Moderna's therapeutics: PD-L1 (mRNA-6981)

Last program update: November 4, 2021

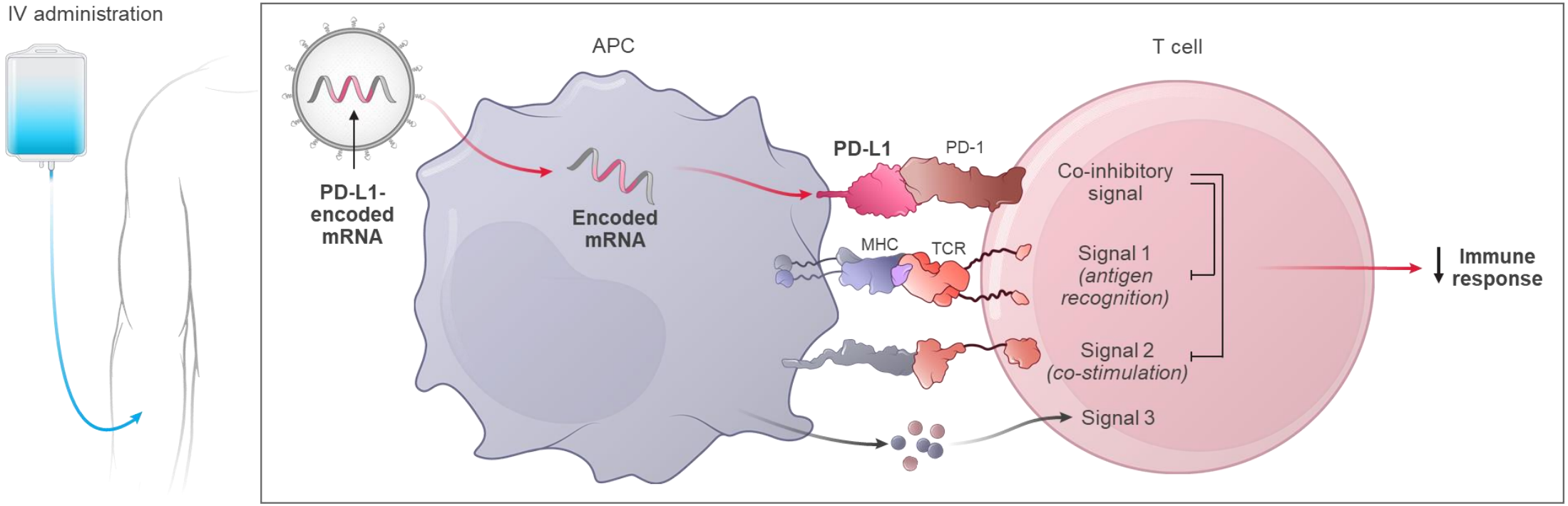
Modality	Program	ID #	Preclinical development	Phase 1	Phase 2	Phase 3	Commercial	Moderna rights
Systemic secreted & cell surface therapeutics	IL-2 *Autoimmune disorders*	mRNA-6231						Worldwide
	Relaxin *Heart failure*	mRNA-0184						Worldwide
	PD-L1 *Autoimmune hepatitis*	**mRNA-6981**						Worldwide
Cancer vaccines	Personalized cancer vaccine (PCV)	mRNA-4157						50-50 global profit sharing with **Merck**
	KRAS vaccine	mRNA-5671						50-50 global profit sharing with **Merck**
Intratumoral Immuno-oncology	OX40L/IL-23/IL-36γ (Triplet) *Solid tumors/lymphoma*	mRNA-2752						Worldwide
	IL-12 *Solid tumors*	MEDI1191						50-50 U.S. profit sharing; **AZ** to pay royalties on ex-U.S. sales
Localized Regenerative Therapeutics	VEGF-A *Myocardial ischemia*	AZD8601						**AZ** to pay milestones and royalties
	Propionic acidemia (PA)	mRNA-3927						Worldwide
	Methylmalonic acidemia (MMA)	mRNA-3705						Worldwide
Systemic Intracellular Therapeutics	Glycogen storage disease type 1a (GSD1a)	mRNA-3745	Open IND					Worldwide
	Phenylketonuria (PKU)	mRNA-3283						Worldwide
	Crigler-Najjar syndrome type 1 (CN-1)	mRNA-3351						Provided to **ILCM** free of charge
Inhaled Pulmonary Therapeutics	Cystic fibrosis (CF)	VXc-522						**Vertex** to pay milestones and royalties

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PD-L1 (mRNA-6981)

mRNA-encoded PD-L1 to send a tolerizing signal to immune cells

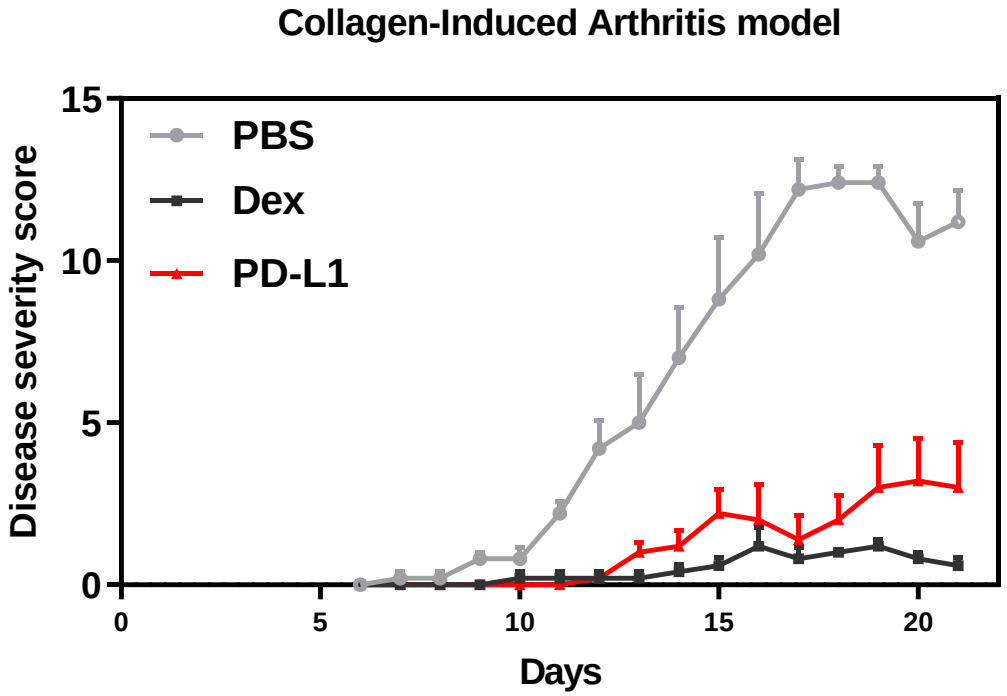
- We intend to influence myeloid cells to provide additional co-inhibitory signals in the context of immune synapses by augmenting endogenous expression of PD-L1
- We believe that this tolerizing signal to lymphocytes may limit autoreactivity in the context of ongoing autoimmune pathology without severe and global suppression of the immune system
- Employs intravenous administration of the same LNP as our mRNA-encoded antibody, mRNA-1944
- First indication intended to be autoimmune hepatitis, a compelling unmet need



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PD-L1 (mRNA-6981)

Preclinical data – demonstrates disease modification in arthritis model



Animals treated with PD-L1 mRNA presented with consistently less severe disease

Rats were given a single injection of chicken collagen type II in incomplete Freund's adjuvant in order to induce chronic arthritis-like symptoms. mRNA-6981 dosed subcutaneously four times per week and compared to a negative PBS control and a positive control of daily high dose dexamethasone (Dex). Arthritis-like symptoms included paw swelling and joint rigidity, which were scored as a proxy for disease severity.

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