

NOVARTIS AG  
Form 6-K  
March 01, 2012

# SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

## FORM 6-K

**REPORT OF FOREIGN PRIVATE ISSUER  
PURSUANT TO RULE 13a-16 or 15d-16 OF  
THE SECURITIES EXCHANGE ACT OF 1934**

**Report on Form 6-K dated February 29, 2012**

**(Commission File No. 1-15024)**

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**Novartis AG**

(Name of Registrant)

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**Switzerland**

(Address of Principal Executive Offices)

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**MEDIA RELEASE • COMMUNIQUE AUX MEDIAS • MEDIENMITTEILUNG**

**Two Phase III studies of Novartis drug INC424 published in NEJM show significant clinical benefit for patients with myelofibrosis**

- *Results of the COMFORT-I and COMFORT-II trials show INC424 significantly reduced disease burden in patients with myelofibrosis*
- *Myelofibrosis is a life-threatening blood cancer associated with progressive, debilitating symptoms that severely impact quality of life and reduce survival*
- *These data provided the basis for worldwide regulatory filings with first actions expected in the second half of 2012*

**Basel, February 29, 2012** *The New England Journal of Medicine (NEJM)* today published the results of the two Phase III trials that found treatment with the investigational Janus kinase (JAK) inhibitor INC424 (ruxolitinib) significantly reduced disease burden in patients with myelofibrosis(1),(2). The results of COMFORT-I and COMFORT-II (COntrolled Myelofibrosis Study with ORal JAK Inhibitor Therapy) were first presented at the 47th American Society of Clinical Oncology (ASCO) annual meeting in June 2011.

Myelofibrosis is an uncommon, life-threatening blood cancer characterized by bone marrow failure, enlarged spleen (splenomegaly), debilitating symptoms, such as fatigue, night sweats and intractable pruritus (itching), poor quality of life and weight loss, as well as shortened survival(3).

Patients living with this malignant disease have a poor quality of life and experience multiple debilitating symptoms, said Claire Harrison, MD, Guy's and St. Thomas' NHS Foundation Trust, Guy's Hospital, London, lead investigator for the COMFORT-II study. Results from these trials are significant because they demonstrate the potential INC424 has to impact the manifestation of the disease and become a new standard of care for many patients with myelofibrosis.

In the COMFORT-II trial, INC424 produced a volumetric spleen size reduction of 35% or greater (roughly equivalent to a reduction in palpable spleen size by 50%) in 28% of patients compared to 0% of patients in the best available therapy (BAT) group at 48 weeks (p<0.001). At week 24, 32% of patients treated with INC424 demonstrated a 35% or greater volumetric spleen size reduction compared to 0% of patients treated with the BAT (p<0.001) for the key secondary endpoint(1). Additionally, INC424 was associated with improvements in myelofibrosis symptoms at each evaluation as compared to the BAT(1).

Continuous INC424 therapy also provided a marked and durable improvement in overall quality of life measures, functioning and symptoms, including appetite loss, dyspnea (shortness of breath), fatigue, insomnia and pain, at week 48, compared to a worsening of symptoms in BAT-treated patients(1). INC424 showed modest toxicity as compared with the BAT, with increased frequency of anemia and thrombocytopenia. The most frequently reported serious adverse event (SAE) was anemia for both groups (INC424, 5%; BAT,

4%). Pneumonia was the only SAE reported in  $\geq 5\%$  of patients in either group (INC424, 1%; BAT, 5%). These findings are consistent with previous investigation of INC424(4).

The COMFORT-I trial, conducted by Incyte Corporation, demonstrated that 41.9% of INC424 treated patients achieved at least a 35% reduction in spleen volume at 24 weeks from baseline compared to 0.7% of patients in the placebo group ( $p < 0.0001$ ). Additionally, an early analysis of COMFORT-I data shows INC424 treatment resulted in an overall survival benefit as compared to placebo (hazard ratio=0.50 [95% confidence interval: 0.25, 0.98]). For patients taking INC424, the most frequently reported grade 3 or higher adverse events were hematologic. Only one patient in each group discontinued for thrombocytopenia and for anemia, respectively. The most common non-hematologic adverse events of any grade reported for patients receiving INC424 or placebo respectively were fatigue (25% vs 34%), diarrhea (23% vs 21%), peripheral edema (19% vs 22%) and ecchymosis (19% vs 9%)(2).

The COMFORT data provided the basis for worldwide regulatory filings and we expect to hear from the regulatory authorities beginning in the second half of 2012, said Hervé Hoppenot, President, Novartis Oncology. We are getting closer to achieving our goal of bringing innovative, pathway-based compounds to patients with myelofibrosis.

Novartis and Incyte Corporation have a worldwide collaboration and license agreement for INC424. Incyte received US Food and Drug Administration (FDA) approval for INC424 in November 2011 under the name Jakafi for the treatment of patients with intermediate or high-risk myelofibrosis. INC424 will be marketed by Incyte in the US.

#### **COMFORT-II trial details**

COMFORT-II is a randomized, open-label, Phase III trial of INC424 versus the BAT that enrolled 219 patients with primary myelofibrosis (MF), post-polycythemia vera myelofibrosis (PPV-MF) or post-essential thrombocythemia myelofibrosis (PET-MF) in 56 study locations. Two-thirds of the patients enrolled received INC424 (starting dose 15 or 20 mg twice daily) and one-third received the investigator-selected BAT(1).

The primary endpoint for COMFORT-II was the proportion of patients achieving a reduction in spleen volume of 35% or more from baseline at week 48 as measured by MRI (or CT scan in applicable patients). Patients continue to receive INC424 therapy beyond week 48 to determine longer-term outcomes of efficacy and safety(1). The study was not powered to detect a statistically significant effect on overall survival.

COMFORT-II was conducted by Novartis in Europe.

#### **COMFORT-I trial details**

COMFORT-I is the first Phase III trial of INC424 and is a randomized, double-blind, placebo-controlled trial that enrolled 309 patients with primary MF, PPV-MF or PET-MF, conducted by Incyte in 89 study locations. Half of the patients enrolled received INC424 (starting dose 15 or 20 mg twice daily) and half received placebo. The primary endpoint was the proportion of patients achieving a reduction in spleen volume of

35% or more from baseline at week 24 as measured by MRI (or CT scan in applicable patients)(2).

COMFORT-I was conducted by Incyte in the US, Canada and Australia.

### **About Myelofibrosis**

In the EU, the disease affects about 0.75 out of every 100,000 people annually(5),(6). Myelofibrosis has a poor prognosis and limited treatment options(3),(4).

Studies show that within 10 years of diagnosis, up to approximately 20% of myelofibrosis patients progress to fatal secondary acute myelogenous leukemia, which is virtually untreatable(7),(8). Although allogeneic stem cell transplantation may cure myelofibrosis, the

procedure is associated with significant morbidity and mortality(9). The five-year survival rate after transplantation is approximately 30%(9).

#### **About INC424**

INC424 is an oral inhibitor of the JAK 1 and JAK 2 tyrosine kinases(4). As part of the Novartis clinical development program, INC424 is being investigated in primary MF as well as PPV-MF and PET-MF. INC424 is also being investigated in clinical trials for the treatment of polycythemia vera (PV)(10).

Novartis licensed INC424 from Incyte for development and potential commercialization outside the US. Incyte has retained rights for the development and potential commercialization of INC424 in the US. Both the European Commission (EC) and the US FDA granted INC424 orphan drug status for myelofibrosis.

#### **Disclaimer**

The foregoing release contains forward-looking statements that can be identified by terminology such as expected, potential, will, expect, goal, similar expressions, or by express or implied discussions regarding potential marketing submissions or approvals for INC424, or the potential timing of such submissions or approvals, or regarding potential future revenues from INC424. You should not place undue reliance on these statements. Such forward-looking statements reflect the current views of the Group regarding future events, and involve known and unknown risks, uncertainties and other factors that may cause actual results with INC424 to be materially different from any future results, performance or achievements expressed or implied by such statements. There can be no guarantee that INC424 will be submitted or approved for sale in any markets, or at any particular time. Nor can there be any guarantee that INC424 will achieve any particular levels of revenue in the future. In particular, management's expectations regarding INC424 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; competition in general; unexpected manufacturing issues; the company's ability obtain or maintain patent or other proprietary intellectual property protection; the impact that the foregoing factors could have on the values attributed to the 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 described herein as anticipated, believed, estimated or expected. Novartis is providing the information in this release as of this date and does not undertake any obligation to update any forward-looking statements 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 areas. In 2011, the Group's continuing operations 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 124,000 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>.



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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: February 29, 2012

By: /s/ MALCOLM B. CHEETHAM

Name: Malcolm B. Cheetham  
Title: Head Group Financial  
Reporting and Accounting