

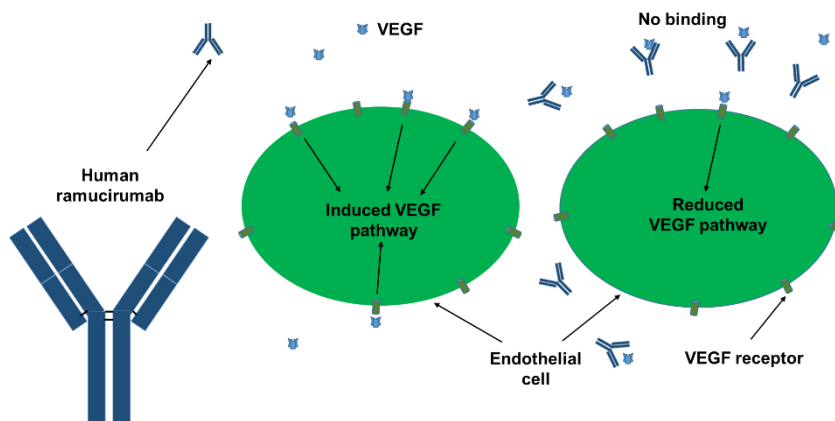
## Ramucirumab – Fact Sheet

### Molecule

Ramucirumab (Cyramza®), originally isolated from a native phage display library, is a fully human monoclonal IgG1 / kappa antibody composed of two heavy chain (γ1-chain) molecules consisting of 446 amino acid residues each and two light chain (κ-chain) molecules consisting of 214 amino acid residues each (combined molecular weight of 143.6 kDa).

### Mode of Action

Similar to bevacizumab, ramucirumab inhibits angiogenesis (formation of new blood vessels) by binding to a specific epitope on the extracellular domain of vascular endothelial growth factor receptor -2 (VEGFR-2) and blocking the interaction of VEGF-A, VEGF-C, or VEGF-D with its receptors. Ramucirumab can therefore slow the growth of new blood vessels in tumors.



### Indication

Cyramza® is indicated for gastric cancer, gastro - oesophageal junction adenocarcinoma, metastatic colorectal cancer, non-small cell lung cancer that has spread to other parts of the body or in patients whose cancer involves mutations in EGFRs, and hepatocellular

carcinoma in patients with a high blood level of alpha fetoprotein.

### Patent Situation

Cyramza® patents will expire in the US in November 2025 and in the EU in May 2023.

### Market and Competitive Field

The originator product Cyramza® was developed by ImClone Systems and is now owned by Eli Lilly. It was approved for its first indication by FDA and EMA in 2014. In 2020, Cyramza® had sales of 0.87 billion €, up from 0.85 billion € in 2019. Biosimilar developments are currently at an early stage.

**VelaLabs Portfolio**

		Ramucirumab
		Cyramza®
	<b>Clone selection/ comparability</b>	
<b>HPLC</b>	Separation based on <b>size</b> (SE-HPLC)	
	Separation based on <b>hydrophobicity</b> (RP-HPLC)	
	Detection of <b>charge variants</b> (CEX-HPLC)	
<b>Binding</b>	Binding to <b>cell surface</b> expressed target (Flow cytometry)	n.a.
	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)	
<b>Effector function</b>	Binding to C1q, <sup>1</sup> <b>CDC surrogate</b> (ELISA)	
	<b>Affinity</b> to recombinant Fc-receptors (SPR-BIACORE)	
	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)	Anti-proliferation
<b>Gly</b>	Glyco-pattern with <b>Lectin Microarray</b> (45 different lectins)	
	<b>(Pre)clinical application</b>	
<b>Clinics</b>	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

	Vela portfolio
	n.a. = not applicable