

NOVARTIS AG  
Form 6-K  
December 12, 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 11, 2008**

**(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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**- Investor Relations Release -**

**Femara® first aromatase inhibitor to indicate survival benefit versus tamoxifen when taken for five years after breast cancer surgery**

- *Femara showed reduced risk of death by 13% (P=0.08), despite inclusion of patients crossing over from tamoxifen to Femara therapy*
- *In a separate censored analysis excluding patients after they crossed over to Femara, reduction in risk of death was 19%*
- *Long-term follow-up from major independent BIG 1-98 trial reinforces starting with Femara as the optimal treatment strategy versus tamoxifen*

**Basel, December 11, 2008** New long-term data from a major international breast cancer study reports that postmenopausal woman with hormone receptor-positive early-stage breast cancer who took Femara® (letrozole) for five years following surgery had a 13% (P=0.08) reduced risk of death, when compared with tamoxifen<sup>(1)</sup>.

These results are from a protocol-defined Intent-to-Treat (ITT) analysis (median follow-up of 76 months) of the Femara and tamoxifen monotherapy arms in the Breast International Group (BIG) 1-98 study. The suggested survival benefit from the ITT analysis is important considering that approximately 25% of patients in the tamoxifen arm selectively crossed over to Femara therapy after the tamoxifen arm was unblinded in 2005. While not statistically significant, these are the first data to suggest a survival benefit for an aromatase inhibitor versus tamoxifen in the monotherapy setting immediately following surgery.

To explore the impact of the selective crossover, an additional analysis was conducted censoring follow-up times at the date of crossover to letrozole. In this analysis, a 19% reduction in risk of death (HR=0.81, 95% CI: 0.69-0.94) was observed in favor of Femara.

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The International Breast Cancer Study Group (IBCSG) presented these results from the BIG 1-98 trial today at the 31st Annual CTBC-AACR San Antonio Breast Cancer Symposium (SABCS), an international scientific symposium for scientists and clinicians in breast cancer.

These data represent an important milestone in the treatment of women with breast cancer. For the first time, we are seeing suggested survival benefit with aromatase inhibitor therapy for five years compared with tamoxifen for the same time period, said Henning T. Mouridsen, MD, PhD, Professor of Oncology, Copenhagen University Hospital and one of the investigators of the BIG 1-98 trial. The potential reduction in the risk of death that we are seeing with letrozole in the adjuvant setting may be a positive result of letrozole's early and sustained reduction in the risk of recurrence and distant metastases.

BIG 1-98 is the only clinical trial designed to explore both a head-to-head comparison of an aromatase inhibitor with tamoxifen during the first five years following breast cancer surgery and the sequencing of both agents to determine the most effective approach to minimizing the risk of recurrence. In the initial adjuvant setting, Femara is the only aromatase inhibitor to have demonstrated an early significant reduction in distant metastases versus tamoxifen, at a median duration of follow-up of 26 months.

Beyond the potential survival benefit or 13% (P=0.08, HR=0.87, 95% CI: 0.75-1.02) reduction in risk of death for Femara patients seen in the ITT analysis, Femara demonstrated significant long-term benefit in reducing the risk of disease free survival events by 12% (P=0.03, HR=0.88, 95% CI: 0.78-0.99) and reducing the risk of distant metastases by 15% (P=0.05, HR=0.85, 95% CI: 0.72-1.00) compared with tamoxifen.

Femara has consistently demonstrated remarkable results and these data reaffirm the benefit of Femara for postmenopausal women with early-stage breast cancer, said Alessandro Riva, MD, Executive Vice President, Head of Global Development at Novartis Oncology. The survival data shown may offer new promise for breast cancer patients.

Also presented at the meeting were results from the Sequential Treatment Analysis (STA) of BIG 1-98 that support the benefit of starting adjuvant treatment with five years of Femara after surgery. This analysis (from randomization) revealed that sequencing hormone therapy following surgery is not superior to five years of Femara alone.

The five-year disease-free survival rates for the three groups of patients in the STA were 87.9% for those patients receiving Femara only, 86.2% for those patients receiving two years of tamoxifen followed by three years of Femara and 87.6% for those patients receiving two years of Femara followed by three years of tamoxifen. The study investigators conclude that sequential treatment does not improve disease free survival compared with Femara alone.

### Study details

This Phase III, randomized, double-blind, controlled clinical trial enrolled postmenopausal women with early breast cancer, in 27 countries<sup>(1)</sup>.

Patients were randomly assigned one of four treatment regimens: (1) five years of tamoxifen only; (2) five years of Femara only; (3) two years of tamoxifen followed by three years of Femara; (4) two years of Femara followed by three years of tamoxifen. In 1998 the first cohort began enrolling patients to receive either Femara or tamoxifen alone. In 1999, the second cohort (solely contributing to the Sequential Treatment Analysis) began enrolling patients to receive Femara or tamoxifen alone, tamoxifen followed by Femara or Femara followed by tamoxifen (n=6,182 patients). Combined, the monotherapy arms of the trial included 4,922 patients who were randomly assigned either Femara or tamoxifen treatment<sup>(1)</sup>. The Primary Core Analysis, reported in 2005, included all 8,010 patients enrolled in the trial.

The primary endpoint of the study was disease-free survival (DFS), defined as the time from randomization to the first of one of the following events: recurrence at local, regional, or distant sites; a new invasive cancer in the contralateral breast; any second, non-breast cancer; or death without a prior cancer event, which is similar but not identical to the endpoint definitions used in other AI adjuvant trials. Other endpoints included time to breast cancer recurrence [including invasive contralateral breast cancer, ignoring second (non-breast) malignancies, and censoring deaths prior to cancer event], time to distant breast cancer recurrence (time to breast cancer recurrence but ignoring local, regional and contralateral breast events), and overall survival.



In 2005, following initial results showing superiority of Femara monotherapy over tamoxifen monotherapy in improving disease-free survival and reducing the risk of recurrence, the tamoxifen-only treatment arm was unblinded and approximately one quarter of those patients selectively crossed over to Femara treatment. The other three treatment arms remained blinded. Subsequent analyses were designed to estimate the extent to which the crossover affected the comparative benefit of Femara<sup>(1)</sup>.

With the long-term follow-up in the analysis conducted more than 10 years after the start of the study, adverse events for Femara and tamoxifen were found to be consistent with the known safety profiles of both drugs. Patients will be monitored for the rest of their lives to track disease status, safety and overall survival<sup>(1)</sup>.

### **About Femara**

Femara is a leading once-daily oral aromatase inhibitor available in more than 100 countries, including the US, major European countries and Japan. It is approved for a number of indications:

- Adjuvant treatment of postmenopausal women with hormone receptor-positive early breast cancer
- Extended adjuvant treatment of hormone-dependent early breast cancer in postmenopausal women who have had prior standard adjuvant tamoxifen therapy for five years
- First-line treatment in postmenopausal women with hormone-dependent advanced breast cancer
- Advanced breast cancer in women with natural or artificially induced postmenopausal status after relapse or disease progression who have been treated with antiestrogens
- Pre-operative therapy in postmenopausal women with localized hormone receptor-positive breast cancer which allows subsequent breast-conserving surgery in patients not originally considered suitable for this type of surgery

Not all indications are available in every country. Subsequent treatment after surgery should be in accordance with the standard of care.

### **Important safety information**

Femara should not be taken by women who have previously had any unusual or allergic reactions to letrozole or any of its ingredients. Femara should not be taken by women who are pregnant or breastfeeding. Only women who are of postmenopausal endocrine status should take Femara. Patients with severe liver impairment should be monitored closely. The use of Femara in patients with significantly impaired kidney function warrants careful consideration.

The most common side effects of Femara are hot flushes, fatigue, joint pain and nausea. Other common side effects are anorexia, appetite increase, peripheral edema, headache, dizziness, vomiting, dyspepsia, constipation, diarrhea, hair loss, increased sweating, rash, muscle pain, bone pain, arthritis, osteoporosis, bone fractures, weight increase, hypercholesterolemia and depression. Other rare, but potentially serious adverse events include leukopenia, cataract, cerebrovascular accident or infarction, thrombophlebitis, pulmonary embolism, arterial thrombosis and ischemic cardiovascular disease.

**Disclaimer**

The foregoing release contains forward-looking statements that can be identified by terminology such as risk, suggested, suggest, potential, m explore, promise, estimate, will, or similar expressions, or by express or implied discussions regarding potential new indications or labeling for Femara or regarding potential future revenues from Femara. 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 Femara to be materially different from any future results, performance or achievements expressed or implied by such statements. There can be no guarantee that Femara will be submitted or approved for any additional indications or labelling in any market. Nor can there be any guarantee that Femara will achieve any particular levels of revenue in the future. In particular, management's expectations regarding Femara 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 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) Mouridsen H for the BIG 1-98 Collaborative Group, Letrozole Alone or in Sequence with Tamoxifen for Postmenopausal Women with Early Breast Cancer. Presented at: the 31st Annual Meeting of the CTRC-AACR San Antonio Breast Cancer Symposium, 31st Annual Meeting, 11 December, 2008. Abstract No. 13.

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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: December 11, 2008

By: /s/ MALCOLM B. CHEETHAM

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