Novartis International AG
Novartis Global Communications
CH-4002 Basel
Switzerland
http://www.novartis.com

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Novartis announces safety and efficacy benefit of Jakavi® in global clinical trial of over 1,000 patients with myelofibrosis

- *Data from ongoing trial reinforces the safety profile of Jakavi® (ruxolitinib) as seen in previous Phase III studies*[1]
- *Patients on Jakavi experienced a reduction in spleen size that was maintained over time and a clinically meaningful improvement in symptoms*[1]
- *Jakavi is the only JAK inhibitor approved in more than 70 countries for patients with myelofibrosis, an uncommon blood cancer marked by debilitating symptoms*[2]

Basel, December 8, 2014 – Novartis today announced data from the largest clinical trial of myelofibrosis patients treated with Jakavi® (ruxolitinib), supporting the safety profile and efficacy benefit as measured in primary and secondary endpoints respectively[1]. In an analysis of 1,144 patients treated with Jakavi to date in this ongoing expanded access study, 69% of patients achieved ≥50% reduction in spleen size from baseline and patients also experienced a clinically meaningful improvement in myelofibrosis symptom score, important treatment goals for patients with myelofibrosis[1,3].

Findings from the study were presented at the 56th Annual Meeting of the American Society of Hematology (ASH) in San Francisco, California.

“Results to date from the JUMP study reinforce the critical role that Jakavi plays in the treatment of myelofibrosis, a life-threatening and debilitating blood cancer with limited treatment options,” said Haifa Kathrin Al-Ali, MD, University Hospital of Leipzig, Leipzig, Germany. “These data provide insight into the real world experience of more than 1,000 patients living with myelofibrosis and further validate the safety and efficacy of Jakavi as an important treatment for myelofibrosis.”

Novartis research and development efforts, in collaboration with Incyte Corporation, include early-phase and post-marketing studies in myelofibrosis and other myeloproliferative neoplasms. More than 50 abstracts on ruxolitinib are being presented at ASH, including three oral presentations exploring combinations of ruxolitinib with various investigational compounds, evaluating the possibility of simultaneously targeting multiple cancer pathways that may be involved in the pathogenesis of myelofibrosis.

“Data presented at ASH demonstrate our ongoing commitment to the myelofibrosis community and reinforce the role of Jakavi as the current standard of care for these patients,” said Alessandro Riva, MD, Global Head, Novartis Oncology Development and Medical Affairs. “It’s exciting to see the depth of research in a rare blood cancer like myelofibrosis. Results from these studies help us to better understand and address the needs of patients and physicians.”

About the JUMP Study

The JUMP study is a Phase IIIb, expanded-access trial for countries with no access to Jakavi outside of a clinical trial. The open-label, multicenter study analyzed 1,144 enrolled myelofibrosis patients who received daily starting doses of either 5 mg, 15 mg or 20 mg of Jakavi twice daily based on platelet counts at baseline. The primary endpoint is assessment of safety and tolerability of Jakavi. Additional analyses included changes in spleen size and symptom scores as measured by the FACT-Lymphoma Total Score (FACT-Lym TS). As of September 22, 2014, 2,138 patients were enrolled at more than 200 study sites in 25 countries, and the final analysis will be performed after all patients have completed 24 months of treatment or ended treatment due to commercial availability[1].

Overall, the safety and efficacy profile of Jakavi was consistent with previous studies[1,4,5]. The most common Grade 3 or 4 hematologic adverse events (AEs) were anemia (33.0%) and thrombocytopenia (12.5%); however, they rarely led to discontinuation (2.6% of discontinuation was due to anemia and 3.2% of discontinuation was due to thrombocytopenia)[1]. The most common nonhematologic AEs were diarrhea (14.5%), fever (13.3%), fatigue (12.9%) and asthenia (12.5%), which were primarily Grade 1 or 2[1].

Also at ASH: MPN Landmark Patient and Physician Survey

Also separately presented for the first time are results from the new MPN Landmark Survey of physicians and patients with myeloproliferative neoplasms (MPNs), a group of related blood cancers, including myelofibrosis[6,7]. The survey, conducted by Incyte Corporation, concluded that an essential goal in disease management should focus on reducing symptom burden and improving quality of life in order to enhance the overall health of patients with myelofibrosis[6,7].

The Landmark Survey found that a remarkable 81% of patients with myelofibrosis reported their myelofibrosis-related symptoms reduced their quality of life[7]. The vast majority of myelofibrosis patients (81%) reported that fatigue was the most severe and common symptom they experienced[7]. According to physicians surveyed, fatigue, abdominal discomfort and pain had the greatest impact on quality of life in their myelofibrosis patients[7]. In fact, both patients and physicians agreed that fatigue is the most urgent symptom myelofibrosis patients would like to resolve[6].

The MPN Landmark Survey is the first large US-based survey to examine both physicians who treat MPNs and patients diagnosed with one of the three MPNs, including myelofibrosis, polycythemia vera (PV) and essential thrombocythemia (ET). The survey was completed by 457 physicians and 813 patients (MF=207; PV=380; ET=226) who filled out an online survey of 59 to 65 questions (depending on the MPN), conducted between May and July 2014. Participants were asked about the overall burden of disease and impact of symptoms on quality of life, productivity, and activities of daily living (ADLs). Symptom severity was determined using the MPN Symptom Assessment Form total symptom scores (MPN-SAF TSS), and descriptive analyses were conducted to identify gaps in perceptions of disease burden and patient-physician communication[6,7].

About Myelofibrosis

Myelofibrosis is a rare, life-threatening blood cancer, with approximately 1 in every 133,000 people estimated to be affected by the disease[2,8,9]. Myelofibrosis develops when uncontrolled signaling in the JAK pathway – which regulates blood cell production – causes the body to make blood cells that do not work properly, which scars the bone marrow and results in an enlarged spleen as well as other severe complications and debilitating symptoms[2,10].

Studies show that patients with myelofibrosis have a decreased life expectancy, with a median overall survival of 5.7 years[11]. Although allogeneic stem cell transplantation may cure myelofibrosis, the procedure is associated with significant morbidity and transplant-related mortality and is available to less than 5% of patients who are young and fit

enough to undergo the procedure[12]. Current myelofibrosis treatment strategies are aimed at reducing spleen size, relieving symptoms, improving quality of life and reducing the risk of complications[3,10].

About Jakavi
Jakavi (ruxolitinib) is an oral inhibitor of the JAK 1 and JAK 2 tyrosine kinases and was approved by the European Commission in August 2012 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 70 countries, including the European Union, Canada, Japan and some countries in Asia, Latin and South America. Additional worldwide regulatory filings are underway.

Novartis licensed ruxolitinib from Incyte Corporation for development and commercialization outside the United States. Both the European Commission and the U.S. Food and Drug Administration (FDA) granted ruxolitinib orphan drug designation for myelofibrosis. Jakavi is marketed in the United States by Incyte Corporation under the name Jakafi® for the treatment of patients with intermediate or high-risk myelofibrosis.

The recommended starting dose for Jakavi in patients with 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 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[13].

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 indication.

Jakavi® 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. The most common adverse drug reactions, occurring at any level of severity (incidence >10%) are urinary tract infections, anemia, thrombocytopenia, neutropenia, hypercholesterolemia, dizziness, headache, alanine aminotransaminase increased, asparte aminotransferase increased and bruising. Other common adverse drug reactions (incidence 1 to 10%) are herpes zoster, weight gain, flatulence and tuberculosis (1%). Progressive multifocal leukencephalopathy (PML) has been reported. Physicians should be alert for neuropsychiatric symptoms suggestive of PML[13]. 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 “commitment,” “will,” “goal,” “should,” or similar terms, or by express or implied discussions regarding potential new indications or labeling 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. 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, cost-saving generic pharmaceuticals, preventive vaccines, over-the-counter and animal health products. Novartis is the only global company with leading positions in these areas. In 2013, the Group achieved net sales of USD 57.9 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 133,000 full-time-equivalent associates and sell products in more than 150 countries around the world. For more information, please visit http://www.novartis.com.

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Novartis Media Relations

Central media line: +41 61 324 2200

Eric Althoff
Novartis Global Media Relations
+41 61 324 7999 (direct)
+41 79 593 4202 (mobile)
eric.althoff@novartis.com

Maureen Byrne
Novartis Oncology
+1 862 778 1518 (direct)
+1 973 714 0063 (mobile)
maureen.byrne@novartis.com

e-mail: media.relations@novartis.com

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For questions about the site or required registration, please contact: journalisthelp@thenewsmarket.com.

Novartis Investor Relations

Central phone:	+41 61 324 7944		
Samir Shah	+41 61 324 7944	**North America:**	
Pierre-Michel Bringer	+41 61 324 1065	Stephen Rubino	+1 862 778 8301
Thomas Hungerbuehler	+41 61 324 8425	Susan Donofrio	+1 862 778 9257
Isabella Zinck	+41 61 324 7188		

e-mail: investor.relations@novartis.com

e-mail: investor.relations@novartis.com