

NOVARTIS AG  
Form 6-K  
June 27, 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 24, 2011**

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

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**Novartis AG**

(Name of Registrant)

**Lichtstrasse 35**

**4056 Basel**

**Switzerland**

(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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**Novartis International AG**

Novartis Global Communications

CH-4002 Basel

Switzerland

<http://www.novartis.com>

**- Investor Relations Release -**

**Novartis drug Votubia® recommended by CHMP for approval in the EU for children and adults with SEGA associated with tuberous sclerosis**

- *If approved, Votubia (everolimus) will be first medication in EU for subependymal giant cell astrocytoma (SEGA) associated with tuberous sclerosis complex (TSC)*
- *CHMP opinion based on Phase II study of 28 patients showing 33% experienced a SEGA tumor reduction of 50% or greater at six months relative to baseline(1)*
- *Brain surgery is only treatment option in EU for growing SEGAs, benign brain tumors that primarily affect children and adolescents(1),(2),(3),(4)*
- *Worldwide regulatory submissions for everolimus to treat this patient population are under way; first approval received in the US in 2010 as Afinitor®*

**Basel, June 24, 2011** The Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) adopted a positive opinion for Votubia® (everolimus) tablets\* for the treatment of patients aged 3 years and older with subependymal giant cell astrocytoma (SEGA) associated with tuberous sclerosis complex (TSC), who require therapeutic intervention but are not amenable to surgery. If approved, Votubia will be the first medication available for these patients in the European Union (EU).

Tuberous sclerosis complex, also known as tuberous sclerosis (TS), may cause benign tumors to form in vital organs and can affect many different parts of the body, most commonly the brain(5),(6). Signs of TSC vary depending on which system and which organs are involved(5). SEGAs, or benign brain tumors, occur in up to 20% of patients with TSC(1). Tuberous sclerosis complex is also associated with a variety of resulting disorders including seizures, swelling in the brain (hydrocephalus), developmental delays and skin lesions(1),(2),(5). Currently, brain surgery is the only treatment option for patients in the EU with growing SEGAs associated with TSC(1).

The CHMP positive opinion is for a conditional approval based on a prospective, open-label, single-arm, Phase II study of 28 patients. Results showed that 78% of patients (21 of 27) experienced a reduction of 30% or greater in the size of their largest SEGA and 33% (9 of 27) experienced a reduction of 50% or greater at six months relative to baseline<sup>1</sup>.

The positive CHMP opinion for Votubia is encouraging as it may lead to the approval of the first medication in the European Union for patients with this challenging disease, said Hervé Hoppenot, President of Novartis Oncology. Our focus on tuberous sclerosis complex research reflects the commitment Novartis has made to develop innovative therapies to help address unmet medical needs.

The European Commission generally follows the recommendations of the CHMP and delivers its final decision within three months of the CHMP recommendation. The decision will be applicable to all 27 EU member states plus Iceland and Norway.

Regulatory approvals have already been granted for SEGA associated with TSC in the United States, Switzerland, Brazil, Colombia, Guatemala, the Philippines and South Korea. Additional submissions to global regulatory agencies are under way worldwide.

Everolimus targets mTOR, a protein that acts as an important regulator of tumor cell division, blood vessel growth and cell metabolism<sup>8</sup>. Tuberous sclerosis complex is caused by defects in the TSC1 and/or TSC2 genes<sup>5</sup>. When these genes are defective, mTOR activity is increased, which can cause uncontrolled tumor cell growth and proliferation, blood vessel growth and altered cellular metabolism, leading to the formation of benign tumors throughout the body, including the brain<sup>1</sup>. By inhibiting mTOR activity in this protein pathway, everolimus may reduce cell proliferation, blood vessel growth and glucose uptake related to SEGA associated with TSC1.

Tuberous sclerosis complex is a genetic disorder affecting approximately one to two million people worldwide<sup>5</sup>. In Europe, the prevalence in the general population is estimated to be nearly nine cases per 100,000<sup>(7)</sup>.

#### **About the Phase II Study**

This prospective, open-label, single-arm study was conducted in 28 patients aged three years and above (median age=11, range 3-34) with evidence of serial SEGA growth<sup>(1)</sup>.

In the study, 78% of patients (21 of 27) experienced a reduction of 30% or greater in the size of their largest SEGA and 33% (9 of 27) experienced a reduction of 50% or greater at six months relative to baseline. This evidence is based on an analysis of change in SEGA volume. No patient developed a new SEGA, had worsening hydrocephalus or required surgery or other therapy for SEGA while receiving everolimus<sup>(1)</sup>.

The most common adverse reactions reported (incidence  $\geq 10\%$ ) in the prospective, open-label, single-arm trial were infections, increased aspartate transaminase (AST), mouth sores, increased cholesterol, decreased white blood cell count, increased alanine transaminase (ALT), increased triglycerides, decreased hemoglobin, fever, decreased glucose, acneiform dermatitis, increased glucose, diarrhea, decreased platelet counts, acne, cough and increased creatinine. The only grade 3 adverse reactions were infections (single cases of sinusitis, pneumonia, tooth infection and viral bronchitis), and single cases of mouth sores, elevated AST concentrations and decreased neutrophil count. No grade 4 adverse reactions were reported. However, the reliability of the frequency of adverse reactions and laboratory abnormalities reported in this trial is limited because of the small number of patients.

All data from the Phase II study submitted to the EMA are based on the cut-off date of December 9, 2009.

#### **About everolimus**

Votubia® (everolimus) tablets is approved in Switzerland for the treatment of patients 3 years of age and older, with SEGA associated with TS, for whom surgery is not a suitable option. Should everolimus be approved in the EU, the trade name will be Votubia. In the US, Afinitor® (everolimus) tablets is approved to treat patients with SEGA associated with TS who require therapeutic intervention but are not candidates for

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curative surgical resection. The effectiveness of everolimus is based on an analysis of change in SEGA volume. Clinical benefit such as improvement in disease-related symptoms or increase in overall survival has not been shown.

Afinitor is approved in the US for the treatment of progressive neuroendocrine tumors of pancreatic origin in patients with unresectable, locally advanced or metastatic disease. The FDA

determined that the safety and effectiveness of Afinitor in the treatment of patients with carcinoid tumors have not been established. Novartis has submitted a marketing application for everolimus to the European Medicines Agency (EMA) for this use, and additional regulatory submissions are under way worldwide.

Afinitor is approved in the EU for the treatment of patients with advanced renal cell carcinoma (RCC) whose disease has progressed on or after treatment with vascular endothelial growth factor (VEGF)-targeted therapy and also in the US for the treatment of patients with advanced RCC after failure of treatment with sunitinib or sorafenib.

In the EU, everolimus is available in different dosage strengths for the non-oncology patient population under the trade name Certican® for the prevention of organ rejection in heart and kidney transplant recipients. In the US, everolimus is available in different dosage strengths under the trade name Zortress® for the prophylaxis of organ rejection in adult patients at low-moderate immunologic risk receiving a kidney transplant.

Everolimus is exclusively licensed to Abbott and sublicensed to Boston Scientific for use in drug-eluting stents.

Not all indications are available in every country. Because of the uncertainty of clinical trials, there is no guarantee that everolimus will become commercially available for additional indications anywhere else in the world.

#### **Important Safety Information about Votubia/Afinitor**

Votubia can cause serious side effects including lung or breathing problems, infections, and renal failure which can lead to death. Mouth ulcers and mouth sores are common side effects. Votubia can affect blood cell counts, kidney and liver function, blood sugar and cholesterol levels. Votubia may cause fetal harm in pregnant women. Women taking Votubia should not breast feed.

The most common adverse drug reactions (incidence  $\geq 15\%$ ) are mouth ulcers, rash, diarrhea, fatigue, acneiform dermatitis, infections, weakness, nausea, peripheral swelling, decreased appetite, headache, pneumonitis, abnormal taste, nose bleeds, mucosal inflammation, weight decreased and vomiting. The most common grade 3-4 adverse drug reactions (incidence  $\geq 2\%$ ) are mouth ulcers, fatigue, decreased white blood cell count, diarrhea, infections, pneumonitis and diabetes mellitus. Cases of hepatitis B reactivation and pulmonary embolism have been reported.

#### **Disclaimer**

The foregoing release contains forward-looking statements that can be identified by terminology such as recommended, will, may, commitment, recommendations, under way, or similar expressions, or by express or implied discussions regarding potential new indications or labeling for everolimus or regarding potential future revenues from everolimus. 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 everolimus to be materially different from any future results, performance or achievements expressed or implied by such statements. There can be no guarantee that everolimus 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 everolimus will achieve any particular levels of revenue in the future. In particular, management's expectations regarding everolimus 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; 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

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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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#### **References**

- (1) Krueger, et al. Everolimus for Subependymal Giant-Cell Astrocytomas in Tuberous Sclerosis. *New Eng J Med* 2010;363:1801-11.
- (2) Adriaensen ME, et al. Prevalence of subependymal giant cell tumors in patients with tuberous sclerosis and a review of the literature. *Eur J Neurol* 2009;16:691-6.
- (3) Nabbout R, et al. Early diagnosis of subependymal giant cell astrocytoma in children with tuberous sclerosis. *J Neurol Neurosurg Psychiatry* 1999;66:370-375.
- (4) Medkour A, et al. Neonatal Subependymal Giant Cell Astrocytoma. *Pediatr Neurosurg* 2002;36:271-274.
- (5) National Institute of Neurological Disorders and Stroke. Tuberous Sclerosis Fact Sheet. Available at [http://www.ninds.nih.gov/disorders/tuberous\\_sclerosis/detail\\_tuberous\\_sclerosis.htm](http://www.ninds.nih.gov/disorders/tuberous_sclerosis/detail_tuberous_sclerosis.htm). Accessed June 2011.
- (6) Inoki, et al. Tuberous sclerosis complex, implication from a rare genetic disease to common cancer treatment. *Human Molecular Genetics* 2009;18(1):R94-R100.
- (7) Orphanet Report Series. Prevalence of rare diseases: Bibliographic Data. Available at [http://www.orpha.net/orphacom/cahiers/docs/GB/Prevalence\\_of\\_rare\\_diseases\\_by\\_alphabetical\\_list.pdf](http://www.orpha.net/orphacom/cahiers/docs/GB/Prevalence_of_rare_diseases_by_alphabetical_list.pdf). Accessed June 2011.
- (8) Motzer, et al. Phase 3 Trial of Everolimus for Metastatic Renal Cell Carcinoma. *Cancer* 2010 Sep;116(18):4256-4265.

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**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

e-mail: media.relations@novartis.com

**Nicole Riley**

Novartis Oncology

+1 862 778 3110

nicole.riley@novartis.com

**Novartis Investor Relations**

<b>Central phone:</b>	+41 61 324 7944		
Susanne Schaffert	+41 61 324 7944	<b>North America:</b>	
Pierre-Michel Bringer	+41 61 324 1065	Richard Jarvis	+1 212 830 2433
Thomas Hungerbuehler	+41 61 324 8425	Jill Pozarek	+1 212 830 2445
Isabella Zinck	+41 61 324 7188	Edwin Valeriano	+1 212 830 2456
e-mail: investor.relations@novartis.com		e-mail: investor.relations@novartis.com	

**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 24, 2011

By: /s/ MALCOLM B. CHEETHAM

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