



Boosting the human immune system
to fight diseases

- ° July 2013
- Discovery & development of mRNA immunotherapies based on research of the VUB Laboratory for Molecular & Cellular Therapy (LMCT)

Milestones

- **10 July 2014:** exclusive license from the VUB on the TriMix Technology and establishment of research collaboration with VUB
- **21 March 2016:** Closing of Series A financing - eTheRNA secures EUR 24 million to develop mRNA-based immunotherapies

eTheRNA Immunotherapies NV

Galileilaan 19 - 2845 Niel | Belgium

Dirk Reyn (CEO)
Dirk.Reyn@etherna.be

Kris Thielemans (CSO)
Kris.Thielemans@etherna.be

[T] +32 (3) 369 17 40
[E] info@etherna.be
[W] www.etherna.be



Developing mRNA immunotherapies

eTheRNA NV is a spin-off company of the VUB established under the leadership of Prof. Kris Thielemans, head of the **VUB Laboratory for Molecular and Cellular Therapy (LMCT)** that is focusing on the development of mRNA immunotherapies. VUB granted eTheRNA the worldwide exclusive license rights for the **TriMix technology**.

TriMix technology

The TriMix technology is built around a unique IP-protected mix of three plasmid-derived mRNA strands (coding for CD40L, CD70 and constitutive active TLR4).

This mix of mRNA-strands mimics the process to activate dendritic cells (DC) for stimulating the immune system in the most potent and physiological way. When combined with disease specific antigens, the TriMix product also mimics the process to educate dendritic cells accordingly.

TriMix can be used to prevent and treat cancer, infectious diseases, immune diseases and allergies. The TriMix technology is suitable for both *ex vivo* and *in vivo* applications, which represents its most distinguishing characteristic.

For *ex vivo* application, autologous dendritic cells are matured and educated in test tubes and subsequently injected into patients. For *in vivo* application, the TriMix solution – either alone or in combination with antigens – is directly injected into the patients, and interacts with the dendritic cells present in the body.

The *ex vivo*, autologous TriMix-DC product – in combination with tumor associated

antigens encoding mRNA - has been validated in preclinical models in mice, as well as in four clinical studies: two phase I studies and two phase IIa studies in melanoma patients - as stand-alone and in combination with ipilimumab. Studies (in collaboration with Prof. Bart Neyns - UZ-VUB) in melanoma patients demonstrated benefits for several parameters: 1-year survival, best overall response, disease control and progression free survival.

Preclinical data for the *in vivo* TriMix product are supportive for further clinical development of the TriMix technology as a unique off-the-shelf vaccine for intra-nodal, intra-dermal and intra-tumor application. Development work by eTheRNA is ongoing in Melanoma, Triple Negative Breast cancer and infectious disease. Other studies in collaboration with VUB are ongoing in cancer (HCC, multiple myeloma) and non-cancer (HIV, HPV) indications.

eTheRNA

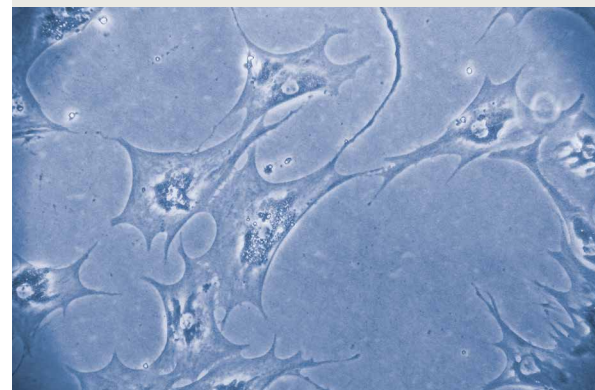
eTheRNA has secured the financial resources required to initiate the clinical validation of the *in vivo* off-the-shelf TriMix product - for intra-nodal, intra-dermal and intra-tumor applications, to continue the development of the *ex vivo* TriMix product and to optimize its existing mRNA manufacturing activities.

eTheRNA has established a preferential research collaboration with the VUB, in particular with the LMCT team of Prof. Kris Thielemans and with the UZ-VUB team of Prof. Bart Neyns, as well as other departments within the UZ-VUB.

eTheRNA's focus

Treatment of:

- cancer with focus on melanoma and Triple Negative Breast cancer
- viral infections with focus on HPV and HepB



"The TriMix technology platform allows for multiple approaches: *ex vivo* - maturation and education of DCs in the test tube and subsequent injection of DCs in patients - and *in vivo* - direct injection in patients of TriMix alone or in combination with antigens."

Dirk Reyn, CEO



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Interface

Knowledge & Technology Transfer Interface
Vrije Universiteit Brussel • Pleinlaan 2 • B-1050 Brussel • Belgium
[E] techtransfer@vub.ac.be • [W] www.vubtechtransfer.be • [T] +32 (0)2 629 22 07



Vrije
Universiteit
Brussel