

NOVARTIS AG  
Form 6-K  
June 06, 2011

# 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 June 4, 2011**

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

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(Name of Registrant)

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(Address of Principal Executive Offices)

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Indicate by check mark whether the registrant files or will file annual reports under cover of Form 20-F or Form 40-F:

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Yes:  **No:**

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**- Investor Relations Release -**

**Novartis JAK inhibitor INC424 shows significant clinical benefit for myelofibrosis patients in two Phase III studies at ASCO**

- *Myelofibrosis is a life-threatening blood cancer characterized by bone marrow failure, enlarged spleen and debilitating symptoms, including fatigue and pain*
- *Phase III trial (COMFORT-II) demonstrated INC424 significantly reduced enlarged spleen size, a major characteristic of the disease, when compared to best available therapy at 48 weeks*
- *A separate Phase III trial (COMFORT-I) of INC424 showed significant spleen size reduction and symptom improvement when compared to placebo at 24 weeks*
- *Both studies met their primary endpoint and provide the basis for worldwide filings to begin in Q2 2011 in myelofibrosis, for which there are limited treatment options*

**Basel, June 4, 2011** Novartis announced today results from two pivotal Phase III studies demonstrating the effects of investigational Janus kinase (JAK) inhibitor INC424 (ruxolitinib) in treating patients with myelofibrosis, a blood cancer with limited treatment options. These data are being presented at the 47th American Society of Clinical Oncology (ASCO) annual meeting in Chicago(1),(2),(3). Novartis and Incyte have a worldwide collaboration and license agreement for INC424.

The Phase III trial COMFORT-II (COntrolled Myl<sup>o</sup>Fibrosis Study with ORal JAK Inhibitor Therapy) demonstrated that INC424 produced a volumetric spleen size reduction of 35% or greater in 28.5% of myelofibrosis patients compared to 0% of patients in the best available therapy arm at 48 weeks (p<0.0001). The trial also met a key secondary endpoint with 31.9% of INC424 patients demonstrating a 35% or greater volumetric spleen size reduction by week 24 compared to 0% in best available therapy patients (p<0.0001)(1). Further, data showed a marked improvement in overall quality of life measures, functioning and symptoms relative to the best available therapy arm(1).

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COMFORT-I, conducted by Incyte, is a Phase III clinical trial comparing INC424 to placebo at 24 weeks. Results showed that 41.9% of myelofibrosis patients who received INC424 achieved at least a 35% reduction in spleen volume at 24 weeks from baseline compared to 0.7% of patients in the placebo arm ( $p < 0.0001$ ). COMFORT-I also met key secondary endpoints with statistical significance, including improvement of debilitating symptoms and demonstrating clinically relevant durations of spleen size reduction(2).

These data show that INC424 may offer a significant advance in treating patients impacted by myelofibrosis, a serious malignant disease with limited available treatment options, said Alessandro Vannucchi, MD, Professor, Department of Hematology, University of Florence,

Hospital Careggi, Italy, investigator for the COMFORT-II study. By targeting the JAK pathway, which is autonomously activated in patients with myelofibrosis even in the absence of the most common JAK mutation, INC424 delivered rapid and durable spleen size reduction in these patients.

Myelofibrosis is an uncommon blood cancer characterized by bone marrow failure, enlarged spleen (splenomegaly), a variety of symptoms that can be debilitating and serious complications. It is associated with significantly reduced quality of life and shortened survival(4). A high unmet medical need exists for the treatment of myelofibrosis, caused by abnormal signaling in the JAK pathway, which regulates blood cell production(3),(5). Abnormal signaling initiates faulty blood cell production resulting in an enlarged spleen and other severe complications(5).

The COMFORT clinical program is the largest ever conducted in myelofibrosis patients and findings support INC424 as a significant advance for patients affected by this life-threatening blood cancer, said Hervé Hoppenot, President, Novartis Oncology. These studies further demonstrate Novartis' goal of bringing innovative, pathway-based compounds to patients with unmet medical needs.

Results of the COMFORT clinical trials will also be presented at the 16th Congress of the European Hematology Association (EHA) from June 9-12 in London. Both studies met their primary endpoint and form the basis of worldwide regulatory filings planned to begin in the second quarter of 2011 by Novartis and Incyte.

#### **COMFORT-II study details**

COMFORT-II is a randomized, open-label Phase III study of INC424 versus best available therapy (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 in Europe. Two-thirds received INC424 (starting dose 15 or 20 mg twice daily) and one-third received BAT, which was administered at doses and schedules determined by the investigator(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). Secondary endpoints included spleen size reduction at 24 weeks, duration of spleen size reduction, time to treatment response, change in bone marrow histomorphology, leukemia-free survival, progression-free survival and overall survival. Patients continue to receive INC424 therapy and to be followed to determine longer-term outcomes(1).

The safety profile of INC424 was consistent with previous studies. Only 8.2% and 5.5% of patients discontinued the study because of an adverse event in the INC424 and BAT arms, respectively. For patients in the INC424 arm, the most commonly reported grade 3 or higher adverse events were hematologic. Based on laboratory assessments, the percentage of patients with grade 3 or 4 low platelet counts at any time during the study was 8.3% on INC424 vs 7.2% on BAT. The percentage of patients with grade 3 or 4 low hemoglobin values at any time during the study was 42.4% on INC424 vs 31.4% on BAT. Both thrombocytopenia and anemia were effectively managed in this clinical setting with appropriate dose modifications and/or transfusions. Only one patient in each arm discontinued for thrombocytopenia and no patient discontinued for anemia. The most commonly reported grade 3 or higher non-hematologic adverse events in the INC424 arm were abdominal pain (3.4% vs 2.7% in the BAT arm), back pain (2.1% vs 0% in the BAT arm), weight gain (2.1% vs 0% in the BAT arm), and fever (2.1% vs 0% in the BAT arm)(1).

COMFORT-II was conducted by Novartis in Europe.

**COMFORT-I study details**

COMFORT-I is the first Phase III study of INC424 and is a randomized, double-blind, placebo-

controlled study that enrolled 309 patients with primary MF, PPV-MF or PET-MF, conducted by the collaboration partner Incyte Corporation in 89 study locations in the US, Canada and Australia. Half of patients 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). Secondary endpoints included duration of maintenance of a 35% or greater reduction in spleen volume from baseline and the proportion of patients with 50% or more reduction in symptom improvement as measured by the modified Myelofibrosis Symptom Assessment Form electronic diary.(2)

In general, the safety profile of patients treated with INC424 was consistent with the findings of the COMFORT-II trial and INC424 was well tolerated. Overall, 10.3% and 9.3% of patients discontinued the study because of an adverse event in the INC424 and placebo arms, respectively. For patients in the INC424 arm, the most commonly reported grade 3 or higher adverse events were hematologic. The percentage of patients with grade 3 or 4 low platelet counts at any time during the study was 12.9% on INC424 vs 1.3% in the placebo arm. The percentage of patients with grade 3 or 4 low hemoglobin values at any time during the study was 45.2% on INC424 vs 19.2% in the placebo arm. Only one patient in each arm discontinued for thrombocytopenia and for anemia. 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 23%) and ecchymosis (19% vs 9%).

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

#### **About myelofibrosis**

Myelofibrosis is an uncommon, life-threatening blood cancer characterized by bone marrow failure, enlarged spleen (splenomegaly), debilitating symptoms, such as fatigue, night sweats and pruritus, poor quality of life, weight loss as well as shortened survival(4). In the EU, the disease affects about 0.75 out of every 100,000 people annually(6),(7). In the US, myelofibrosis affects about 1.5 out of every 100,000 people annually(8). 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(9),(10). Although allogeneic stem cell transplantation may cure myelofibrosis, the procedure is associated with significant morbidity and mortality and is usually appropriate only in a very small subset of younger patients, typically less than 5% of patients(5),(11). The five-year survival rate after transplantation is approximately 50%(11).

#### **About INC424**

INC424 is an oral inhibitor of the JAK1 and JAK2 tyrosine kinases(3). INC424 is being investigated in primary myelofibrosis as well as post-polycythemia vera myelofibrosis (PPV-MF) and post-essential thrombocythemia myelofibrosis (PET-MF). INC424 is also being investigated in clinical trials for the treatment of polycythemia vera (PV)(1),(2),(12).

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 Food and Drug Administration (FDA) have granted INC424 orphan drug status for myelofibrosis.





## Disclaimer

The foregoing release contains forward-looking statements that can be identified by terminology such as to begin in Q2 2011, may, will, planned, potential, mission, promise, continue to receive INC424 therapy and to be followed to determine longer-term outcomes, or 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 the potential long-term impact of INC424 therapy, 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 management 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 market, or at any particular time. Nor can there be any guarantees regarding the long-term impact of treatment with INC424. Neither 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 clinical trial results, including unexpected new clinical data and unexpected additional analysis of existing clinical data; unexpected regulatory actions or delays or government regulation generally; the company's ability to obtain or maintain patent or other proprietary intellectual property protection; competition in general; government, industry and general public pricing pressures; 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 healthcare solutions that address the evolving needs of patients and societies. Focused solely on healthcare, Novartis offers a diversified portfolio to best meet these needs: innovative medicines, eye care, cost-saving generic pharmaceuticals, consumer health products, preventive vaccines and diagnostic tools. Novartis is the only company with leading positions in these areas. In 2010, the Group's continuing operations achieved net sales of USD 50.6 billion, while approximately USD 9.1 billion (USD 8.1 billion excluding impairment and amortization charges) was invested in R&D throughout the Group. Headquartered in Basel, Switzerland, Novartis Group companies employ approximately 119,000 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: June 4, 2011

By: /s/ MALCOLM B. CHEETHAM

Name: Malcolm B. Cheetham

Title: Head Group Financial Reporting and Accounting