

NOVARTIS AG  
Form 6-K  
July 01, 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 July 1, 2010**

**(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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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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**Novartis International AG**

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**- Investor Relations Release -**

**Phase III study shows Novartis drug Afinitor® more than doubles time without tumor growth in advanced pancreatic NET patients**

- *Everolimus extended median progression-free survival from 4.6 to 11.0 months vs. placebo and reduced risk of cancer progression by 65%(1)*
- *Patients with advanced pancreatic neuroendocrine tumors (NET) have a rare and aggressive form of cancer with limited treatment options(2),(3)*
- *Worldwide regulatory filings planned for everolimus as first mTOR inhibitor treatment for patients with advanced pancreatic NET*

**Basel, July 1, 2010** Novartis announced today that results of a Phase III study show Afinitor® (everolimus) tablets plus best supportive care (BSC) more than doubled progression-free survival, or time without tumor growth, versus placebo plus BSC in patients with advanced pancreatic neuroendocrine tumors (NET). The study, RADIANT-3 (RAD001 In Advanced Neuroendocrine Tumors), was presented at the 12th World Congress on Gastrointestinal Cancer and is part of the largest clinical trial program in patients with advanced NET(1).

Afinitor is approved 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 (4).

Findings from the RADIANT-3 study demonstrated that everolimus extended the median time without tumor growth from 4.6 to 11.0 months when compared with placebo. Additionally, the data showed everolimus reduced the risk of cancer progression by 65% (hazard ratio=0.35 [95% confidence interval, 0.27 to 0.45]; p<0.0001)(1).

It is encouraging to see that by targeting the mTOR pathway, treatment with everolimus can provide a significant progression-free survival advantage over placebo in patients with advanced pancreatic NET, said James Yao, MD, Associate Professor of Medicine, The University of

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Texas MD Anderson Cancer Center. These results further validate earlier trials and demonstrate the potential benefit everolimus can provide to these patients.

Pancreatic NET can grow aggressively and at time of diagnosis nearly 60% of all patients have advanced disease, meaning the cancer has spread to other parts of the body and has become more difficult to treat(2),(3). The median overall survival for patients with advanced pancreatic NET is 24 months(5). Currently, surgery and chemotherapy are the only available treatment options for patients with advanced pancreatic NET(2).

Our commitment to patients with advanced NET continues with the RADIANT trial program, which is the largest in patients with advanced NET, said Hervé Hoppenot, President, Novartis

Oncology. With this study, Novartis continues to make progress towards our goal of providing patients with treatment options for this rare and hard to treat cancer.

### **About RADIANT-3**

RADIANT-3 is a Phase III prospective, double-blind, randomized, parallel group, placebo-controlled, multicenter study. The trial examined the efficacy and safety of everolimus plus BSC versus placebo plus BSC in 410 patients with advanced pancreatic NET, also known as islet cell tumors. Patients who met the study entry criteria were randomized 1:1 to receive either daily everolimus (10 mg) or daily placebo orally(1).

The primary endpoint of RADIANT-3 is progression-free survival. Secondary endpoints include safety, objective response rate and overall survival. Additional study findings will be submitted for presentation at the 35th European Society for Medical Oncology Congress (ESMO) in Milan, Italy later this year.

In the study, everolimus had a safety profile consistent with previous studies of this drug. Adverse events observed (>20%) in the everolimus arm included stomatitis (53.9%), rash (52.5%), diarrhea (46.6%), fatigue (43.6%), edema peripheral (35.8%), nausea (31.9%), headache (29.9%), pyrexia (29.4%), decreased appetite (28.9%), vomiting (28.4%), weight loss (27.9%), abdominal pain (23.5%), anemia (22.1%), cough (21.6%) and epistaxis (21.1%)(1).

### **About neuroendocrine tumors (NET)**

Neuroendocrine tumors arise from cells that can produce and secrete a variety of hormones that regulate bodily functions. There are many types of NET that can occur throughout the body; however, most are found in the gastrointestinal tract, pancreas and lungs(5). Because NET are relatively rare, there is no routine screening and patients often experience delays of five to seven years before receiving an accurate diagnosis(5),(6). As a result of this, patients with NET often have advanced disease when diagnosed(6). Although considered a rare cancer, the incidence of NET is increasing dramatically, having quadrupled in the past 30 years(5).

### **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 prevention of rejection of kidney transplants in adult patients at low-to-moderate immunologic risk.

With once-daily dosing Afinitor works by targeting mTOR in cancer cells, a protein that acts as a central regulator of tumor cell division, blood vessel growth and cell metabolism.

As an investigational compound the safety and efficacy profile of everolimus has not yet been established in NET. Access to everolimus for NET has been carefully controlled and monitored in clinical trials designed to better understand the potential benefits and risks of the compound. For more information about ongoing everolimus clinical trials, healthcare professionals can visit [www.theWIDEprogram.com](http://www.theWIDEprogram.com). Because of the uncertainty of clinical trials, there is no guarantee that everolimus will become commercially available for NET 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 risk, planned, encouraging, can, potential, commitment, goal, 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 submitted or 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>.

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## References

- (1) Yao, et al. Everolimus versus placebo in patients with advanced pancreatic neuroendocrine tumors (pNET) (RADIANT-3). 12th World Congress on Gastrointestinal Cancer, Barcelona. July 1, 2010.
- (2) National Library of Medicine and the National Institutes of Health. Pancreatic islet cell tumor. Available at <http://www.nlm.nih.gov/medlineplus/ency/article/000393.htm>. Accessed May 2010.
- (3) Halfdanarson, et al. Pancreatic neuroendocrine tumors (PNETs): incidence, prognosis and recent trend toward improved survival. *Annals of Onc* 19: 1727-1733, 2008.
- (4) Afinitor® (everolimus) tablets EU summary of product characteristics. Basel, Switzerland: Novartis International AG; August 2009.
- (5) Yao, et al. One Hundred Years After Carcinoid: Epidemiology of and Prognostic Factors for Neuroendocrine Tumors in 35,825 Cases in the United States. *Journal of Clinical Oncology*. June 20 2009; vol. 26, number 18.
- (6) Modlin, et al. Priorities for Improving the Management of Gastroenteropancreatic Neuroendocrine Tumors. *J Natl Cancer Inst* 2008;100:1282-1289.

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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: July 1, 2010

By: /s/ MALCOLM B. CHEETHAM

Name: Malcolm B. Cheetham

Title: Head Group Financial  
Reporting and Accounting