eTheRNA immunotherapies

International Cancer Cluster Showcase, Philadelphia

v1.0; June 2019

eTheRNA immunotherapies
Boosting the human immune system to fight diseases

eTheRNA: Origins and status

- Founded in VUB, Brussels
- First-in-class mRNA platforms with two product development streams:
  - Immuno-stimulatory therapeutics
  - Therapeutics modifying the tumour micro-environment
- Completed FIH translational study for intranodal delivery showing safety and immune responses – basis for next study in IN combination study (with pembrolizumab)
- Generated unprecedented pre-clinical data with mRNA in a proprietary formulation for IV administration transitioning into clinical development in Series B. The IV platform can form a basis for multiple partnerships
- Early data support the combination of IV TriMix mRNA with neoantigens
- Early *in vivo* data for a novel mRNA TME-modifying therapeutic with intra-tumoural delivery
- Established in house CMC capability with full control over GMP manufacturing – no development bottleneck

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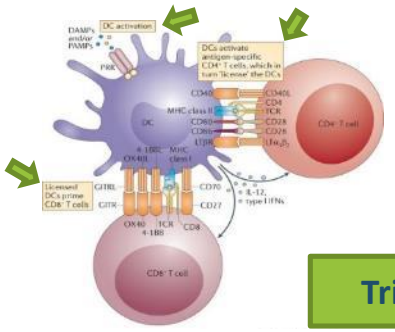
eTheRNA platforms and pipeline

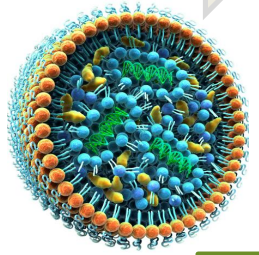
Platforms

Ex vivo — Loco-regional (IN/IT) — Systemic

Route of administration



TriMix



Immuno TriMix

- Trimix
- LNP
- Antigens or therapeutic agents

Products

	Indication	Stage	Mode	Administration	Commercial Route
Oncology	Metastatic melanoma	Phase I/II	Immuno-stimulation	Loco-regional (IN)	Orphan disease Partner late
	HNSCC	Preclinical	Immuno-stimulation	Systemic (IV)	Partner at preclinical
	Undisclosed	Lead opt'n	TME modification	Loco-regional (IT)	Partner at Phase II
	CNS	Discovery	TME modification	Loco-regional (IT)	Partner at Phase II
Non - oncology	Infectious disease	Discovery	Immuno-stimulation	Systemic (IV)	Co-develop/early partner
	Autoimmune	Discovery	Immuno-stimulation	To be determined	Co-develop/early partner

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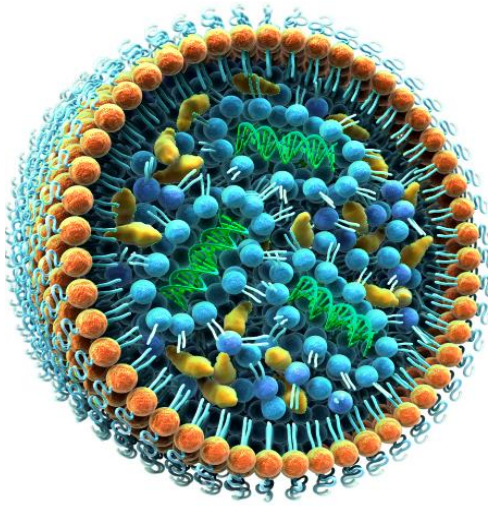
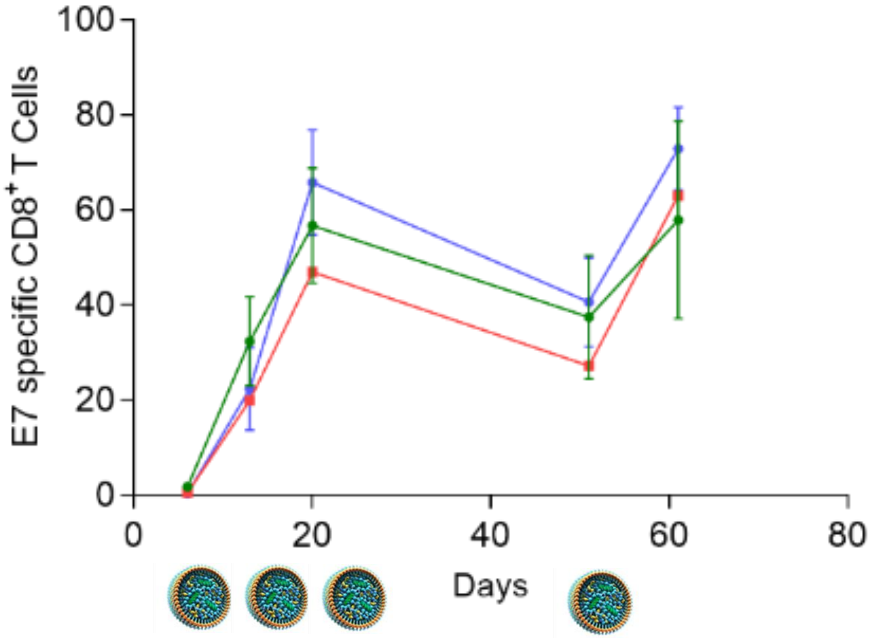
Immuno-stimulatory therapeutics

Product	Discovery	Preclinical	Preclinical IND enabling	Phase I/II
E011-MEL (IN) =>EI-101	Metastatic melanoma: Combo with aPD1			
ETR-IV-01	HNSCC			



API comprises:
- TriMix
- Interchangeable TAAs or neoantigens
- Proprietary LNP

Key outcomes:
- Anti-tumour effects via:
  - DC activation
  - T cell proliferation
- Boostable response
- Immune memory



- **Unprecedented magnitude** of antigen specific T cell responses (>60% of CD8 T cells are antigen specific) after priming
- **Extended contraction phase**
- **High % multifunctional T cells** (IFN-g/TNF-a)
- **Stunning recall response** – IV formulation vaccines can be boosted

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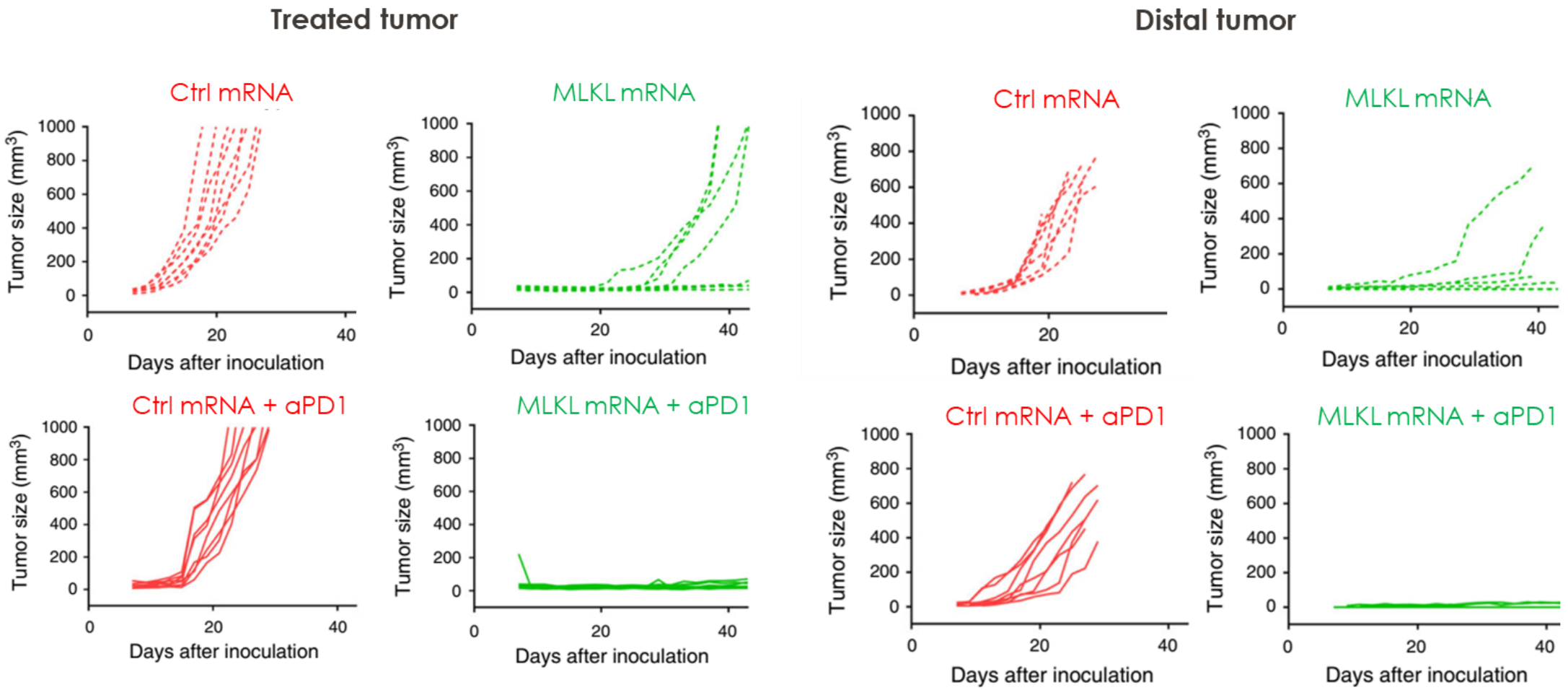
MLKL exhibits abscopal effects and synergizes with aPD1 therapy



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Mid-term deliverables

Raising Series B will deliver the following by 2021:

- Completion of Phase I/II, intranodal administration in metastatic melanoma
- Completion of FIH Phase I/II of proprietary formulation, IV administered immuno-stimulant TriMix and TAAs in HNSCC
- IND ready second IV product
- Possible partnering in IV platform
- IND ready TME modifying IT delivered mRNA
- Continuation of mRNA platform extension and IP generation

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