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Novartis receives EC Approval for Beovu®, a next-generation anti-VEGF treatment for wet AMD, a leading cause of blindness worldwide

- *Beovu (brolucizumab) is the only anti-VEGF treatment approved in Europe for wet AMD that offers the option to start eligible patients on three-month dosing intervals immediately after the loading phase*[1]
- *For the more than 20 million people worldwide who are living with wet AMD, frequent injections are a common reason patients drop off existing treatments*[2-4]
- *Approval is based on two head-to-head clinical trials, HAWK and HARRIER, in which Beovu achieved robust vision gains that were non-inferior to aflibercept at year one (primary endpoint)*[1,5]
- *Beovu also demonstrated superior fluid resolution versus aflibercept at week 16 and year one (secondary endpoints)*[1,5]

Basel, February 17, 2020 – Novartis today announced the European Commission (EC) has approved Beovu® (brolucizumab) injection for the treatment of wet age-related macular degeneration (AMD). Beovu is the first EC-approved anti-VEGF treatment to demonstrate superior resolution of retinal fluid (IRF/SRF), a key marker of disease activity, versus aflibercept (secondary endpoints)[1,5]. Beovu also offers the ability to start eligible wet AMD patients on a three-month dosing interval immediately after the loading phase[1,5]. The EC decision is applicable to all 27 European Union member states as well as the UK, Iceland, Norway and Liechtenstein.

“Currently, wet AMD patients, who are often older, can face significant challenges in managing their disease. We believe that Beovu, and its ability to resolve fluid, brings great therapeutic value that will help physicians optimize treatments for patients based on disease activity,” said Marie-France Tschudin, President Novartis Pharmaceuticals. “With the approval of this innovative biologic, Novartis is continuing to reimagine medicine for people living with wet AMD.”

“Drying the retina is one of the main goals in the treatment of wet AMD with anti-VEGF therapy,” said Frank Holz, MD, FEBO, FARVO, Professor and Chairman, Department of Ophthalmology, University of Bonn, Germany. “Beovu, with its superior fluid resolution as demonstrated in the HAWK and HARRIER trials, will provide physicians with a new option to treat wet AMD.”

Wet AMD is a chronic, degenerative eye disease caused by an excess of VEGF, a protein that promotes the growth of abnormal blood vessels underneath the macula, the area of the retina responsible for sharp, central vision[6,7]. The disease is a leading cause of severe vision loss and blindness in people over age 65, affecting more than 20 million people worldwide[3,4,8]. In the EU, an estimated 1.7 million people are affected by wet AMD[9]. Early symptoms of wet AMD include blurry or wavy vision[7]. As the disease progresses, patients lose central vision, making it difficult to see objects directly in front of them[7].

The EC approval was based on findings from the Phase III HAWK and HARRIER clinical trials, in which Beovu met the primary endpoint, demonstrating gains in best corrected visual acuity (BCVA) that were non-inferior to aflibercept at year one (week 48)[1,5]. Vision gains at year one were maintained at year two[1,5].

In fluid-related secondary endpoints, Beovu outperformed aflibercept[1,5]. Significantly fewer patients had intra-retinal and/or sub-retinal fluid (IRF/SRF), two fluids which may disrupt the normal retinal structure and cause damage to the macula (31% for brolucizumab 6 mg vs. 45% for aflibercept in HAWK; 26% vs. 44%, respectively, in HARRIER at year one)[1,5,10]. Additionally, Beovu showed superior reductions in central subfield thickness, another indicator of retinal fluid, at week 16 and at year one[1,5]. Differences seen at year one were maintained at year two[1,5]. In both trials, 30% fewer patients had signs of disease activity with Beovu versus aflibercept as early as week 16[11].

In HAWK and HARRIER, over half of patients were maintained on the three-month dosing interval (56% in HAWK and 51% in HARRIER) at year one[1,5]. The remaining patients in the study were treated on a two-month dosing interval[1,5].

“Today’s approval is a step forward for patients in Europe who have been looking for a new treatment option which may help them maintain their sight — and their independence — for longer,” said Christina Fasser, President, Retina International. “This can really help to alleviate a burden, not only on the patient themselves, but also on those who care for them."

In October 2019, Novartis received approval from the U.S. Food and Drug Administration for Beovu for the treatment of wet AMD[12]. Beovu received Swissmedic approval in Switzerland[13] and Australian TGA approval[14] in January 2020, both for the treatment of wet AMD. Novartis is committed to bringing Beovu to patients worldwide, and additional regulatory filings are currently underway in Canada, Japan and Brazil.

About Beovu (brolucizumab)
Beovu (brolucizumab, also known as RTH258) is the most clinically advanced humanized single-chain antibody fragment (scFv)[5,15]. 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[15-17].

The proprietary innovative structure results in a small molecule (26 kDa) with potent inhibition of, and high affinity to, all VEGF-A isoforms[16]. Beovu is engineered to deliver the highest concentration of drug, providing more active binding agents than other anti-VEGFs[5,15]. In preclinical studies, Beovu inhibited activation of VEGF receptors through prevention of the ligand-receptor interaction[16-18]. Increased signaling through the VEGF pathway is associated with pathologic ocular angiogenesis and retinal edema[19]. Inhibition of the VEGF pathway has been shown to inhibit the growth of neovascular lesions and suppress endothelial cell proliferation and vascular permeability[19].

About the HAWK and HARRIER studies
With more than 1,800 patients across nearly 400 centers worldwide, HAWK (NCT02307682) and HARRIER (NCT02434328) are the first and only global head-to-head trials in patients with wet AMD that prospectively demonstrated efficacy at week 48 using an innovative q12w/q8w regimen, with a majority of patients on q12w immediately following the loading phase[5]. Both studies are 96-week prospective,

randomized, double-masked multi-center studies and part of the Phase III clinical development of Beovu[5]. The studies were designed to compare the efficacy and safety of intravitreal injections of brolucizumab 6 mg (HAWK and HARRIER) and 3 mg (HAWK only) versus aflibercept 2 mg in patients with wet AMD[5].

About wet age-related macular degeneration
Wet AMD 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 million people worldwide[3,4,8]. Wet AMD occurs when abnormal blood vessels form underneath the macula, the area of the retina responsible for sharp, central vision[7,20,21]. These blood vessels are fragile and leak fluid, disrupting the normal retinal architecture and ultimately causing damage to the macula[7,20,21].

Early symptoms of wet AMD include distorted vision (or metamorphopsia) and difficulties seeing objects clearly[22]. Prompt diagnosis and intervention are essential[21]. As the disease progresses, cell damage increases, further reducing vision quality[7]. This progression can lead to a complete loss of central vision, leaving the patient unable to read, drive or recognize familiar faces and potentially depriving them of their independence[7,23]. Without treatment, vision can rapidly deteriorate[24].

About Novartis in ophthalmology
At Novartis, our mission is to discover new ways to improve and extend people's lives. In ophthalmology, we develop and deliver life-changing medicines and therapies for diseases and conditions from front to back of the eye, enabled by data and transformative technologies. Our ophthalmic solutions reach more than 150M people per year, from premature infants to the elderly.

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About Novartis

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