Novartis International AG
Novartis Global Communications
CH-4002 Basel
Switzerland

https://twitter.com/novartisnews

MEDIA UPDATE

Novartis announces positive results from year two of the Phase III trial of Beovu® in diabetic macular edema

- *Results from year two of the Phase III KESTREL clinical trial confirmed year one findings, with an overall favorable benefit-risk profile for Beovu® (brolucizumab) 6 mg in patients with visual impairment due to diabetic macular edema (DME)*[1,2]
- *Beovu showed visual acuity gains that were consistent with year one, and sustained average reductions in central subfield thickness at year two (week 100)*[1]
- *More Beovu patients experienced resolution of intraretinal and/or subretinal fluid versus aflibercept at year two*[1]
- *Of Beovu patients who completed the first 12-week dosing interval following the loading phase, 70% remained on 12-week dosing through year two, showing the potential for DME patients to receive fewer injections versus aflibercept*[1]

Basel, December 9, 2021 — Novartis today announced the first interpretable results from year two (week 100) of the Phase III KESTREL study. KESTREL assessed the safety and efficacy of Beovu® (brolucizumab) 6 mg in patients with visual impairment due to diabetic macular edema (DME). Results from year two confirmed the visual acuity gains, fluid reduction findings and safety profile from year one, while addressing the burden of frequent treatments for DME patients[1,2].

Results from year two of KESTREL were consistent with those seen at year one, including maintenance of best-corrected visual acuity (BCVA) and sustained reductions in central subfield thickness (CSFT)[1,2]. Additionally, numerically fewer Beovu patients had intraocular fluid and/or sub-retinal fluid (IRF/SRF) versus patients treated with aflibercept[1]. CSFT is a key indicator of fluid in the retina, and fluid is a key marker of disease activity[3,4].

More than 40% of Beovu patients were maintained on 12-week dosing intervals, and 70% of patients who completed the first 12-week cycle after loading remained on 12-week dosing through year two, showing the potential for Beovu to offer fluid resolution in more DME patients with fewer injections versus aflibercept[1].

“With an average age at diagnosis of 48 years, DME primarily affects working-age adults, which means managing their vision, in addition to multiple comorbidities related to diabetes, may result in loss of work productivity and employment instability[5,6],” said Dr. David M Brown MD, Director of Research, Retina Consultants of Texas. “The extended dosing and fluid resolution observed in year two of the KESTREL clinical trial suggest Beovu has the potential to help appropriate patients more conveniently and effectively manage their disease with dosing intervals every 12 weeks after an initial loading phase.”

Further details of year-two findings from the KESTREL trial, along with findings from KITE*, another pivotal Phase III trial of Beovu in DME, will be presented at upcoming medical congresses.

About the KESTREL year two safety results
In KESTREL (NCT03481634), rates of intraocular inflammation (IOI) were 4.2% for Beovu 6 mg, 5.3% for Beovu 3 mg and 1.1% for aflibercept; retinal vasculitis (RV) rates were 0.5% for Beovu 6 mg, 1.6% for Beovu 3 mg and 0% for aflibercept[1]. Rates of retinal vascular occlusion (RO) were 1.6% for both Beovu 6 mg and 3 mg versus 0.5% for aflibercept[1]. The majority of IOI events were manageable and resolved without any clinical complications[1]. There were no vascular events reported in year two (weeks 52-100)[1]. No new RV events were reported during year two of KESTREL[1]. Of the four new RO events reported during year two (two in Beovu 6 mg, one in Beovu 3 mg and one in aflibercept), none were associated with IOI or RV[1].

Brolucizumab 6 mg is the commercialized dose of Beovu in wet age-related macular degeneration (AMD)[7]. Novartis is committed to bringing Beovu 6 mg to DME patients and has submitted data from KESTREL and KITE (NCT03481660), to global health authorities in H2 2021.

About the KESTREL and KITE clinical trials
KESTREL and KITE are global, randomized, double-masked, Phase III, two-year studies comparing the safety and efficacy of Beovu and aflibercept in the treatment of patients with visual impairment due to DME[8,9].

KESTREL and KITE involved 926 total patients in 36 countries[8,9]. In the loading phase of both trials, patients in the Beovu arms were treated every six weeks for a total of five doses; patients in the aflibercept arms were treated every four weeks for a total of five doses, in line with its label at the start of the studies[8,9]. Following the loading phase, patients in the Beovu arms were subsequently treated every 12 weeks, with those demonstrating disease activity moved to dosing every eight weeks for the remainder of the study[8,9]. At week 72 of KITE, Beovu patients dosed every 12 weeks could be extended to dosing every 16 weeks, and patients dosed every eight weeks could be extended to every 12 weeks[9].

About diabetic macular edema (DME)
DME is a common microvascular complication in patients with diabetes that may have a debilitating impact on visual acuity, eventually leading to blindness[10]. DME is the leading cause of blindness in adults in developed countries, affecting 12% of patients with type 1 diabetes and 28% of those with type 2 diabetes[10].

Consistently high blood sugar levels associated with diabetes can damage small blood vessels in the eye, causing them to leak fluid[11]. This damage leads to an excess of vascular endothelial growth factor (VEGF)[10,11]. VEGF is a protein that stimulates the growth of blood vessels[10,11]. At elevated levels in DME, VEGF stimulates the growth of abnormal, leaky blood vessels[10,11]. The resulting accumulation of fluid (known as edema) in the macula can lead to vision impairment or even vision loss[10,11]. The macula is the area of the retina responsible for sharp, central vision[11]. Early symptoms of DME include blurry or wavy central vision and distorted color perception, although the disease can also progress without symptoms at early stages[11,12].

About Beovu (brolucizumab) 6 mg
Beovu (brolucizumab, also known as RTH258) 6 mg is approved for the treatment of wet age-related macular degeneration (AMD) in more than 70 countries, including in the US, EU, UK, Japan, Canada and Australia[7,13-16]. Additional trials, which study the effects of brolucizumab in patients with wet AMD, diabetic macular edema (DME), and proliferative diabetic retinopathy (PDR), are currently ongoing.

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.

**Kite Pharma, Inc. is neither a sponsor of nor associated with Novartis' KITE trial.*

Disclaimer
This media update 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," "may," "could," "would," "expect," "anticipate," "look forward," "believe," "committed," "investigational," "pipeline," "launch," or similar terms, or by express or implied discussions regarding potential marketing approvals, new indications or labeling for the investigational or approved products described in this media update, 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 media update 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; 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, economic and business conditions, including the effects of and efforts to mitigate pandemic diseases such as COVID-19; safety, quality, data integrity 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 media update as of this date and does not undertake any obligation to update any forward-looking statements contained in this media update 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 nearly 800 million people globally and we are finding innovative ways to expand access to our latest treatments. About 108,000 people of more than 140 nationalities work at Novartis around the world. Find out more at https://www.novartis.com.

Novartis is on Twitter. Sign up to follow @Novartis at **https://twitter.com/novartisnews**
For Novartis multimedia content, please visit **https://www.novartis.com/news/media-library**
For questions about the site or required registration, please contact media.relations@novartis.com

References

1. Data on file. KESTREL (year two) first interpretable results. Novartis, 2021.
2. Brown D, Wolf S, Garweg JG, et al. Brolucizumab for the treatment of visual impairment due to diabetic macular edema: 52-week results from the KESTREL & KITE studies. Presented at: The Association for Research in Vision and Ophthalmology 2021 Annual Meeting. May 2021.
3. Kang SW, Park CY, Ham D-I. 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. Arnold J, Markey CM, Kurstjens NP, Guymer GH. The role of sub-retinal fluid in determining treatment outcomes in patients with neovascular age-related macular degeneration--a phase IV randomised clinical trial with ranibizumab: the FLUID study. *BMC Ophthalmol*. 2016;143(4):679-680.
5. Petrella RJ, Blouin J, Davies B, Barbeau M. Prevalence, Demographics, and Treatment Characteristics of Visual Impairment due to Diabetic Macular Edema in a Representative Canadian Cohort. *J Ophthalmol.* 2012;2012:159167.
6. Kiss S, Chandwani HS, Cole AL, Patel VD, Lunacsek OE, Dugel PU. Comorbidity and health care visit burden in working-age commercially insured patients with diabetic macular edema. *Clin Ophthalmol*. 2016;10:2443-2453.
7. Beovu [US prescribing information] East Hanover, NJ. Novartis Pharmaceuticals Corp; 2020.
8. Data on file. KESTREL clinical trial protocol (CRTH258B2301). Novartis, 2021.
9. Data on file. KITE clinical trial protocol (CRTH258B2302). Novartis, 2021.
10. Romero-Aroca P. Managing diabetic macular edema: The leading cause of diabetes blindness. *World J Diabetes*. 2011;2(6):98-104.
11. National Eye Institute. Macular Edema. Available at: https://www.nei.nih.gov/learn-about-eye-health/eye-conditions-and-diseases/macular-edema. Accessed December 2021.
12. National Eye Institute. Diabetic Retinopathy. Available at: https://www.nei.nih.gov/learn-about-eye-health/eye-conditions-and-diseases/diabetic-retinopathy. Accessed December 2021.
13. Beovu [summary of product characteristics] Basel, Switzerland. Novartis; 2020.
14. Pharma Japan. National Health Insurance Pricing. Available at: https://pj.jiho.jp/sites/default/files/pj/document/2020/05/New%20Drugs%20to%20Be%20Added%20to%20NHI%20Price%20List%20on%20May%2020_1.pdf. Accessed December 2021.
15. Canadian Agency for Drugs and Technologies in Health. CADTH Canadian Drug Expert Committee Recommendation. Available at: https://cadth.ca/sites/default/files/cdr/complete/SR0632%20Beovu%20-%20CDEC%20Final%20Recommendation%20%E2%80%93%20May%2025%2C%202020_for%20posting.pdf. Accessed December 2021.
16. Beovu [prescription medicine decision summary] Australia. Novartis: 2020.

# # #

Novartis Media Relations
E-mail: media.relations@novartis.com

Amy Wolf
Novartis External Communications
+41 79 576 07 23
amy.wolf@novartis.com

Meghan O'Donnell
Novartis Division Communications
+41 79 797 9102
meghan.odonnell@novartis.com

Julie Masow
Novartis US External Communications
+1 862 579 8456
julie.masow@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	+1 862 345 4440
Thomas Hungerbuehler	+41 61 324 8425	Alina Levchuk	+1 862 778 3372
Isabella Zinck	+41 61 324 7188	Parag Mahanti	+1 973-876-4912