exploRNA

Spin-off from UW

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ExploRNA's Scientific Team is a group of experienced researchers in mRNA chemistry and immuno-oncology

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Business strategy

mRNA technology has emerged as both a disruptive and highly promising new class of medicines

DNA

DNA stores instructions for proteins in the nucleus

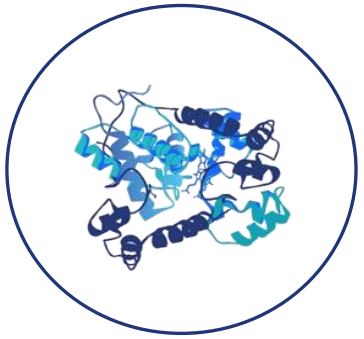
Transcription

mRNA

mRNA is a temporary set of instructions for cells to make proteins

Translation

Protein



Proteins form the basis of life by performing the functions required by every cell

Using mRNA as a therapeutic is a cutting-edge approach

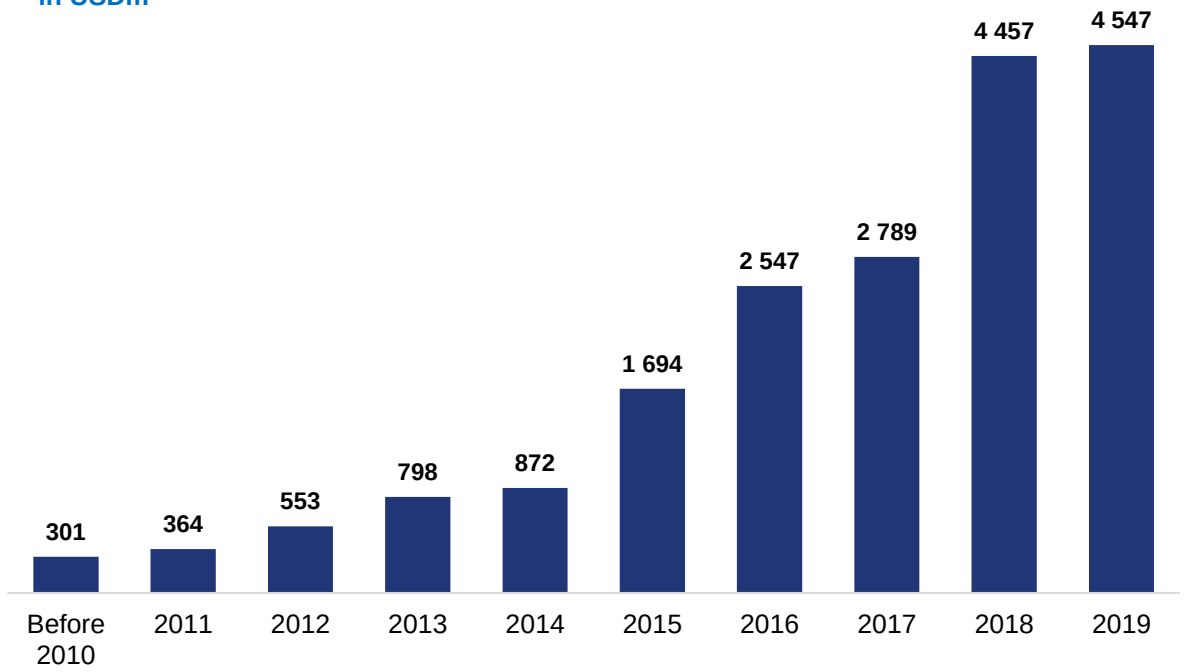
mRNA based drugs deliver a defined genetic message into the cells to produce any kind of protein

Ability to set instruction for cells allows mRNA therapeutics to be used for any disease

mRNA drugs have the potential to transform standards of drug discovery and manufacturing

Given the broad potential applications, mRNA has captured significant interest of leading biotech investors

Cumulative investments in mRNA sector
in USDm



- Novel mRNA technology is presently **one of the most promising innovations**, with a wide range of applications
- Rapidly growing investments in mRNA technology lead to the establishment, in a relatively short period of time, of **multibillion dollars ventures** such as Moderna, BioNTech or CureVac
- Given the significant potential of the technology platform, and broad applications, many **'Big-Pharma' players are aggressively competing to find new investment** targets in mRNA therapeutics
- In 2018, mRNA companies lead in the size of fundraised capital (Moderna – **USD 625m**, BioNTech **USD 270m**). Moderna as well conducted a successful IPO on NASDAQ with a valuation of **USD 7.5bn**

Leading Investors in mRNA sector

AstraZeneca · Bayer · Boehringer Ingelheim · Lilly · Merck · Pfizer · Roche · Sanofi · Vertex

Broad application of mRNA platforms are a key factor in signing partnership agreements before Phase 1

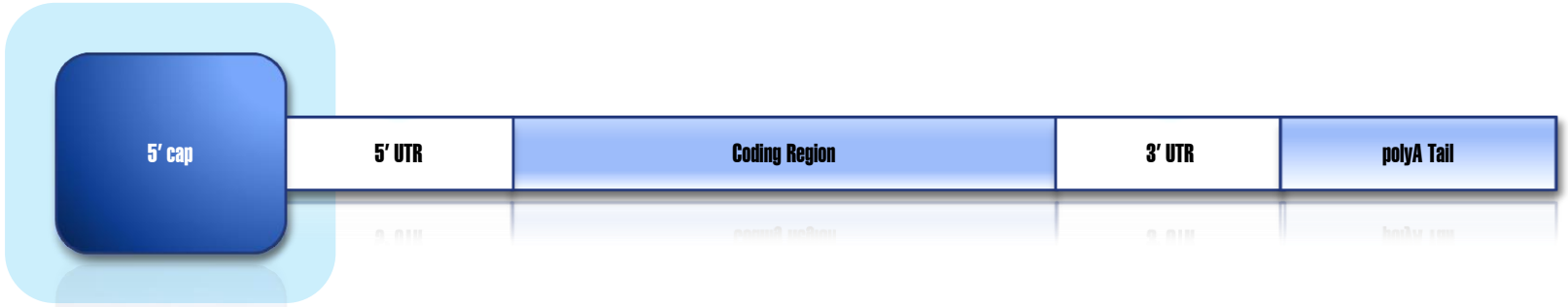
- Given the wide range of potential mRNA applications, ‘Big-Pharma’ companies have **evolved internal strategies** and focused their BD&L activities on **trying to license entire technology platforms,** versus for only selected therapeutic indications
- Most leading mRNA companies are **aiming to establish broad platforms** that will extend R&D programs into multiple therapeutic directions
- Technology **platforms have the potential to accelerates R&D and commercialization** of new drug candidates
- mRNA technology platforms can **strengthen a company’s value proposition**, **de-risk** R&D pipelines and **boost the enterprise valuation**
- ‘Big-Pharma’ players are not only looking for a higher valuation but also want to **‘close’ the market for competitors** by signing exclusive licensing agreements

Selected licensing agreements in mRNA therapeutics

mRNA company	Indication	Licensees	Deal Timing
moderna	Cancer Infectious diseases Rare diseases	MERCK, VERTEX, AstraZeneca	Pre-Phase I
BIONTECH	Cancer Infectious diseases Rare diseases	BAYER, Lilly, Pfizer, Roche, SANOFI	Pre-Phase I
CUREVAC	Cancer vaccines	Lilly, Boehringer Ingelheim	Pre-Phase I
TranslateBIO	Infectious diseases	SANOFI PASTEUR	Pre-Phase I
ethris	Respiratory diseases	AstraZeneca, MedImmune	Pre-Phase I

Adaptation of mRNA as a potential therapeutic requires modifications

mRNA Structure



Modification of the 5’ cap plays an essential role in adapting mRNA as a potential therapeutic

mRNA as a therapeutic must first be modified to have extended stability, half life, and translational efficiency

The 5’ cap has a vital role in recognizing and binding to the ribosome

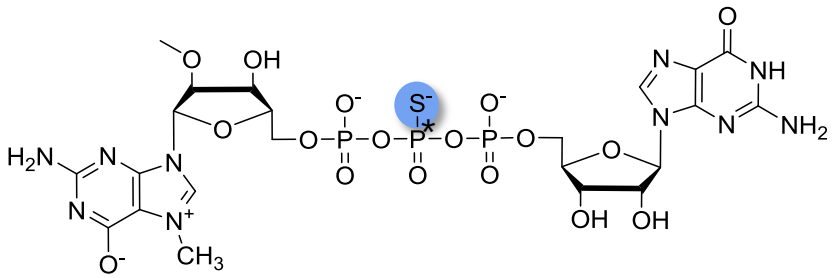
5’ mRNA caps can be used to increase the stability of mRNA and improve its translational properties

Novel capping technologies enabled mRNA therapeutics to advance to the clinic

1st generation cap modification was a significant breakthrough and the foundation for BioNtech's mRNA platform

Prof. Jemielity and his team developed 1st generation cap analogs (*β-S-ARCA*)

- Professor Jemielity's team of scientists at the University of Warsaw, are renowed international experts in mRNA chemistry and mRNA therapeutics
- The team developed the 1st generation cap analogs (*β-S-ARCA*) characterized by high stability and efficient translation of desirable proteins *in vivo*



β-S-ARCA cap analogs were licensed to BioNTech in 2011

- 1st generation mRNA cap analogs became the base for BioNTech's mRNA pipeline
- In the following years BioNTech went on to sublicense the mRNA technology to "big-Pharma" partners such as Sanofi, Roche and Pfizer
- BioNTech have raised more than $1b in total equity funding
- The technology is now under investigation in the clinic

BIONTECH Innovative Manufacturing Services

BioNTech licensees

Pfizer Roche SANOFI

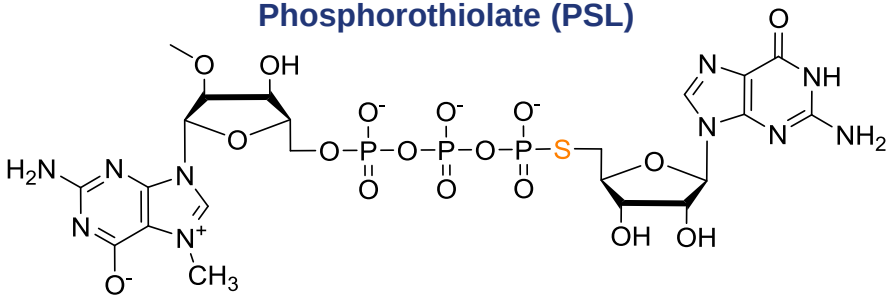
ExploRNA has developed an improved "*next generation*" cap structure

Next generation has significant advantages versus earlier research

1st generation		Next generation
	More time & cost-efficient mRNA synthesis pathway	Improved vs 1st generation
	Ability to be stored for long periods of time	Improved vs 1st generation
	Easier to upscale	Improved vs 1st generation
	Equivalent or better translation efficiency in vitro and in living cells	As good as or better than 1st generation
	Increased mRNA half-life in vivo	As good as or better than 1st generation
	Higher stability (resistance to Dcp2 de-capping)	As good as or better than 1st generation
	Efficient expression of desirable proteins in vivo	As good as or better than 1st generation

Patent protected next generation cap modifications(1)

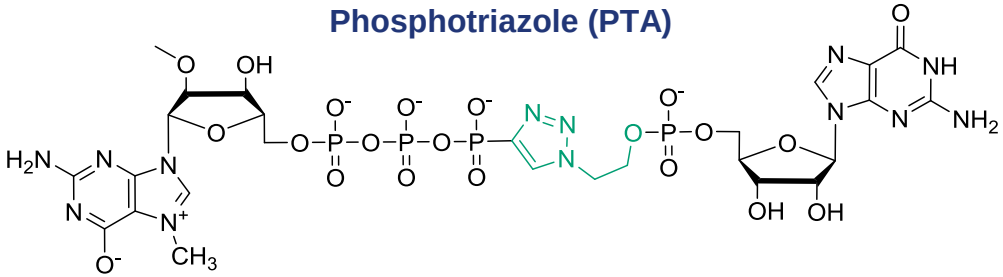
Phosphorothiolate (PSL)



5'-Phosphorothiolate Dinucleotide Cap Analogues: Reagents for Messenger RNA Modification and Potent Small-Molecular Inhibitors of Decapping Enzymes

Journal of the American Chemical Society, April 2018

Phosphotriazole (PTA)



A novel route for preparing 5' cap mimics and capped RNAs: phosphate-modified cap analogues obtained via click chemistry

Chemical Science, January 2017

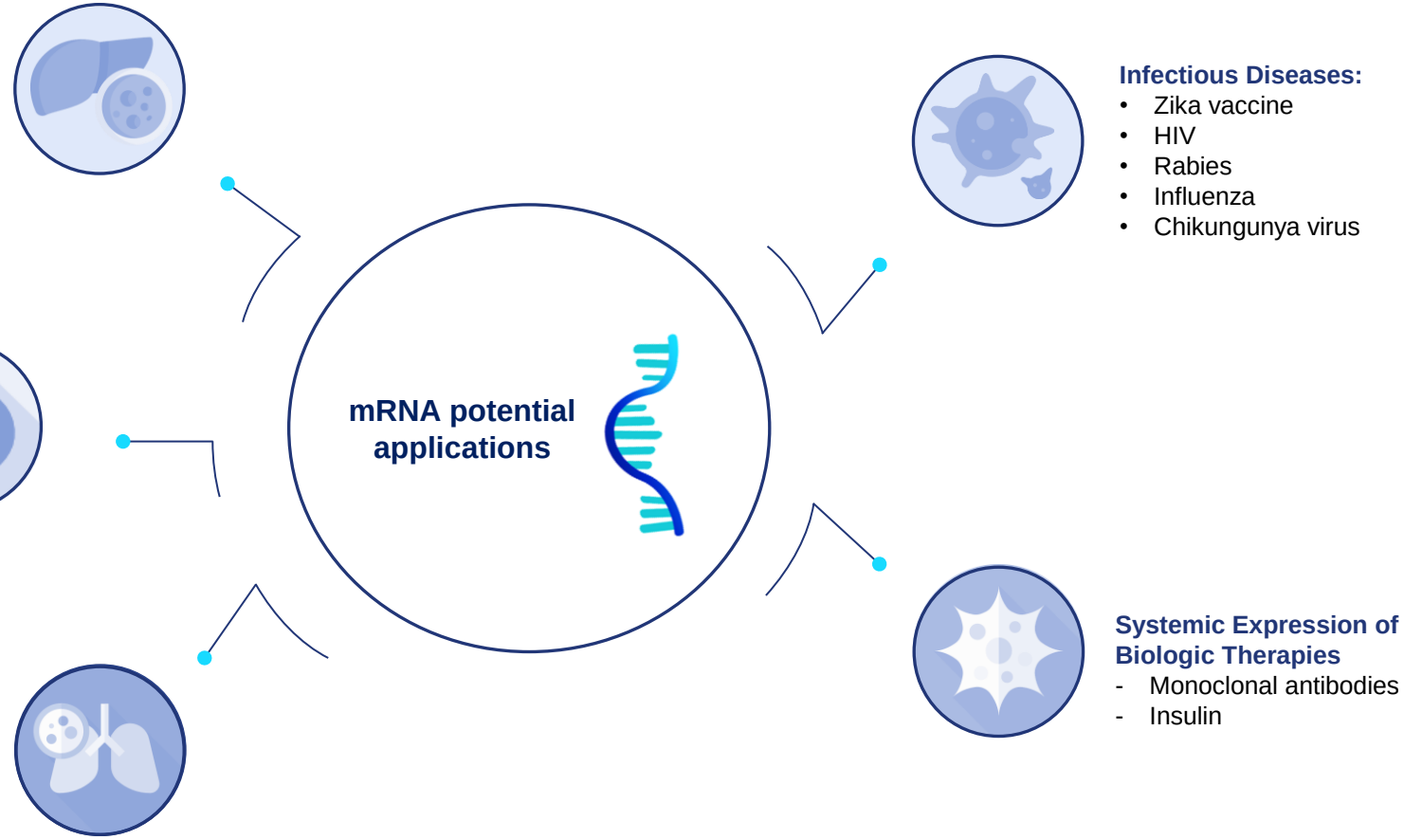
(1) ExploRNA exclusively licensed 2 patents from the University of Warsaw (patent application numbers: PCT/IB2017/050447 and PCT/IB2017/054221)

Modified mRNA has the potential for a wide range of applications which represents a significant market opportunity

Cancer Immunotherapies[(1)]:
- Solid tumors / PCV
- Neo-antigen vaccines
- Pro-immunogenic cytokines

Autoimmune Diseases[(1)]:
- Multiple Sclerosis
- Expression of cytokines to drive immune response mediated by regulatory T cells

Rare Diseases:
- Cystic Fibrosis
- Heptatic Monogenic Rare diseases



Infectious Diseases:
- Zika vaccine
- HIV
- Rabies
- Influenza
- Chikungunya virus

Systemic Expression of Biologic Therapies
- Monoclonal antibodies
- Insulin

mRNA has the potential to treat any disease where expression of protein(s) will drive the alleviation of the symptoms or causes of the disease

(1) Current ExploRNA's therapeutic focus

ExploRNA’s research and development strategy

Therapies based on known targets for mRNA

- Low risk of entry strategy, whereby ExploRNA will be fast followers to therapies developed by market leaders.
- Targets are selected based on a large potential market size to allow for multiple therapies.

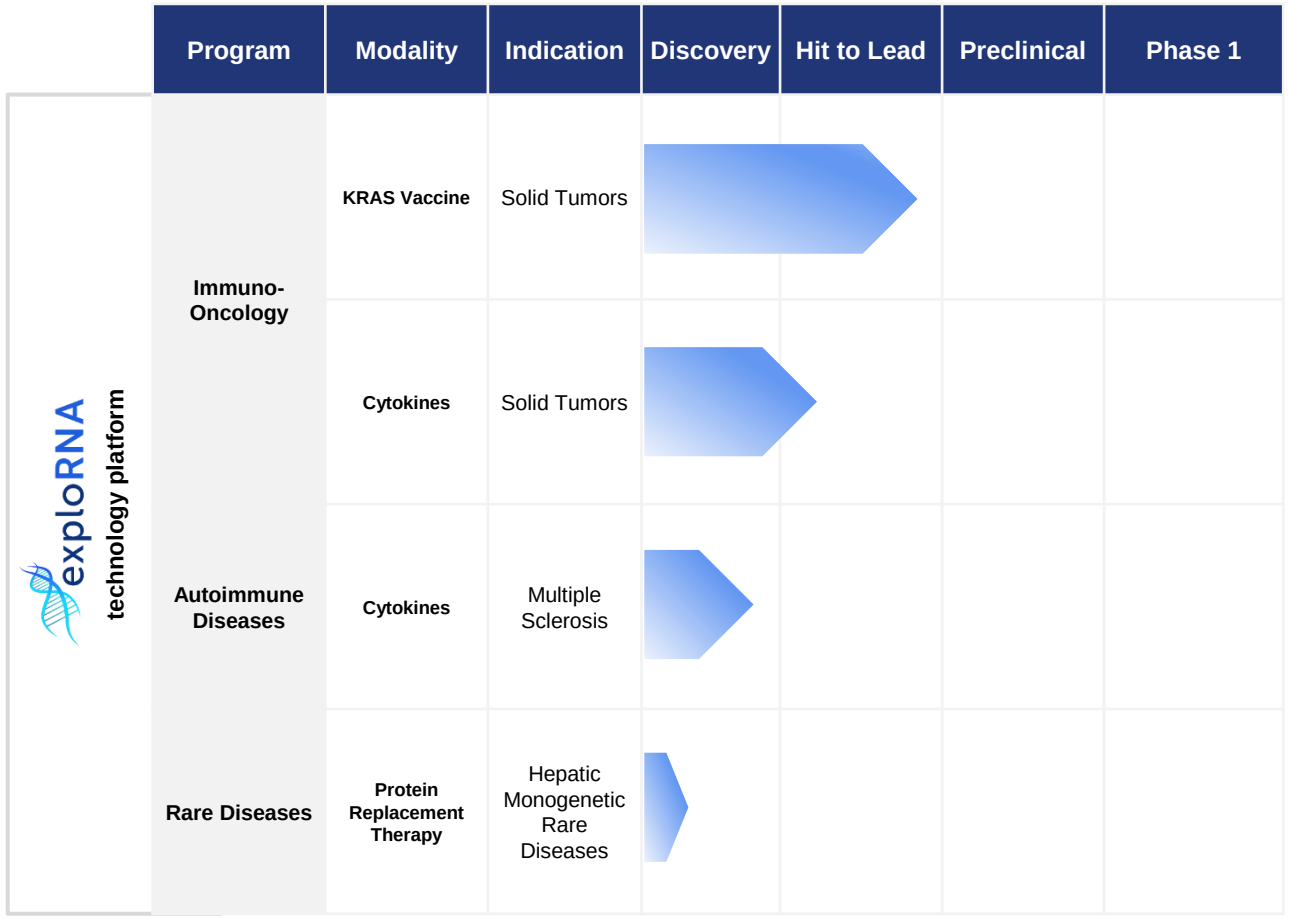
Therapies based on known disease targets

- Therapies based on known disease targets that are not yet being considered by competitor mRNA companies.
- mRNA would allow for improved efficacy and cost efficiency over current accepted therapies.
- Examples include the targeting of Treg cell population for the treatment of multiple sclerosis.

Therapies that are designed to tackle novel targets

- Therapies that are designed to tackle novel targets in diseases with high unmet need.
- Once the applicability of mRNA as a therapeutic has been demonstrated novel areas can be entered.
- Targets will be isolated from collaboration with Polish and International Research Organizations.

ExploRNA is developing a novel therapeutics pipeline based on their proprietary "*next generation*" mRNA cap technology

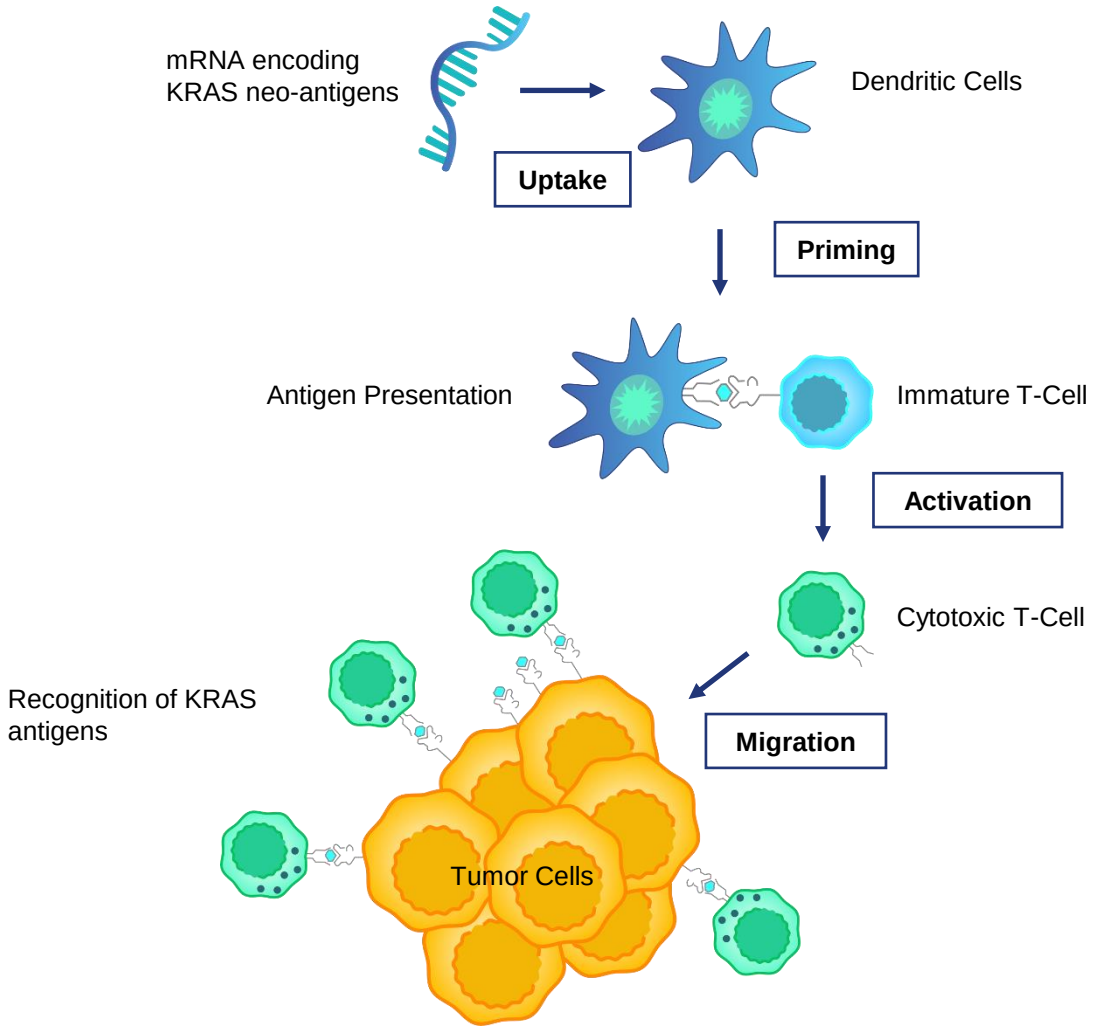


- mRNA **technology platform** has a **significant potential** in any indication where protein expression would lead to the alleviation of the underlying cause of a disease
- ExploRNA's key development areas include **immuno-oncology** due to its transformative potential, and **autoimmune and rare diseases** due to the high unmet needs and strong market potential
- In immuno-oncology, ExploRNA will target **tumor specific antigen vaccines** and **therapeutics that promote the over-expression of cytokines** in the tumor microenvironment to initiate the attack of cancer cells by the immune system
- **The mechanism of action** of ExploRNA's approach is **unique** to any therapeutic that is currently on the market and provides significant potential for patients that do not respond to current medications

ExploRNA's lead program is an anti-KRAS therapeutic vaccine

Anti-Kras Vaccine

- Mutations in the **KRAS protein** are present in approximately **22%** of cancers
- KRAS mutants are particularly prevalent in **non-small cell lung cancer (NSCLC), colorectal cancer (CRC) and pancreatic cancer**
- **90% of patients with pancreatic cancer** have KRAS mutations
- KRAS mutants are linked to **poor survival outcomes** and a lack of response to current front-line treatments
- No small molecule inhibitors have been successfully developed for KRAS and it is considered the biggest **"undruggable"** target in oncology
- A KRAS vaccine "teaches" the immune system to detect KRAS mutants on cancer cells and target these cells for removal
- mRNA allows for rapid uptake of different KRAS neo-antigens by dendritic cells allowing for a multiple faceted response to different KRAS mutants present in different subsets of patients



ExploRNA

- **ExploRNA Therapeutics** is a privately owned “spin-off” company from the **University of Warsaw** and is led by **Professor Jacek Jemielity**, Head of the Bioorganic Chemistry Laboratory at the Center of New Technologies (CeNT) at the University of Warsaw

- ExploRNA has **exclusively licensed** intellectual property developed by Professor Jemielity’s group on synthetic 5’ caps for mRNA that stabilize the nucleic acid enabling its application as a therapeutic

- ExploRNA’s **two lead development programs** will focus on **tumor specific antigen vaccines** and the **expression of cytokines** to promote cytotoxic T cells to eliminate tumor growth

- ExploRNA’s **next generation** mRNA is expected to have **significantly improved** benefits in stability, translational efficiency, and cost of synthesis

- ExploRNA has recently ExploRNA’s mRNA therapeutics will compete in a **multi-billion global marketplace** that is **growing** at approximately **30%** per year