NOVARTIS AG
Form 6-K
March 08, 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 March 7, 2012

(Commission File No. 1-15024)

Novartis AG

(Name of Registrant)

Lichtstrasse 35

4056 Basel

Switzerland

(Address of Principal Executive Offices)

Indicate by check mark whether the registrant files or will file annual reports under cover of Form 20-F or Form 40-F:

Form 20-F: x Form 40-F: o

Indicate by check mark if the registrant is submitting the Form 6-K in paper as permitted by Regulation S-T Rule 101(b)(1):

Yes: o **No**: x

Indicate by check mark if the registrant is submitting the Form 6-K in paper as permitted by Regulation S-T Rule 101(b)(7):

Yes: o **No**: x

Indicate by check mark whether the registrant by furnishing the information contained in this form is also thereby furnishing the information to the Commission pursuant to Rule 12g3-2(b) under the Securities Exchange Act of 1934.

Yes: o **No**: x

Novartis International AG
Novartis Global Communications
CH-4002 Basel
Switzerland
http://www.novartis.com

MEDIA RELEASE • COMMUNIQUE AUX MEDIAS • MEDIENMITTEILUNG

Data in NEJM shows Novartis drug Signifor® is first therapy to provide rapid, durable benefit for Cushing s disease patients in Phase III study

- *Study met primary endpoint showing Signifor (pasireotide) normalized cortisol overproduction, a critical factor in controlling the debilitating endocrine disorder*(1),(2),(3)

- *Cortisol levels decreased quickly in the majority of patients and levels were normalized in 26.3% of patients treated with pasireotide 900µg twice daily*(1)

- *Results showed pasireotide improved key clinical manifestations of the disease, including reductions in blood pressure, cholesterol, weight and body mass index*(1)

- *Caused by an underlying pituitary tumor, Cushing s disease most commonly affects women from 20 to 50 years old*(2),(4)

Basel, March 7, 2012 A study published in *The New England Journal of Medicine* (NEJM) found that the investigational drug Signifor® (SOM230, pasireotide), normalized cortisol levels and showed clinical benefit in patients with Cushing s disease(1). This study, which was first presented at the 14th Congress of the European Neuroendocrine Association in September 2010, is the first Phase III trial to demonstrate the efficacy of a medical therapy for Cushing s disease.

Cushing s disease is a debilitating endocrine disorder caused by excess cortisol in the body due to the presence of a non-cancerous pituitary tumor. There are currently no approved medicines that target Cushing s disease(5).

In the study, patients were randomized to receive pasireotide subcutaneous (sc) injection in doses of 900µg or 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. UFC levels were normalized in 26.3% and 14.6% of patients with Cushing s disease 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(1).

While rare, Cushing s disease is a serious disease with no cure and very limited treatment options, said Annamaria Colao, MD, lead study investigator and Professor of Endocrinology, Chief of the Neuroendocrine Unit at the Department of Molecular and Clinical Endocrinology and Oncology, Federico II University of Naples. These data on pasireotide are the first to show a therapeutic treatment can help patients achieve biochemical control of their Cushing s disease, while improving associated symptoms.

Study results also showed that cortisol levels decreased quickly in the majority of patients, with a median decrease of approximately 50% by month two, and remained stable in both groups through the end of the study. 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(1).

The trial, which represents the largest randomized study to evaluate a medical therapy in patients with Cushing s disease, is the basis for regulatory submissions for pasireotide under way worldwide for the treatment of this condition. In January, pasireotide received a positive CHMP opinion for the treatment of Cushing s disease, and if approved in the EU the brand name will be Signifor.

These positive study results demonstrate thapasireotide has the potential to be an important therapeutic option for patients living with Cushing s disease and reinforces Novartis commitment to develop therapies to help address unmet medical needs, said Hervé Hoppenot, President, Novartis Oncology. We look forward to working with regulatory authorities worldwide to help bring this novel treatment option to market.

About the Study

PASPORT-CUSHINGS (PASireotide clinical trial PORTfolio - CUSHING S disease) is a prospective randomized, double-blindPhase III study conducted at 68 sites in 18 countries. The study evaluated the efficacy and safety of pasireotide 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 are not candidates for surgery(1).

Patients with primarily moderate to severe hypercortisolism were randomized to receive pasireotide 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. The primary endpoint was met in patients treated with 900µg sc twice daily. Secondary endpoints included safety, proportion of patients with UFC ≤ ULN at months 3, 6 and 12 regardless of dose titration, proportion of patients with partial UFC control (defined as UFC > ULN and ≥50% reduction from baseline); changes from baseline in plasma adrenocorticotropic hormone (ACTH), UFC, serum and salivary cortisol over time and changes from baseline in clinical signs, symptoms and health-related quality of life(1).

After six months, the primary efficacy responder rate was 26.3% (95% confidence interval [CI], 16.6 to 35.9) and 14.6% (95% 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 25.0% and 13.4%, respectively, for the 900µg and 600µg groups. The median reduction in UFC after six months was 47.9% for both groups. The median reduction in UFC after 12 months was 62.4% (900µg) and 67.6% (600µg). In patients with full or partial control of UFC levels at months 1 or 2, 71.4% remained on treatment until month 12 compared with 24.6% of those uncontrolled at months 1 and 2(1).

As may be expected with a treatment that lowers cortisol levels in Cushing s disease, 13 patients experienced adverse events associated with cortisol levels below the normal range. This was managed by dose reduction without loss of efficacy. There were no deaths during pasireotide treatment. Forty patients reported serious AEs (SAE); 19 were drug-related, including nine patients with a glucose related SAE (n=5 diabetes mellitus; n=4 hyperglycemia)(1).

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 ACTH-secreting pituitary adenoma(5). 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(6). It most commonly affects adults who are as young as 20 to 50 years and affects women three times more often than men(2),(4). 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(2).

About pasireotide

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

For the treatment of Cushing s diseasepasireotide 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.

Information about Novartis clinical trials for pasireotide can be obtained by healthcare professionals at 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 three times the upper limit of normal (ULN) and bilirubin greater than two times ULN have also been observed. Patients need to be monitored closely for liver function for the first three 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 five times 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.

Treatment with pasireotide leads to rapid suppression of ACTH (adrenocorticotropic 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 can, potential, commitment, look forward to, expected, will, 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, or at any particular time. 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

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.

References

(1) Colao, A. A 12-Month Phase III Study of Pasireotide in Cushing s Disease. New Engl J Med. 2012; 366:32-42.

(2) National Endocrine and Metabolic Diseases Information Service. Cushing s SyndromeAvailable at: http://endocrine.niddk.nih.gov/pubs/cushings/Cushings_Syndrome_FS.pdf. Accessed December 2011.

(3) Boscaro, M. Treatment of Pituitary-Dependent Cushing s Disease with the Multireceptor Ligand Somatostatin Analog Pasireotide (SOM230): A Multicenter, Phase II Trial. *J Clin Endocrin Metabol*. 2009;94(1):115-122.

(4) Newell-Price, J. The Diagnosis and Differential Diagnosis of Cushing s Syndrome and Pseudo-Cushing s States. Endocrine Reviews. 1998;19(5): 647-672 .

(5) Pedroncelli, A. Medical Treatment of Cushing s Disease: Somatostatin Analogues and Pasireotide. *Neuroendocrinology.* 2010;92(suppl1):120-124.

(6) Lindholm, J. Incidence and Late Prognosis of Cushing s Syndrome: A Population-Based Study. The Journal of Clinical Endocrinology & Metabolism. 2001;86(1): 117-121.

# # #

Novartis Media Relations

Central media line : +41 61 324 2200

Eric Althoff

Novartis Global Media Relations

+41 61 324 7999 (direct)

+41 79 593 4202 (mobile)

eric.althoff@novartis.com

Nicole Riley

Novartis Oncology

+1 862 778 3110 (direct)

+1 862 926 9040 (mobile)

nicole.riley@novartis.com

For Novartis multimedia content, please visit www.thenewsmarket.com/Novartis
For questions about the site or required registration, please contact: journalisthelp@thenewsmarket.com.

Novartis Investor Relations

Central phone:	+41 61 324 7944		
Susanne Schaffert	+41 61 324 7944	**North America:**	
Pierre-Michel Bringer	+41 61 324 1065	Helen Boudreau	+1 212 830 2404
Thomas Hungerbuehler	+41 61 324 8425	Jill Pozarek	+1 212 830 2445
Isabella Zinck	+41 61 324 7188	Edwin Valeriano	+1 212 830 2456

e-mail: investor.relations@novartis.com

e-mail: investor.relations@novartis.com

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:	March 7, 2012	By:	/s/ MALCOLM B. CHEETHAM
		Name:	Malcolm B. Cheetham
		Title:	Head Group Financial Reporting and Accounting