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IL-2 mutein (mRNA-6231)

Last program update: February 26, 2020

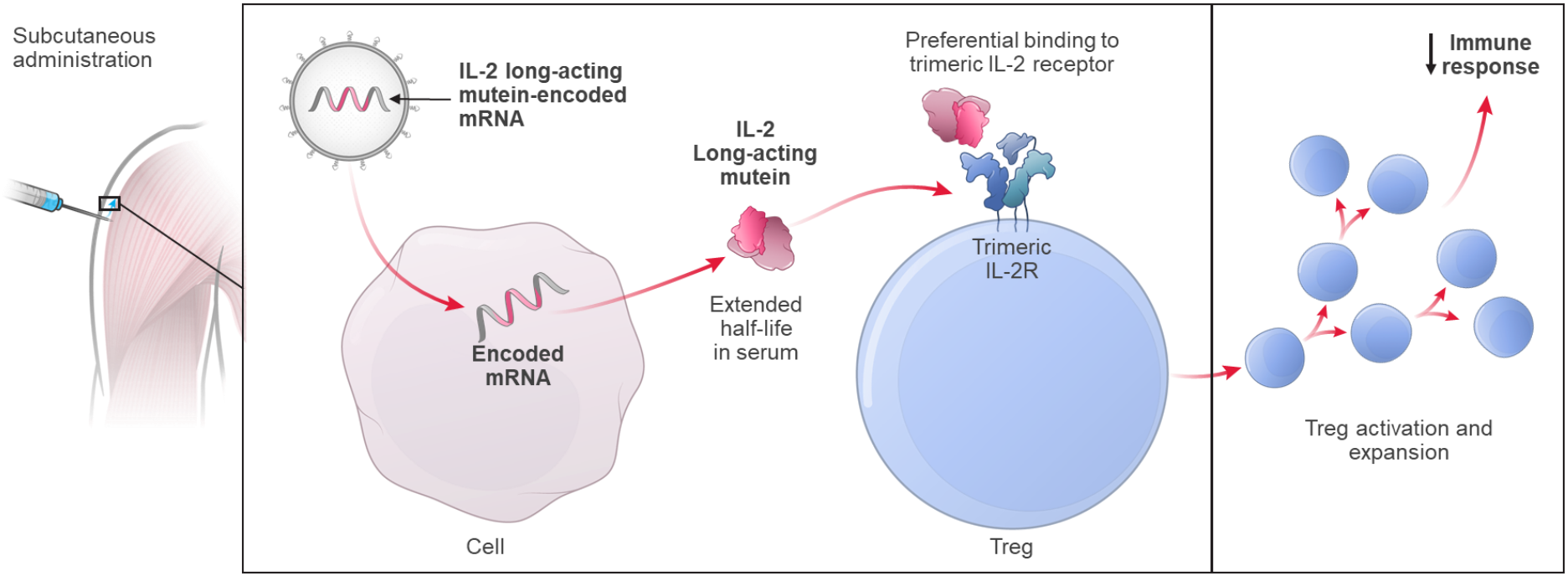
Modality	ID #	Program *Indication*	Preclinical development	Phase 1	Phase 2	Phase 3 and commercial	Moderna rights
Systemic secreted & cell surface therapeutics	mRNA-1944	Antibody against Chikungunya virus					Worldwide *DARPA funded*
	AZD7970	Relaxin *Heart failure*					50-50 U.S. profit sharing; AZ to 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-6231 announced in January 2020

IL-2 mutein (mRNA-6231)

mRNA-encoded IL-2 modified for the expansion of regulatory T cells

- Modified IL-2 is longer acting and more selective for the high affinity IL-2 receptor which is expressed mainly by regulatory T cells
- First intended subcutaneous administration of the LNP successfully used in a clinical trial for our mRNA-encoded antibody, mRNA-1944
- Recombinant IL-2 based therapeutics are being clinically evaluated for a wide range of autoimmune conditions



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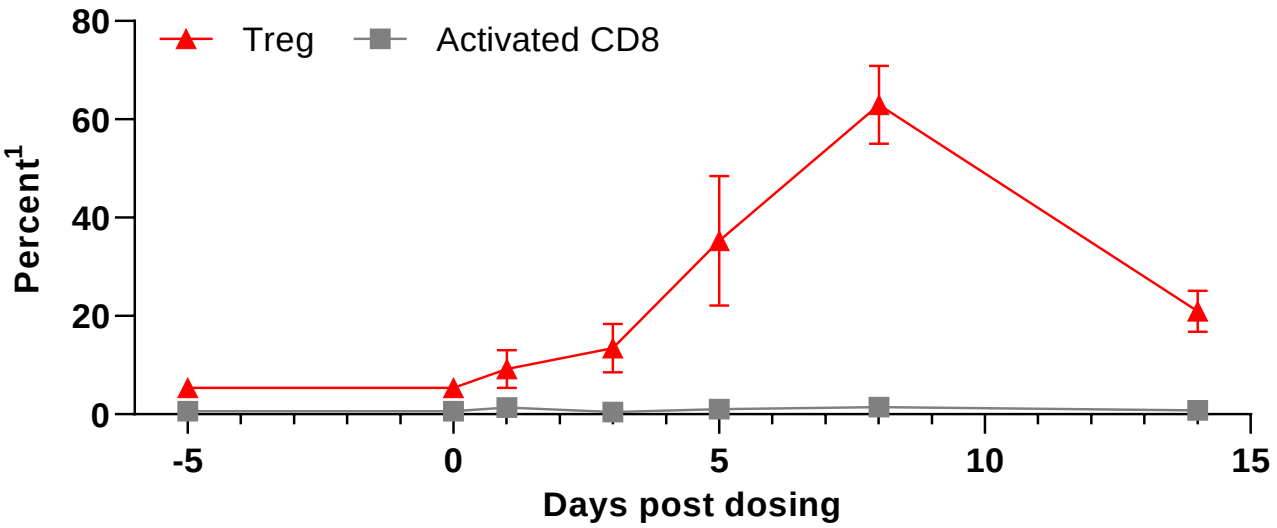
Preclinical data – demonstrates preferential expansion of Treg in NHP



- Treg increased ~12 fold at their peak[2]
- Activated CD8+ T cells did not significantly increase over baseline[3]

NHP were dosed subcutaneously with a single dose of mRNA-6231 and T cells in the peripheral blood were monitored on days 1, 3, 5, 8, and 14

1. Percent either Treg or activated CD8 out of total CD4+ or CD8+ respectively
2. Treg defined as CD3+CD4+Foxp3+, increase represents an average over 4 animals, maximum is day 8 post-dosing
3. Activated CD8+ defined as CD3+CD8+ CD25+

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