

NOVARTIS AG  
Form 6-K  
December 15, 2008

# 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 December 12, 2008

(Commission File No. 1-15024)

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**Novartis AG**

(Name of Registrant)

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(Address of Principal Executive Offices)

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Yes: o      **No: x**

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**- Investor Relations Release -**

**Afinitor<sup>®</sup> shows potential to reverse resistance to Herceptin<sup>®</sup>\* in metastatic breast cancer patients, leading to Phase III trial**

- *Afinitor (RAD001) combined with Herceptin and chemotherapy in two separate Phase I trials halted tumor growth in 77% and 62% of patients, respectively*
- *Novartis to start Phase III clinical trial program to explore Afinitor, an oral mTOR inhibitor, as combination treatment with Herceptin and chemotherapy*

**Basel, December 12, 2008** New data from two early clinical studies show that Afinitor<sup>®</sup> (everolimus) may overcome resistance to Herceptin<sup>®</sup> (trastuzumab)\* in women with HER2- positive metastatic breast cancer<sup>(1),(2)</sup>. These results support the initiation of a Phase III clinical trial program to fully explore the potential of Afinitor, also known as RAD001, in breast cancer.

Two Phase I studies were presented today during the CTRC-AACR San Antonio Breast Cancer Symposium. Initial results from both studies were released earlier this year at the American Society of Clinical Oncology (ASCO) annual meeting.

Updated results from the first Phase I trial show that the combination of Afinitor with Herceptin and weekly Taxol<sup>®</sup> (paclitaxel)\*\* halted tumor growth in 77% of patients with HER2-positive metastatic breast cancer with documented resistance to Herceptin. In addition, the data demonstrated the first complete response in the trial.

In addition, updated data from the second Phase I study show promising anticancer activity for Afinitor in combination with Herceptin and Navelbine<sup>®</sup> (vinorelbine)\*\*\* in heavily pretreated Herceptin-resistant patients with HER2-positive metastatic breast cancer. In the study, Afinitor in combination with Herceptin and Navelbine halted tumor growth in 62% of patients<sup>(2)</sup>.

Data presented at this meeting affirm the potential of Afinitor to reverse Herceptin resistance and restore patient response to treatment, said Ruth O. Regan, MD, Emory University School of Medicine, Atlanta, GA. These findings are important for patients with HER2-positive metastatic breast cancer who develop resistance to Herceptin.

Preclinical data have shown that Afinitor, an inhibitor of mTOR, acts on the pathway that mediates Herceptin resistance and has the potential to help restore response in these patients. Afinitor works through direct antitumor activity and through its influence on two of the most important pathways for breast cancer, the erbB receptor and the HER2 pathways.

We are encouraged by the benefit Afinitor provided to advanced breast cancer patients in these early trials, said Alessandro Riva, MD, Executive Vice President & Global Head of Development,

Novartis Oncology. Novartis is committed to further evaluating the potential of Afinitor in combination with Herceptin as a new treatment regimen in breast cancer, as well as to studying its role in treating other tumor types.

Novartis will initiate a worldwide Phase III clinical trial program to further evaluate the potential of Afinitor in combination with Herceptin and chemotherapy in patients with HER2-positive metastatic breast cancer.

**Study details: abstract #3119**

An open-label, multicenter Phase I dose escalation trial evaluated daily Afinitor (5 mg, 10 mg) and weekly Afinitor (30 mg, 50 mg and 70 mg) regimens in combination with Taxol (80 mg/m<sup>2</sup> IV over 60 min on days 1, 8 and 15 every 28 days) and Herceptin (2 mg/kg IV over 30 min) in heavily pretreated patients with HER2-positive metastatic breast cancer with prior resistance to Herceptin (1).

Across treatment arms, there was an overall disease control rate of 77% (complete response/partial response/stable disease  $\geq 16$  weeks). Twenty-two heavily pretreated patients were evaluable for efficacy: treatment arms included five patients assigned to Afinitor 5 mg daily, eight to Afinitor 10 mg daily and nine to Afinitor 30 mg weekly. Among the five patients evaluated in the 5 mg daily treatment arm, one patient had a complete response and four patients had partial responses. In the 10 mg daily treatment arm, one patient had a partial response, six patients had stable disease and one patient had progressive disease. Among the nine patients evaluated in the 30 mg weekly treatment arm, three patients had partial responses, five patients had stable disease and one patient had progressive disease. The critical dose-limiting toxicities occurring in the first cycle of treatment included febrile neutropenia, oral mucositis and confusion, occurring in the 5 mg daily, 10 mg daily and 30 mg weekly treatment groups, respectively(1). The most commonly reported grade 3/4 adverse events ( $\geq 10\%$ ) suspected of being related to study treatment were neutropenia, lymphopenia, stomatitis, leukopenia, alopecia and anemia.

**Study details: abstract #406**

An open-label, multicenter, Phase I trial evaluated daily Afinitor (2.5 mg, 5 mg, 10 mg) and weekly Afinitor (20 mg, 30 mg, 50 mg and 70 mg) in combination with Navelbine (25 mg/m<sup>2</sup> IV over 10-15 min on days 1 and 8 every 21 days) and Herceptin (2 mg/kg IV over 30 min). All patients entering the study had progression on, or shortly after, treatment with Herceptin and all had received prior taxane. The median number of prior chemotherapy regimens was 3 (range: 1-5)(2).

Across treatment arms, there was an overall disease control rate of 62% (complete response/partial response/stable disease  $\geq 16$  weeks). Thirty-four heavily pretreated patients were evaluated to date (fifteen patients assigned to Afinitor 5 mg daily, six to Afinitor 20 mg weekly, and thirteen to Afinitor 30 mg weekly). Among the fifteen patients in the 5 mg daily treatment arm, one patient had a complete response, two patients had partial responses, nine patients had stable disease and three patients had progressive disease. Among the six patients in the 20 mg weekly treatment arm, one patient had a partial response, three patients had stable disease and two patients had progressive disease. Among the thirteen patients evaluated in the 30 mg weekly treatment arm, two patients had partial responses, nine patients had stable disease and two patients had progressive disease. The critical dose-limiting toxicities (i.e., dose-limiting toxicities in cycle 1) occurring in the 5 mg daily treatment group included grade 3/4 neutropenia, grade 3 stomatitis, grade 3 fatigue and grade 3 anorexia. In the 30 mg weekly treatment group, grade 3/4 neutropenia was the only critical dose-limiting toxicity. There were no critical dose-limiting toxicities in the 20 mg weekly Afinitor treatment arm. The most commonly reported grade 3/4 adverse events ( $\geq 10\%$ ) suspected of being related to study treatment was neutropenia,

stomatitis and leukopenia(2).

## About breast cancer

Worldwide, breast cancer is the fifth most common cause of cancer death. Every year breast cancer causes 548,000 deaths worldwide<sup>(3)</sup>. The incidence of breast cancer is rising among women in many European countries, affecting up to one in 16 women<sup>(4)</sup>.

Inside a breast there are many lobes, ducts and vessels that support several important functions in the body, including reproductive needs and fighting infection. In breast cancer, some of the cells in the breast begin growing abnormally and divide more rapidly than healthy cells. The quick division of cells may cause spreading through the breast, to the lymph nodes or to other parts of the body.

## About Afinitor

Afinitor, an oral once-daily inhibitor of mTOR, is an investigational drug being studied in multiple tumor types. In cancer cells, Afinitor provides continuous inhibition of mTOR, a protein that acts as a central regulator of tumor cell division, cell metabolism and blood vessel growth.

The safety and efficacy profile of Afinitor has not yet been established in oncology and there is no guarantee that Afinitor will become commercially available for oncology indications. The active ingredient in Afinitor is everolimus, which is available in different dosage strengths under the trade name Certican<sup>®</sup> for the prevention of organ rejection in heart and kidney transplant recipients. Certican was first approved in the EU in 2003.

In addition to breast cancer, Afinitor is being evaluated as a single agent or in combination with existing therapies in renal cell carcinoma, neuroendocrine tumors, lymphoma, gastric, lung and other cancers, as well as tuberous sclerosis complex.

## Disclaimer

The foregoing release contains forward-looking statements that can be identified by terminology such as potential, to start, to explore, may, to fully explore, promising, encouraged, committed, will, to further evaluate, or similar expressions, or by express or implied discussions regarding potential regulatory filings or marketing approvals 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 sale for any oncology indication 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,

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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 AG 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 2007, the Group's continuing operations (excluding divestments in 2007) achieved net sales of USD 38.1 billion and net income of USD 6.5 billion. Approximately USD 6.4 billion was invested in R&D activities throughout the Group. Headquartered in Basel, Switzerland, Novartis Group companies employ approximately 97,000 full-time associates and operate in over 140 countries around the world. For more information, please visit <http://www.novartis.com>.

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## References

- (1) O'Regan, R., et al. RAD001 (everolimus) in Combinations with Weekly Paclitaxel and Trastuzumab in Patients with HER-2-Overexpressing Metastatic Breast Cancer with Prior Resistance to Trastuzumab: A Multicenter Phase I Clinical Trial. Poster presented at SABCS 2008.
- (2) Fasolo, A., et al. Multicenter Phase I Clinical Trial of Daily and Weekly Everolimus (RAD001) in Combination with Vinorelbine and Trastuzumab in Patients with HER-2-Overexpressing in Metastatic Breast Cancer with Prior Resistance to Trastuzumab. Poster presented at SABCS 2008.
- (3) World Health Organization. Media Centre: Cancer Fact Sheet <http://www.who.int/mediacentre/factsheets/fs297/en/>
- (4) World Health Organization Regional Office for Europe. Reproductive Health and Research: Breast Cancer [http://www.euro.who.int/reproductivehealth/areas/20071101\\_6](http://www.euro.who.int/reproductivehealth/areas/20071101_6)

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\* In the US, Herceptin is a registered trademark of Genentech, Inc. Internationally, Herceptin is a registered trademark of Roche.

\*\* Taxol is a registered trademark of Bristol-Myers Squibb Company.

\*\*\* Navelbine is a registered trademark of Pierre Fabre Pharmaceuticals Inc.

**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: December 12, 2008

By: /s/ MALCOLM B. CHEETHAM  
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Reporting and Accounting