Novartis International AG
Novartis Global Communications
CH-4002 Basel
Switzerland

http://www.novartis.com/
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Novartis receives positive CHMP opinion for Beovu® (brolucizumab) for the treatment of wet AMD

- *In two head-to-head clinical trials, patients on Beovu achieved vision gains that were non-inferior to aflibercept at year one*[1]
- *In a pre-specified secondary endpoint, fewer patients had intra-retinal fluid and/or sub-retinal fluid at week 16 and year one with Beovu*[1]
- *In a key pre-specified secondary endpoint, over half of Beovu 6mg patients (56% in HAWK and 51% in HARRIER) were maintained on three-month dosing intervals immediately after the loading phase through year one*[1]
- *Frequent injections are a common reason patients drop off treatment for wet AMD, a leading cause of blindness that affects more than 20M people worldwide*[2-4]

Basel, December 13, 2019 — Novartis today announced that the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) has adopted a positive opinion for Beovu® (brolucizumab 6 mg), also known as RTH258, an investigational product for the treatment of wet age-related macular degeneration (AMD).

“Today’s CHMP opinion brings us another step closer to providing wet AMD patients in Europe with a new treatment option,” said Nikos Tripodis, Worldwide Franchise Head, Novartis Ophthalmology. “At Novartis, we remain committed to reimagining treatments for patients suffering from wet AMD, a leading cause of blindness worldwide.”

Wet AMD is caused by uncontrolled VEGF, a protein that promotes abnormal blood vessel formation underneath the macula, the area of the retina responsible for sharp, central vision[5,6]. These blood vessels are fragile and leak fluid, disrupting the normal retinal architecture and ultimately causing damage to the macula[5,6]. By inhibiting VEGF, Beovu is designed to suppress the growth of abnormal blood vessels and the potential for fluid leakage into the retina[1].

The positive CHMP opinion is based on findings from the Phase III, global, head-to-head HAWK and HARRIER clinical trials, in which Beovu demonstrated non-inferiority versus aflibercept in mean change in best-corrected visual acuity from baseline to year one[1]. In both trials, approximately 30% of patients treated with Beovu gained at least 15 letters at year one[1].*

In pre-specified secondary endpoints, fewer patients treated with Beovu 6mg versus aflibercept had intra-retinal and/or sub-retinal fluid at week 16 (35% fewer patients in both HAWK and

HARRIER) and at year one (30% fewer patients in HAWK and 41% fewer patients in HARRIER)[1]. Significant reductions in central subfield thickness were also seen with Beovu[1].

Additionally, over half (56% in HAWK and 51% in HARRIER) of patients treated with Beovu 6mg maintained a three-month dosing interval immediately after the loading phase through year one[1]. Beovu patients who started on three-month dosing intervals after the loading phase had an 85% (HAWK) and 82% (HARRIER) probability of remaining on this interval through year one[1].

Beovu exhibited an overall safety profile comparable to aflibercept. The most common adverse events (≥5% of patients) with Beovu were vision blurred, cataract, conjunctival hemorrhage, vitreous floaters and eye pain[1].

In October 2019, Novartis received the first, and so far the only, approval for Beovu from the U.S. Food and Drug Administration in the treatment of wet AMD. The European Commission will consider the CHMP opinion as it makes its final decision on the marketing authorization for Beovu. The decision is expected within three months.

*Patients receiving Beovu showed a numerical improvement in treatment versus aflibercept, but the p values did not result in statistical significance.

About Beovu (brolucizumab)
Beovu (brolucizumab, also known as RTH258) is the most clinically advanced humanized single-chain antibody fragment (scFv)[1,7]. 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[7-9].

The proprietary innovative structure results in a small molecule (26 kDa) with potent inhibition of, and high affinity to, all VEGF-A isoforms[8]. Beovu is engineered to deliver the highest concentration of drug, providing more active binding agents than other anti-VEGFs[1,7]. In preclinical studies, Beovu inhibited activation of VEGF receptors through prevention of the ligand-receptor interaction[8-10]. Increased signaling through the VEGF pathway is associated with pathologic ocular angiogenesis and retinal edema[5]. Inhibition of the VEGF pathway has been shown to inhibit the growth of neovascular lesions and suppress endothelial cell proliferation and vascular permeability[5].

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[1]. Both studies are 96-week prospective, randomized, double-masked multi-center studies and part of the Phase III clinical development of Beovu[1]. 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[1].

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[3,4,11]. Wet AMD occurs when abnormal blood vessels form underneath the macula, the area of the retina responsible for sharp, central vision[6,12,13]. These blood vessels are fragile and leak fluid, disrupting the normal retinal architecture and ultimately causing damage to the macula[6,12,13].

Early symptoms of wet AMD include distorted vision (or metamorphopsia) and difficulties seeing objects clearly[14]. Prompt diagnosis and intervention are essential[13]. As the disease progresses, cell damage increases, further reducing vision quality[6]. 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[6,15]. Without treatment, vision can rapidly deteriorate[16].

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.

Disclaimer
This press release contains forward-looking statements within the meaning of the United States Private Securities Litigation Reform Act of 1995 that can generally be identified by words such as “positive CHMP opinion,” “investigational,” “another step closer,” “committed,” “potential,” “so far,” “will,” “expected,” “within three months,” “can,” “potentially,” “mission,” or similar terms, or by express or implied discussions regarding potential marketing approvals, new indications or labeling for Beovu, or regarding potential future revenues from Beovu. 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 Beovu 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 Beovu will be commercially successful in the future. In particular, our expectations regarding Beovu could be affected by, among other things, regulatory actions or delays or government regulation generally; the uncertainties inherent in research and development, including clinical trial results and additional analysis of existing clinical data; global trends toward health care cost containment, including government, payor and general public pricing and reimbursement pressures and requirements for increased pricing transparency; our ability to obtain or maintain proprietary intellectual property protection; the particular prescribing preferences of physicians and patients; general political and economic conditions; safety, quality or manufacturing issues; potential or actual data security and data privacy breaches, or disruptions of our information technology systems, 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 is reimagining medicine to improve and extend people’s lives. As a leading global medicines company, we use innovative science and digital technologies to create transformative treatments in areas of great medical need. In our quest to find new medicines, we consistently rank among the world’s top companies investing in research and development. Novartis products reach more than 750 million people globally and we are finding innovative ways to expand access to our latest treatments. About 109,000 people of more than 140 nationalities work at Novartis around the world. Find out more at.
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Novartis Media Relations
E-mail: media.relations@novartis.com

Antonio Ligi
Novartis External Communications
+41 61 324 1374 (direct)
antonio.ligi@novartis.com

Amy Wolf
Global Head, Ophthalmology Communications
+41 61 696 5894 (direct)
+41 79 576 0723 (mobile)
amy.wolf@novartis.com

Eric Althoff
Novartis US External Communications
+1 646 438 4335
eric.althoff@novartis.com

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

Central		North America	
Samir Shah	+41 61 324 7944	Sloan Simpson	+1 862 778 5052
Pierre-Michel Bringer	+41 61 324 1065	Cory Twining	+1 862 778 3258
Thomas Hungerbuehler	+41 61 324 8425		
Isabella Zinck	+41 61 324 7188		