

NOVARTIS AG
Form 6-K
February 09, 2018

UNITED STATES

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 November 10, 2017

(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: Form 40-F:

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: **No:**

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: **No:**

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: **No:**

Novartis International AG
Novartis Global Communications
CH-4002 Basel
Switzerland

<http://www.novartis.com>

MEDIA RELEASE • COMMUNIQUE AUX MEDIAS • MEDIENMITTEILUNG

Novartis brolocizumab (RTH258) demonstrates superiority versus aflibercept in key secondary endpoint measures of disease activity in nAMD, a leading cause of blindness

Brolocizumab, the first and only anti-VEGF to maintain a majority of patients on a 12-week treatment schedule immediately following loading phase in Phase III trials, met primary endpoint of non-inferiority vs aflibercept

Significantly fewer brolocizumab patients showed signs of disease activity as well as retinal fluid (IRF and/or SRF)—key markers used by physicians to determine injection frequency in clinical practice

Brolocizumab delivered superior reductions in retinal thickness (CST) due to fluid accumulation versus aflibercept

Overall ocular and non-ocular adverse event rates for brolocizumab were comparable to aflibercept in both studies

Basel, November 10, 2017 – Novartis, a global leader in ophthalmology, announced further positive results from two Phase III studies of brolocizumab versus aflibercept. Results showed non-inferiority in primary endpoint, superiority in key retinal health outcomes, and long-lasting effect in patients with neovascular age-related macular degeneration (nAMD), a leading cause of blindness. The results of the head-to-head trials, HAWK and HARRIER, were presented at the American Academy of Ophthalmology (AAO) 2017 Annual Meeting¹.

In neovascular AMD, abnormal blood vessels leak fluid into the eye, ultimately causing damage and blindness². At week 16, relative to aflibercept, 35% fewer brolocizumab 6 mg patients showed presence of IRF and/or SRF in HAWK, and 33% fewer in HARRIER (P<0.0001 for both)¹. Again at week 48, relative to aflibercept, 31% fewer patients on brolocizumab 6 mg had intra-retinal fluid (IRF) and/or sub-retinal fluid (SRF) in HAWK, and 41% fewer

in HARRIER ($P < 0.0001$ for both)¹. The absence of fluid for patients in the brolocizumab arm suggests the potential for a long-lasting effect and decreased treatment need.

Additionally, brolocizumab 6 mg patients demonstrated superior reductions in central subfield thickness (CST)¹. In nAMD, an elevated CST—as measured by optical coherence tomography (OCT)—is a key indicator of abnormal fluid accumulation in the retina³. Significantly improved CST reductions were evident at week 16 ($P = 0.0016$ in HAWK and $P < 0.0001$ in HARRIER) and at week 48 ($P = 0.0023$ and $P < 0.0001$, respectively)¹.

Brolocizumab met the primary efficacy endpoint of noninferiority to aflibercept in mean change in best-corrected visual acuity (BCVA) from baseline to week 48 in both trials¹. These results were achieved while a majority of brolocizumab patients—57% in HAWK and 52% in HARRIER—were maintained on a q12w dosing interval immediately following the loading phase through week 48¹.

“HAWK and HARRIER demonstrated that brolocizumab has the potential to positively impact disease management and provide long-lasting treatment effect,” said Dr. Pravin U. Dugel, Managing Partner, Retinal Consultants of Arizona; Clinical Professor, Roski Eye Institute, Keck School of Medicine, University of Southern California; and principal investigator of both trials. “HAWK and HARRIER showed that brolocizumab outperformed aflibercept on disease activity assessments, including key measures of disease progression seen on OCT, which forms the basis of a clinician’s treatment decisions. Importantly, improvements in these key OCT measures were seen as early as week 16 and maintained at week 48, with a majority of brolocizumab patients on a 12-week treatment interval.”

Frequent injections into the eye, a standard requirement for nAMD therapies, can be a significant hardship for patients and burden on caregivers^{4,5}. Brolocizumab is the first and only anti-vascular endothelial growth factor (anti-VEGF) treatment for nAMD to demonstrate robust visual gains with a majority of patients maintained on a less-frequent 12-week (q12) treatment interval immediately following the loading phase in randomized clinical trials¹.

“Having delivered on our non-inferiority endpoint with a majority of patients on a q12 week interval, we’re truly excited to share these data showing that brolocizumab clearly improves key anatomical outcomes that are biomarkers of disease,” said Vas Narasimhan, Global Head, Drug Development and Chief Medical Officer, Novartis. “Brolocizumab represents a major scientific and clinical advancement for patients, caregivers and retina specialists around the world.”

With brolocizumab, significantly fewer patients had active disease at week 16 in a matched head-to-head comparison. Active disease was observed in 23.5% of brolocizumab 6 mg patients versus 33.5% of aflibercept patients in HAWK, and in 21.9% of brolocizumab patients versus 31.4% of aflibercept patients in HARRIER (P=0.0022 for both)¹.

Brolocizumab safety was comparable to aflibercept with the overall incidence of adverse events balanced across all treatment groups in both studies¹. The most frequent ocular adverse events (greater than 5% of patients in any treatment arm) for brolocizumab 3 mg, 6 mg and aflibercept, respectively, in HAWK were reduced visual acuity (8.7%, 6.9% and 8.9%), conjunctival hemorrhage (8.4%, 6.4% and 5.6%), vitreous floaters (6.7%, 5.0% and 3.1%) and eye pain (5.9%, 4.4% and 4.2%)⁶. The incidences of these events for brolocizumab 6 mg and aflibercept, respectively, in HARRIER were reduced visual acuity (5.9% and 6.2%), conjunctival hemorrhage (1.9% and 3.3%), vitreous floaters (3.0% and 0.8%) and eye pain (2.7% and 3.3%)⁶. The most frequent non-ocular adverse events were typical of those reported in an nAMD population; there were no notable differences between arms⁶. The incidence of arterial thrombotic events (ATE) was 3.9%, 2.5% and 5.5% (brolocizumab 3 mg, brolocizumab 6 mg and aflibercept respectively) in HAWK and 1.6% and 1.1% (brolocizumab 6 mg and aflibercept, respectively) in HARRIER¹.

About brolocizumab (RTH258)

Brolocizumab (RTH258) is a humanized single-chain antibody fragment (scFv) and the most clinically advanced, humanized single-chain antibody fragment to reach this stage of development. Single-chain antibody fragments are

highly sought after in drug development due to their small size, enhanced tissue penetration, rapid clearance from systemic circulation and drug delivery characteristics^{7,8,9}.

The proprietary innovative structure results in a small molecule (26 kDa) with potent inhibition of, and high affinity to, all VEGF-A isoforms^{7,10}. In preclinical studies, brolicizumab inhibited activation of VEGF receptors through prevention of the ligand-receptor interaction^{7,8,9,10}. Increased signaling through the VEGF pathway is associated with pathologic ocular angiogenesis and retinal edema¹¹. Inhibition of the VEGF pathway has been shown to inhibit the growth of neovascular lesions, resolve retinal edema and improve vision in patients with chorioretinal vascular diseases¹².

About HAWK and HARRIER study design

With more than 1,800 patients across 400 centers worldwide, HAWK and HARRIER are the first and only global head-to-head trials in patients with nAMD that prospectively demonstrated efficacy at week 48 using an innovative q12w/q8w regimen, with a majority of patients on q12w immediately following the loading phase¹. Both studies are 96-week prospective, randomized, double-masked multi-center studies and part of the Phase III clinical development of brolocizumab^{13,14}.

The studies were designed to compare the efficacy and safety of intravitreal injections of brolocizumab 6 mg and 3 mg (HAWK only) versus aflibercept 2 mg in patients with nAMD. The primary efficacy objective of HAWK and HARRIER trials was to confirm that brolocizumab is noninferior to aflibercept in mean change in BCVA from baseline to Week 48. Secondary endpoints include average mean change in BCVA from baseline over the period week 36-48, the proportion of patients on a q12w interval at week 48 and anatomical parameters^{13,14}.

In both trials, patients were randomized to either brolocizumab or aflibercept. Immediately following the 3-month loading phase, patients in the brolocizumab arms received a q12w dosing interval with an option to adjust to a q8w dosing interval based on masked disease activity assessments at defined visits. Aflibercept was dosed bi-monthly according to its label^{13,14}.

Week 16 was an important pre-defined data point, as it represents a timepoint when the treatment assessment for brolocizumab and aflibercept were identical, providing an opportunity to observe how both drugs performed in a matched comparison¹.

About neovascular age-related macular degeneration (nAMD or wet AMD)

nAMD is the leading cause of severe vision loss and legal blindness in people over the age of 65 in North America, Europe, Australia and Asia, impacting an estimated 20 to 25 million people worldwide^{15,16}. nAMD occurs when abnormal blood vessels form underneath the macula, the area of the retina responsible for sharp, central vision. These blood vessels are fragile and leak fluid, disrupting the normal retinal architecture and ultimately causing damage^{17,18,19}.

Early symptoms of nAMD include distorted vision or metamorphopsia and difficulties seeing objects clearly²⁰. Prompt diagnosis and intervention are essential. As the disease progresses, cell damage increases, further reducing vision quality. This progression can lead to a complete loss of central vision, leaving the patient unable to read, drive or recognize familiar faces¹⁷. Without treatment, vision can rapidly deteriorate²¹.

About Novartis in ophthalmology

Novartis is a leading ophthalmology company, with therapies that treat both front and back of the eye disorders, including retina diseases, glaucoma, dry eye and other external eye diseases. In 2016, approximately 200 million patients worldwide were treated with Novartis ophthalmic products.

Disclaimer

This press release contains forward-looking statements within the meaning of the United States Private Securities Litigation Reform Act of 1995. Forward-looking statements can generally be identified by words such as “potential,” “can,” “will,” “plan,” “expect,” “anticipate,” “look forward,” “believe,” “committed,” “investigational,” “pipeline,” “launch,” or by express or implied discussions regarding potential marketing approvals, new indications or labeling for the investigational or approved products described in this press release, or regarding potential future revenues from such products. You should not place undue reliance on these statements. Such forward-looking statements are based on our current beliefs and expectations regarding future events, and are subject to significant known and unknown risks and uncertainties. Should one or more of these risks or uncertainties materialize, or should underlying assumptions prove incorrect, actual results may vary materially from those set forth in the forward-looking statements. There can be no guarantee that the investigational or approved products described in this press release will be submitted or approved for sale or for any additional indications or labeling in any market, or at any particular time. Nor can there be any guarantee that such products will be commercially successful in the future. In particular, our expectations regarding such products could be affected by, among other things, the uncertainties inherent in research and development, including clinical trial results and additional analysis of existing clinical data; regulatory actions or delays or government regulation generally; our ability to obtain or maintain proprietary intellectual property protection; the particular prescribing preferences of physicians and patients; global trends toward health care cost containment, including government, payor and general public pricing and reimbursement pressures; general economic and industry conditions, including the effects of the persistently weak economic and financial environment in many countries; safety, quality or manufacturing issues, and other risks and factors referred to in Novartis AG’s current Form 20-F on file with the US Securities and Exchange Commission. 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, cost-saving generic and biosimilar pharmaceuticals and eye care. Novartis has leading positions globally in each of these areas. In 2016, the Group achieved net sales of USD 48.5 billion, while R&D throughout the Group amounted to approximately USD 9.0 billion. Novartis Group companies employ approximately 121,000 full-time-equivalent associates. Novartis products are sold in approximately 155 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>

For Novartis multimedia content, please visit www.novartis.com/news/media-library

For questions about the site or required registration, please contact media.relations@novartis.com

References

1. Dugel P, et al. HAWK & HARRIER: 48-week results of 2 multi-centered, randomized, double-masked trials of brolucizumab versus aflibercept for neovascular AMD. Presented at: The American Academy of Ophthalmology 2017 Annual Meeting on November 10, 2017, New Orleans.
2. NHS Choices. Macular Degeneration. Available at <http://www.nhs.uk/Conditions/Macular-degeneration/Pages/Introduction.aspx> (link is external). Accessed November 2017.
3. Kang SW, et al. The correlation between fluorescein angiographic and optical coherence tomographic features in clinically significant diabetic macular edema. *Am J Ophthalmol* 2004;137(2):313-322.
4. Mantel I. Optimizing the Anti-VEGF Treatment Strategy for Neovascular Age-Related Macular Degeneration: From Clinical Trials to Real-Life Requirements. *Translational Vision Science & Technology*. 2015;4(3):6.
5. Gohil R, et al. Caregiver Burden in Patients Receiving Ranibizumab Therapy for Neovascular Age Related Macular Degeneration. *PLoS ONE*. 2015;10(6):e0129361.
6. Data on file.
7. Escher D, et al. Single-chain antibody fragments in ophthalmology. Oral presentation at EURETINA congress. 2015. Abstract. Available at: <http://www.euretina.org/nice2015/programme/free-papers-details.asp?id=4072&day=0> (link is external). Accessed November 2017.
8. Nimz EL, et al. Intraocular and systemic pharmacokinetics of brolucizumab (RTH258) in nonhuman primates. The Association for Research in Vision and Ophthalmology (ARVO) annual meeting. 2016. Abstract 4996.
9. Gaudreault J, et al. Preclinical pharmacology and safety of ESBA1008, a single-chain antibody fragment, investigated as potential treatment for age related macular degeneration. ARVO Annual meeting abstract. *Invest Ophthalmol Vis Sci* 2012;53:3025. <http://iovs.arvojournals.org/article.aspx?articleid=2354604> (link is external).
10. Tietz J, et al. Affinity and Potency of RTH258 (ESBA1008), a Novel Inhibitor of Vascular Endothelial Growth Factor A for the Treatment of Retinal Disorders. *IOVS*. 2015; 56(7): 1501.
11. Qazi Y, et al. Mediators of ocular angiogenesis. *J. Genet.* 2009;88(4):495-515.
12. Kim R. Introduction, mechanism of action and rationale for anti-vascular endothelial growth factor drugs in age-related macular degeneration. *Indian J Ophthalmol*. 2007;55(6):413-415.

13. ClinicalTrials.gov. Identifier NCT02307682. Available at <https://clinicaltrials.gov/ct2/show/NCT02307682> (link is external). Accessed November 2017.
14. ClinicalTrials.gov. Identifier NCT02434328. Available at <https://clinicaltrials.gov/ct2/show/NCT02434328> (link is external). Accessed November 2017.
15. Schmidt-Erfurth U, et al. Guidelines for the management of neovascular age-related macular degeneration by the European Society of Retina Specialists (EURETINA). Br J Ophthalmol. 2014;98:1144-1167.
16. Chopdar A, et al. Age related macular degeneration. BMJ. 2003;26(7387):485-488.
17. World Health Organization. Priority eye diseases: Age-related macular degeneration. Available at <http://www.who.int/blindness/causes/priority/en/index7.html> (link is external). Accessed November 2017.
18. NHS Choices. Macular Degeneration. Available at <http://www.nhs.uk/Conditions/Macular-degeneration/Pages/Introduction.aspx> (link is external). Accessed November 2017.
19. National Eye Institute. Facts About Age-Related Macular Degeneration. Available at https://nei.nih.gov/health/maculardegen/armd_facts (link is external). Accessed November 2017.
20. NHS Choices. Macular degeneration - Symptoms. Available at <http://www.nhs.uk/Conditions/Macular-degeneration/Pages/Symptoms.aspx> (link is external). Accessed November 2017.
21. van Lookeren Campagne M, et al. Mechanisms of age-related macular degeneration and therapeutic opportunities. J Pathol. 2014; 232(2):151-64. doi: 10.1002/path.4266.

###

Novartis Media Relations

Central media line: +41 61 324 2200
E-mail: media.relations@novartis.com

| | |
|--|--|
| Eric Althoff | Amy Wolf |
| Novartis Global Media Relations | Global Head, Ophthalmology Communications |
| +41 61 324 7999 (direct) | +41 61 696 5894 (direct) |
| +41 79 593 4202 (mobile) | +41 79 576 0723 (mobile) |
| eric.althoff@novartis.com | amy.wolf@novartis.com |

Novartis Investor Relations

Central investor relations line: +41 61 324 7944
E-mail: investor.relations@novartis.com

Edgar Filing: NOVARTIS AG - Form 6-K

Central

Samir Shah

+41 61 324 7944

Pierre-Michel Bringer

+41 61 324 1065

Thomas Hungerbuehler

+41 61 324 8425

Isabella Zinck

+41 61 324 7188

North America

Richard Pulik

+1 212 830 2448

Cory Twining

+1 212 830 2417

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: November 13, 2017 By: /s/ PAUL PENEPEM
Name: Paul Penepent
Head Group Financial
Title: Reporting and
Accounting