater than 45% and had increased three or more percentage points from the time they entered the trial (e.g., at baseline), or hematocrit greater than 48%. A second, preplanned analysis was performed at 80 weeks (18 months) evaluating durability of primary response, hematocrit control, spleen size reduction, complete hematologic remission and safety. Also at this 80 week data cutoff, a separate analysis evaluating hematologic parameters was assessed by baseline level[1].

About Polycythemia Vera
PV is a rare and incurable blood cancer associated with an overproduction of blood cells in the bone marrow that affects roughly one to three people per 100,000 globally[3,7]. The disease is driven by the dysregulation of the JAK-STAT pathway[8]. It is typically characterized by elevated hematocrit, the volume percentage of red blood cells in whole blood, which can lead to a thickening of the blood and an increased risk of blood clots, as well as an elevated white blood cell and platelet count[3]. This can cause serious cardiovascular complications, such as stroke and heart attack, resulting in increased morbidity and mortality[9]. Additionally, patients with PV may have an enlarged spleen and symptoms that are frequent and burdensome, with an overall impact on quality of life similar to that seen with myelofibrosis[5,10].

A common PV treatment includes phlebotomy, a procedure to remove blood from the body to reduce the concentration of red blood cells, which is used to help maintain a hematocrit level below 45%[3,9]. However, phlebotomy is usually unsuitable as a permanent treatment option due to its inability to control symptoms or effectively manage

the overproduction of red blood cells, therefore cytoreductive agents, such as hydroxyurea, may be added[9]. For patients requiring phlebotomy in combination with hydroxyurea, hematocrit may fluctuate and remain at unsafe levels for significant periods of time[11]. Unfortunately, approximately 25% of patients with PV become resistant to or intolerant of hydroxyurea treatment according to ELN criteria, resulting in inadequate disease control and an increased risk of progression[2].

About Jakavi
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 (also known as chronic idiopathic myelofibrosis), post-polycythemia vera myelofibrosis or post-essential thrombocythemia myelofibrosis. Jakavi is approved in more than 80 countries for patients with myelofibrosis, including countries in the European Union, Canada, Japan and countries in Asia, Latin and South America. Additional worldwide regulatory filings are underway in myelofibrosis and PV.

Novartis licensed ruxolitinib from Incyte Corporation for development and commercialization outside the United States. Jakavi is marketed in the United States by Incyte Corporation as Jakafi® for the treatment of patients with PV who have had an inadequate response to or are intolerant of hydroxyurea and for the treatment of patients with intermediate or high-risk myelofibrosis.

The recommended starting dose of Jakavi in PV is 10 mg given orally twice daily. The recommended starting dose of Jakavi in myelofibrosis is 15 mg twice daily for patients with a platelet count between 100,000 cubic millimeters (mm^3) and 200,000 mm^3, and 20 mg twice daily for patients with a platelet count of >200,000 mm^3. Doses may be titrated based on safety and efficacy. There is limited information to recommend a starting dose for myelofibrosis and PV patients with platelet counts between 50,000/mm^3 and <100,000/mm^3. The maximum recommended starting dose in these patients is 5 mg twice daily, and patients should be titrated cautiously[12].

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 the approved indications.

Jakavi Important Safety Information for Treatment of Myelofibrosis (MF) and Polycythemia Vera (PV)
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

The foregoing release contains forward-looking statements that can be identified by words such as “can,” “currently,” “commitment,” “underway,” or similar terms, or by express or implied discussions regarding potential new indications or labeling for Jakavi, regarding potential future marketing approvals for Jakavi, or regarding potential future revenues from Jakavi. You should not place undue reliance on these statements. Such forward-looking statements are based on the current beliefs and expectations of management 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 Jakavi will be submitted or approved for any additional indications or labeling in any market, or at any particular time. Neither can there be any guarantee that Jakavi will be submitted or approved for sale in any additional markets, or at any particular time. Nor can there be any guarantee that Jakavi will be commercially successful in the future. In particular, management’s expectations regarding Jakavi could be affected by, among other things, the uncertainties inherent in research and development, including unexpected clinical trial results and additional analysis of existing clinical data; unexpected regulatory actions or delays or government regulation generally; the company’s ability to obtain or maintain proprietary intellectual property protection; general economic and industry conditions; global trends toward health care cost containment, including ongoing pricing pressures; unexpected manufacturing issues, 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 provides innovative healthcare solutions that address the evolving needs of patients and societies. Headquartered in Basel, Switzerland, Novartis offers a diversified portfolio to best meet these needs: innovative medicines, eye care and cost-saving generic pharmaceuticals. Novartis is the only global company with leading positions in these areas. In 2014, the Group achieved net sales of USD 58.0 billion, while R&D throughout the Group amounted to approximately USD 9.9 billion (USD 9.6 billion excluding impairment and amortization charges). Novartis Group companies employ approximately 120,000 full-time-equivalent associates. Novartis products are available in more than 180 countries around the world. For more information, please visit http://www.novartis.com.

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References

1. Kiladjian JJ, Vannucchi AM, Greisshammer M, et al. Ruxolitinib versus Best Available Therapy in Patients with Polycythemia Vera: 80-week Follow-up from the RESPONSE Trial. Abstract #S447. 20th Congress of the European Hematology Association (EHA) Vienna, Austria, 2015.
2. Alvarez-Larran A, Pereira A, Cervantes F, et al. Assessment and Prognostic Value of The European LeukemiaNet Criteria for Clinicohematologic Response, Resistance, and Intolerance to Hydroxyurea in Polycythemia Vera. *Blood*. 2012;119(6):1363-1369.
3. Leukemia & Lymphoma Society. “Polycythemia Vera Facts.” Available at: http://www.lls.org/content/nationalcontent/resourcecenter/freeeducationmaterials/mpd/pdf/polycythemiavera.pdf. Accessed June 2015.
4. Barbui T, Barosi G, Birgegard G, et al. Philadelphia-Negative Classical Myeloproliferative Neoplasms; Critical Concepts and Management Recommendations from European LeukemiaNET. *J Clin Oncol*. 2011;29(6):761-770.
5. Emanuel R, Dueck A, Geyer H, et al. Myeloproliferative Neoplasm (MPN) Symptom Assessment Form Total Symptom Score: Prospective International Assessment of an Abbreviated Symptom Burden Scoring System Among Patients with MPNs. *J Clin Oncol*. 2012;30(33):4098-4103.

6. Harrison C, Masszi T, Zachee P, et al. Complete Hematologic Control with Ruxolitinib in Patients with Polycythemia Vera (PV) Resistant to or Intolerant of Hydroxyurea. Abstract #E1353. 20th Congress of the European Hematology Association (EHA) Vienna, Austria, 2015.
7. Titmarsh G, Duncombe A, McMullin M, et al. How Common are Myeloproliferative Neoplasms? A Systematic Review and Meta-analysis. *Am J Hematol*. 2014:1-7.
8. Schafer AI. Molecular Basis of the Diagnosis and Treatment of Polycythemia Vera and Essential Thrombocythemia. *Blood.* 2006;107(11):4214-4222.
9. Finazzi G and Barbui T. How I Treat Patients with Polycythemia Vera. *Blood*. 2007;109(12):5104-5111.
10. Mesa RA, Niblack J, Wadleigh M, et al. The Burden of Fatigue and Quality of Life in Myeloproliferative Disorders (MPDs): An International Internet-based Survey of 1,179 MPD Patients. *Cancer*. 2007;109(1):68-76.
11. Marchioli R, Finazzi G, Specchia G, et al. Cardiovascular Events and Intensity of Treatment in Polycythemia Vera. *N Engl J Med*. 2013;368:22-33.
12. Jakavi® (ruxolitinib) tablets: EU Summary of Product Characteristics. Novartis; Mar 2015.

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