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PD-L1 (mRNA-6981)

Last program update: February 26, 2020

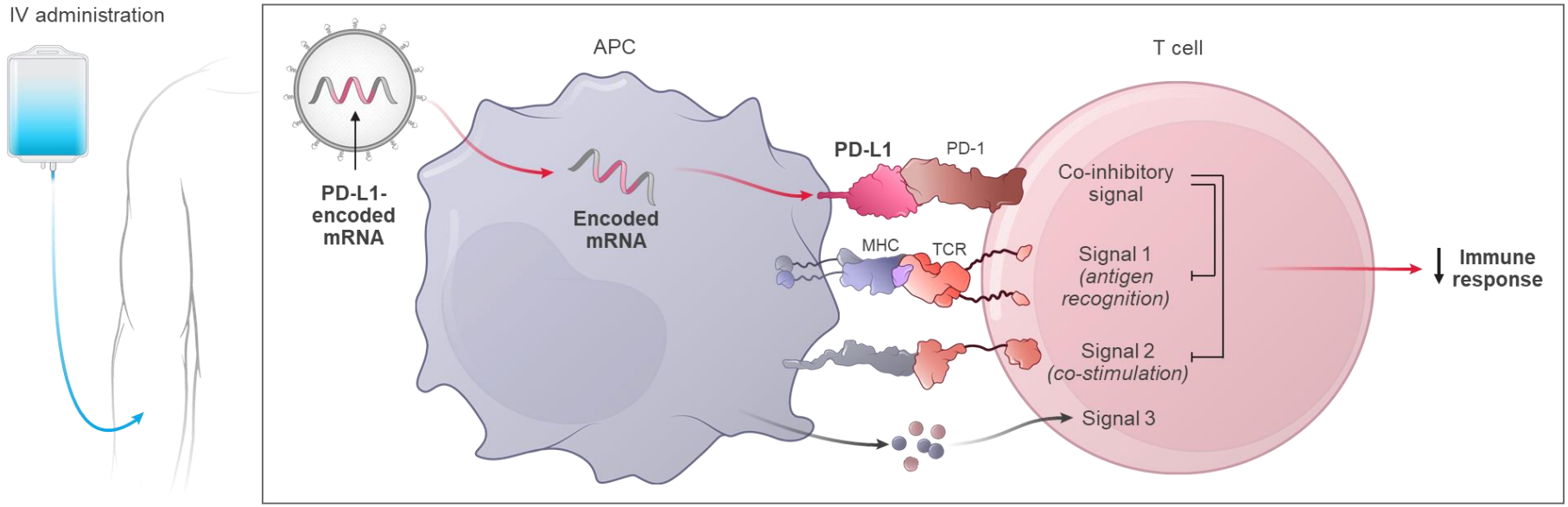
Modality	ID #	Program *Indication*	Preclinical development	Phase 1	Phase 2	Phase 3 and commercial	Moderna rights
Systemic secreted & cell surface therapeutics	mRNA-1944	Antibody against Chikungunya virus					Worldwide *DARPA funded*
	AZD7970	Relaxin *Heart failure*					50-50 U.S. profit sharing; AZ to pay royalties on ex-U.S. sales
	mRNA-3630	α-GAL *Fabry disease*					Worldwide
	mRNA-6981	PD-L1 *Autoimmune hepatitis*					Worldwide
	mRNA-6231	IL-2 *Autoimmune disorders*					Worldwide

mRNA-6981 announced in January 2020

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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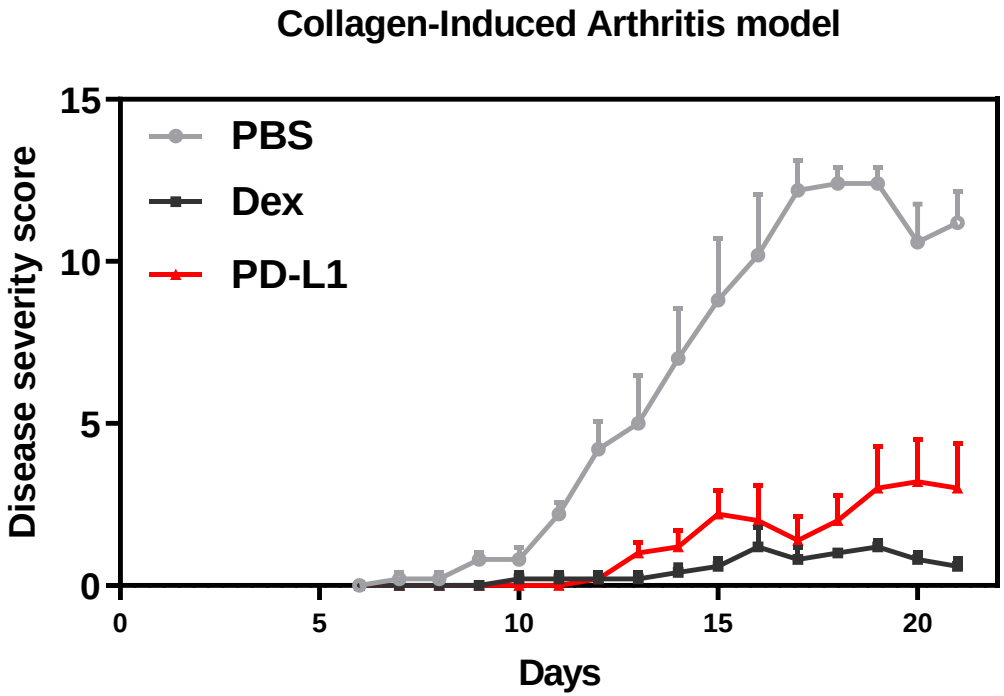
Preclinical data – demonstrates disease modification in arthritis model



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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