

NOVARTIS AG  
Form 6-K  
June 08, 2010

## 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 5, 2010

(Commission File No. 1-15024)

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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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Indicate by check mark if the registrant is submitting the Form 6-K in paper as permitted by Regulation S-T Rule 101(b)(1):

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Yes:  No:

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**- Investor Relations Release -**

**Study at ASCO shows Novartis drug Afinitor® first to shrink SEGA brain tumors in children and adults with tuberous sclerosis**

- *Phase II study shows meaningful reduction in brain tumor size in 75% of patients with subependymal giant cell astrocytomas (SEGAs) from baseline to six months<sup>1</sup>*
- *SEGAs are benign brain tumors associated with tuberous sclerosis (TS) that primarily affect children and adolescents and can cause severe brain swelling<sup>2</sup>*
- *No patient developed new tumors or needed brain surgery, the only current treatment option for patients with SEGAs that are growing<sup>1</sup>*
- *Novartis submitted file to FDA based on this study of 28 patients and is enrolling the EXIST Phase III trials to further study everolimus in patients with TS*

**Basel, June 5, 2010** Novartis announced today that results from a Phase II study show Afinitor® (everolimus) tablets is the first medication in a clinical trial to decrease the size of subependymal giant cell astrocytomas (SEGAs), benign brain tumors associated with tuberous sclerosis (TS)<sup>1,2</sup>. In this study of 28 patients presented today at the 46th American Society of Clinical Oncology (ASCO) annual meeting in Chicago, 75% of patients experienced a reduction of 30% or greater in the size of their brain tumors from baseline to six months (p<0.001)<sup>1</sup>.

Everolimus is approved under the trade name Afinitor® (everolimus) tablets for the treatment of patients with advanced renal cell carcinoma whose disease has progressed on or after treatment with vascular endothelial growth factor (VEGF)-targeted therapy.

Tuberous sclerosis is a genetic disorder that causes tumors to form in many vital organs. It is estimated to affect 25,000 to 40,000 people in the US and one to two million worldwide<sup>3</sup>. These tumors can grow in any organ, but typically occur in the brain, kidneys, heart, eyes, lungs and skin<sup>3</sup>. Common symptoms include seizures, mental retardation, autism, behavior problems and kidney and skin abnormalities<sup>3</sup>.

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SEGAs, occurring in 5-20% of patients with TS, primarily affect children and adolescents and can cause severe swelling in the brain or hydrocephalus<sup>1,2</sup>. Currently, the only treatment option for patients with growing SEGAs is brain surgery<sup>1</sup>. Patients enrolled in the study had evidence of established SEGA growth. The data show everolimus significantly decreased the size of SEGAs and no patient required surgery or developed new SEGAs while receiving everolimus.

These data formed the basis for a regulatory submission to the US Food and Drug Administration (FDA) for the treatment of patients with SEGA associated with TS. Everolimus has orphan drug designation for TS in the US. Orphan drugs are those developed to treat diseases affecting fewer than 200,000 people nationally<sup>4,5</sup>.

Our hope is to offer these patients the first approved medication to treat SEGAs associated with tuberous sclerosis, said Herve Hoppenot, President of Novartis Oncology. As part of our worldwide everolimus development program, Novartis has launched the EXIST Phase III trial program to continue to evaluate the impact of everolimus in the fight against tuberous sclerosis.

Tuberous sclerosis is caused by defects in the *TSC1* and *TSC2* genes that negatively control mTOR, a protein that acts as a central regulator of tumor cell division, blood vessel growth, cell metabolism and cell orientation in neurons<sup>3,6</sup>. By inhibiting mTOR activity in this protein pathway, everolimus may inhibit tumor growth and resulting symptoms caused by tumor growth in the brain, including hydrocephalus<sup>1,7</sup>.

### **About the Phase II study**

In this open-label study, 28 patients aged three years and above (median age=11, range 3-34) with evidence of established SEGA growth received everolimus orally at a dose of 3 mg/m<sup>2</sup>/day (once-daily or on an alternate day regimen), which was subsequently adjusted subject to tolerability to attain a whole blood trough concentration of 5-15 ng/mL. The median duration of treatment was 21.5 months. The study met its primary endpoint of change in primary SEGA lesion volume from baseline to six months (or at the last available assessment if a patient discontinued treatment prior to month 6). Results from the independent central review assessment showed that 75% (21 of 28 patients) experienced a reduction in SEGA volume of 30% or greater from baseline to six months (p<0.001)<sup>1</sup>.

Study findings also showed that everolimus was associated with a clinically relevant reduction in overall frequency of seizures (p=0.022). Of 16 patients with seizures at the start of the study for whom video-EEGs were available, 9 experienced decreases in seizure frequency, 6 reported no change and 1 experienced an increase (median change -1.0, p=0.022). A reduction was also evident in the proportion of patients experiencing seizures on a daily basis from 7 of 26 patients at baseline to 2 of 25 patients at month 6 (based on caregiver observation)<sup>1</sup>.

In the study, everolimus had a safety profile consistent with previous studies with this drug. The most common adverse events (≥10%) included: stomatitis or mouth sores (79%), upper respiratory tract infection (79%), sinusitis (39%), middle ear infection (36%), fever (36%), convulsion (25%), acne-like skin inflammation (25%), diarrhea (25%), cellulitis (21%), vomiting (21%), body tinea or fungal infection (18%), cough (18%), headache (18%), personality change (18%), rash (18%), contact dermatitis (14%), dizziness (14%), gastroenteritis (14%), external ear infection (14%), allergic rhinitis or inflammation of nasal passages (14%), skin infection (14%), acne (11%), constipation (11%), dry skin (11%), gastric infection (11%), hypertriglyceridemia or **high blood triglyceride levels(11%), skin disorder (11%) and** leukopenia or decreased white blood cell count (11%). Grade three adverse events included convulsion (7%), stomatitis (4%), sinusitis (4%), vomiting (4%), dizziness (4%), leukopenia (4%), pneumonia (4%), aspiration or breathing in a foreign object (4%), viral bronchitis (4%), cyclic neutropenia or cyclical decrease in white blood cell count (4%), sleep apnea syndrome or suspension of breathing while asleep (4%) and tooth infection (4%). A single grade 4 convulsion was reported.

### **About the EXIST trial program**

Two Phase III trials called EXIST (EXamining everolimus In a Study of TS) have been initiated and are currently enrolling patients to further explore the potential of everolimus for the treatment of TS<sup>8,9</sup>.

The EXIST-1 study will examine everolimus treatment in patients with SEGAs, including tumor shrinkage, as well as evaluate the effect of everolimus treatment on seizures and skin abnormalities associated with TS<sup>8</sup>. The EXIST-2 study will evaluate everolimus in patients with angiomyolipoma associated with either TS or sporadic lymphangioleiomyomatosis (LAM)<sup>9</sup>. Angiomyolipomas, benign tumors of blood vessels, muscle and fat typically located in the kidney, are common in patients with TS<sup>3,10</sup>. The trials are currently enrolling patients in 11 countries,



including Australia, Belgium, Canada, France, Germany, Italy, the Netherlands, Poland, Russia, the UK and the US<sup>8,9</sup>.

For more information about the EXIST studies and other everolimus clinical trials across tumor types, healthcare professionals can visit [www.theWIDEprogram.com](http://www.theWIDEprogram.com).

### **About everolimus**

In the European Union (EU), everolimus is approved under the trade name Afinitor® (everolimus) tablets 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. In the US, Afinitor is approved 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 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.

As an investigational compound, the safety and efficacy profile of everolimus has not yet been established in TS. The dosage strength of everolimus when used for studying the TS patient population is different from that when used for its approved RCC indication. Everolimus is available for TS through carefully controlled and monitored clinical trials. These trials are designed to better understand the potential benefits and risks of the compound. Because of the uncertainty of clinical trials, there is no guarantee that everolimus will become commercially available for TS anywhere in the world.

### **Afinitor (everolimus) tablets important safety information**

Afinitor is contraindicated in patients with hypersensitivity to everolimus, to other rapamycin derivatives or to any of the excipients.

Cases of non-infectious pneumonitis have been described; some of these have been severe and occasionally fatal. Management of pneumonitis may require dose adjustment and/or interruption, or discontinuation of treatment and/or addition of corticosteroid therapy.

Afinitor is immunosuppressive. Localized and systemic bacterial, fungal, viral or protozoal infections (e.g. pneumonia, aspergillosis, candidiasis, hepatitis B reactivation) have been described; some of these have been severe and occasionally fatal. Pre-existing infections should be treated prior to starting treatment. Patients and physicians should be vigilant for symptoms and signs of infection; in case of emergent infections, appropriate treatment should be promptly instituted and interruption or discontinuation of Afinitor should be considered. Patients with systemic invasive fungal infections should not receive Afinitor.

Mouth ulcers, stomatitis and oral mucositis have been seen in patients treated with Afinitor. Monitoring of renal function, blood glucose and complete blood counts is recommended prior to initiation and periodically during treatment.

Afinitor is not recommended in patients with severe hepatic impairment. Use of live vaccines should be avoided. Afinitor is not recommended during pregnancy or for women of childbearing potential not using contraception. Afinitor may cause fetal harm in pregnant women. Women taking Afinitor should not breast feed.

Avoid concurrent treatment with strong CYP3A4 and PgP inhibitors and use caution with moderate inhibitors. Avoid concurrent treatment with strong CYP3A4 or PgP inducers.



The most common adverse reactions ( $\geq 10\%$ ) include stomatitis, rash, fatigue, asthenia, diarrhea, anorexia, nausea, mucosal inflammation, vomiting, cough, infections, peripheral edema, dry skin, epistaxis, pneumonitis, pruritus, dyspnea and dysgeusia. Common adverse reactions ( $\geq 1$  to  $<10\%$ ) include headache, dry mouth, pyrexia, weight loss, hand-foot syndrome, abdominal pain, erythema, insomnia, dyspepsia, dysphagia, hypertension, increased daytime urination, dehydration, chest pain, hemoptysis and exacerbation of diabetes mellitus. Uncommon adverse reactions ( $<1\%$ ) include ageusia, congestive cardiac failure, new-onset diabetes mellitus, impaired wound healing, grade 1 hemorrhage and hepatitis B reactivation.

#### **Disclaimer**

The foregoing release contains forward-looking statements that can be identified by terminology such as can, to further study, encouraged, hope, to continue to evaluate, may, to further explore, potential, will, or similar expressions, or by express or implied discussions regarding potential new indications or labeling for Afinitor or regarding potential future revenues from Afinitor. 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 Afinitor to be materially different from any future results, performance or achievements expressed or implied by such statements. There can be no guarantee that Afinitor will be approved for any additional indications or labeling in any market. Nor can there be any guarantee that Afinitor will achieve any particular levels of revenue in the future. In particular, management's expectations regarding Afinitor 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, cost-saving generic pharmaceuticals, preventive vaccines, diagnostic tools and consumer health products. Novartis is the only company with leading positions in these areas. In 2009, the Group's continuing operations achieved net sales of USD 44.3 billion, while approximately USD 7.5 billion was invested in R&D activities throughout the Group. Headquartered in Basel, Switzerland, Novartis Group companies employ approximately 100,000 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>. For more information about the 2010 ASCO Annual Meeting on Twitter, search for #ASCO10.

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Media materials can be accessed at: <http://www.novartisoncology.com/media/index.jsp>

**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 5, 2010

By: /s/ MALCOLM B. CHEETHAM

Name: Malcolm B. Cheetham  
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Reporting and Accounting