**Category**

Best Pharmaceutical Product

**General Information**

**Company Name ***

Genentech, A Member of the Roche Group

**Product/Solution Name ***

VABYSMO

**Compound/Tech Name***

RG 7716; faricimab-svoa; RO 6867461; Vabysmo™

**Trade Name ***

Faricimab-svoa; Vabysmo™, VABYSMO®

**Corporate Name ***

**Date of Approval ***

2022-01-31

**Indications ***

Vabysmo (faricimab-svoa) is a prescription medicine given by injection into the eye, used to treat adults with neovascular (wet) age-related macular degeneration (AMD) and diabetic macular edema (DME).

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**Therapeutic Areas ***

Retinal vascular diseases:neovascular (wet) age-related macular degeneration (nAMD), diabetic macular edema (DME)

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**Background information and need for drug / device**
**(please be as specific as possible in your description; limit 500 words)**

Vabysmo is the first breakthrough innovation in retinal eye care for more than 17 years and sets a new paradigm for the treatment of (wet) neovascular age-related macular degeneration (nAMD) and for diabetic macular edema (DME). nAMD affects an estimated 14 million people, past the age of 50 [1]

and DME is a common eye complication of diabetes [2]. Our scientists previously recognized that targeting vascular endothelial growth factors (VEGFs) addressed the abnormal blood vessel proliferation and fluid leakage that eventually lead to blindness in retinal vascular diseases. Since VEGFs play critical normal roles in the body, blocking their pathological activities specifically in the eye requires direct intravitreal (IVT) injections of the medication in the retina by trained practitioners [3,4]. Anti-VEGF therapies have revolutionized eye care for millions of people worldwide, who previously had few, if any, treatment options for disease management. However, the chronicity (often monthly injections) and invasiveness of the treatment makes it burdensome for patients to adhere to. Additionally, anti-VEGF therapies only target a subset of the disease pathology, highlighting the unmet need for more comprehensive and robust treatments which require fewer IVT injections [5]. Many pharmaceutical companies have tried, unsuccessfully, over the years to address this need until now. Vabysmo builds on the already proven concept, and established infrastructure, of anti-VEGF therapies, and blocks an additional growth factor (ANG-2) that plays critical and complementary deleterious pathological roles in nAMD and DME. Vabysmo's dual inhibition provides rapid and robust drying of retinal fluid, which can be sustained for longer periods of time, resulting in patients being able to extend the interval between their treatments by 3-4 months apart [6,7].

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**History of the development of the solution/product ***
**(please be as specific as possible in your description; 500 words)**

Our thinking is that blocking only one cytokine is insufficient to treat complex diseases such as nAMD or DME and we set our sights on the Ang-Tie pathway, another critical vasculature regulator in physiology [8]. Pathologically, increases in Angiopoietin-2 growth factor (ANG-2) compete with ANG-1 binding to the Tie receptor, resulting in inflammation, cell death and vascular leakage. Moreover, ANG-2 potentiates the effects of VEGF-A in pathologic new vessel formation and leakage [9]. Due to the complexity of treating retinal diseases by IVT injections, combination therapy with dual agents present challenges ranging from the need for two independent IVT injections to non-optimal formulations with two agents that can affect intraorbital pressure. We therefore engineered Vabysmo, our first-in-class humanized bi-specific antibody designed for intraocular use, as a single molecule blocking two pathways. Using our proprietary CrossMAb technology [10], we engineered the antigen-binding fragments to independently bind and inhibit both VEGF-A and ANG-2 with high affinity and specificity and in a synergistic manner, without binding ANG-1. Specific modifications to the tail (Fc) region results in decreased inflammation and ensures faster clearance out of the body. After thorough testing in preclinical models [11, 12, 13], as well as Phase 1 and 2 studies [14, 15], we launched extensive global Phase 3 and 4 programs for Vabysmo in DME and nAMD, as well as for retinal vein occlusion (RVO). Year one Phase 3 results for Vabysmo trials for DME and nAMD involving over 4500 patients confirmed the effectiveness and durability of treatment, while requiring fewer intra-eye maintenance injections (every 3-4 months rather than every 2 months for anti-VEGF monotherapy) [6,7]. To date, Vabysmo has been approved in over 60 countries and over a million doses have been administered to patients [16], who find that they can extend the time between their treatments, without vision loss.

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**Why this drug or device is innovative, the broad implications for future research, and/or how it will improve the human condition ***

Vabysmo is the first bispecific antibody for use in the retina that was designed using our novel CrossMAb technology. Besides nMAD and DME, data from our global Phase III studies show that Vabysmo is an equally effective treatment for branch and central retinal vein occlusion diseases (RVO) [17]. These data have been submitted for regulatory approval as a third treatment indication for Vabysmo. nData from clinical trials [6,7] and mounting real world evidence [18, 16] show that Vabysmo is a safe, effective and durable new generation eye medicine that requires fewer maintenance IVT injections, thus dramatically improving the quality of life for patients. Additionally, our patients are experiencing more robust improvements with Vabysmo compared to anti-VEGF therapies, for example faster and better drying of the retina. Our thinking is that this is because Vabysmo targets multiple pathological features of retinal diseases beyond new vessel formation and inspires us to keep innovating, based on rigorous scientific data, to systematically address other key pathological pathways in retinal vascular disease, such as inflammation, to deliver next-generation medicines. With Vabysmo, we are entering a new era of being able to tailor IVT injections, based on evaluation of the patient's anatomy and vision outcomes, ranging from one to four months apart. Our recent two-year Phase 3 nAMD data show that more than 60% of patients receiving Vabysmo can be treated every 4 months, which is an increase from 45% at year one [19].nOur Phase IV Elevatum study evaluates the use of Vabysmo in underrepresented patient populations (Black, African American, Hispanic, Latin American and Indigenous people) who are at higher risk of developing diabetic macular edema (DME) [20] and speaks to our commitment of improving the overall standard of care by including a diversity of populations, perspectives and experiences. The future for treating retinal vascular diseases is looking brighter.

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**Please provide appropriate references (PubMed, Abstract, Website) ***

1. https://pubmed.ncbi.nlm.nih.gov/18484796/n2. https://pubmed.ncbi.nlm.nih.gov/26605370/n3. https://pubmed.ncbi.nlm.nih.gov/17021318/n4. https://pubmed.ncbi.nlm.nih.gov/19118696/n5. https://pubmed.ncbi.nlm.nih.gov/27330279/n6. https://pubmed.ncbi.nlm.nih.gov/35085503/n7. https://pubmed.ncbi.nlm.nih.gov/35085502/n8. https://pubmed.ncbi.nlm.nih.gov/33136975/n9. https://pubmed.ncbi.nlm.nih.gov/33136975/n10.https://pubmed.ncbi.nlm.nih.gov/30453028/n11.https://pubme articleid=2772952n14. https://pubmed.ncbi.nlm.nih.gov/31047438/n15.https://pubmed.ncbi.nlm.nih.gov/32729897/n16.Conference presentation - Eandi C. et al. Presented at SFO 2023, Paris, France, 6-8 May 2023n17.https://www.gene.com/media/press-releases/14983/2023-02-09/new-phase-iii-data-show-genentechs-vabysn18.https://pubmed.ncbi.nlm.nih.gov/36959312/n19.https://www.gene.com/media/press-releases/14960/2022-07-14/new-two-year-data-confirm-genentechs-vabn20.https://clinicaltrials.gov/ct2/show/NCT05224102n

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