

NOVARTIS AG  
Form 6-K  
April 26, 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 April 26, 2012

(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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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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Yes:  No:

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

**Novartis drug Signifor® approved in the EU as the first medication to treat patients with Cushing's disease**

- *Signifor is first targeted approach for Cushing's disease, a debilitating endocrine disorder caused by an underlying pituitary tumor that triggers excess cortisol(1),(2),(3)*
- *Majority of patients in the Phase III clinical trial experienced a rapid and sustained decrease in mean cortisol levels with a subset of patients achieving normalization*
- *With reduced cortisol levels, key clinical manifestations of the disease improved, including reductions in blood pressure, cholesterol, weight and body mass index(1)*

**Basel, April 26, 2012** Novartis announced today that the European Commission has approved Signifor® (pasireotide) for the treatment of adult patients with Cushing's disease for whom surgery is not an option or for whom surgery has failed(1). Signifor is the first medicine to be approved in the European Union (EU) targeting Cushing's disease.

The approval is based on data from the largest randomized Phase III study to evaluate a medical therapy in patients with Cushing's disease, a disorder caused by excess cortisol in the body due to the presence of a non-cancerous pituitary tumor(1),(2),(3). In the study, mean urinary-free cortisol (UFC) levels were normalized in 26.3% and 14.6% of the 162 patients randomized to receive Signifor 900µg and 600µg subcutaneous (sc) injection twice daily, respectively, at month six. The primary endpoint, the proportion of patients who achieved normalization of UFC after six months without dose up-titration relative to randomized dose, was met in patients treated with 900µg twice daily(4).

In addition, the study showed the majority of the patients remaining on the study at month six (91 out of 103 patients; 88%) had any reduction in their mean UFC(5). The median reduction in mean UFC was 47.9% in both dose groups. Reductions in UFC were rapid and sustained through the end of the study, with the majority of patients experiencing a decrease within the first two months(4).

Overall reductions in the clinical manifestations of Cushing's disease, including blood pressure, total cholesterol, weight and body mass index, were observed at months six and twelve in patients with both full and partial mean UFC control, with the greatest reductions observed in patients with normalized UFC levels(1),(4).

As the first therapeutic option to specifically target Cushing's disease, Signifor has the potential to redefine treatment of this debilitating disease, said Hervé Hoppenot, President, Novartis Oncology. By focusing research efforts on our understanding of this rare disease where there is significant unmet need, we have been able to successfully bring a novel treatment option to patients in the European Union.

Cushing's disease most commonly affects adults as young as 20 to 50 years and affects women three times more often than men. It may present with weight gain, central obesity, a round, red and full face, severe fatigue and weakness, striae (purple stretch marks), high blood pressure, depression and anxiety(2),(3),(6),(7).

Patients with Cushing's disease often struggle with a variety of debilitating health issues associated with the overproduction of cortisol and previously were faced with a treatment approach limited to surgery, said Ellen van Veldhuizen, board member of the Dutch Adrenal Society. The approval of pasireotide as a new treatment option that may help patients with Cushing's disease is welcome news.

The decision follows the positive opinion the Committee for Medicinal Products for Human Use (CHMP) adopted for Signifor in January 2012 for the treatment of Cushing's disease and applies to all 27 EU member states, plus Iceland and Norway. Signifor 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(8),(9). Additional regulatory submissions for pasireotide for the treatment of Cushing's disease are under way worldwide.

### **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. 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. It is a rare but serious disease that affects approximately one to two patients per million per year. The first line and most common treatment approach for Cushing's disease is surgical removal of the tumor(2),(3),(10).

### **About PASPORT-CUSHINGS**

PASPORT-CUSHINGS (PASireotide clinical trial PORTfolio - CUSHING\_S disease) is a prospective, randomized, double-blind Phase III study conducted at 68 sites in 18 countries. The study evaluated the efficacy and safety of Signifor in 162 adult patients with persistent or recurrent Cushing's disease and UFC levels greater than 1.5 times the upper limit of normal (ULN), as well as in patients with newly diagnosed Cushing's disease who were not candidates for surgery(4).

Patients with primarily moderate to severe hypercortisolism were randomized to receive Signifor sc injection in doses of 900µg (n=80) or 600µg (n=82) 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, which was met in patients treated with 900µg twice daily(4).

### **About Signifor (pasireotide)**

Signifor® (pasireotide) is approved in the European Union (EU) for the treatment of adult patients with Cushing's disease for whom surgery is not an option or for whom surgery has failed. For the treatment of Cushing's disease, Signifor 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. Signifor is a multireceptor targeting somatostatin analog (SSA) that binds with high affinity to four of the five somatostatin receptor subtypes (sst 1, 2, 3 and 5)(1),(3),(11).

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 Signifor**

Signifor is contraindicated in patients with hypersensitivity to the active substances in Signifor or to any of the excipients and in patients with severe liver impairment.

Alterations in blood glucose levels have been frequently reported in healthy volunteers and patients treated with Signifor. Glycemic status should be assessed prior to starting treatment with Signifor. Patients need to be monitored for hyperglycemia; if hyperglycemia develops, the initiation or adjustment of antidiabetic treatment is

recommended. Dose reduction or treatment discontinuation should be considered if uncontrolled hyperglycemia persists. After treatment discontinuation, glycemic monitoring (e.g. FPG or HbA1c) should be done according to clinical practice.

Monitoring of liver function is recommended prior to starting treatment with Signifor and after one, two, four, eight and twelve weeks during treatment and thereafter as clinically indicated. Therapy should be discontinued if the patient develops jaundice, other clinical signs of significant liver dysfunctions, sustained AST (aminotransferases) or ALT (alanine aminotransferase) increase five times the upper limit of normal (ULN) or greater, or if ALT or AST increase three times ULN with concurrent bilirubin elevation greater than two 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. Electrocardiography should be performed prior to the start of Signifor therapy and as clinically indicated thereafter.

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

Monitoring of gallbladder and pituitary hormones is recommended prior to initiating treatment and periodically thereafter.

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

Signifor may affect the way other medicines work, and other medicines can affect how Signifor 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 Signifor 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 Signifor was similar to that of other somatostatin analogs with the exception of the greater degree of hyperglycemia(1).

#### **Disclaimer**

The foregoing release contains forward-looking statements that can be identified by terminology such as potential, under way, or similar expressions, or by express or implied discussions regarding potential future marketing approvals for Signifor or regarding potential future revenues from Signifor. 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 Signifor to be materially different from any future results, performance or achievements expressed or implied by such statements. There can be

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no guarantee that Signifor, or its LAR version, will be approved for sale, or for any additional indications, in any market, or at any particular time. Nor can there be any guarantee that Signifor will achieve any particular levels of revenue in the future. In particular, management's expectations regarding Signifor 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; government, industry and general public pricing pressures; the company's ability to

obtain or maintain patent or other proprietary intellectual property protection; competition in general; unexpected manufacturing issues; 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 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 2011, the Group's continuing operations achieved net sales of USD 58.6 billion, while approximately USD 9.6 billion (USD 9.2 billion excluding impairment and amortization charges) was invested in R&D throughout the Group. Novartis Group companies employ approximately 124,000 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: April 26, 2012

By: /s/ MALCOLM B. CHEETHAM

Name: Malcolm B. Cheetham  
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