

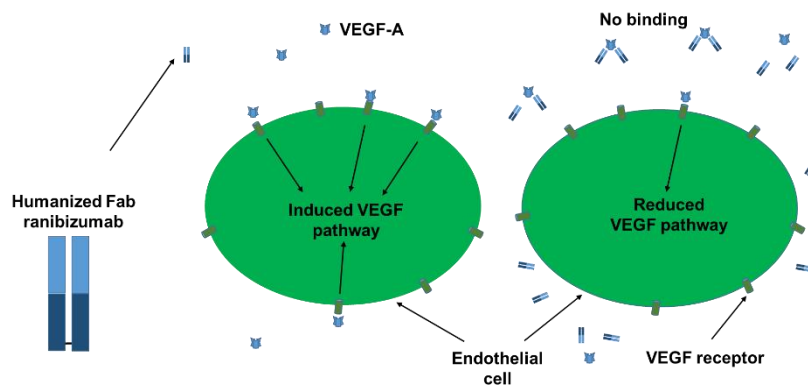
## Ranibizumab – Fact Sheet

### Molecule

Ranibizumab (Lucentis®) is a humanized monoclonal truncated antibody (Fab-fragment) created from the same parent mouse antibody as bevacizumab. It has a molecular weight of approximately 48 kDa and its effectiveness is very similar to that of bevacizumab.

### Mode of Action

Ranibizumab binds to the receptor binding site of active forms of vascular endothelial growth factor A (VEGF-A), including the biologically active, cleaved form of this molecule, VEGF110. The binding of ranibizumab to VEGF-A prevents the interaction of VEGF-A with its receptors (VEGFR1 and VEGFR2) on the surface of endothelial cells, reducing endothelial cell proliferation, vascular leakage, and new blood vessel formation.



### Indication

Lucentis® is indicated for the treatment of neovascular (wet) age-related macular degeneration, macular edema following retinal vein occlusion, diabetic macular edema, diabetic retinopathy, and myopic choroidal neovascularization.

### Patent Situation

Relevant patents for Lucentis® expired / will expire in US in 2020 and in EU in 2022, however, there are still uncertainties about patent term extensions.

### Market and Competitive Field

Ranibizumab was developed by Genentech (Roche) and is marketed in the US by Genentech and elsewhere by Novartis under the brand name Lucentis®. The originator product was first approved by FDA in 2006 and by EMA in 2007. In 2020, Lucentis® had global sales of 1.63 billion € (Novartis), and 1.33 billion € (Genentech / Roche). Several ranibizumab biosimilars are in development, one product is already marketed in India.

		Ranibizumab
		Lucentis®
		Razumab®
	<b>Clone selection/ comparability</b>	
HPLC	Separation based on <b>size</b> (SE-HPLC)	
	Separation based on <b>hydrophobicity</b> (RP-HPLC)	
	Detection of <b>charge variants</b> (CEX-HPLC)	
Binding	Binding to <b>cell surface</b> expressed target (Flow cytometry)	c.l.d.
	Binding to <b>soluble target</b> (ELISA)	
	Binding to specific <b>antibody or antigen</b> (SPR-BIACORE, ELISA)	
	<b>Affinity/ kinetic</b> to recombinant target (SPR-BIACORE)	
Effector function	Binding to C1q, <sup>1</sup> <b>CDC surrogate</b> (ELISA)	neg. assay
	<b>Affinity</b> to recombinant Fc-receptors (SPR-BIACORE)	n.a.
	Reporter gene assays, <sup>2</sup> <b>ADCC surrogate</b> (Luminescence)	n.a.
	<sup>1</sup> <b>CDC</b> (Flow cytometry)	n.a.
	<sup>2</sup> <b>ADCC</b> (DELFI, Fluorescence)	n.a.
	Additional <b>bioassays</b> (Luminescence, fluorescence)	
Gly	Glyco-pattern with <b>Lectin Microarray</b> (45 different lectins)	n.a.
	<b>(Pre)clinical application</b>	
Clinics	Pharmacokinetics – <b>PK</b> (ECL, ELISA)	
	Pharmacodynamics – <b>PD</b> (ECL, ELISA, flow cytometry, bioassay)	
	Immunogenicity - <sup>3</sup> <b>ADAs</b> (ECL, Biacore, ELISA, neutr. assay)	

<sup>1</sup>CDC = Complement Dependent Cytotoxicity  
<sup>2</sup>ADCC = Antibody Dependent Cellular Cytotoxicity  
<sup>3</sup>ADA = Anti-Drug Antibody

	VelaLabs portfolio
	VelaLabs planned
	c.l.d. = cell line dependent
	n.a. = not applicable
	In development