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FORM 6-K

REPORT OF FOREIGN PRIVATE ISSUER

PURSUANT TO RULE 13a-16 or 15d-16 OF

THE SECURITIES EXCHANGE ACT OF 1934

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Yes: **No**:

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MEDIA RELEASE • COMMUNIQUE AUX MEDIAS • MEDIENMITTEILUNG

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

- Brolucizumab, 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 brolucizumab 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*

- *Brolucizumab delivered superior reductions in retinal thickness (CST) due to fluid accumulation versus aflibercept*

- *Overall ocular and non-ocular adverse event rates for brolucizumab 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 brolucizumab 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 Meeting[1].

In neovascular AMD, abnormal blood vessels leak fluid into the eye, ultimately causing damage and blindness[2]. At week 16, relative to aflibercept, 35% fewer brolucizumab 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 brolucizumab 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 brolucizumab arm suggests the potential for a long-lasting effect and decreased treatment need.

Additionally, brolucizumab 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 retina[3]. 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].

Brolucizumab 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 trials[1]. These results were achieved while a majority of brolucizumab patients—57% in HAWK and 52% in HARRIER—were maintained on a q12w dosing interval immediately following the loading phase through week 48[1].

“HAWK and HARRIER demonstrated that brolucizumab 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 brolucizumab 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 brolucizumab 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 caregivers4,5. Brolucizumab 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 trials[1].

“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 brolucizumab clearly improves key anatomical outcomes that are biomarkers of disease,” said Vas Narasimhan, Global Head, Drug Development and Chief Medical Officer, Novartis. “Brolucizumab represents a major scientific and clinical advancement for patients, caregivers and retina specialists around the world.”

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

Brolucizumab 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 brolucizumab 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 brolucizumab 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% (brolucizimab 3 mg, brolucizumab 6 mg and aflibercept respectively) in HAWK and 1.6% and 1.1% (brolucizumab 6 mg and aflibercept, respectively) in HARRIER[1].

About brolucizumab (RTH258)

Brolucizumab (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, brolucizumab 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 edema[11]. 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 diseases[12].

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 brolucizumab[13,14].

The studies were designed to compare the efficacy and safety of intravitreal injections of brolucizumab 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 brolucizumab 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 brolucizumab or aflibercept. Immediately following the 3-month loading phase, patients in the brolucizumab 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 brolucizumab and aflibercept were identical, providing an opportunity to observe how both drugs performed in a matched comparison[1].

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 clearly[20]. 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 faces[17]. Without treatment, vision can rapidly deteriorate[21].

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.

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About 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

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