

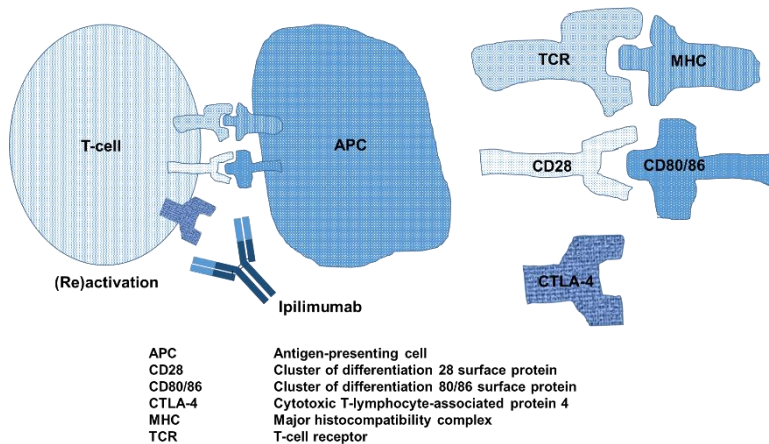
## Ipilimumab – Fact Sheet

### Molecule

Ipilimumab (Yervoy®) is targeting the immune checkpoint T-lymphocyte-associated protein 4 (CTLA-4). It is a fully humanized monoclonal antibody with two heavy chains and two kappa light chains linked together by disulfide bonds. The molecular weight is approximately 148 kDa.

### Mode of Action

The anti-CTLA-4 blocking antibody ipilimumab was the first immune checkpoint inhibitor to be approved for the treatment of cancer. CTLA-4 is a B7/CD28 family member that inhibits T-cell functions. It is constitutively expressed by regulatory T-cells but can also be upregulated by other T-cell subsets, especially CD4+ T-cells, upon activation. CTLA-4 mediates immunosuppression by indirectly diminishing signaling through the co-stimulatory receptor CD28. Cancer cells can thus avoid immune recognition and immune-mediated destruction. The function of ipilimumab is thus a (re)activation of the immune system.



### Indication

Yervoy® is indicated for unresectable or metastatic melanoma, as an adjuvant in the treatment of cutaneous melanoma, to treat microsatellite-high or mismatch repair deficient metastatic colorectal cancer, hepatocellular carcinoma, and in combination with nivolumab (Opdivo®) for advanced renal cell carcinoma.

### Patent Situation

Yervoy® patents will expire in the US in 2023 and in the EU in 2021. Basic patents related to anti-CTLA4 have been already expired.

### Market and Competitive Field

The originator product Yervoy® was developed by Bristol-Myers Squibb and Medarex. The first approvals by FDA and EMA were in 2011. In 2019, Yervoy® had sales of 1.36 billion €, up from 1.22 billion € in 2018. Biosimilar developments are currently at an early stage.

**VelaLabs Portfolio**

		Ipilimumab
		Yervoy®
	<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)	
	<sup>1</sup> <b>CDC</b> (Flow cytometry)	
	<sup>2</sup> <b>ADCC</b> (DELFI, Fluorescence)	
<b>Gly</b>	Additional <b>bioassays</b> (Luminescence, fluorescence)	
	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

	VelaLabs portfolio
	VelaLabs planned
n.a.	not applicable