NOVARTIS AG
Form 6-K
September 21, 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 September 21, 2012**

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

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# Novartis AG

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

**Novartis drug Votubia® recommended by CHMP for EU approval to treat patients with non-cancerous kidney tumors associated with TSC**

- *Votubia (everolimus) would be the first non-surgical treatment option in the EU for kidney tumors associated with tuberous sclerosis complex (TSC)(1)*

- *Kidney tumors, or renal angiomyolipomas, affect up to 80% of patients with TSC and growing tumors may lead to life-threatening complications(2)*

**Basel, September 21, 2012** 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 adult patients with renal angiomyolipoma associated with tuberous sclerosis complex (TSC) who are at risk of complications (based on factors such as tumor size or presence of aneurysm, or presence of multiple or bilateral tumors) but who do not require immediate surgery. Votubia would be the first medication available in the European Union (EU) for these patients(1).

Today s positive CHMP opinion for Votubia is important for patients in the EU with TSC, as renal angiomyolipoma is among the most difficult-to-treat manifestations of this debilitating disease, said Hervé Hoppenot, President, Novartis Oncology. There remain many unmet medical needs in TSC, and Novartis is committed to understanding and improving the lives of people affected by this rare disease through clinical research, education and collaboration with the global TSC community.

In the EU, 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. In Europe, everolimus has orphan drug designation for TSC. Orphan drugs are those that treat a condition which affects no more than five in 10,000 people in the EU(3).

The CHMP positive opinion is based on data from the Phase III EXIST-2 (EXamining everolimus In a Study of TSC) trial, which found that 42% of patients on everolimus experienced an angiomyolipoma response versus 0% of patients in the placebo arm ($p<0.0001$). The evidence is based on analysis of change in sum of angiomyolipoma volume. Median time to angiomyolipoma progression was 11.4 months in the placebo arm and was not reached in the everolimus arm ($p<0.0001$). Among the 97% of patients with skin lesions, one of the key concerns for the majority of patients with TSC, a 26% response rate was seen with everolimus versus 0% with placebo ($p=0.0002$)(4).

Everolimus works by inhibiting mTOR, a protein implicated in many tumor-causing pathways(2),(5). TSC is caused by defects in the *TSC1* and/or *TSC2* genes(2). 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(5),(6).

*Known as Afinitor® (everolimus) tablets for this patient population in the US. If approved in the EU for this patient population, the trade name will be Votubia.

According to preclinical studies, by inhibiting mTOR activity in this signaling pathway, everolimus reduces cell proliferation and blood vessel growth(1),(5).

**About Renal Angiomyolipomas**

Up to 80% of patients with TSC a genetic disorder affecting approximately one to two million people worldwide that may cause non-cancerous tumors to form in many organs will develop renal angiomyolipomas. Typical symptom onset occurs between the ages of 15 and 30 and prevalence increases with age. Over time, these tumors may grow large enough to cause severe internal bleeding, require emergency surgical interventions, such as embolization and nephrectomy, or lead to kidney failure(2). The tumors can be difficult to manage as they are often multiple and form in both kidneys at the same time(1),(2). In the EU, approximately 7,000 TSC patients have large growing AML tumors (> 3 cm) at risk of bleeding(7),(8),(9).

**About EXIST-2**

EXIST-2 is the first double-blind, randomized, placebo-controlled, international, multicenter Phase III study for the treatment of patients with renal angiomyolipoma associated with TSC. Trial patients (median age=31, range 18-61) were randomized 2:1 to receive either everolimus (n=79) or placebo (n=39) at a daily dose of 10 mg. The median duration of blinded study treatment was 48 weeks in the everolimus arm and 45 weeks in the placebo arm(4).

In the study, 42% of patients on everolimus (33 of 79; 95% confidence interval [CI] 30.8-53.4) experienced an angiomyolipoma response versus 0% on placebo (0 of 39; 95% CI 0.0-9.0; p<0.0001), defined as a 50% or greater reduction in the sum of angiomyolipoma volume relative to baseline, the absence of new tumor growth at least 1 cm in longest diameter, absence of kidney volume increase of 20% or greater and no renal angiomyolipoma-related bleeding of Grade 2 or higher(4).

Everolimus demonstrated superiority to placebo for both supportive efficacy outcomes measured: time to angiomyolipoma progression and skin lesion response rate. There were three patients in the everolimus arm and eight patients in the placebo arm with documented angiomyolipoma progression by central radiologic review. The time to angiomyolipoma progression was statistically significantly longer in patients on everolimus (hazard ratio [HR] 0.08, 95% CI 0.02-0.37; p<0.0001). Skin lesion response rate was significantly higher in the everolimus arm. A partial clinical response in skin lesions (corresponding to a 50% or greater improvement) was observed by Physician Global Assessment in 26% of patients on everolimus, compared with 0% of patients on placebo (p=0.0011). No complete responses were observed(4).

The most common adverse reactions reported in the everolimus arm during the double-blind period (with an incidence at least 15%) included stomatitis, hypercholesterolemia, aphthous stomatitis, mouth ulceration, and acne. The most common Grade 3 adverse reactions in the everolimus arm (with an incidence of at least 2%) were amenorrhea, aphthous stomatitis, and mouth ulceration. The most common laboratory abnormalities (incidence ≥ 50%) were hypercholesterolemia, hypertriglyceridemia and anemia. The most common Grade 3-4 laboratory abnormality (incidence ≥ 3%) was hypophosphatemia(4).

**About everolimus**

Everolimus is approved as Afinitor® (everolimus) tablets in the United States (US) for the treatment of adult patients with renal angiomyolipomas and tuberous sclerosis complex (TSC), not requiring immediate surgery. The effectiveness of Afinitor in treatment of renal angiomyolipoma is based on an analysis of durable objective responses in patients treated for a median of 8.3 months. Further follow-up of patients is required to determine long-term outcomes. Should everolimus be approved in the European Union (EU) for this patient population,

the trade name will be Votubia.

Everolimus is also approved in the US as Afinitor and Afinitor Disperz in pediatric and adult patients with tuberous sclerosis complex (TSC) for the treatment of subependymal giant cell astrocytoma (SEGA) that requires therapeutic intervention but cannot be curatively resected. The effectiveness is based on demonstration of durable objective response, as evidenced by reduction in SEGA tumor volume. Improvement in disease-related symptoms and overall survival in patients with SEGA and TSC have not been demonstrated. In the EU, everolimus is approved as Votubia® (everolimus) tablets for the treatment of patients aged 3 years and older with SEGA associated with TSC who require therapeutic intervention but are not amenable to surgery. The evidence is based on analysis of change in SEGA volume. Further clinical benefit, such as improvement in disease-related symptoms, has not been demonstrated.

Everolimus is approved as Afinitor in 90 countries including the US and throughout the EU in the adult oncology settings of advanced renal cell carcinoma following progression on or after vascular endothelial growth factor (VEGF)-targeted therapy in the EU and after failure of treatment with sunitinib or sorafenib in the US. Afinitor is approved for the treatment of locally advanced, metastatic or unresectable progressive neuroendocrine tumors of pancreatic origin in adults in the US and EU. Afinitor is also approved in the EU for the treatment of hormone receptor-positive (HR+), HER2/neu-negative (HER2-) advanced breast cancer, in combination with exemestane, in postmenopausal women without symptomatic visceral disease after recurrence or progression following a non-steroidal aromatase inhibitor, and in the US for the treatment of postmenopausal women with advanced hormone receptor-positive, HER2-negative breast cancer (advanced HR+ breast cancer) in combination with exemestane after failure of treatment with letrozole or anastrozole.

Everolimus is also available from Novartis for use in other non-oncology patient populations under the brand names Certican® and Zortress® and is exclusively licensed to Abbott and sublicensed to Boston Scientific for use in drug-eluting stents.

Indications vary by country and not all indications are available in every country.

**Important Safety Information about Votubia/Afinitor**

Votubia/Afinitor 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/Afinitor can affect blood cell counts, kidney and liver function, and blood sugar and cholesterol levels. Votubia/Afinitor may cause fetal harm in pregnant women. Highly effective contraception is recommended for women of child-bearing potential while receiving Afinitor and for up to 8 weeks after ending treatment. Women taking Votubia/Afinitor should not breast feed.

The most common adverse drug reactions (incidence $\geq$15%) are mouth ulcers, diarrhea, feeling weak or tired, skin problems (such as rash or acne), infections, nausea, swelling of extremities or other parts of the body, loss of appetite, headache, inflammation of lung tissue, abnormal taste, nose bleeds, inflammation of the lining of the digestive system, weight decreased and vomiting. The most common Grade 3-4 adverse drug reactions (incidence $\geq$2%) are mouth ulcers, feeling tired, low white blood cells (a type of blood cell that fights infection), diarrhea, infections, inflammation of lung tissue, diabetes and amenorrhea. Cases of hepatitis B reactivation and blood clot in the lung and leg have been reported.

**Disclaimer**

The foregoing release contains forward-looking statements that can be identified by terminology such as recommended, will, committed, generally follows and delivers, further follow to determine long-term outcomes, 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 new 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; unexpected manufacturing issues; 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 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 126,000 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) Ewalt D, et al. Long-term outcome of transcatheter embolization of renal angiomyolipomas due to tuberous sclerosis complex. J Urol. 2005;174:1764-1766.

(2) 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. Accessed September 2012.

(3) European Medicines Agency. Orphan drugs and rare diseases at a glance. Available at http://www.ema.europa.eu/docs/en_GB/document_library/Other/2010/01/WC500069805.pdf. Accessed September 2012.

(4) Novartis Data on File.

(5) Motzer, et al. Phase 3 Trial of Everolimus for Metastatic Renal Cell Carcinoma. Cancer. 2010 Sep;116(18):4256-4265.

(6) Krueger D, et al. Everolimus for Subependymal Giant-Cell Astrocytomas in Tuberous Sclerosis. N Engl J Med. 2010 Nov;363(19):1801-11.

(7) Dixon B, et al. Tuberous Sclerosis Complex Renal Disease. Nephron Exp Nephrol. 2011:118:e15 e20.

(8) O Callaghan F, et al. An epidemiological study of renal pathology in tuberous sclerosis complex. BJU International. 2004:94:853-857.

(9) Cox J, et al. The natural history of renal angiomyolipomata (AMLs) in Tuberous Sclerosis Complex (TSC). European Renal Association - European Dialysis and Transplant Association Congress. 2012, Paris, France.

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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**

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|---|---|---|---|
| Date: | September 21, 2012 | By: | /s/ MALCOLM B. CHEETHAM |
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