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FORM 6-K

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Novartis AG

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Two-year data show new Novartis drug Jakavi® significantly reduced myelofibrosis disease burden and suggest overall survival advantage

- *Jakavi demonstrated rapid reductions in spleen size and improved quality of life in Phase III studies, with results sustained over two years*

- *COMFORT-II follow-up results show Jakavi may improve overall survival vs. best available therapy*

- *MF is a life-threatening blood cancer associated with progressive, debilitating symptoms that severely impact quality of life and reduce overall survival*

- *Until recently, treatment options have been very limited Jakavi is now approved in the EU and Canada with additional worldwide regulatory filings underway*

Basel, December 11, 2012 Novartis today announced long-term follow-up data from the COMFORT-I and COMFORT-II Phase III studies in myelofibrosis. In these studies, Jakavi® (INC424, ruxolitinib) treatment resulted in sustained reductions in spleen size, a hallmark of myelofibrosis, while also improving quality of life and extending overall survival compared to placebo or the best available therapy (BAT).

Results are being presented at the 54th American Society of Hematology (ASH) Annual Meeting and Exposition in Atlanta.

A two-year follow-up analysis of COMFORT-II showed Jakavi was associated with sustained reductions in splenomegaly (enlarged spleen). Overall, 48.3% of patients treated with Jakavi achieved a ≥35% reduction in spleen volume, and the majority of reductions were sustained with continued treatment over two years. In a rigorous intent-to-treat analysis, Jakavi-treated patients showed an overall survival advantage compared

to patients receiving BAT (HR=0.51; 95% CI, 0.26-0.99; p=0.041)(1), which was defined by protocol as any commercially available agent (monotherapy or in combination) or no therapy at all. A total of 61.6% of BAT patients switched to Jakavi treatment, but remained categorized as BAT patients during the follow-up analyses(1).

As these Phase III studies continue over the long term, it is encouraging to see how treatment with Jakavi consistently alleviates the myelofibrosis disease burden and may improve overall survival, said Dr. Francisco Cervantes, Hematology Department, Hospital Clínic, IDIBAPS, University of Barcelona. Just one year ago, we didn t have a truly effective treatment to offer our patients with myelofibrosis. Now, it appears we can significantly improve a patient s quality of life while also potentially extending their life.

In COMFORT-I, which compared the use of Jakavi versus placebo, researchers presented long-term follow-up data evaluating the efficacy and safety of Jakavi. Similar to COMFORT-II, Jakavi was associated with sustained reductions in spleen volume. Mean spleen volume reduction in the Jakavi arm was 31.6% at week 24, and maintained through week 96 (34.9%)(2). Among patients with a ≥35% reduction in spleen volume, response was maintained with a median duration of 108 weeks. The study demonstrated

a continued overall survival benefit in favor of Jakavi, as 83% of patients on Jakavi survived at the 102 week follow-up period, compared to 73% of patients on placebo (HR=0.58; 95% CI, 0.36-0.95; p=0.028)(2). Overall survival favored Jakavi across subgroups, including starting dose as well as baseline risk status and hemoglobin(2).

The COMFORT program, which supported the European Commission approval for Jakavi, is the most extensive clinical trial program in myelofibrosis to date and continues to demonstrate significant results for Jakavi-treated patients, said Hervé Hoppenot, President, Novartis Oncology. We are encouraged by these findings and look forward to evaluating how Jakavi may help patients with other myeloproliferative neoplasms associated with a similar mechanism of disease.

Myelofibrosis develops when uncontrolled signaling in the JAK pathway which regulates blood cell production causes bone marrow scarring and faulty blood cell production, resulting in severe complications. Jakavi directly targets an underlying mechanism of myelofibrosis, significantly reducing splenomegaly and improving debilitating symptoms regardless of JAK mutational status, disease subtype or any prior treatment, including hydroxyurea(3),(4),(5),(6).

While Jakavi has proven to provide patient benefits regardless of mutational status, an analysis of patients with the *JAK2V617F* mutation within the COMFORT-II study was also presented at ASH. Findings demonstrate the disease-modifying effects of Jakavi. Patients bearing the *JAK2V617F* mutation who received Jakavi had greater reductions in the presence of cancerous cells with the mutated *JAK2V617F* allele (allele burden) compared with BAT(5). Allele burden reductions among Jakavi-treated patients were gradual and sustained over the duration of the study, whereas BAT-treated patients demonstrated zero reductions. Among patients with ≥20% allele burden reduction, sustained spleen volume reductions were observed to week 72(5).

COMFORT-II Long-Term Study Background

The COMFORT-II (COntrolled MyeloFibrosis Study with ORal JAK Inhibitor Therapy) study randomized 219 patients to receive Jakavi (15 or 20 mg BID) or BAT (2:1 randomization for Jakavi vs. BAT). A total of 73.3% (107/146) of patients in the Jakavi arm entered the extension phase vs. 61.6% (45/73) in the BAT arm, and 55.5% (81/146) of those originally randomized to Jakavi remained on treatment at the time of this analysis(1). Overall survival was estimated using the Kaplan-Meier method. In the analysis of COMFORT-II data examining *JAK2V617* allele burden reduction, allele burden was measured from blood samples using allele-specific quantitative real-time polymerase chain reaction (qPCR)(5).

No specific long-term safety signals emerged during the two-year follow-up period. In the primary analysis of the COMFORT-II study published in *The New England Journal of Medicine* in February 2012 (median treatment duration of 50.1 weeks; Jakavi, 51.4 weeks; BAT, 45.1 weeks), the most common grade 3/4 hematologic adverse events (AEs) in either arm (Jakavi, BAT) were anemia (42.4%; 31.4%) and thrombocytopenia (8.3%; 7.2%), and were manageable with either dose reduction or occasional interruption(4). In the Jakavi arm, mean hemoglobin levels decreased over the first 12 weeks of treatment and then recovered to levels similar to the BAT from week 24 onward(4).

One patient in each arm discontinued for thrombocytopenia, and no patients discontinued for anemia. One week after discontinuing Jakavi, these patients experienced a return of myelofibrosis symptoms that were present before initiating therapy. Since the core study has completed, all patients either entered the extension phase or discontinued from the study. A total of 107 of the 146 patients on Jakavi entered the extension phase in addition to 45 of the 73 patients previously treated with BAT (median treatment duration of 83.3 weeks; Jakavi, 111.4 weeks [randomized and extension phases]; BAT, 45.1 weeks [randomized treatment only per primary analysis].

Grade 3/4 hematologic abnormalities in the extension phase for Jakavi were consistent with the primary analysis: anemia (40.4%); lymphopenia (22.6%) and thrombocytopenia (9.6%)(1).

COMFORT-I Long-Term Study Background

This study randomized 309 patients to Jakavi or placebo. The primary analysis occurred when all patients completed 24 weeks of therapy, and all patients receiving placebo were eligible to cross over to Jakavi after the primary analysis. Quality of life was evaluated beyond week 24 using the European Organization for Research and Treatment of Cancer QoL Questionnaire-Core 30, and overall survival was assessed according to original randomized treatment(2).

The AE profile with long-term treatment is consistent with what has been previously reported(2). Of 34 patients randomized to Jakavi who discontinued after the primary analysis, 4 discontinued for an AE. In patients who continued on Jakavi therapy, anemia and thrombocytopenia remained the most frequently reported AEs. New onset of grade 3 or 4 anemia and thrombocytopenia was reported in 12 and 5 patients, respectively. One patient discontinued for anemia. Overall, among all patients randomized to Jakavi, grade 3 and 4 anemia regardless of baseline hemoglobin was reported in 37.4% and 14.8% of patients, respectively. Similarly, grade 3 and 4 thrombocytopenia was reported in 11.0% and 5.2% of patients, respectively. These rates were similar to those reported in the primary analysis. By week 36, the proportion of patients receiving red blood cell transfusions decreased to the level seen with placebo and remained stable thereafter(2).

Rates of non-hematologic AEs adjusted for increased follow-up duration remained similar to those seen at the time of the primary data analysis(2). No additional cases of acute myeloid leukemia (AML) in patients randomized to Jakavi were reported. Two patients originally randomized to placebo developed AML, 21 and 178 days after crossover to Jakavi. There continued to be no reports of a withdrawal syndrome after Jakavi discontinuation(2).

About Myelofibrosis

Myelofibrosis is a life-threatening blood cancer with a poor prognosis and limited treatment options(7),(8). Studies show that patients with myelofibrosis have a decreased life expectancy, with a median overall survival of 5.7 years(9). 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(10).

About Jakavi

Jakavi® (INC424, ruxolitinib) is an oral inhibitor of the JAK 1 and JAK 2 tyrosine kinases(4) 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 available in more than 30 countries including the European Union and Canada, with additional global regulatory filings underway.

Novartis licensed INC424 (ruxolitinib) from Incyte Corporation for development and commercialization outside the United States. Both the European Commission and the US Food and Drug Administration (FDA) granted INC424 (ruxolitinib) orphan drug status 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 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(11).

Jakavi is a registered trademark of Novartis AG in countries outside the United States. Jakafi is a registered trademark of Incyte Corporation.

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 severe hepatic or 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, bruising, bleeding and increased blood pressure. Other common adverse drug reactions (incidence 1 to 10%) are herpes zoster, weight gain, flatulence and tuberculosis (1%).

Please see full Prescribing Information for Jakavi available at www.jakavi.com.

Disclaimer

The foregoing release contains forward-looking statements that can be identified by terminology such as suggest, may, encouraging, potentially, encouraged, look forward to, or similar expressions, or by express or implied discussions regarding potential future revenues from Jakavi. You should not place undue reliance on these statements. Such forward-looking statements reflect the current views of management regarding future events, and involve known and unknown risks, uncertainties and other factors that may cause actual results with Jakavi to be materially different from any future results, performance or achievements expressed or implied by such statements. There can be no guarantee that Jakavi will achieve any particular levels of revenue in the future. In particular, management s expectations regarding Jakavi could be affected by, among other things, unexpected regulatory actions or delays or government regulation generally; unexpected clinical trial results, including unexpected new clinical data and unexpected additional analysis of existing clinical data; government, industry and general public pricing pressures; unexpected manufacturing issues; competition in general; the company s ability to obtain or maintain patent or other proprietary intellectual property protection; the impact that the foregoing factors could have on the values attributed to the Novartis Group s assets and liabilities as recorded in the Group s consolidated balance sheet, and other risks and factors referred to in Novartis AG s current Form 20-F on file with the US Securities and Exchange Commission. Should one or more of these risks or uncertainties materialize, or should underlying assumptions prove incorrect, actual results may vary materially from those anticipated, believed, estimated or expected. 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 and diagnostic tools, over-the-counter and animal health products. Novartis is the only global company with leading positions in these

4

areas. In 2011, the Group achieved net sales of USD 58.6 billion, while approximately USD 9.6 billion (USD 9.2 billion excluding impairment and amortization charges) was invested in R&D throughout the Group. Novartis Group companies employ approximately 127,000 full-time-equivalent associates and operate in more than 140 countries around the world. For more information, please visit http://www.novartis.com.

Novartis is on Twitter. Sign up to follow @Novartis at http://twitter.com/novartis.

References

(1) Cervantes, F, et al. Long-Term Safety, Efficacy, and Survival Findings From COMFORT-II, a Phase 3 Study Comparing Ruxolitinib with Best Available Therapy (BAT) for the Treatment of Myelofibrosis (MF). *Blood.* 2012. Abstract #801. American Society of Hematology (ASH) 2012 Annual Meeting. Atlanta, GA.

(2) Verstovsek S et al. Long-Term Outcome of Ruxolitinib Treatment in Patients with Myelofibrosis: Durable Reductions in Spleen Volume, Improvements in Quality of Life, and Overall Survival Advantage in COMFORT-I. *Blood.* 2012. Abstract #800. ASH 2012 Annual Meeting. Atlanta, GA.

(3) Verstovsek S, Mesa RA, Gotlib J, et al. A Double-Blind, Placebo-Controlled Trial of Ruxolitinib for Myelofibrosis. *New Eng J Med*. 2012 March 1: 366:799-807.

(4) Harrison C, Kiladjian JJ, Al-Ali HK, et al. JAK Inhibition with Ruxolitinib versus Best Available Therapy for Myelofibrosis. *New Eng J Med*. 2012: March 1;366:787-98.

(5) Vannucchi A, Kiladjian JJ, Gisslinger H, et al. Reductions in JAK2V617F Allele Burden with Ruxolitinib Treatment in COMFORT-II, a Phase III Study Comparing the Safety and Efficacy of Ruxolitinib to Best Available Therapy (BAT). 2012. Abstract #802. ASH 2012. Annual Meeting, Atlanta, GA.

(6) Harrison C, Kiladjian JJ, Gisslinger H, et al. Association of Cytokine Levels and Reductions in Spleen Size in COMFORT-II, a Phase 3 Study Comparing Ruxolitinib to Best Available Therapy (BAT). Abstract # 6625. American Society of Clinical Oncology 2012 Annual Meeting, Chicago, IL.

(7) Verstovsek S, Kantarjian H, Mesa RA, et al. Safety and Efficacy of JAK1 & JAK2 Inhibitor, INCB018424, in Myelofibrosis. *New Eng J Med*. 2010 September 16;363(12):1117-1127.

(8) Mesa RA, Schwagera S, Radia D, et al. The Myelofibrosis Symptom Assessment Form (MFSAF): an evidence-based brief inventory to measure quality of life and symptomatic response to treatment in myelofibrosis. *Leuk Res*. 2009;33:1199-1203.

(9) Cervantes F, Dupriez B, Pereira A, et al. New prognostic scoring system for primary myelofibrosis based on a study of the International Working Group for Myelofibrosis Research and Treatment. *Blood*. 2009;113:2895 2901.

(10) Patriarca F, Bacigalupo A, Sperotto A, et al. Allogeneic hematopoietic stem cell transplantation in myelofibrosis: the 20-year experience of the Gruppo Italiano Trapianto di Midollo Osseo (GITMO). *Haematologica.* 2008;93(10):1514-1522.

(11) JAKAVI [Summary of Product Characteristics]. Basel, Switzerland: Novartis Pharma AG; 2012.

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SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

Novartis AG

Date:	December 11, 2012	By:	/s/ MALCOLM B. CHEETHAM
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