

NOVARTIS AG  
Form 6-K  
September 23, 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 September 22, 2010**

(Commission File No. 1-15024)

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(Name of Registrant)

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**Switzerland**

(Address of Principal Executive Offices)

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Yes:       No:

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**- Investor Relations Release -**

**Novartis drug SOM230 is first medical therapy to show efficacy in a Phase III trial in Cushing's disease, a debilitating hormonal disorder**

- *SOM230 reduced urinary free cortisol (UFC) levels in majority of patients; 26% of patients randomized to SOM230 900µg achieved normal UFC levels*
- *With reduced UFC levels, clinical symptoms improved including lower blood pressure, total cholesterol and weight loss*
- *Cushing's disease is caused by a pituitary tumor that triggers excess cortisol; can lead to severe cardiovascular, metabolic problems and death*
- *This pivotal trial is the largest study of a medical therapy in Cushing's disease and will be basis for first regulatory filing planned by year end*

**Basel, September 22, 2010** Novartis announced today that the results of a Phase III study of SOM230 (pasireotide) showed a reduction in cortisol levels in patients with Cushing's disease, a condition in which a benign (non-cancerous) pituitary tumor causes the adrenal glands to produce excess cortisol and can be fatal(1). Results will be presented at the 14th Congress of the European Neuroendocrine Association (Enea).

At six months, the majority of evaluable patients (91/103) experienced a reduction from baseline in urinary free cortisol (UFC) levels, the main measure of biochemical control of the disease. UFC levels were normalized in 26% of patients randomized to SOM230 900µg twice daily, meeting the primary endpoint of the study. Additionally, median UFC was reduced by 48% in both the 900µg and 600µg dose groups. After 12 months of treatment, results confirmed the durability of the effect(1).

On average, as UFC levels were reduced, clinical symptoms of Cushing's disease improved including reduction of blood pressure, total cholesterol, weight and body mass index (BMI)(1).

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Cushing's disease is caused by a benign tumor in the pituitary gland that secretes adrenocorticotropic hormone (ACTH), which triggers the adrenal glands to produce excess cortisol. Cortisol is a powerful steroid hormone that regulates a broad range of physiologic functions, including metabolism and immunity(2). Cushing's disease can cause severe cardiovascular and metabolic-related illnesses or death(3),(4). There are currently no approved medicines to treat Cushing's disease(1).

Up to half of patients with Cushing's disease cannot be cured with currently available options, which include surgery or radiotherapy of the tumor, leaving a critical need for medical treatments, said Annamaria Colao, MD, Professor of Endocrinology and Chief of the Neuroendocrine Unit at the Department of Molecular and Clinical Endocrinology and Oncology, Federico II University of Naples and one of the study investigators. The study findings show that SOM230 has the

potential to directly target the underlying pituitary tumor and suppress cortisol production, thereby helping patients achieve biochemical control of their Cushing's disease and the associated debilitating symptoms.

PASPORT-CUSHINGS (PASireotide clinical trial PORTfolio - CUSHING'S disease) is the largest randomized study to evaluate a medical therapy in patients with Cushing's disease(1). The trial is part of a large-scale global clinical development program to assess the efficacy and safety of SOM230 in a range of pituitary and neuroendocrine tumors(6).

Positive results from this trial bring us one step closer to providing physicians with a new treatment option to offepeople living with the physically and emotionally debilitating symptoms associated with Cushing's disease, said Hervé Hoppenot, President, Novartis Oncology.

These data will form the basis for the first regulatory filing of SOM230 planned this year. SOM230 has orphan drug designation for Cushing's disease in the US and Europe(7),(8). In the US, orphan drugs are those developed to treat diseases affecting fewer than 200,000 people(9). In Europe, orphan drugs are those developed to treat conditions affecting fewer than five in 10,000 people(8).

#### Study details

PASPORT-CUSHINGS is a prospective Phase III study of 162 patients conducted at 68 sites in 18 countries. The study evaluated the efficacy and safety of SOM230 in patients with persistent or recurrent Cushing's disease, as well as in patients with newly diagnosed Cushing's disease who are not candidates for surgery(1),(10).

Patients with primarily moderate to severe hypercortisolism were randomized to receive SOM230 subcutaneous (sc) injection in doses of 600µg (n=82) or 900µg (n=80) twice daily. The primary endpoint was the proportion of patients who achieved normalization of UFC after six months without dose up-titration relative to randomized dose(1). UFC is typically used to diagnose and monitor Cushing's disease. In this test, urine is collected over 24 hours to assess average cortisol secretion(2). The primary endpoint was met for the higher dose tested (900µg sc twice daily)(1). Secondary endpoints included safety, time to response, response duration and changes from baseline in clinical signs, symptoms, tumor volume and health-related quality of life(10).

After six months, the primary efficacy responder rate was 26.3% (95% CI, 16.6 to 35.9) and 14.6% (95% confidence interval [CI], 7.0 to 22.3), respectively, for the 900µg and 600µg groups. Based on pre-specified criteria (lower bound of 95% CI >15%), the 900µg group met the primary endpoint and the 600µg group did not meet the primary endpoint. After 12 months, the proportion of responders regardless of dose up-titration was 13.4% and 25.0%, respectively, for the 600µg and 900µg groups. The median reduction in UFC after six months was 47.9% for both groups. The median reduction in UFC after 12 months was 67.6% (600µg) and 62.4% (900µg). Patients who showed little to no improvement in UFC levels (<50% reduction from baseline) by month two were unlikely to show improvement by month six or 12. The most frequently reported adverse events suspected by the investigators to be related to the study drug were diarrhea (58%), nausea (46.9%), hyperglycemia (38.9%), cholelithiasis (29.6%), abdominal pain (20.4%), diabetes mellitus (17.9%), fatigue (11.7%) and increased glycosylated hemoglobin (10.5%), with most events being Grade 1-2. Overall, the tolerability profile of SOM230 is similar to other somatostatin analogs with the exception of the greater degree of hyperglycemia, which appears manageable with early detection and appropriate intervention following established treatment guidelines. As may be expected with a treatment that lowers cortisol levels in Cushing's disease, 13 (8.0%) patients experienced adverse events associated with cortisol levels below the normal range. This was managed by dose reduction without loss of efficacy(1).

**About Cushing's disease**

Cushing's disease is a rare but serious disease that affects approximately 10 to 15 patients per million per year. It most commonly affects adults who are as young as 20 to 50 years and affects

women three times more often than men. Cushing's disease presents with weight gain, central obesity, moon face, severe fatigue and weakness, striae (purple stretch marks), depression and anxiety(2),(5). To date, no known causes or risk factors have been identified for the development of the benign tumors in the pituitary gland that cause Cushing's disease.

Complications of Cushing's disease can include osteoporosis and subsequently fractures, insulin resistance with higher prevalence of impaired glucose tolerance and diabetes mellitus, high blood pressure, lipid disorders, infections, kidney stones and mental illnesses, including depression and psychosis(1),(3),(4). Cardiovascular complications resulting from untreated Cushing's disease, including coronary artery disease, congestive heart failure and stroke, contribute to a mortality rate up to four times higher than the healthy population(4).

The most common treatment approach for Cushing's disease is surgical removal of the tumor. Persistent disease and/or relapse can occur in up to 50% of surgery patients(2),(5). If surgery is not appropriate or effective, other treatment options include radiation to the pituitary gland, stereotactic radiosurgery or gamma knife radiation, removal of the adrenal glands and inhibition of cortisol production(2).

#### **About SOM230 (pasireotide)**

SOM230 is an investigational pituitary-directed therapy that targets the cause of Cushing's disease, with the aim to control excess cortisol secretion and its debilitating complications(1),(2). SOM230 targets multiple subtypes of the receptor for somatostatin (sst), a hormone that controls the pituitary gland. Its highest affinity is to sst5, a receptor subtype frequently expressed by the pituitary tumors associated with Cushing's disease. Currently approved somatostatin analogs preferentially bind to sst2 and are not effective in Cushing's disease(6).

SOM230 is currently being studied as a twice-daily sc injection, as well as a long-acting release (LAR) once-monthly intramuscular injection for the treatment of multiple disease types, including Cushing's disease, carcinoid syndrome and acromegaly(10).

Because it is an investigational compound, the safety and efficacy profile of SOM230 has not yet been established. Access to this investigational compound is available only through carefully controlled and monitored clinical trials. These trials are designed to better understand the potential benefits and risks of the compound. There is no guarantee that SOM230 will become commercially available(6).

Information about Novartis clinical trials for SOM230 can be obtained by healthcare professionals at [www.pasporttrials.com](http://www.pasporttrials.com).

#### **Disclaimer**

The foregoing release contains forward-looking statements that can be identified by terminology such as will, planned, potential, or similar expressions, or by express or implied discussions regarding regulatory submissions or approvals for SOM230, or the timing of such submissions or approvals, or regarding potential future revenues from SOM230. 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 SOM230 to be materially different from any future results, performance or achievements expressed or implied by such statements. There can be no guarantee that SOM230 will be submitted or approved for sale in any market, or for any particular indication, or at any particular time. Nor can there be any guarantee that SOM230 will achieve any particular levels

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of revenue in the future. In particular, management's expectations regarding SOM230 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 102,000 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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**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: September 22, 2010

By: /s/ MALCOLM B. CHEETHAM

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