

NOVARTIS AG  
Form 6-K  
January 20, 2012

# 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 January 20th 2012**

**(Commission File No. 1-15024)**

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(Name of Registrant)

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(Address of Principal Executive Offices)

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**MEDIA RELEASE • COMMUNIQUE AUX MEDIAS • MEDIENMITTEILUNG**

**Novartis drug Signifor® recommended by CHMP for EU approval to treat patients with Cushing's disease**

- *If approved, Signifor (SOM230, pasireotide) would be the first approved medication targeting Cushing's disease(1)*
- *In clinical trials, pasireotide suppresses overproduction of cortisol caused by an underlying pituitary tumor, a critical factor in controlling the disease(2),(3),(4)*
- *A debilitating endocrine disorder, Cushing's disease most commonly affects women from 20 to 50 years old(2),(5)*

**Basel, January 20, 2012** The Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) adopted a positive opinion for Signifor® (SOM230, pasireotide) for the treatment of Cushing's disease. There are currently no approved medicines in the European Union (EU) targeting Cushing's disease, a debilitating endocrine disorder caused by excess cortisol in the body due to the presence of a non-cancerous pituitary tumor(1),(2).

We are pleased with the decision by the CHMP in support of pasireotide in the European Union, said Hervé Hoppenot, President, Novartis Oncology. We are now one step closer to being able to offer patients in Europe the first approved medical treatment for Cushing's disease.

In the EU, the European Commission generally follows the recommendations of the CHMP and delivers its final decision within three months of the CHMP recommendation. The decision will be applicable to all 27 EU member states plus Iceland and Norway. Pasireotide has orphan drug designation for Cushing's disease, a condition which affects no more than five in 10,000 people in the EU, the threshold for orphan designation(6).

The CHMP positive opinion is based on data from the Phase III PASPORT-CUSHINGS (PASireotide clinical trial PORTfolio - CUSHING'S disease) trial, the largest randomized study to evaluate a medical therapy in patients with Cushing's disease(4).

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In the study, patients were randomized to receive pasireotide subcutaneous (sc) injection in doses of 900µg and 600µg twice daily. For the 900µg group, the study met the primary endpoint of normalizing urinary-free cortisol (UFC) levels, the key measure of biochemical control of the disease(4).

Urinary-free cortisol levels were normalized in 26.3% and 14.6% of patients randomized to receive pasireotide 900µg and 600µg twice daily, respectively, at six months of treatment. After 12 months of treatment, results confirmed the durability of the effect. On average, as UFC levels were reduced, clinical manifestations of Cushing's disease improved including reduction of blood pressure, total cholesterol, weight and body mass index(4).

The most frequently reported adverse events (AE) (>10%) by investigators for pasireotide were diarrhea, nausea, hyperglycemia, cholelithiasis, abdominal pain, diabetes mellitus, injection site reactions, fatigue and increased glycosylated hemoglobin (HbA1c), with most events being Grade 1-2. The tolerability profile of pasireotide was similar to that of other somatostatin analogs with the exception of the greater degree of hyperglycemia(4).

### **About Cushing's disease**

Cushing's syndrome is an endocrine disorder caused by excessive cortisol, a vital hormone that regulates metabolism, maintains cardiovascular function and helps the body respond to stress(2). Cushing's disease is a form of Cushing's syndrome, in which excess cortisol production is triggered by an adrenocorticotropic hormone (ACTH)-secreting pituitary adenoma(1). The first-line and most common treatment approach for Cushing's disease is surgical removal of the tumor(2).

Cushing's disease is a rare but serious disease that affects approximately one to two patients per million per year(7). It most commonly affects women from 20 to 50 years old(2),(5). Cushing's disease may present with weight gain, central obesity, moon face, severe fatigue and weakness, striae (purple stretch marks), buffalo hump, depression and anxiety(1),(5).

### **About pasireotide**

Pasireotide, an investigational multireceptor targeting somatostatin analog (SSA), binds with high affinity to four of the five somatostatin receptor subtypes (sst 1, 2, 3 and 5)(1).

For the treatment of Cushing's disease, pasireotide has been studied as a twice-daily subcutaneous (sc) injection and is currently being evaluated as a long-acting release (LAR), once-monthly intramuscular (IM) injection as part of a global Phase III program. Pasireotide LAR is also being studied in three large-scale, global Phase III clinical trial programs: two in patients with acromegaly and one in patients with metastatic carcinoid tumors whose disease-related symptoms are inadequately controlled by somatostatin analogs.

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

### **Important Safety Information about pasireotide**

Pasireotide is contraindicated in patients with hypersensitivity to pasireotide or to any of the excipients and in patients with severe liver impairment. Hyperglycemia is commonly reported as an adverse event and elevated glucose was the most frequently reported Grade 3 laboratory abnormality (23.2% of patients) in the Phase III study in Cushing's disease patients. Glycemic status should be assessed prior to starting treatment with pasireotide. Patients need to be monitored for hyperglycemia; if hyperglycemia develops, the initiation or adjustment of antidiabetic treatment is recommended.

Mild transient elevations in AST (aminotransferases) are commonly observed in patients treated with pasireotide. Rare cases of concurrent elevations in ALT (alanine aminotransferase) greater than 3 times the upper limit of normal (ULN) and bilirubin greater than 2 times ULN have also been observed. Patients need to be monitored closely for liver function for the first 3 months and thereafter as clinically indicated. Therapy should be discontinued if the patient develops jaundice, other clinical signs of significant liver dysfunctions, sustained AST or ALT increase 5 times ULN or greater, or if ALT or AST increase 3 times ULN with concurrent bilirubin elevation greater than 2 times ULN.

Patients with cardiac disease and/or risk factors for bradycardia need to be closely monitored. Caution is to be exercised in patients who have or may develop QT

prolongation. Hypokalemia or hypomagnesemia must be corrected prior to initiating therapy and monitored thereafter.

Treatment with pasireotide leads to rapid suppression of ACTH (adrenocorticotrophic hormone) secretion in Cushing's disease patients. Patients need to be monitored for signs and symptoms of hypocortisolism. Temporary exogenous steroid (glucocorticoid) replacement therapy and/or dose reduction or interruption of pasireotide therapy may be necessary.

Pasireotide should not be used during pregnancy unless clearly necessary. Breast feeding should be discontinued during treatment with pasireotide.

Pasireotide may affect the way other medicines work, and other medicines can affect how pasireotide works. Caution is to be exercised with the concomitant use of drugs with low therapeutic index mainly metabolized by CYP3A4, bromocriptine, cyclosporine, anti-arrhythmic medicines or drugs that may lead to QT prolongation.

The most frequently reported adverse events (AE) (>10%) by investigators for pasireotide were diarrhea, nausea, hyperglycemia, cholelithiasis, abdominal pain, diabetes mellitus, injection site reactions, fatigue and increased glycosylated hemoglobin (HbA1c), with most events being Grade 1-2. The tolerability profile of pasireotide was similar to that of other somatostatin analogs with the exception of the greater degree of hyperglycemia.

#### **Disclaimer**

The foregoing release contains forward-looking statements that can be identified by terminology such as would, will, being evaluated, being studied, or similar expressions, or by express or implied discussions regarding potential marketing approvals for pasireotide or regarding potential future revenues from pasireotide. 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 pasireotide to be materially different from any future results, performance or achievements expressed or implied by such statements. There can be no guarantee that pasireotide will be approved for sale in any market. Nor can there be any guarantee that pasireotide will achieve any particular levels of revenue in the future. In particular, management's expectations regarding pasireotide could be affected by, among other things, unexpected regulatory actions or delays or government regulation generally; unexpected clinical trial results, including unexpected new clinical data and unexpected additional analysis of existing clinical data; competition in general; government, industry and general public pricing pressures; unexpected manufacturing issues; the company's ability to obtain or maintain patent or other proprietary intellectual property protection; 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**

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Novartis provides innovative healthcare solutions that address the evolving needs of patients and societies. Headquartered in Basel, Switzerland, Novartis offers a diversified portfolio to best meet these needs: innovative medicines, eye care, cost-saving generic pharmaceuticals, preventive vaccines and diagnostic tools, over-the-counter and animal health products. Novartis is the only global company with leading positions in these



areas. In 2010, the Group's continuing operations achieved net sales of USD 50.6 billion, while approximately USD 9.1 billion (USD 8.1 billion excluding impairment and amortization charges) was invested in R&D throughout the Group. Novartis Group companies employ approximately 121,000 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: January 20th 2012

By: /s/ MALCOLM B. CHEETHAM

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