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Cancer Vaccine Industry

Overview

Q4 2022

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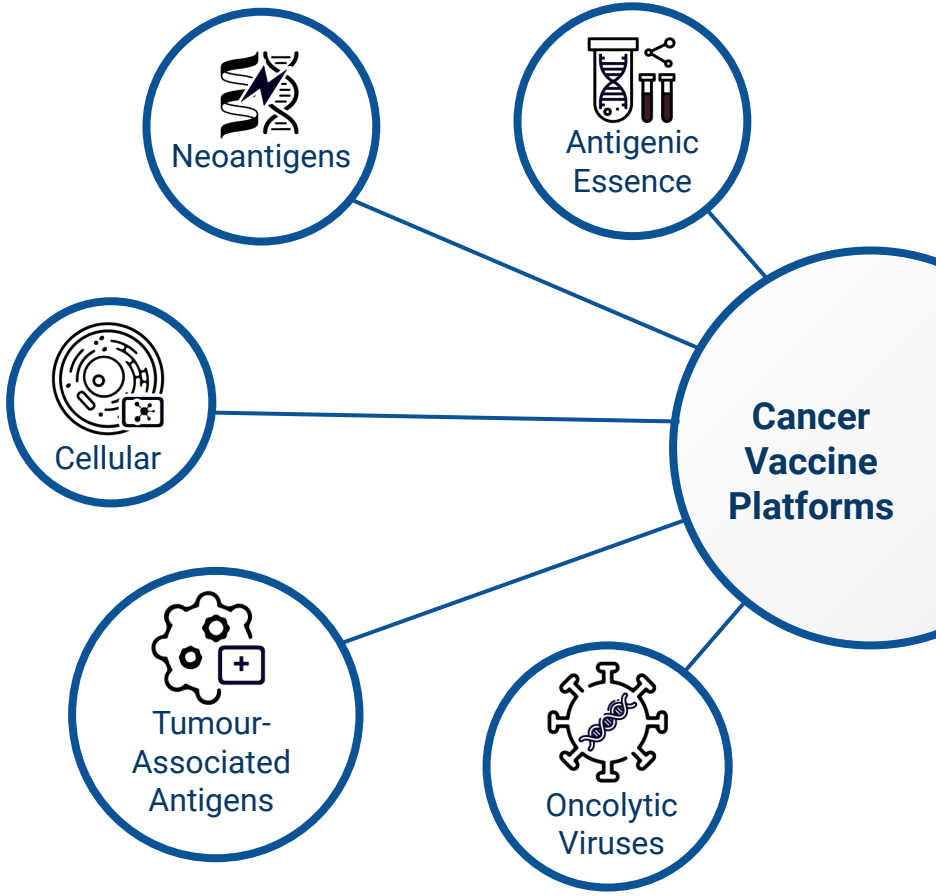
Intro: What is a Cancer Vaccine?

The most powerful weapon against malignancies can be hidden inside the host human body, and it is called **immune system**. Cancer mechanisms usually trick our immune system, but a proper therapy can turn our immunity back against the tumour.

This is the aim of **cancer vaccination — to activate host immunity cells to destroy the tumour cells.**

A number of **FDA-approved vaccines** are cancer prevention vaccines, proving that cancer vaccines are more than just a pipe dream.

Researchers nowadays are developing vaccines with the goal of reliably and effectively inducing the immune system to target cancer cells. Additionally, they are looking into additional strategies to improve the immune system's response to malignant cells.



Cancer Vaccine Platforms Classification

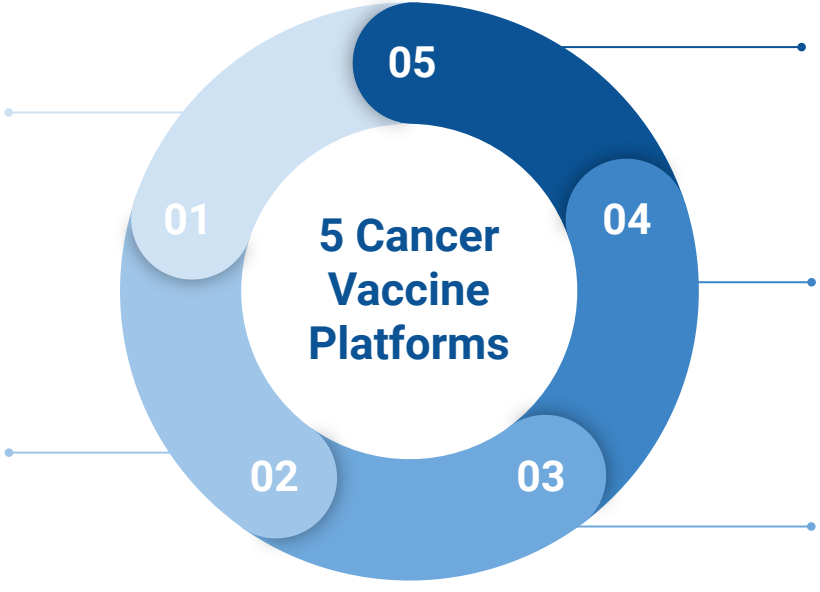
There are multiple platforms developed to obtain cancer vaccines. In this report we are going to discuss **five such platforms**, which serve as a basement for vaccines creation. Some of these cancer vaccine platforms **overlap and evolve out of each other** while other still have some unique distinguishable features, which was a reason for suggested classification.

Neoantigen Platform

Developing vaccines based on specific class of antigens which include those created by tumour viruses that have integrated into the genome and those produced by mutant proteins. They are abundantly expressed only in cancer cells and have a high immunogenicity and tumour heterogeneity.

Tumour-Associated Antigens Platform

Developing vaccines based on antigens that are inappropriately expressed by cancer cells. The antigens are present in both healthy and cancerous cells, with the only difference being the degree of exposure or presentation by the cell.



Oncolytic viruses platform

Developing vaccines through viruses modified to target cancer cells and enhance the immune response to completely destroy the tumour.

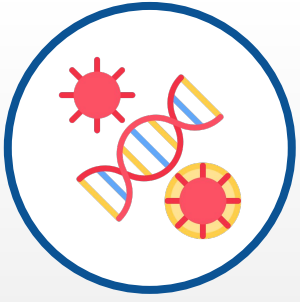
Antigenic Essence Platform

Developing vaccines by using surface-presented antigens, recognised by human immune system.

Cellular Platform

Developing vaccines by considering all cellular antigens, including tumour-associated antigens (TAA) and neoantigens. Whole-cell platforms, as opposed to TAA or neoantigen platforms, contain both recognised and uncharacterised TAA and tumour-specific antigens TSA.

Intro: Where is Cancer Vaccination Right Now?



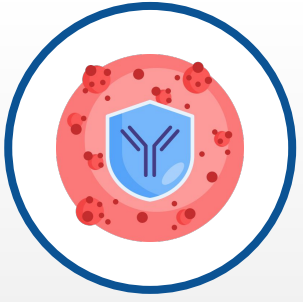
We learnt how to target tumours through their unique mutations – **neoantigens.**

To prevent **tumour escape,** we need to target multiple antigens on the tumour cell.

cytotoxic CD8+ T-cells

We targeted **cytotoxic CD8+ T-cells** to kill the cancer cells.

We need to engage **both CD8+ and memory CD4+ T-cells** to prolongate the effect.



We found out that the **tumour lysates** can activate the immune response to cancer.

Off-tumour effects became a severe reason for cellular damage, so scientists are working to decrease them.

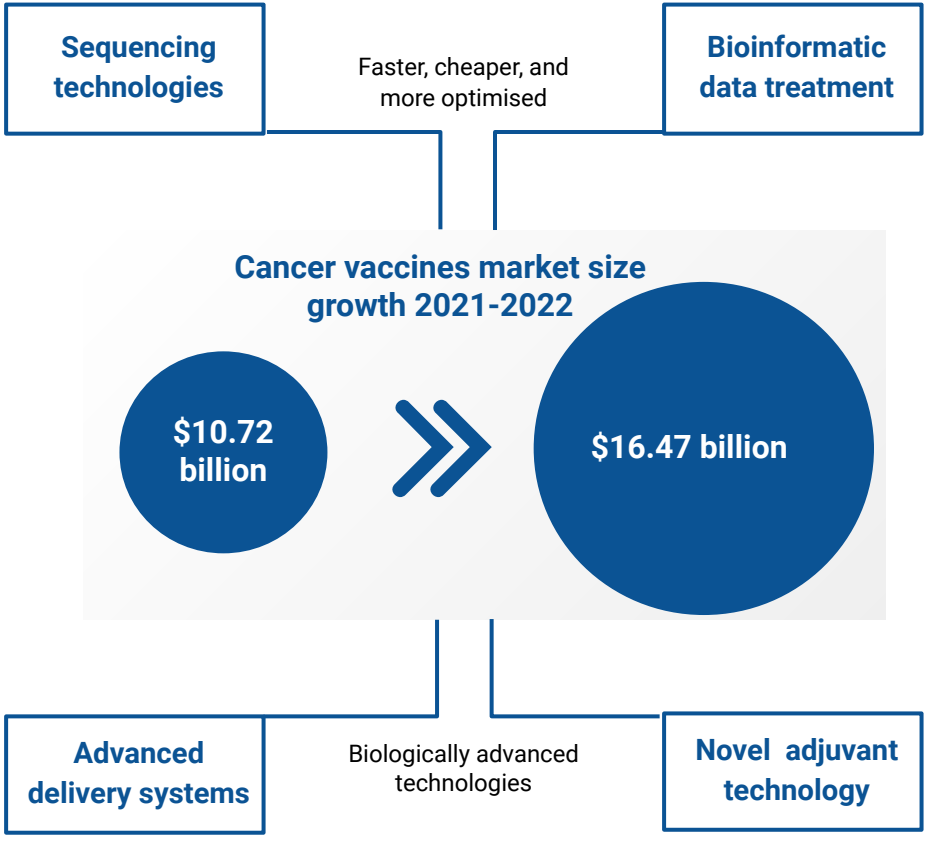
Cancer Vaccine Industry

At first, cancer vaccines did not succeed: the enthusiasm and interest towards this technology dropped after seeing the high level of adverse effects versus low efficacy.

However, with the development of **sequencing technologies**, innovative **delivery systems, bioinformatic data treatment strategies,** and vaccine **adjuvants**, cancer vaccines have more and more prominent chances to become deeply integrated into the market.

In 2021, the **market size** of cancer vaccines was estimated as US$10.72 billion, and it has reached **$16.47 billion in 2022.**

Considering this tendency, it is reasonable to say that cancer vaccines start forming a **separate branch of industry.**



Cancer Vaccines by Antigen Type

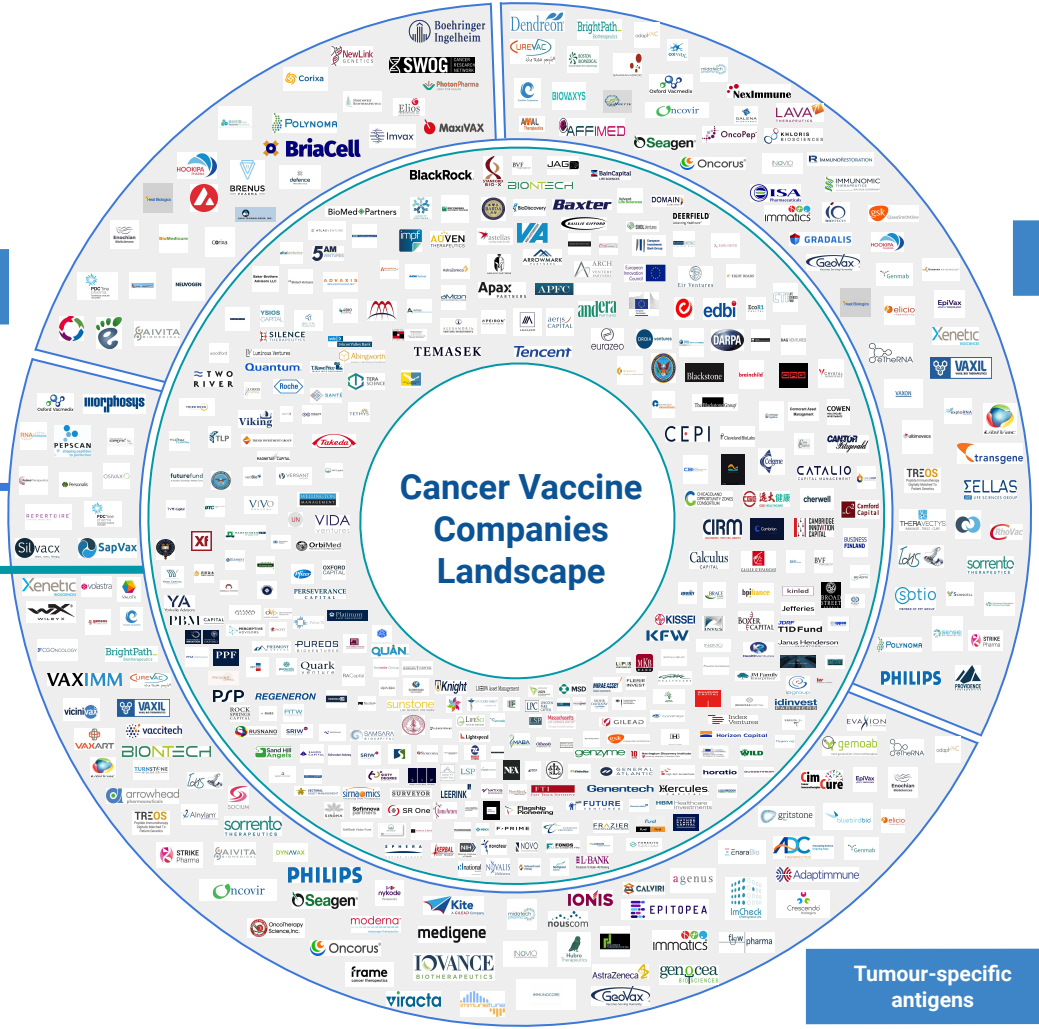
Companies – 150
Investors – 350

Whole-cell antigens

Tumour-associated antigens

Companies

Investors



Tumour-specific antigens

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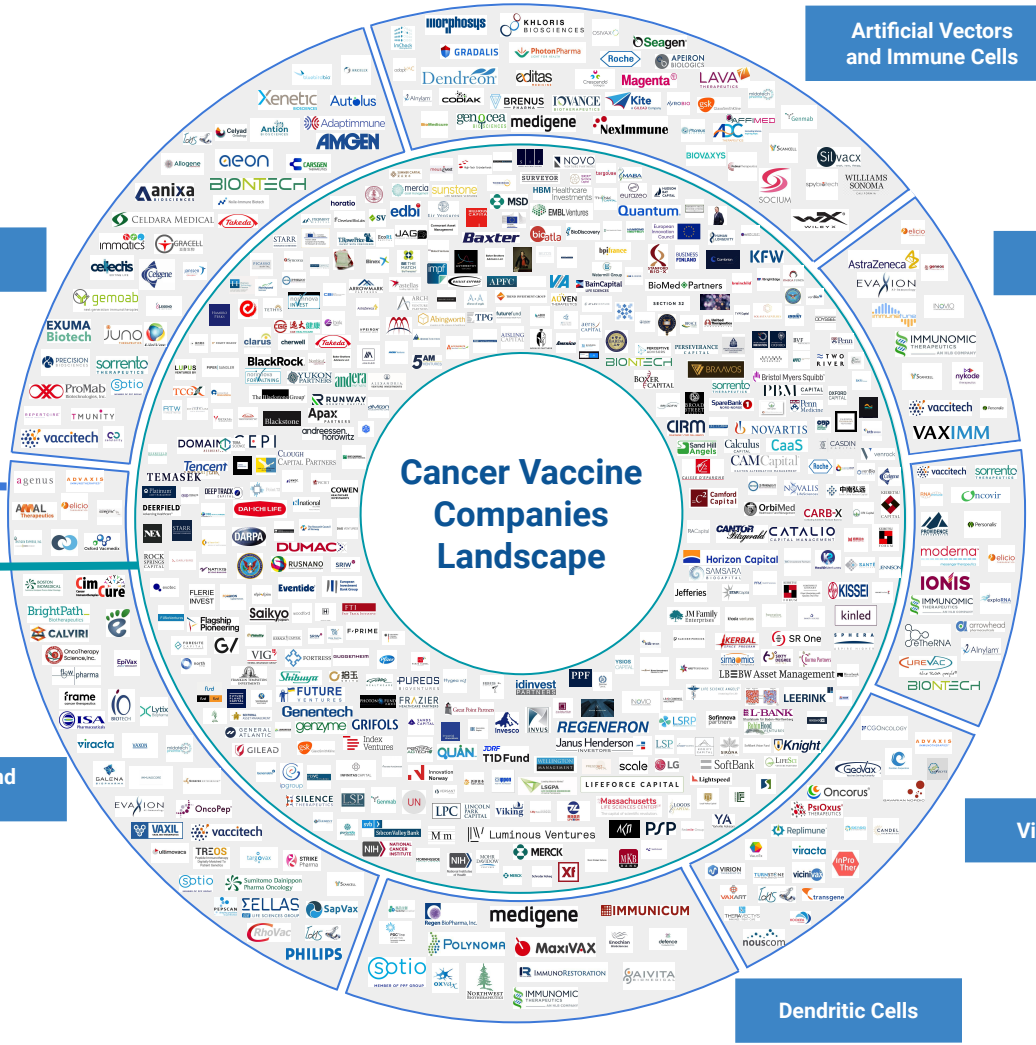
Cancer Vaccines and Cell Immunotherapies by Delivery Form

Companies – 170
Investors – 420



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Level of Cancer Vaccine Innovation of 40 Leading Companies in Drug Discovery Sector

Innovative Approach

1	AiVita Biomedical
2	Arrowhead Pharmaceuticals (NASDAQ:ARWR)
3	Biobohemia
4	CimCure
5	Editas Medicine
6	Epitopea
7	Genocea Biosciences (NASDAQ:GNCA)
8	Gradalis
9	Gritstone Oncology (NASDAQ:GRTS)
10	Heat Biologics (NASDAQ:HTBX)
11	Hookipa Biotech (NASDAQ: HOOK)
12	ImCheck
13	IO Biotech
14	Ionis Pharma (NASDAQ:IONS)
15	Iovance Biotherapeutics (NASDAQ: IOVA)
16	NexImmune (NASDAQ:NEXI)
17	Oxford Vacmedix
18	Rubius Therapeutics (NASDAQ:RUBY)
19	Scancell Holdings (LSE:SCLP)
20	Sorrento Therapeutics (NASDAQ:SRNE)

Classic Approach

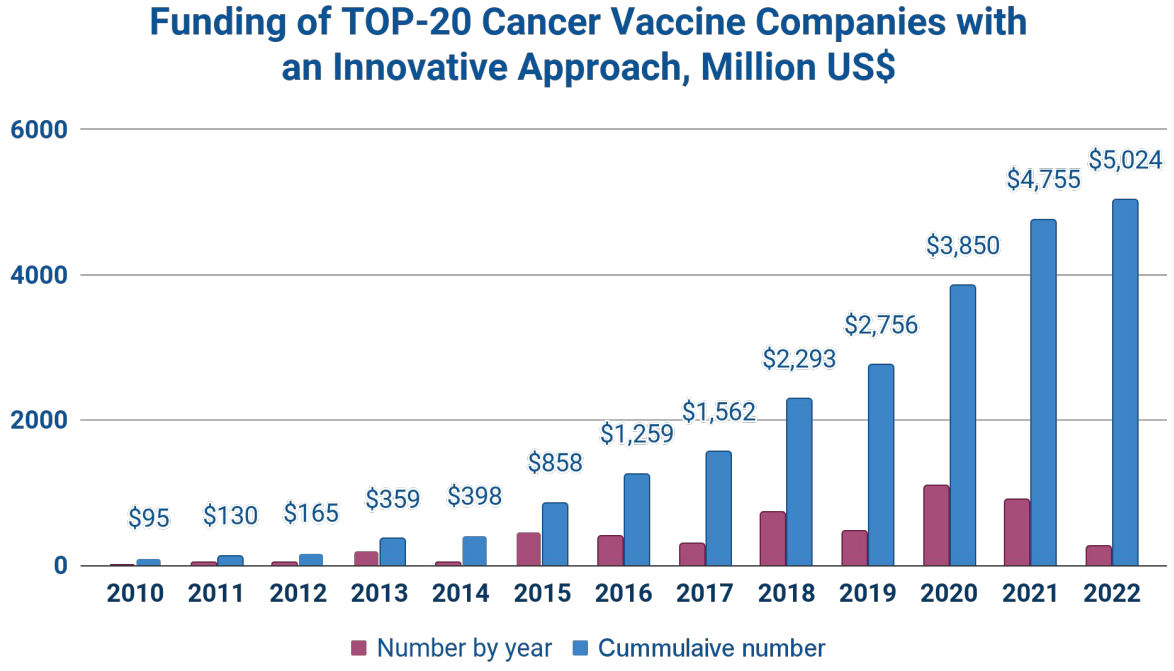
1	Adaptimmune (NASDAQ: ADAP)
2	ADC Therapeutics (NYSE: ADCT)
3	Affimed Therapeutics (NASDAQ: AFMD)
4	Agenus Inc. (NASDAQ:AGEN)
5	AstraZeneca (NSE:ASTRAZEN)
6	BioNTech (NASDAQ:BNTX)
7	Brenus Pharma
8	CureVac (NASDAQ:CVAC)
9	Enochian Biosciences (NASDAQ:ENOB)
10	Gilead
11	GlaxoSmithKline (NYSE:GSK)
12	Immunomic Therapeutics
13	Inovio Pharmaceuticals (NASDAQ:INO)
14	Moderna Therapeutics (NASDAQ:MRNA)
15	Northwest Biotherapeutics (OTC:NWBO)
16	Nykode Therapeutics
17	OncoPep
18	PsiOxus Therapeutics
19	Transgene (EPA: TNG)
20	Vaccitech

Methodology: database creation followed by the detailed analysis of every individual use case by the quantitative and qualitative features such as cancer vaccine category; complexity and development possibilities of the technology; number of similar products on the market/development pipelines; novelty of the product; addressment of the unmet needs, etc.

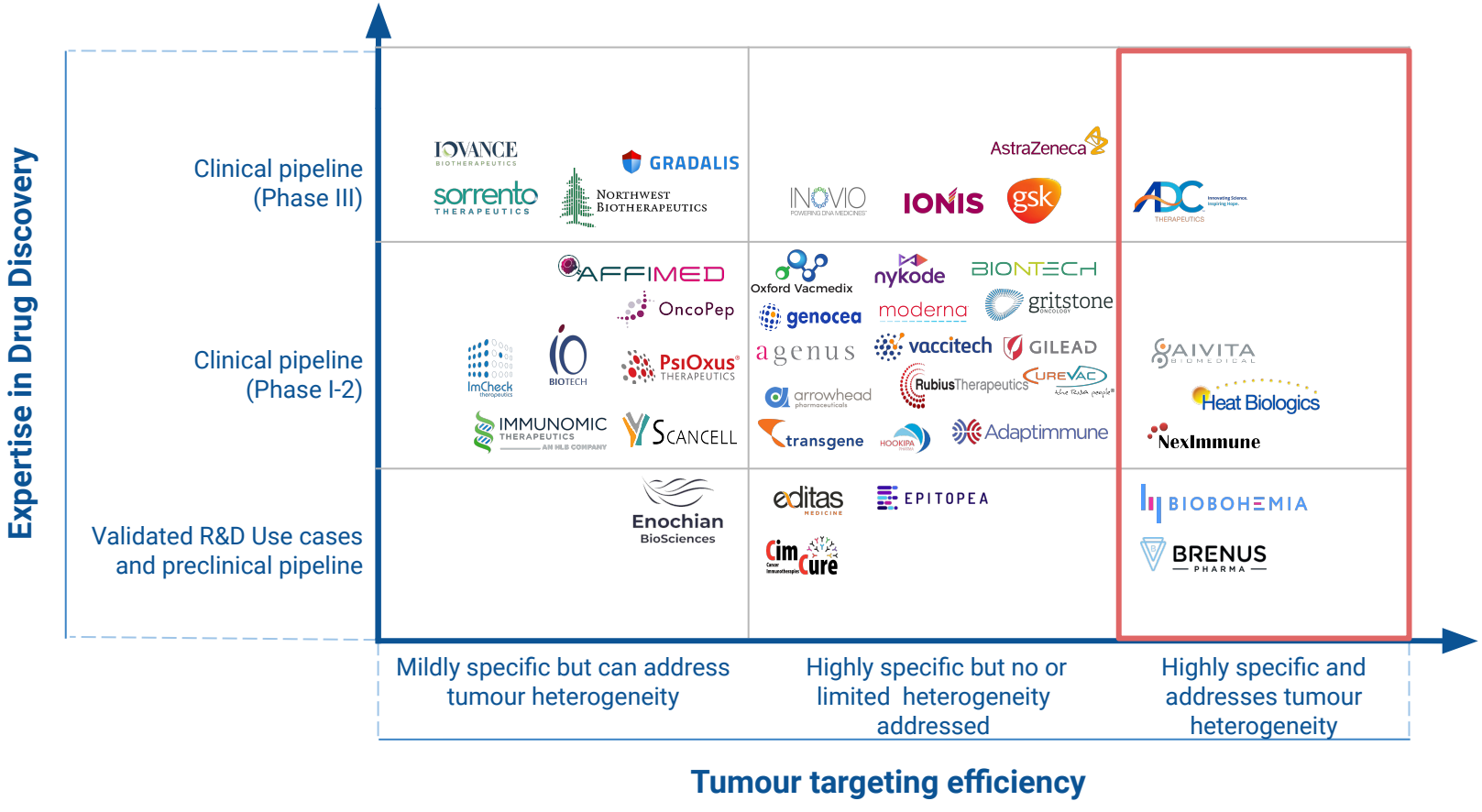
Comparison of Top-40 Leading Drug Discovery Companies Expertise in Cancer Vaccines R&D

Cancer vaccines development shifted into the direction of more **specific tumour targeting** due to **neoantigen platform**. Still, the tremendous majority of such neoantigen vaccines don't overcome the problem of tumour escape mutations and the heterogeneity of cancer cells.

Only restricted number of **innovative platforms** try to face and solve both issues of **highly specific tumour targeting and escape mutations prevention.** They apply **new approaches** on already developed platforms (such as whole-cell, neoantigen, TAA) or initialise **new platform (antigenic essence).**



Comparison of Top-40 Leading Drug Discovery Companies Expertise in Cancer Vaccines R&D

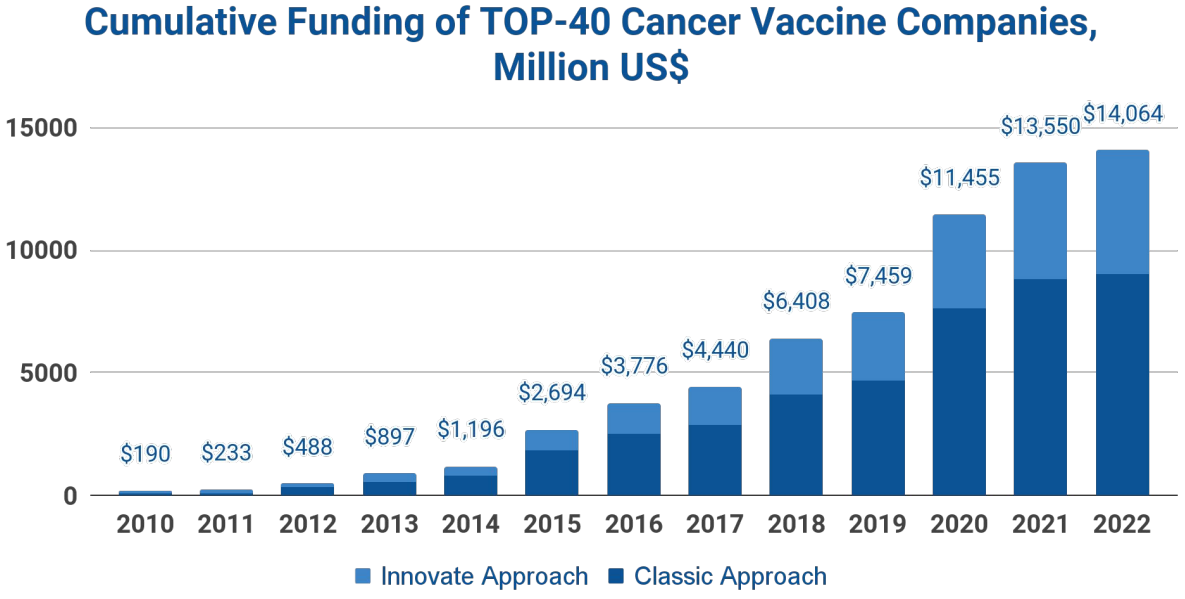


Comparison of Top-40 Leading Drug Discovery Companies Expertise in Cancer Vaccines R&D

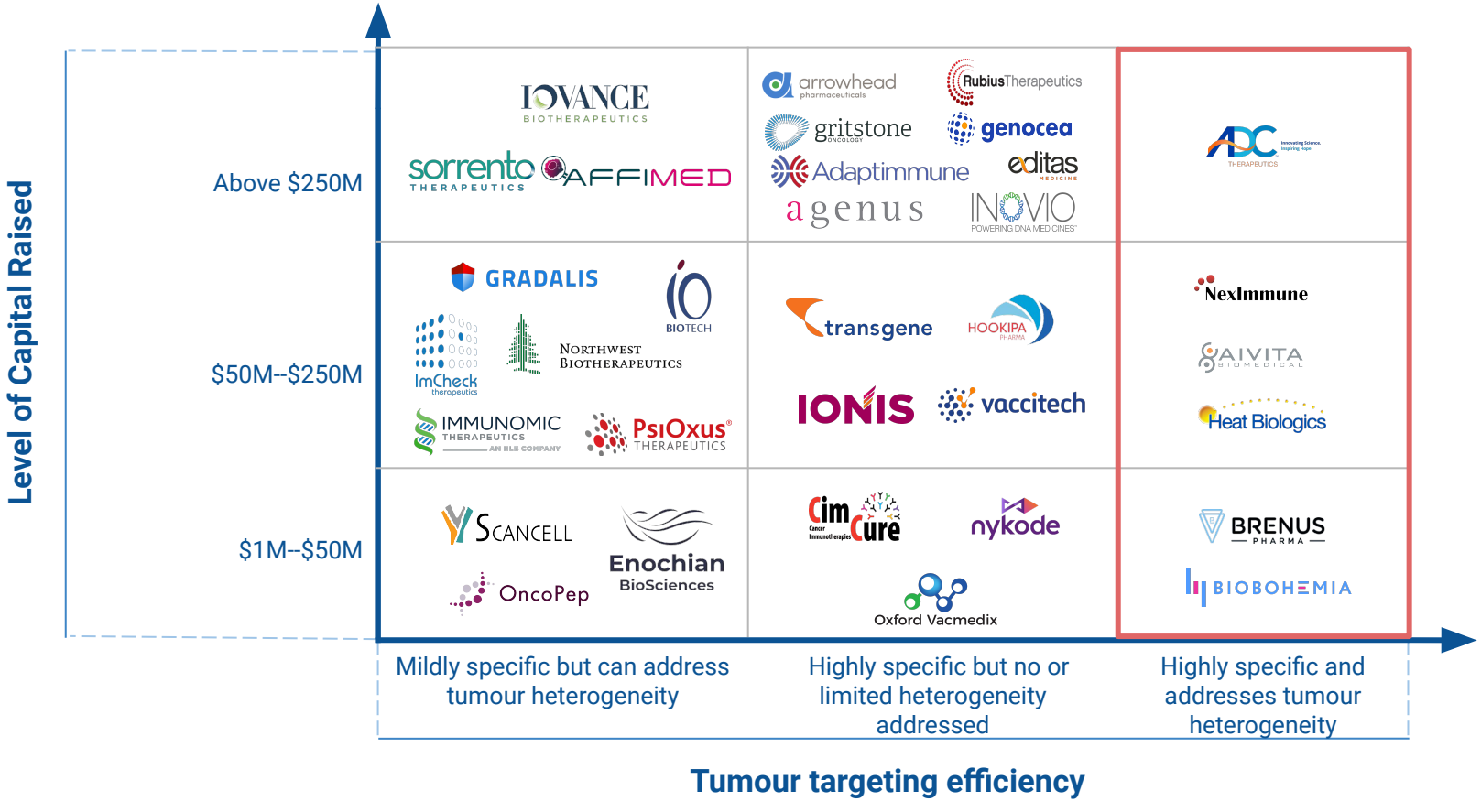
Cancer vaccine leaders belong both to Big Pharma companies with multiple directions and to fast-growing start-ups that are oriented on cancer vaccine development only.

Such **Big Pharma** companies mostly keep up with **mainstream approaches** like neoantigens in the form of mRNA vaccines (Moderna Therapeutics and BioNTech) and raise funding from various sources.

At the same time, there is a **drastic growth** experienced by companies who apply more **innovative approaches.** According to the study of TOP-15 cancer vaccine companies with innovative approach, as of Q2 2021, they already raised roughly twice as much as during the whole 2020 (**$850 million and $484 million,** correspondingly).



Comparison of Top-35 Leading Drug Discovery Companies Expertise in Cancer Vaccines R&D



Neoantigen Platform

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DNA sequencing – first stage for neoantigens identification

Neoantigen Platform: Overview

Neoantigens represent a large platform in the field of cancer vaccines and generally in tumour immunotherapy.

Neoantigens include antigens produced by **tumour viruses** integrated into the genome and antigens originated by **mutant proteins,** which are abundantly expressed specifically in cancer cells and have strong immunogenicity and tumour heterogeneity.

Currently, a **considerable number of neoantigens** have been discovered that are unique to tumour cells and are not affected by immune tolerance mechanism.

Neoantigens

Shared

Common across different cancer patients and not present in the normal genome

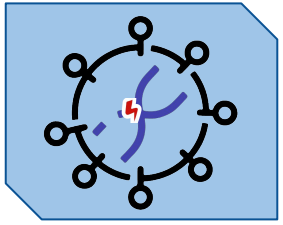
Shared neoantigens that are highly immunogenic have the potential to be screened for use as broad-spectrum therapeutic cancer vaccines for patients with the same mutated gene.

Private

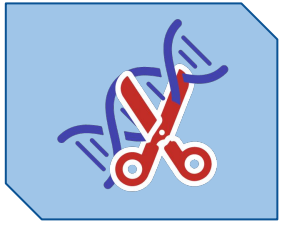
Unique to most neoantigens and completely different from patient to patient

Personalised neoantigen preparation drug can only be specifically targeted to each patient, that is, personalised therapy

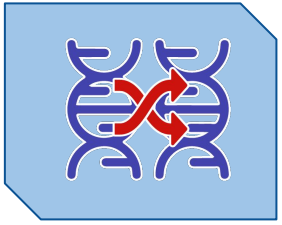
Viral infection



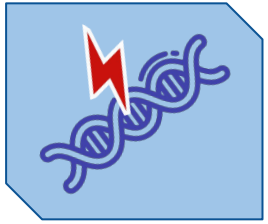
Alternative splicing



Gene rearrangement

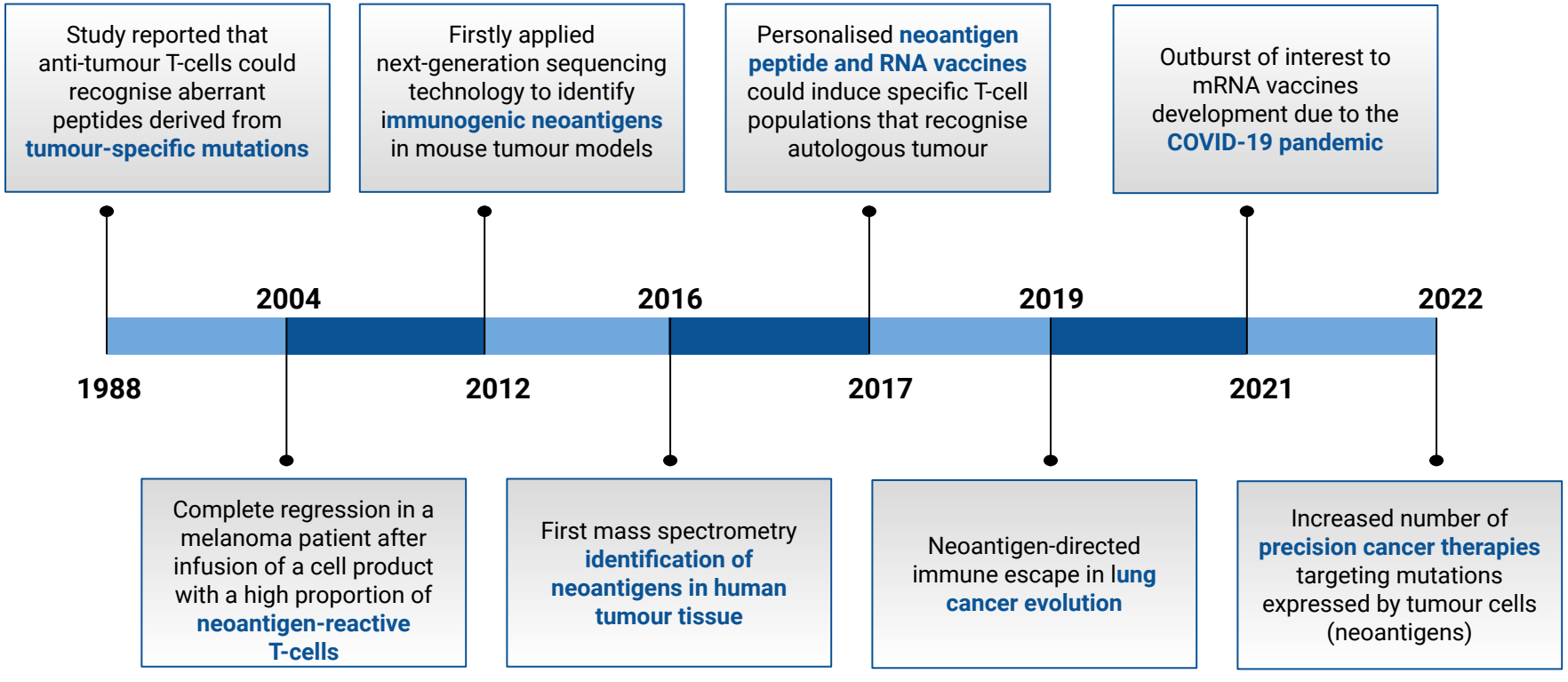


Protein coding sequence mutation



Zhang et al., Frontiers in Immunology (2021)

Neoantigen Platform: Development Milestones



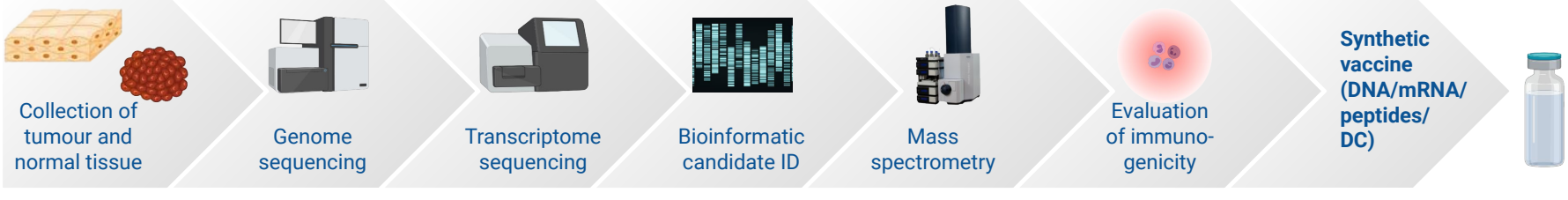
Jiang et al., Journal of Hematology & Oncology (2019)

Neoantigen Platform: Cancer Vaccines in Development

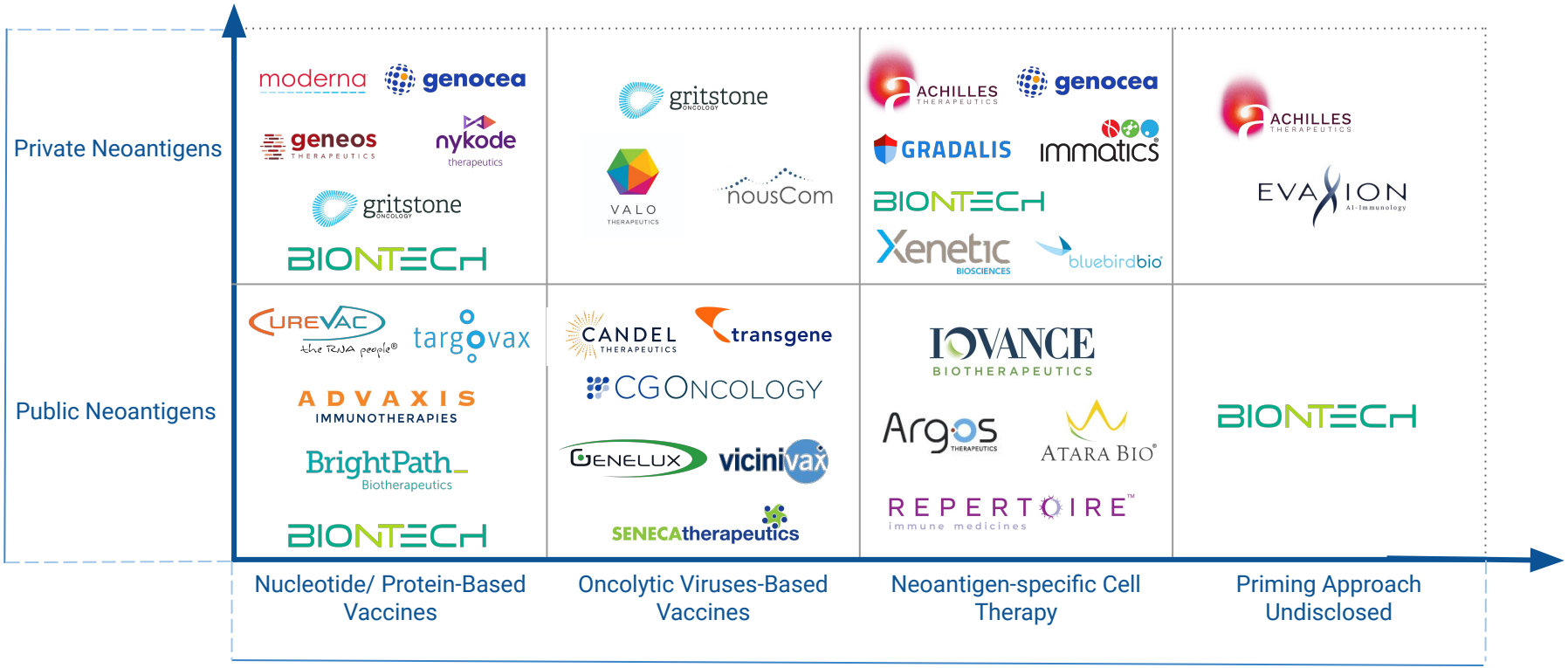
There are no yet approved neoantigen vaccines. However, according to ClinicalTrials.gov search, there are **190 cases** of neoantigen studies, and none of them has yet entered the third clinical phase (not considering HPV-vaccines). It is **30 more cases,** compared to the search results in Q3 2021, which demonstrates a tremendous growth of interests in this cancer-vaccines platform. Many of these studies have shown a good application value of neoantigen (Search term 'neoantigen').

However, the study of neoantigen therapy starts relatively late and is still in the laboratory stage. The **first stages** of neoantigen vaccines development are **complex and time consuming.** Even though genome and transcriptome sequencing technologies are actively developing, they remain a milestone, together with **bioinformatic treatment of data.** As a result, the complications of neoantigen platform overlap with the well-known issues of sequencing cost, speed, data storage, and analysis. However, with the rapid digitalisation and a broad introduction of Artificial Intelligence (AI), smart robotics, and data storage technologies, these issues are expected to be at least reduced, if not almost fully eliminated.

Step-by-Step Scheme of Neoantigen Cancer Vaccine Development



Landscape of Selected Neoantigen Companies

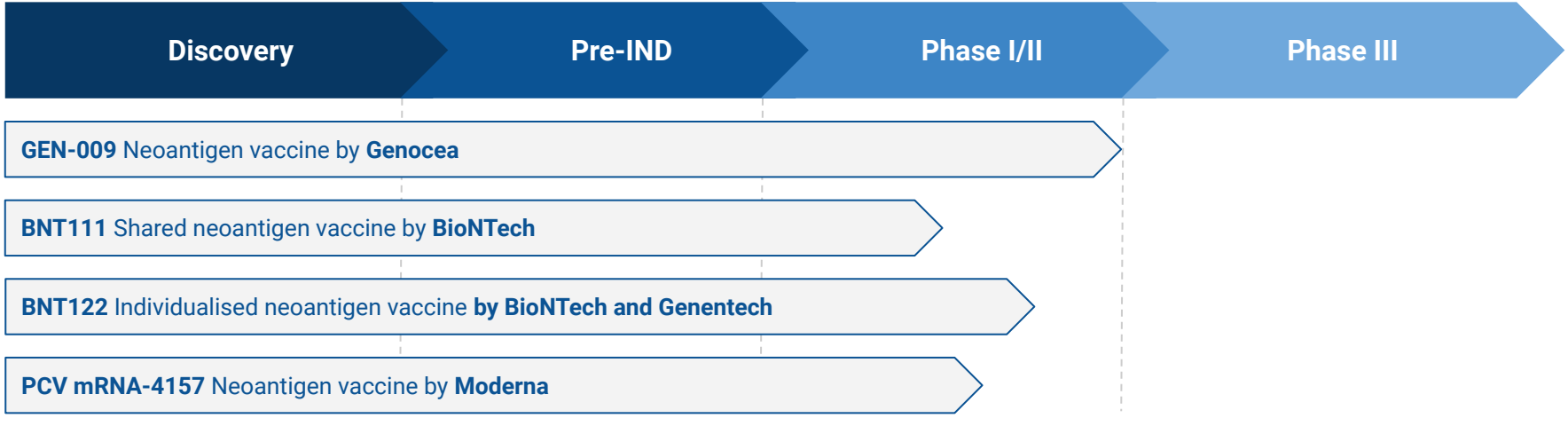


Neoantigen Platform: Cancer Vaccines in Development

Genocea Biosciences GEN-009 vaccine trial (NCT03633110) is now on the Phase I/IIa clinical trials and has shown the best efficacy among the current neoantigen personalisation therapies, with an estimated completion date of December 2022. The purpose of this study was to evaluate the safety, tolerability, immunogenicity, and anti-tumour activity of the personalised vaccine GEN-009 for the treatment of patients with **solid tumours,** which is targeted at a **broad range of cancers**. The results so far show that 40 doses of the vaccine have been administered and no dose limiting toxicity (DLT) occurred, and, so far, no patients who have received the vaccine have relapsed.

BioNTech and Moderna are Big Pharma leaders in development of cancer vaccines of various forms based of neoantigens. **BioNTech** has six cancer vaccines in development with **shared neoantigens** (FixVac platform) and two cancer vaccines owned together with **Genentech** based on **individualised approach** (iNeST platform).

Neoantigen Cancer Vaccines Development Pipeline



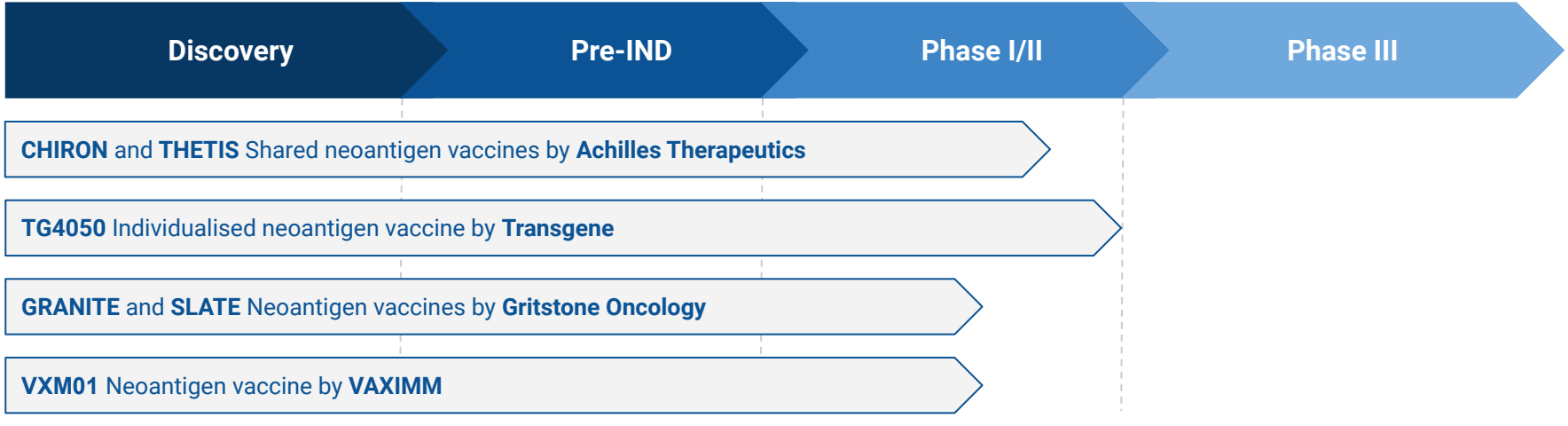
Neoantigen Platform: Cancer Vaccines in Development

Achilles Therapeutics is a biopharmaceutical company developing precision **T-cell therapies** that target **clonal neoantigens**. Currently, they have **two vaccine trials** that are **at the Phase I/IIa clinical trials**: **Chiron** for therapy of **advanced nonsmall cell lung cancer** and **Thetis** for therapy of **melanoma**. The purpose of this study was to evaluate the safety and clinical activity of neoantigen reactive T-cells.

Transgene finished **Phase I clinical trial** studies of personalised neoantigen vaccine **TG4050** in **ovarian carcinoma** and **head and neck carcinoma.** This cancer vaccine is based on Transgene's **myvac® platform** and powered by **NEC's cutting-edge AI capabilities**.

Granite and **Slate** are two cancer vaccines developed by **Gritstone Oncology**. Both of them are now at **Phase I/IIa clinical trials** for the treatment of different types of solid tumours.

Neoantigen Cancer Vaccines Development Pipeline



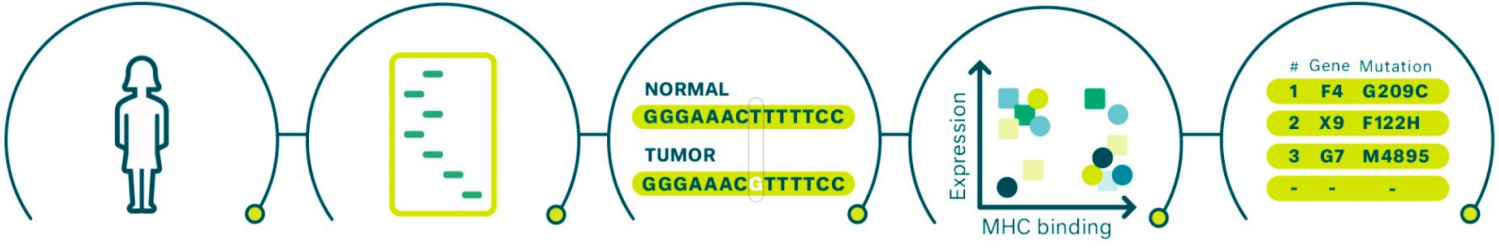
Neoantigen Platform: Key Players

BioNTech — Big Pharma company that mostly specialises on various cancer immunotherapies. They own technologies with

- developed mRNA platform;
- cell therapies;
- antibodies;
- small molecule immunomodulators.

BioNTech is oriented on individualised immunotherapy with patient-specific approach. It requires a complex bioinformatic data treatment. That is why the company gathered expertise in bioinformatics of mutation detection, cancer genomics, and immunotherapy.

BioNTech's Validated Patient-Centric Bioinformatic Process

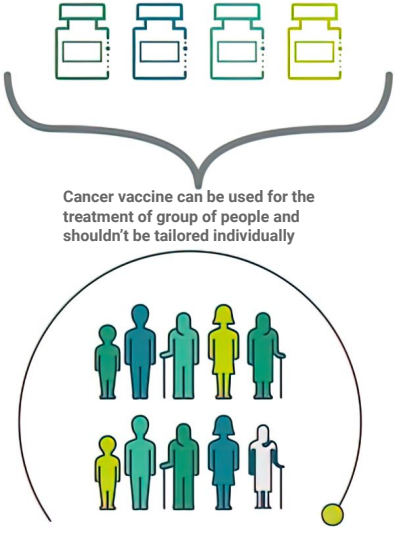


Source — BioNTech Approach

Neoantigen Platform: Key Players

FixVac — cancer vaccine with **shared neoantigens.**

Contains selected combinations of unmodified, pharmacologically optimised mRNA, encoding known for cancer-specific shared antigens. mRNA is delivered using lipoplex technology.



BNT 111 — Advanced Melanoma

BNT 112 — Prostate Cancer

BNT 113 — HPV16+ Head and Neck Cancer

BNT 114 — Triple Negative Breast Cancer

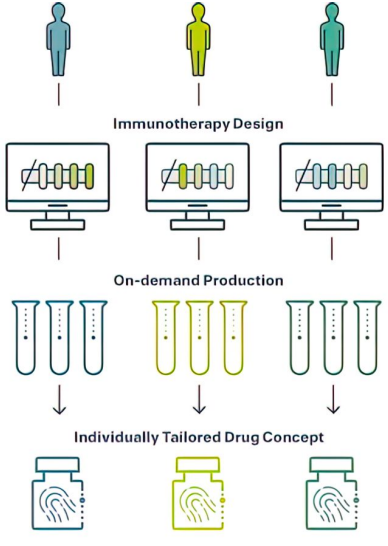
BNT 115 — Ovarian Cancer

BNT 116 — NSCLC

All of them currently are at Phase I of clinical trials

iNeST — Individualised Neoantigen Specific Immunotherapy — cancer vaccine with **private neoantigens.**

Contains unmodified, pharmacologically optimised mRNA encoding up to 20 patient-specific neoantigens, delivered by RNA-LPX formulation.



BNT 122 — Metastatic Melanoma

(currently on the Phase II of clinical trials)

And for locally advanced or metastatic solid tumours

(currently on the Phase I of clinical trials)

Rights are equally shared with Genentech

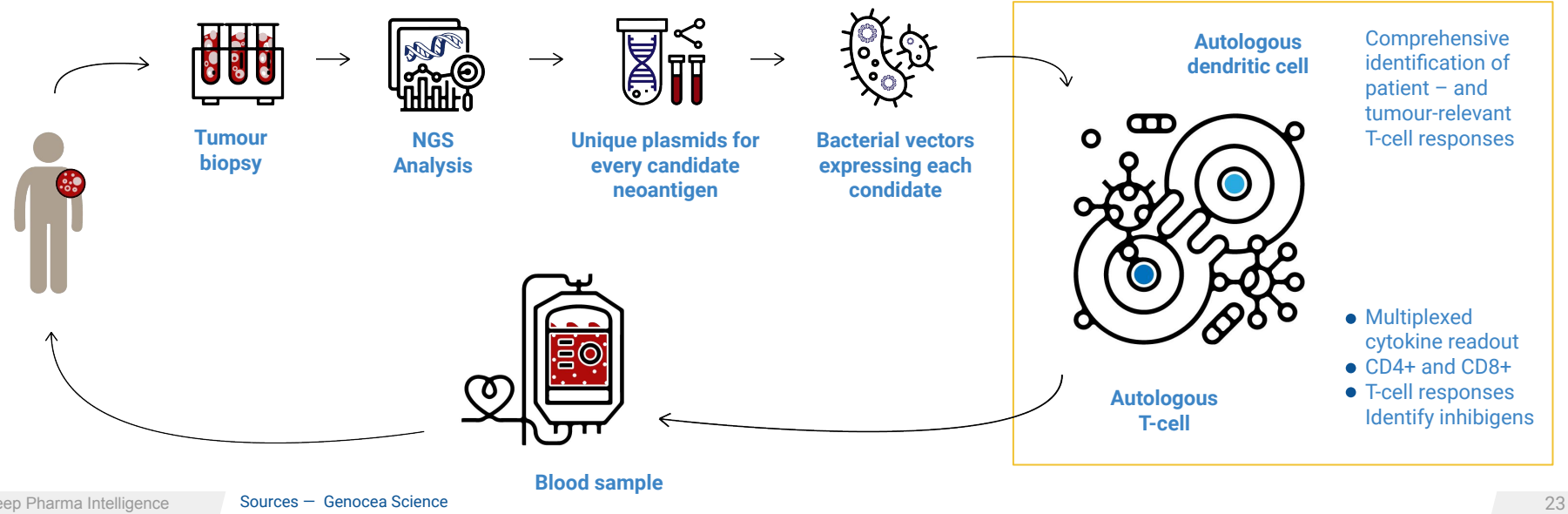
Sources — BioNTech Pipeline, BioNTech Platforms

Neoantigen Platform: Key Players

Genocea Biosciences owns an innovative approach for neoantigen vaccines development – ATLAS platform. It is a unique bioassay that enables a superior, patient biology-driven approach to identify targets of protective T-cell responses. ATLAS zeroes in on only those **surface-presented antigens that trigger anti-tumour T-cell responses.**

ATLAS is unique in the way that it can identify **protumour inhibitory antigens** (Inhibigens), which subvert anti-tumour immune responses. Vaccination with such inhibigens is proved to drive tumour hyperprogression in mice.

How does the Genocea's ATLAS approach work?



Sources — Genocea Science

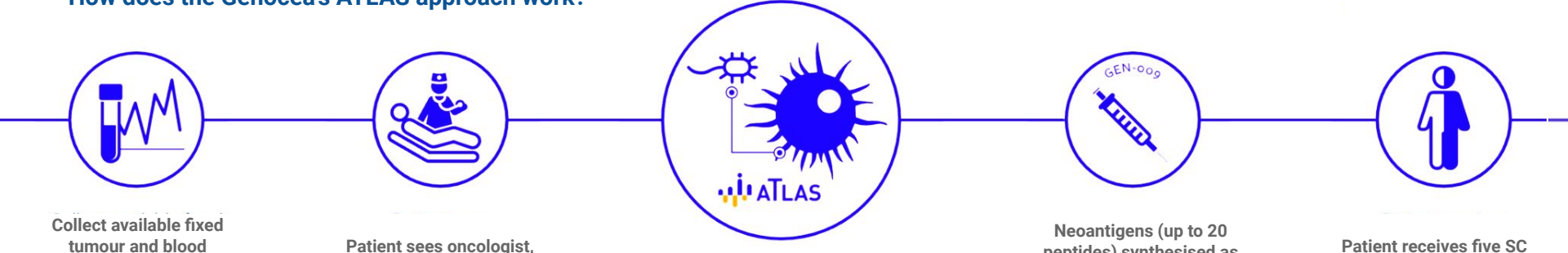
Neoantigen Platform: Key Players

Genocea Biosciences greatly focuses in the **antigen selection** for the best tumour targeting and destruction, which lies at the very basement of the ATLAS platform.

GEN-009 is a neoantigen vaccine candidate in a Phase I/IIa clinical trial to treat a variety of solid tumours. ATLAS identifies neoantigens optimised both to **patients' T-cell responses and their tumours**, underscoring the advantages of the technology for neoantigen selection.

Other vaccine candidate **GEN-011** belongs to the class of **adoptive T-cell therapy**. GEN-011 Neoantigen-activated Peripheral T-cells (NPTs) are peripheral blood T-cells activated by the ATLAS-identified patient-specific neoantigens and expanded to create a **customised therapy.**

How does the Genocea's ATLAS approach work?



Collect available fixed tumour and blood sample and send for sequencing

Patient sees oncologist, begins SoC ICI

Inhibigens and neoantigens identified by ATLAS

Neoantigens (up to 20 peptides) synthesised as peptides and formulated with Poly-ICLC

Patient receives five SC doses over 6 months

Sources — Genocea Pipeline

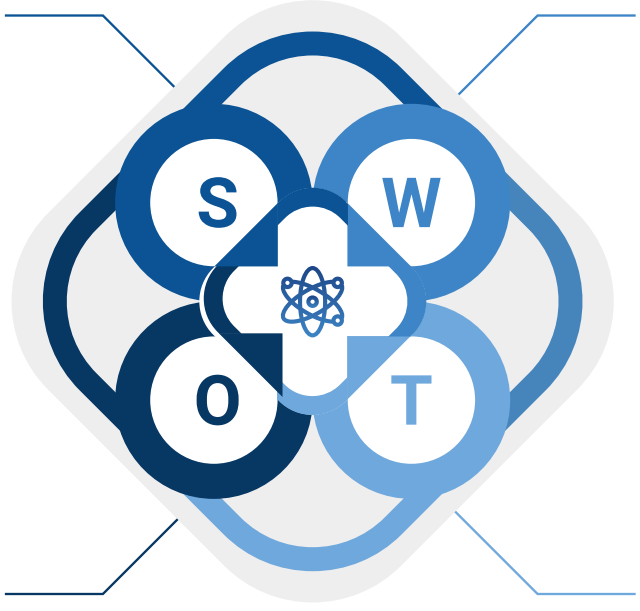
Neoantigen Platform: SWOT Analysis

Strengths

- Great financial support, which moves the platforms faster to clinical research;
- Complete specificity to the tumour cells;
- Already has products in clinical phase of development;
- Cancer vaccine can be delivered in various forms.

Opportunities

- Vaccines possibly can enter the clinical trials Phase III;
- Neoantigen cancer vaccines might be the best personalised solution for cancer treatment.



Weaknesses

- The development cycle of neoantigen vaccine is too long;
- Preparation and delivery of vaccines remains a challenge;
- The heterogeneity of the tumour is difficult to resolve with neoantigen platform;
- Limited number of antigens meet the neoantigen criteria;
- Expensive.

Threats

- Platform has a limited number of directions to develop further in case of failure;
- It might be substituted with novel platforms, which are more cost-effective and highly specific for cancer cells at the same time.

Tumour-Associated Antigens Platform

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Macrophages attacking cancer cells

Tumour-Associated Antigens Platform: Overview

Tumour-Associated Antigens (TAA) are self-proteins that are abnormally expressed by cancer cells.

It means they are **present both in healthy and cancer cells** and differ only by the level of exposure or presentation by cell.

This makes TAA slightly easier to discover, compared to neoantigens, but at the same time TAA might cause **peripheral tolerability issues** in patients, lack of T-cell activation, and collateral damage.

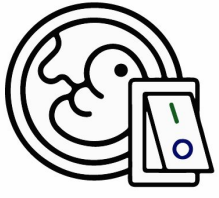
Even though TAA are used for the currently well-developed **CAR-T** technology, they still remain to be challengeable for cancer vaccines development.

Tumour-Associated Antigens

Overexpressed proteins

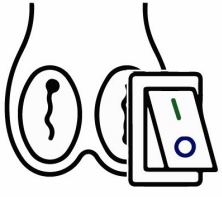
Detected both on healthy and cancer cells of human body, but due to the **higher amount at malignant cells,** their detection will be preferable

Differentiation antigens



Differentiation factors are meant to be present at cells only **during the early development** and are saved only in small subset of cells in developed body

Cancer testis antigens



Are not supposed to be present in healthy adult somatic tissues but are expressed in **testicles in male germ cells**

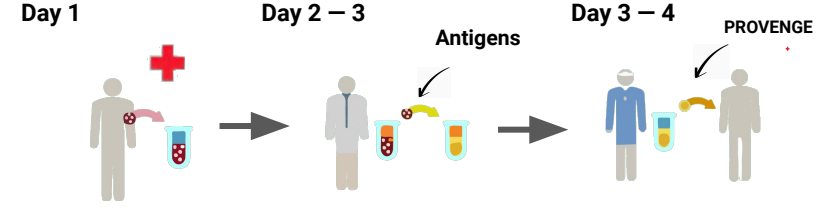
Tumour-Associated Antigens Platform: Development Milestones

Cancer immunotherapy field experienced at least two significant breakthroughs connected with **tumour-associated antigens platform:**

- Promising approval of **Provenge cancer vaccine** (sipuleucel-T) by FDA for the treatment of prostatic cancer, which used tumour-associated antigen as a target;
- Development and approval of multiple **CAR-T therapies** based on targeting of TAA.

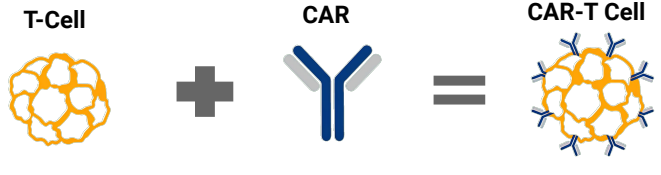
Dendreon

2010 – first FDA-approved cancer vaccine



NOVARTIS Kite Pharma

2017 – first FDA-approved CAR-T

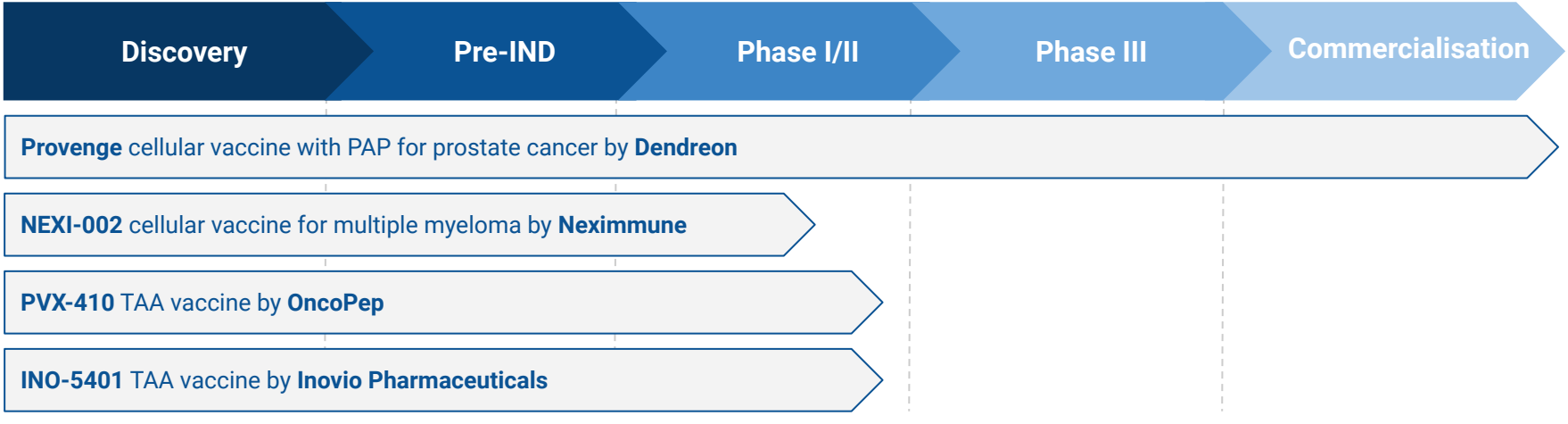


Tumour-Associated Antigens Platform: Cancer Vaccines in Development

Tumour-associated antigens platform is one of the most well-developed platforms. That is why there is plenty of clinical candidates even not considering CAR-T and counting only cancer vaccines. At the moment of our research, there were roughly **200 cases** of tumour-associated antigens studies, according to ClinicalTrials.gov search.

After approval of **Provenge in 2010,** no other cancer vaccine entered the global market. Provenge passed the clinical trials stage with a low efficiency level, but just enough to pass it, so now it is not as frequently used as we wish it to be. And toxic chemotherapy remains to be more effective way to treat prostate cancer.

Tumour-Associated Antigens Cancer Vaccines Development Pipeline



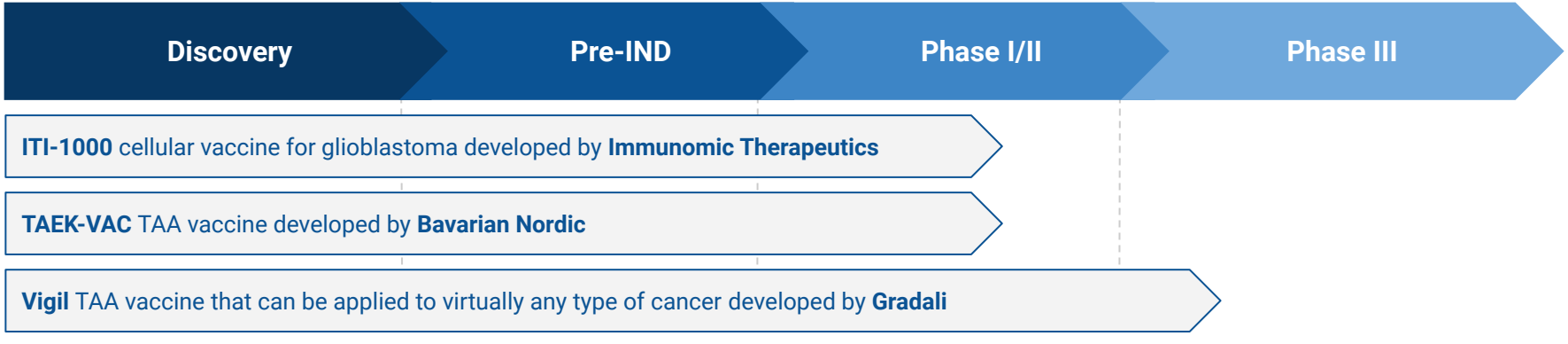
Tumour-Associated Antigens Platform: Cancer Vaccines in Development

ITI-1000 is a **dendritic cell therapy** comprised of autologous dendritic cells, which is now at a **Phase II clinical trial** and was developed by **Immunomic Therapeutics**. ITI-1000 is being tested in a randomised, blinded, and placebo-controlled Phase-II study in patients with **newly-diagnosed glioblastoma (GBM),** which is anticipated to close in 2022.

TAEK-VAC is an innovative immuno-oncology candidate developed by **Bavarian Nordic** using **MVA-BN technology**. In 2021, a **Phase I/II** open label trial of the vaccine administered intravenously to individuals with **advanced HER2 and brachyury-expressing tumours** was started.

Vigil® is a fully personalised, patient-specific cancer immunotherapy that **can be applied to virtually any cancer** developed by **Gradalis.** The most advanced study is continuing now in patient with recurrent/refractory **Ewing's sarcoma**.

Tumour-Associated Antigens Cancer Vaccines Development Pipeline



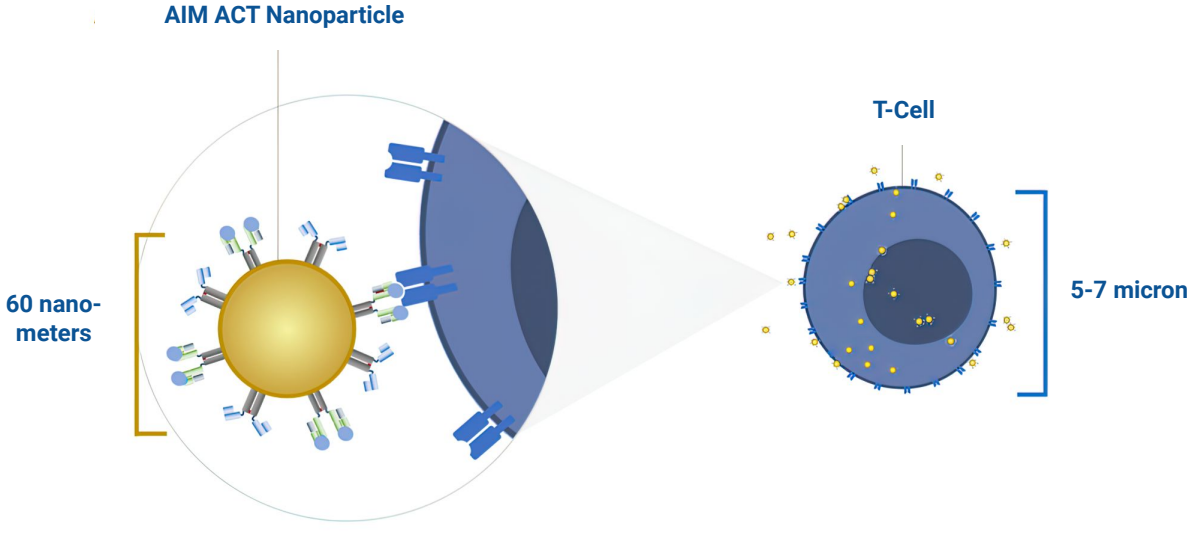
Tumour-Associated Antigens Platform: Key Players

NexImmune — biopharmaceutical company which implements an innovative approach to improve and develop tumour-associated antigens cancer vaccines. They own a nanotechnological Artificial Immune Modulation (AIM) platform.

NexImmune constructs '**synthetic dendritic cells**' in the form of **AIM nanoparticles,** which are capable of directing a specific T-cell-mediated immune response.

During antigen presentation, T-cells can recognise **multiple antigens in the form of peptides.** This produces T-cells with multiple immune targets for a robust anti-tumour activity.

AIM™ Nanoparticles induce the production of both memory cells and cytotoxic effector cells. Effector cells will be the main direct mechanism to destroy tumour cells through the release of cytotoxic granules while memory cells will store in the bloodstream.



Sources — NexImmune Technology

Tumour-Associated Antigens Platform: Key Players

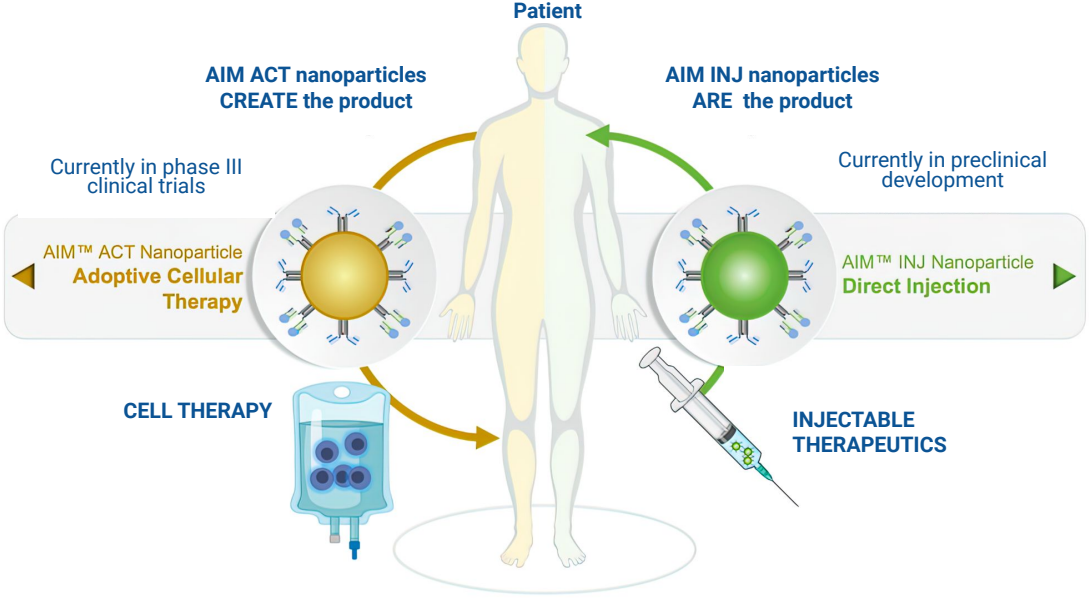
NexImmune is based on few principles in developing cancer vaccines with TAA:

- The ability to expand T-cell populations that recognise and attack **multiple antigen-specific targets;**
- **Consistency** in containing **T-cell subtypes** that support anti-tumour potency, self-renewal, proliferation, and long-term T-cell survival.

Artificial Immune Modulation (AIM) nanoparticles are designed to **mimic the immune functions of natural antigen presenting cells**, such as dendritic cells, by delivering two key immune-directing T-cell signals.

Adoptive cell therapy modality includes cancer vaccines in the form of **donor- or patient-derived T-cells** for AML, multiple myeloma, and solid tumours.

Injectable modality is presented by **injectable AIM nanoparticles** for solid tumours.



Sources — NexImmune Technology

Tumour-Associated Antigens Platform: Key Players

Inovio Pharmaceuticals is a BioTech company which is oriented on **DNA medicines** development.

One of the main focuses of the company is HPV-vaccines with candidates on the third phase of clinical trials. At the same time, there are promising cancer vaccine candidates with **tumour-associated antigens** in the **second phase of clinical trials.**

PRECISELY DESIGNED PLASMIDS (SynCon®)

SynCon uses a proprietary computer algorithm that has been designed to **identify and optimise the DNA sequence** of the target antigen.

PROPRIETARY SMART DEVICES (CELLECTRA®)

INOVIO's DNA medicines deliver **optimised plasmids** directly into cells, intramuscularly or intradermally using one of INOVIO's proprietary hand-held **CELLECTRA® smart devices.**

INO-5401 cancer vaccine

WT1, PSMA, hTERT antigens
for glioblastoma multiforme
(with PD-1 inhibitor)

REGENERON

INO-5151 cancer vaccine

PSA, PSMA antigens
for prostate cancer
(with PD-1 inhibitor and
immune modulator)

PARKER INSTITUTE FOR CANCER IMMUNOTHERAPY

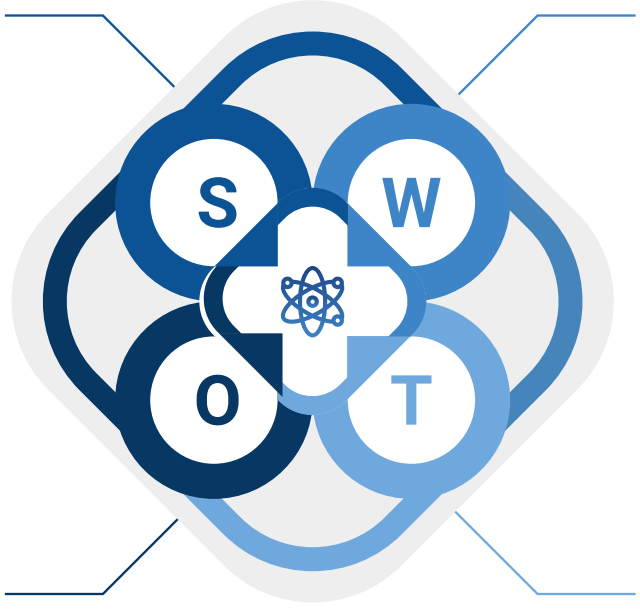
CANCER RESEARCH INSTITUTE

Sources — Inovio DNA Medicines Technology

Tumour-Associated Antigens Platform: SWOT Analysis

Strengths

- There are already examples of FDA approved immunotherapies using TAA;
- Applicable to almost any tumour;
- Lots of accumulated knowledge due to the long-time platform investigation.



Weaknesses

- Cancer vaccines with TAA are not highly specific to tumour cells;
- High number of adverse effects;
- Peripheral tolerability risk.

Opportunities

- Cancer vaccine candidates can enter Phase III of clinical trials;
- Using the experience of FDA-approved immunotherapies can improve the developing products faster.

Threats

- This platform is likely to be pushed out of the cancer vaccines field by platforms with higher specificity;
- Provenge cancer vaccine is seldomly used due to the low activity and high cost even though it was approved by FDA.

Cellular Platform

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Cellular Platform: Overview

Whole-cell platform for cancer vaccines is **the earliest platform** developed with the principle 'vaccinate with something you want to fight against'.

Whole-cell vaccines consist of the **all cellular antigens,** which means there are tumour-associated antigens and neoantigens included. Unlike TAA or neoantigen platform, whole-cell platform contains **both characterised and uncharacterised TAA and TSA.**

This approach is suitable, in theory, for any **solid tumour** regardless its mutation burden, and the general process of its development takes fewer steps, compared to TAA or neoantigen platforms.

Irradiated Gene-Modified Tumour Cells

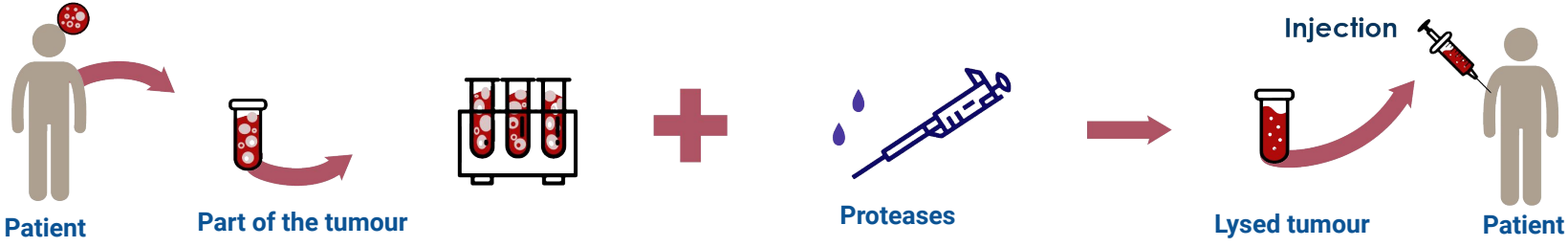
Irradiated gene-modified autologous or allogeneic tumour cells, which were engineered to encode **immunostimulatory agents,** including cytokines and **costimulatory molecules.**

Razi et al., Vaccines for Cancer Immunotherapy (2019)

Cellular Platform: Overview

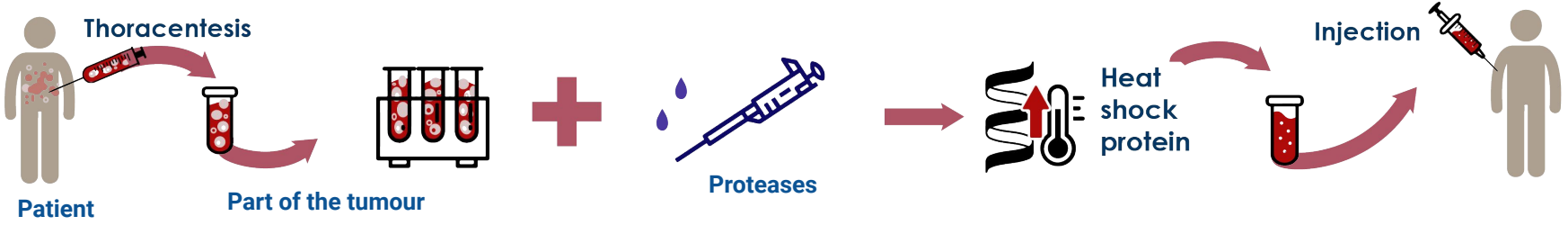
Tumour cell lysates

Whole tumour cell lysates contain all tumour cell antigens. **Autologous or allogeneic lysates** could be prepared in different ways, leading to cell death: Cells can be **frozen and thawed** repeatedly or irradiated with **ultraviolet B** (UVB).



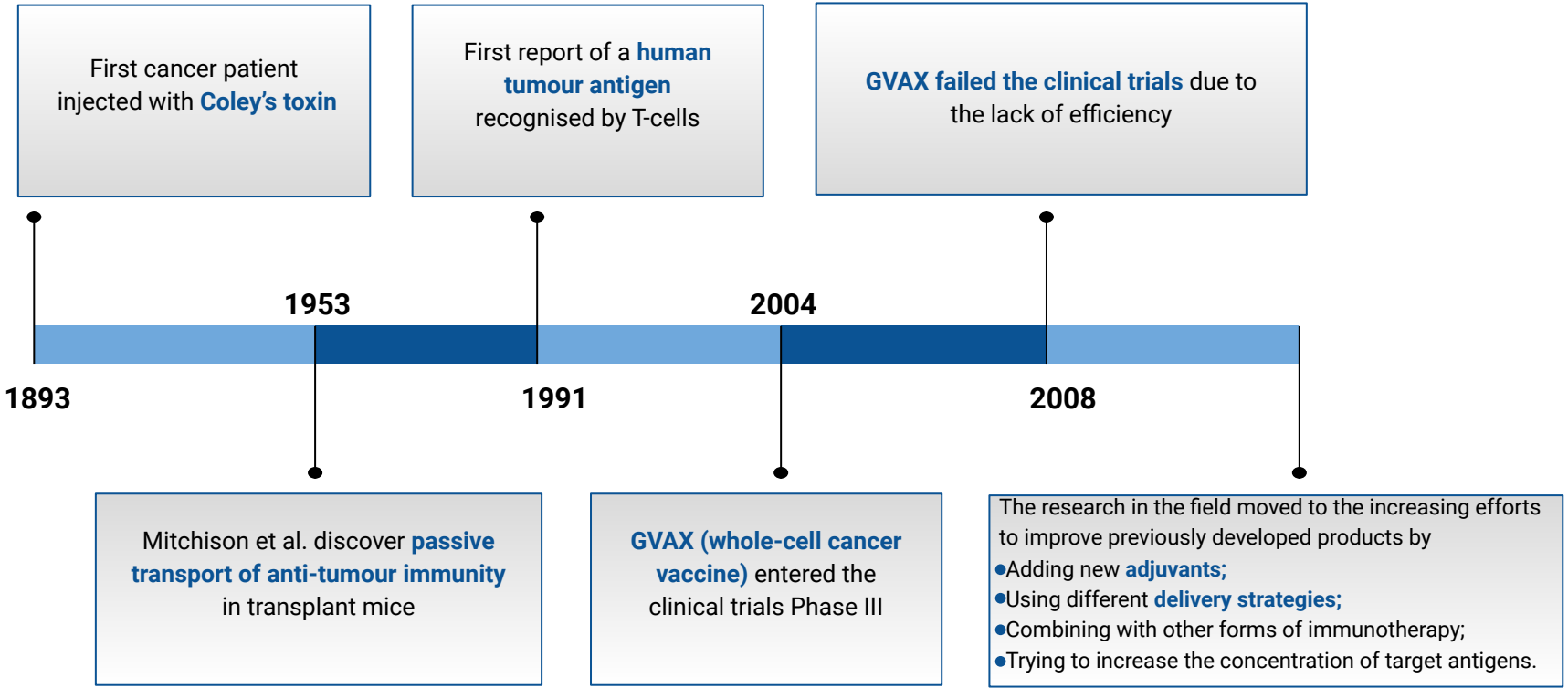
Tumour-Derived Exosomes

Tumour cell derived exosomes could be obtained from ascites, pleural effusion, and plasma samples of patients; such exosomes comprise various tumour antigens, one of the leading antigens investigated is **heat shock protein.**



Razi et al., Vaccines for Cancer Immunotherapy (2019)

Tumour Associated Antigens Platform: Development Milestones



Jiang et al., Journal of Hematology & Oncology (2019)

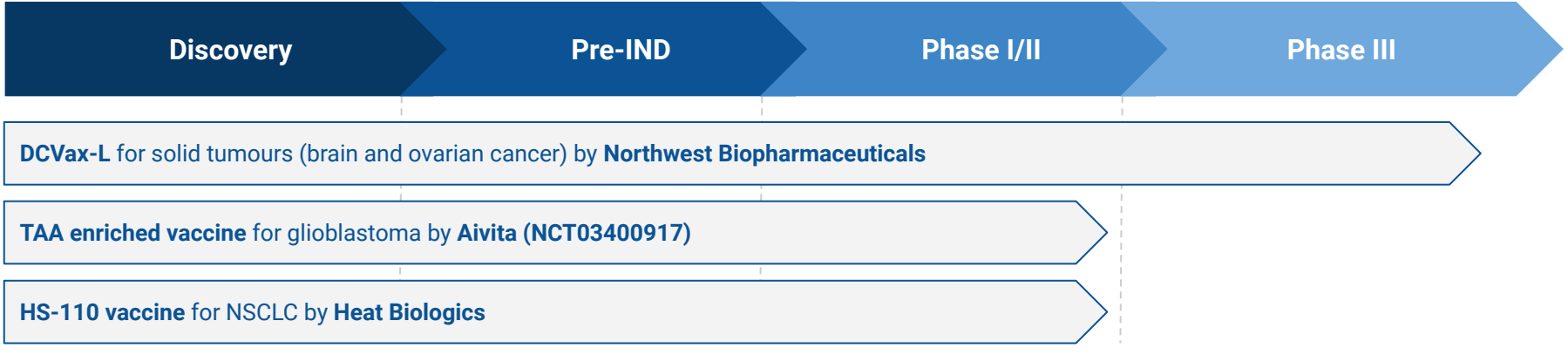
Cellular Platform: Cancer Vaccines in Development

Despite the large number of developed products, none of them has entered the cancer vaccine market yet.

Whole-cell platform for cancer vaccines is an attractive field for various ways of improvement to eliminate its considerable cons ,such as low efficiency and high toxicity. **Heat Biologics** is developing two products: **HS-110 and HS-130** by implementing the pan-antigenic self-adjuvant technology. On the other hand, **Northwest Biopharmaceuticals** has a classic approach for cancer vaccines development but focuses more on clinical application optimisation for clinicians and patients.

Still, history of whole-cell cancer vaccines shows some failures such as one of the most advanced cancer-vaccine candidates, **GVAX,** which resulted into higher mortality level in clinical trial Phase III patients.

Cellular cancer vaccines development pipeline



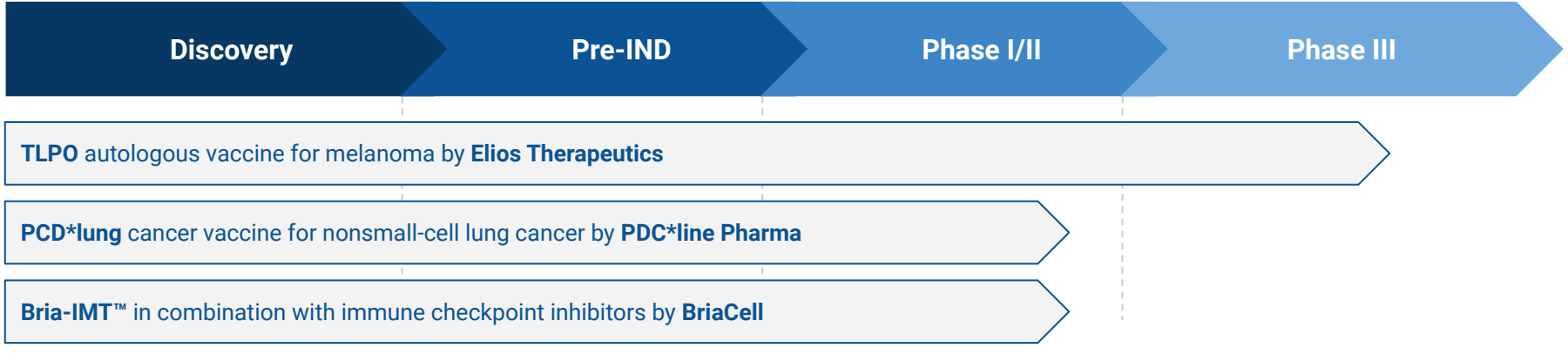
Cellular Platform: Cancer Vaccines in Development

The Tumour Lysate, Particle Only (TLPO) vaccine, developed by **Elios Therapeutics,** is an autologous therapeutic cancer vaccine intended to arouse the immune system to recognize tumour cells and combat a patient's particular cancer. TLPO vaccine research for adjuvant melanoma treatment is currently underway.

PDC*line Pharma developed **PDC*vac** – cancer vaccine based on a cell line of Plasmacytoid Dendritic Cells (PDC*line), their top candidate for nonsmall-cell lung cancer is **PDC*lung**. This vaccine targets common antigens that are widely expressed. In 2019, a **Phase Ib/II trial** assessing its security and biological activity was started.

Bria-IMT™ is a targeted immunotherapy being developed by **BriaCell** for the treatment of advanced breast cancer. This cancer vaccine is currently enrolling in **Phase I/II combination study** with Incyte's checkpoint inhibitor retifanlimab in patients with advanced breast cancer.

Cellular Cancer Vaccines Development Pipeline



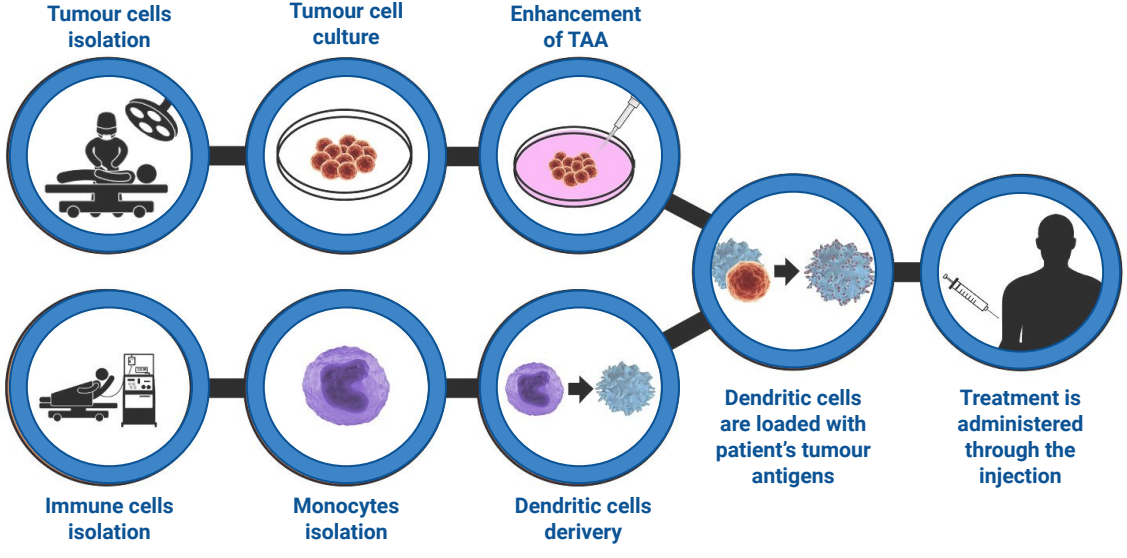
Cellular Platform: Key Players

AiVita Biomedical is a medicine company that develops personalised cancer vaccines with a set of TAA-enriched whole-cell antigens.

Their therapies are oriented to kill **tumour-initiating cells** (a small portion of the tumour mass that is the most prolific in the ability to generate additional cancer cells), while implementing **pan-antigenic approach.**

They developed **AV-GBM-1 –** cancer vaccine in the form of autologous dendritic cells loaded with tumour antigens from a short-term cell culture of autologous tumour cells.

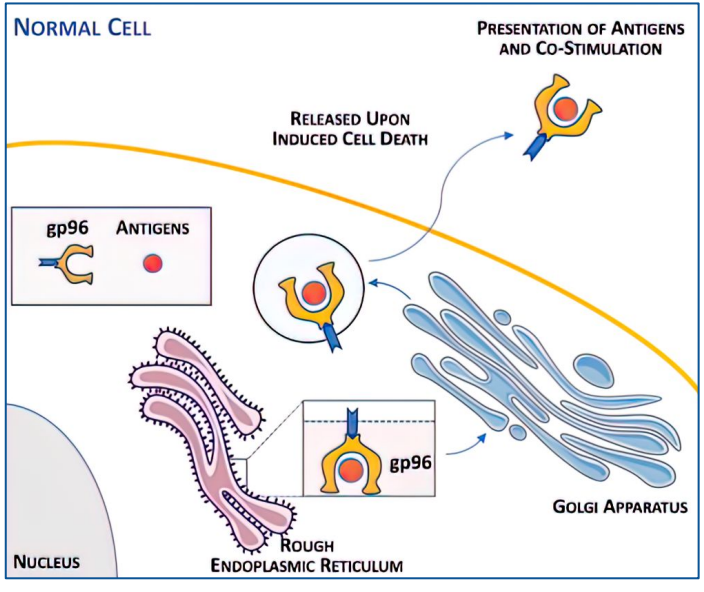
On the first steps the sample of the patient's tumour undergoes cell culture. The aim of this step is **enrichments with tumour-initiating cells** and their amplification. It is the most critical stage since it reduces the nonspecific signals from cells. Selected in such a way, tumour cells are used to **load antigen-presenting (dendritic) cells,** which are delivered to the patient back in the form of subcutaneous injections.



Sources — AiVita Cancer Immunotherapy

Cellular Platform: Key Players

Heat Biologics — is a BioTech clinical-stage company focused on developing its proprietary **'ImPACT' (Immune Pan-Antigen Cytotoxic Therapy)** adjuvant technology. It is first-in-class fully human adjuvant system that functions as both an immune stimulator and an antigen-delivery system.



Leading product — HS-110 (viagenpumatucel-L)

Vaccine derived from irradiated human lung cancer cells genetically engineered to continually secrete **gp96-Ig.**

Clinical Phase II stage, in combination with checkpoint inhibitor

nivolumab (Opdivo®) or

pembrolizumab (Keytruda®)

Bristol Myers Squibb™ MERCK

HS-130

Vaccine derived from irradiated human lung cancer cells expressing the costimulatory fusion protein **OX40L-Ig**

Clinical Phase I stage for a wide range of solid tumours

Sources — Heat Biologics Technology, clinicaltrials.gov

Cellular Platform: Key Players

Northwest Biopharmaceuticals – BioTech company focused on discovering, developing, and commercialising immunotherapy products that generate and enhance immune responses to treat cancer.

This company is fully focused of the development of whole-cell cancer vaccines based on **DCVax technology** (the technology that implements dendritic cells for a cancer treatment) or the direct usage of DC for cancer treatment.

Besides focusing on the development of cancer vaccine candidates, one of the Northwest Biotherapeutics priorities is a user-friendly approach for both patients and physicians.

Simplicity in the vaccine preparation, storage, and delivery is one of the top values, which creates a multidirectional approach with a broad coverage of needs.

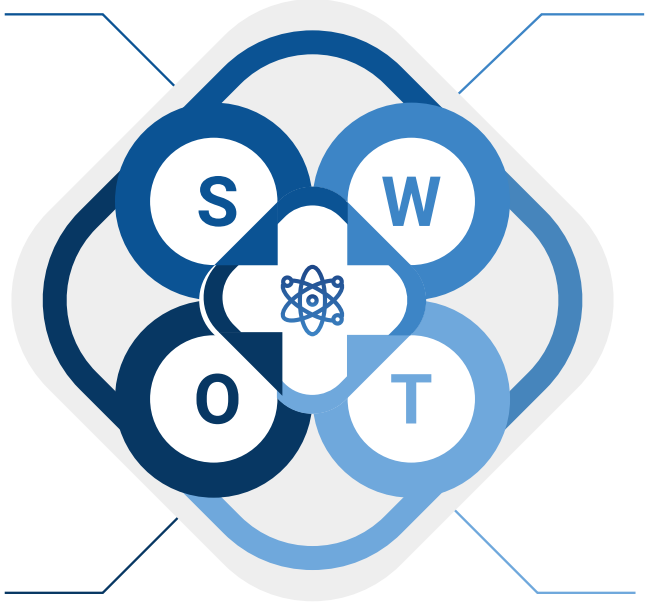
DCVax – L	DCVax-Direct
Dendritic cell cancer vaccine loaded with **cancer antigens from tumour lysate from the patient's own tumour tissue.** DCVax-L is expected to be used for any solid tumour cancers.	The partially matured dendritic cells are **injected directly into the patient's tumour(s)** – it is suitable for the situations in which the tumours are inoperable.

Sources – Northwest Biopharmaceuticals Product Candidates

Cellular Platform: SWOT Analysis

Strengths

- Targeting of all cellular antigens;
- Natural antigens composition;
- Cost-effective.



Weaknesses

- Cellular noise;
- Low concentration of immunogenic antigens;
- Higher toxicity due to nonspecific targeting of healthy cells;
- Low immunogenicity.

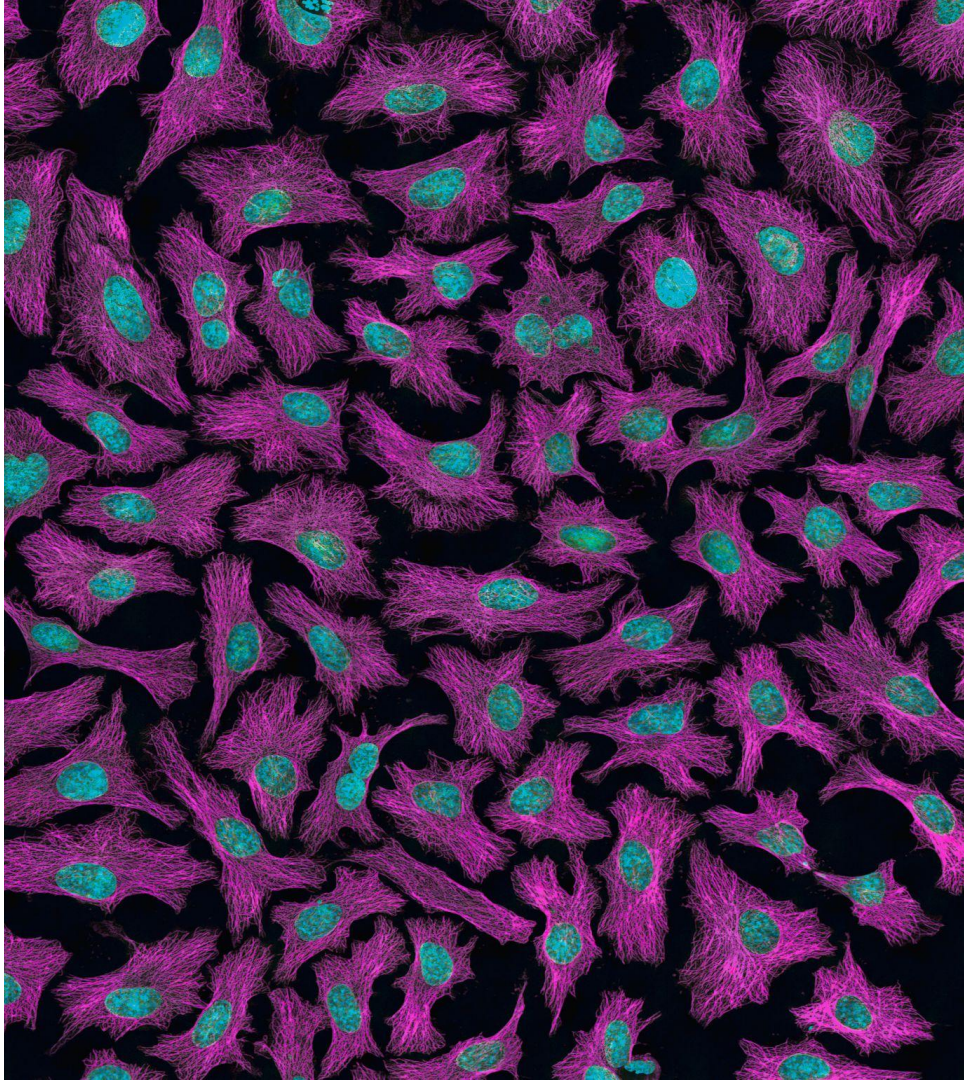
Opportunities

- The vaccines developed earlier in whole-cell platform which failed clinical trials might be upgraded with innovative platform.

Threats

- It might not reach the needed level of efficiency on clinical trials even using adjuvants, checkpoint inhibitors, immune stimulators, etc.
- GVAX (an advanced product in whole-cell cancer vaccine platform) failed clinical Phase III with a high mortality rate.

Antigenic Essence Platform



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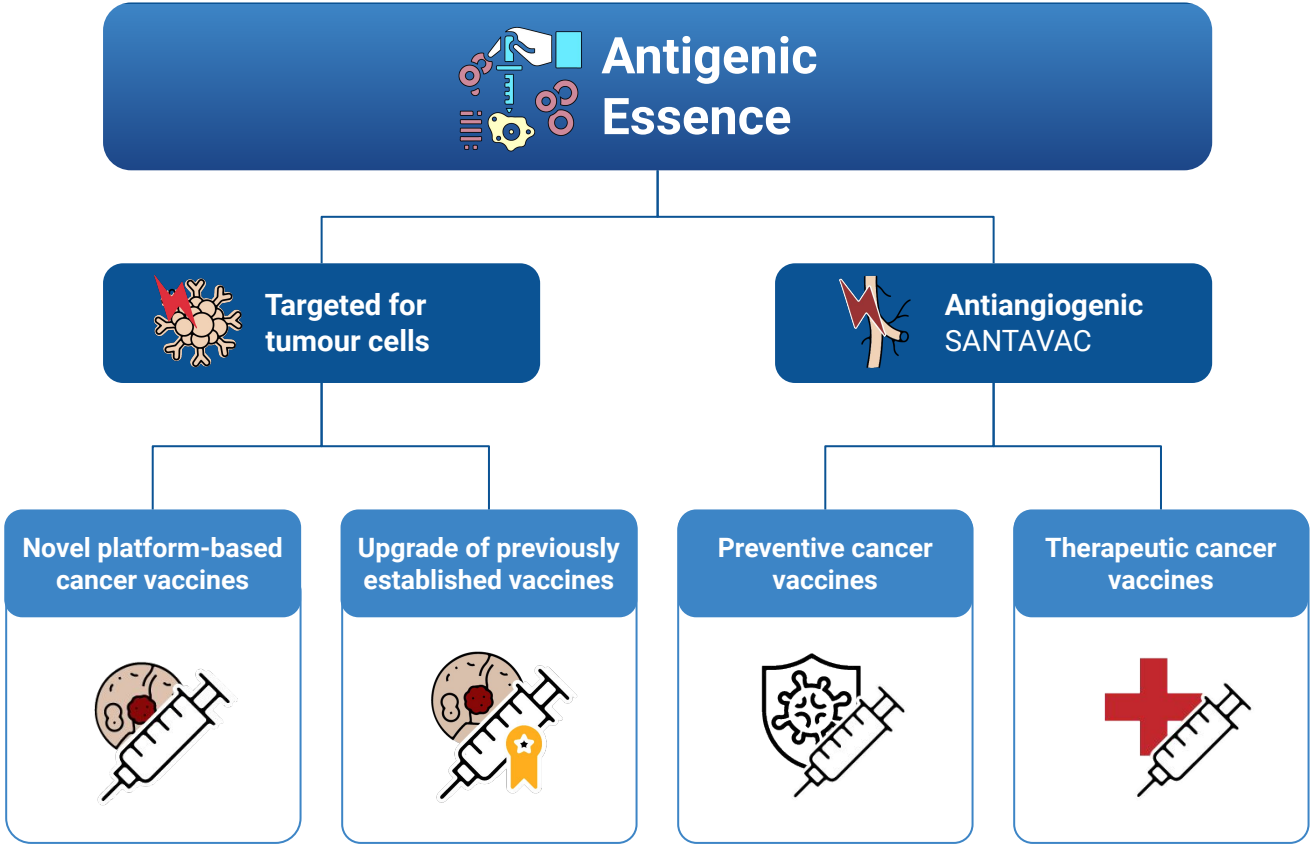
Antigenic Essence Platform: Overview

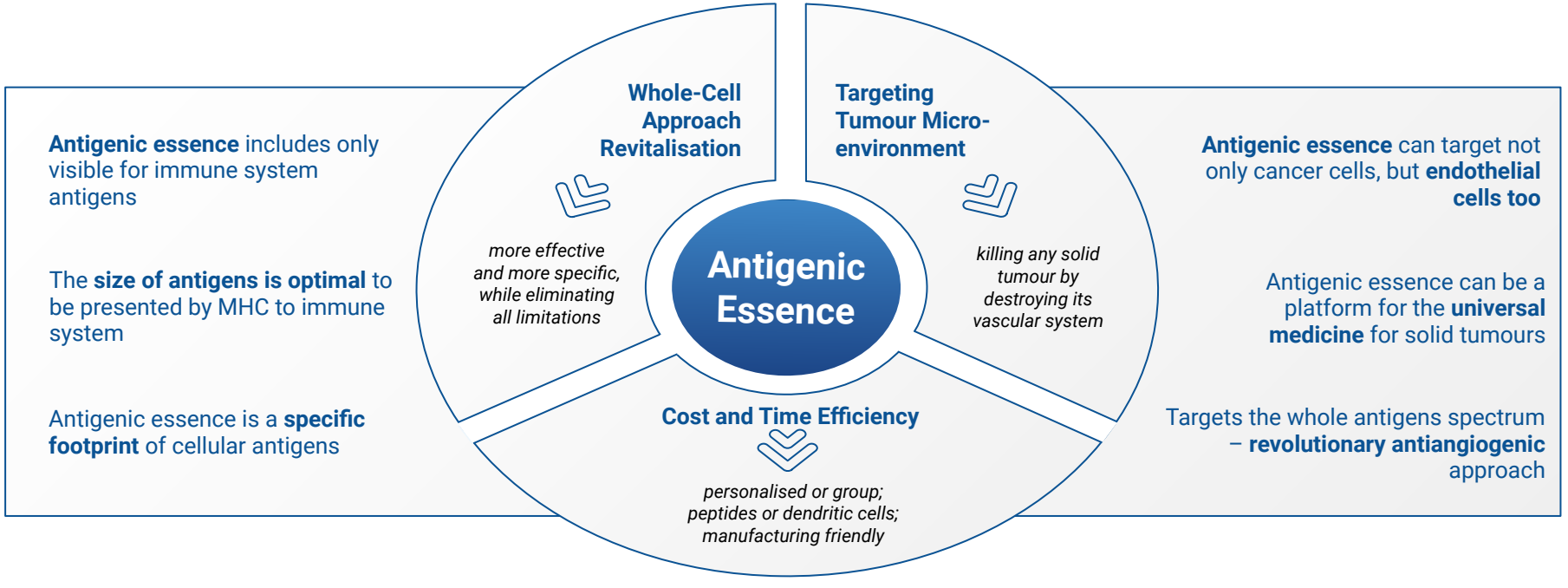
Antigenic essence platform is an **innovative platform** that can be considered as a **cellular vaccines revitalisation.** In it, scientists implemented the lessons from other platforms and created a novel product.

Unlike whole-cell vaccines, antigenic essence includes only **surface-presented antigens** recognised by immune system.

At the same time, unlike neoantigens or tumour-associated antigens, antigenic essence **targets a wide number of antigens** and doesn't require a complex data treatment.

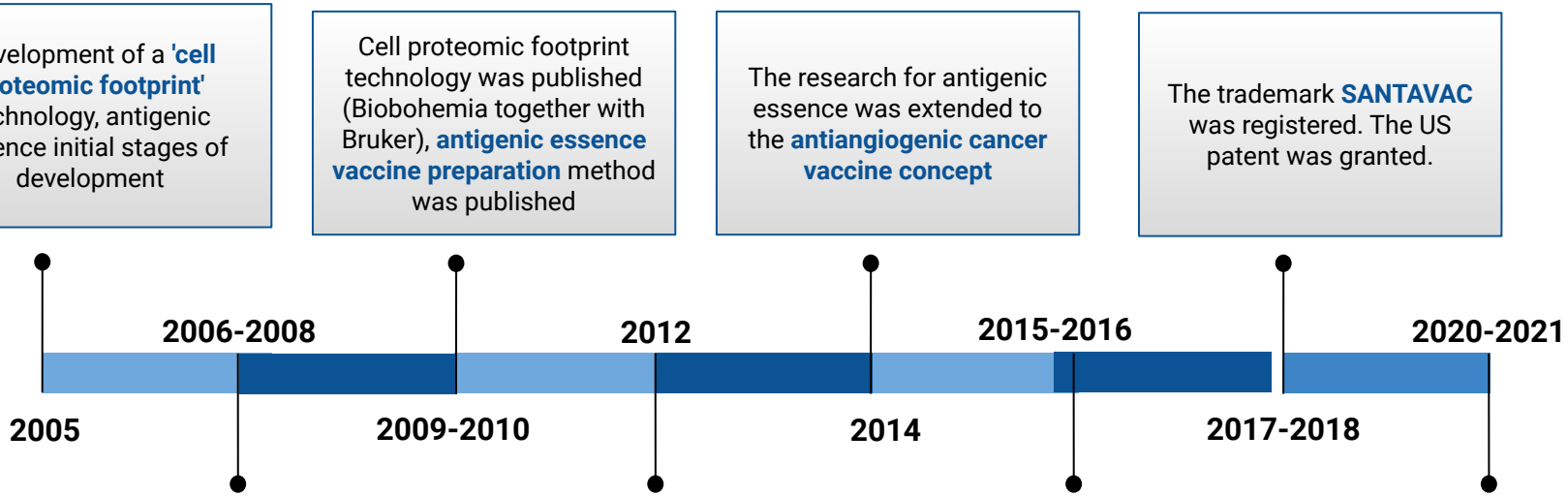


Antigenic Essence Platform: Overview



Overall, it is important to mention that the whole complement of native antigens is inherited via antigenic essence, which is free of any substantial drawbacks. For instance, it solves MHC restriction, allows precise control of antigen composition, lacks cellular ballast (nontarget antigens), and does much more. It makes logical to improve the current cellular cancer vaccines by switching out entire cells with their antigenic components.

Antigenic Essence Platform: Development Milestones



Hamid et al., Cancer Immunology and Immunotherapy (2017)

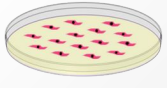
Antigenic Essence Platform: Cancer Vaccines in Development

Antigenic essence platform may be considered as a significant upgrade of whole-cell platform. It means that antigenic essence is

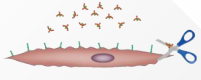
- Cost and time-effective
- Applicable for all solid tumours regardless their mutation burden status
- Applicable both for personalised or group medicine
- Can be used to direct tumour cells or vessels

This platform can be a a solution for previously failed whole-cell cancer vaccines or a good collaborator for developing ideas. Currently, antigenic essence platform is **at the preclinical stage** of development, but according to analysed data, it **should come to final phases of clinical trials** (e.g. **GVAX** and **CanVaxin**) and pass it due to significant revitalisation of the technology.

Step-by-step scheme of antigenic essence cancer vaccine development



Cell line or primary cell culture



Antigenic essence preparation

Complex Omics approaches and bioinformatic data treatment are not needed

Only for quality control of antigenic essence products

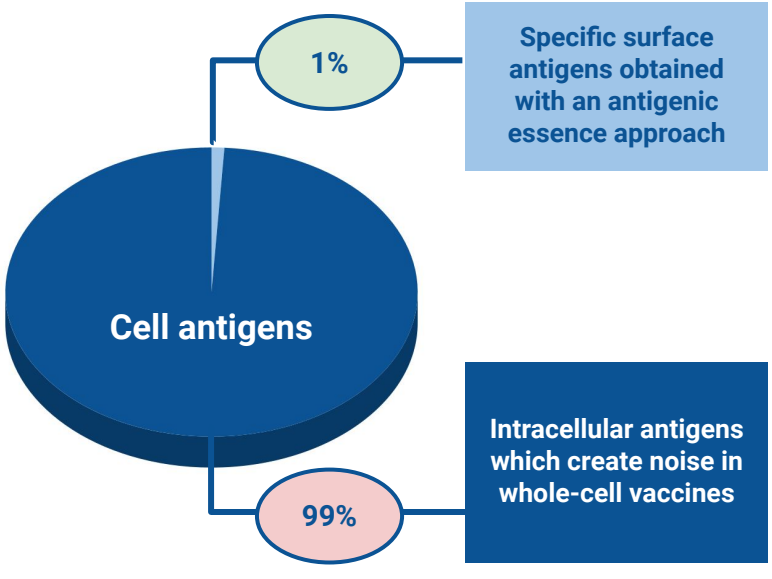
Mass spectrometry

Natural peptides or peptide-loaded DC vaccine

Antigenic Essence Platform: Key Players

Biobohemia, Inc. — a BioTech company focused on the development of cancer vaccines. They fully own an antigenic essence platform which is based on a deep knowledge in proteomics and provides the tool for a revitalisation of cellular vaccines.

The antigenic essence technology allows to control the composition, as well as an efficient purification from ballast substances (cellular 'noise'), and evasion of MHC restrictions.



Naturally produced antigens by the tumour cells tend to induce the most accurate targeting of these cancer cells. Even though such native-cell antigens are obtained by the appliance of cellular vaccines platform, **whole-cell vaccines also have a tremendous majority of ballast intracellular proteins. This cellular noise**

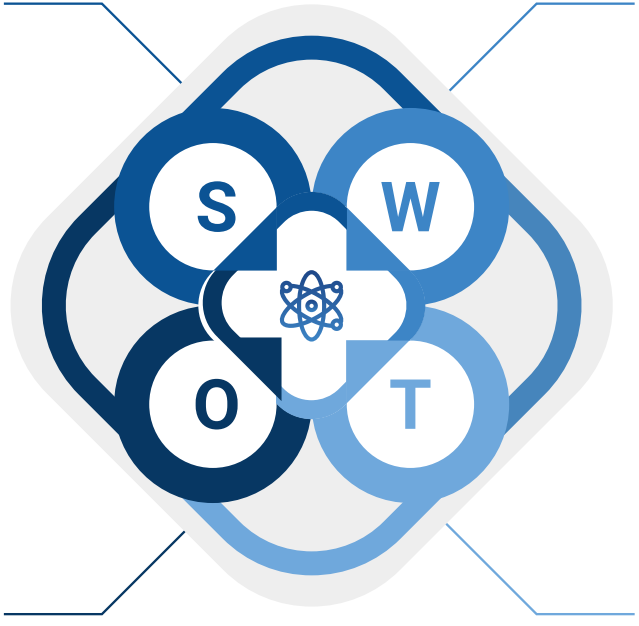
- **dillutes target antigens,**
- **results into the undesired immune response, and**
- **reduces the cancer vaccine specificity.**

That is why antigenic essence platform met the need to develop a novel cell-based cancer vaccine free from intracellular immunogenic molecules.

Antigenic Essence Platform: SWOT Analysis

Strengths

- Innovative platform which eliminates all the cons of previously developed platforms;
- Targeting of only surface antigens visible for immune system;
- High concentration of antigens;
- Controllable set of antigens in doses.



Weaknesses

- Not directed to target nonsolid tumours (20% of cancer cases);
- Low public awareness about the new technology.

Opportunities

- Can be used to upgrade cellular vaccines developed earlier;
- Can become a new emergent star of cancer vaccines market;
- Potentially can cure any solid tumour;
- Can become a leader in preventive cancer vaccines field.

Threats

- The platform is not validated in preclinical study although preliminary validation is strong;
- Operational capacity, structuring business processes.

Oncolytic Viruses Platform

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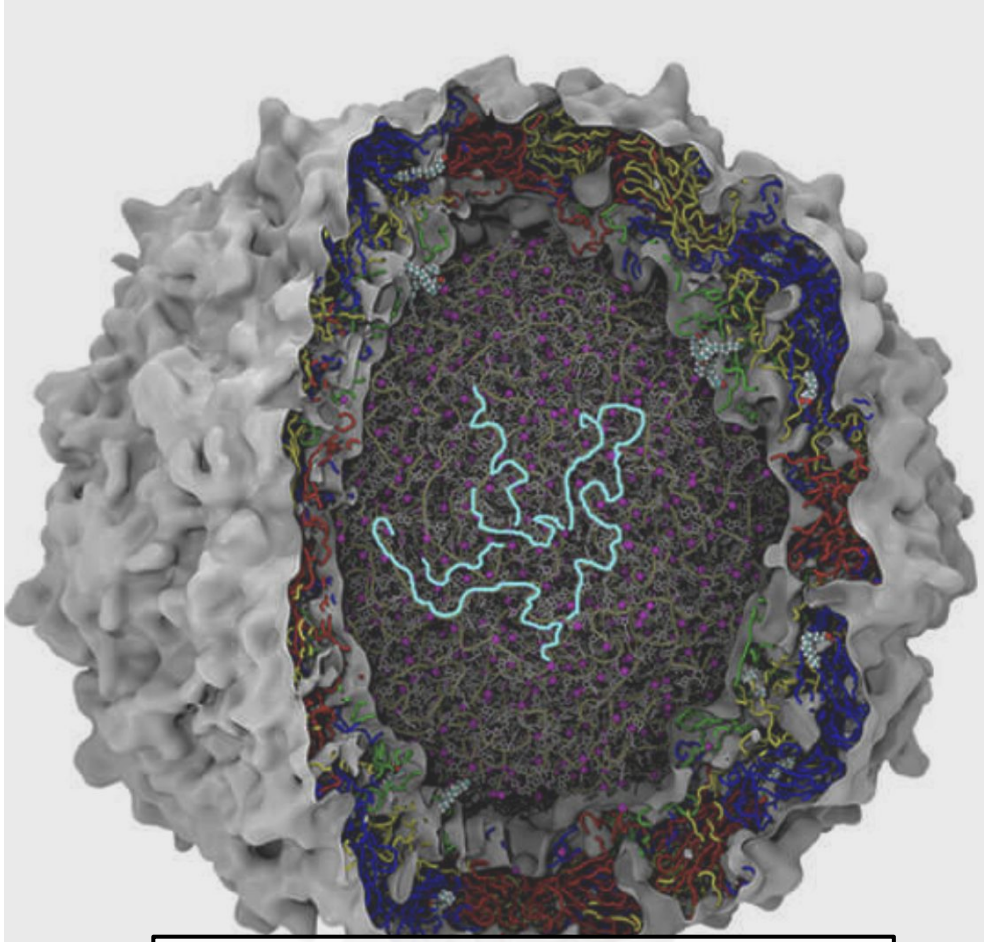


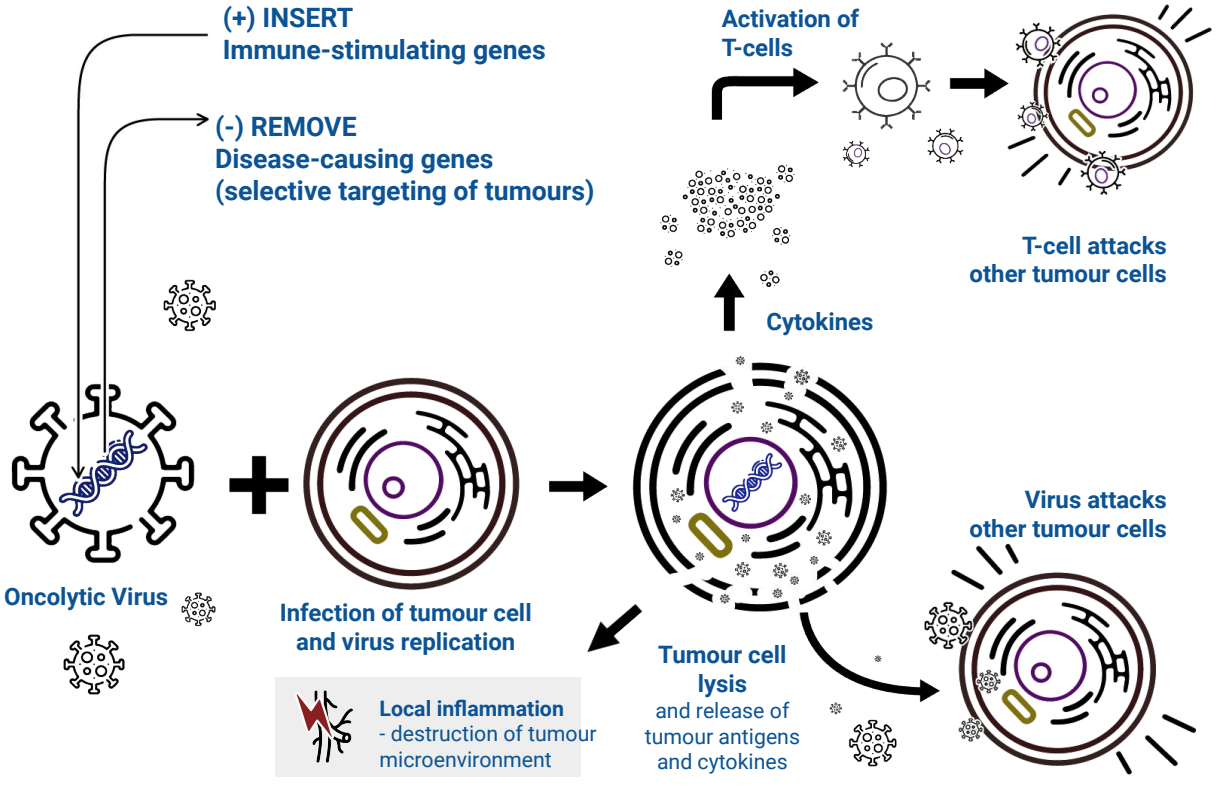
Engineered oncolytic poliovirus for cancer treatment
Credit: Duke Cancer Institute and cancer.gov

Oncolytic Viruses Platform: Overview

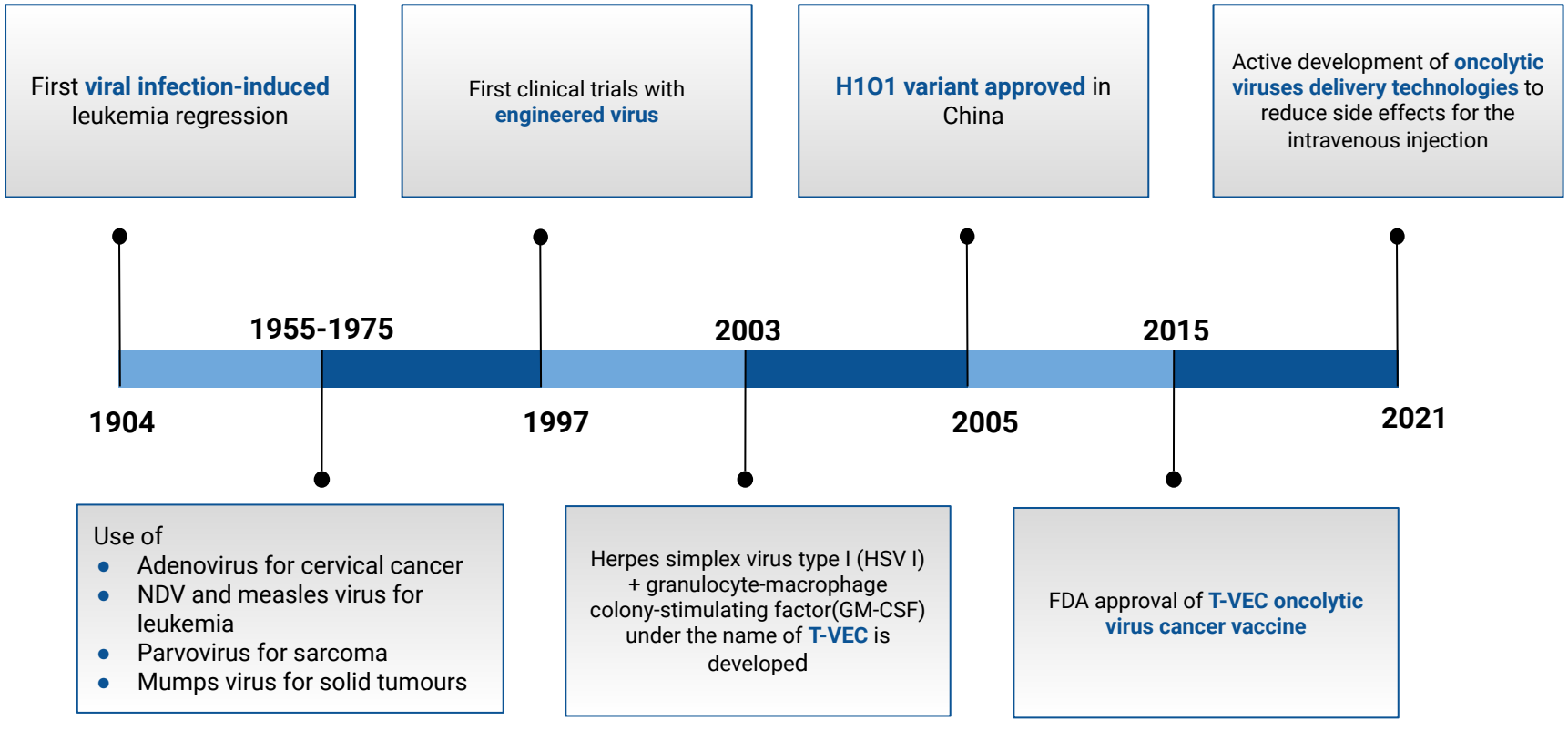
Oncolytic virotherapy is based on the property of some viruses to infect the cells and induce the cell lysis.

In case of cancer vaccination, these viruses are **modified to target cancer cells** and enhance the immune response to completely destroy the tumour.

Oncolytic viruses cancer vaccines platform is greatly based on the neoantigens and tumour-associated antigens platforms since the viruses are 'taught' to target such antigens on the cancer cells. But due to the drastic uniqueness of the mechanism of action of such vaccines, it is fair enough to separate them from other molecular and cellular cancer vaccines.



Oncolytic Viruses Platform: Development Milestones

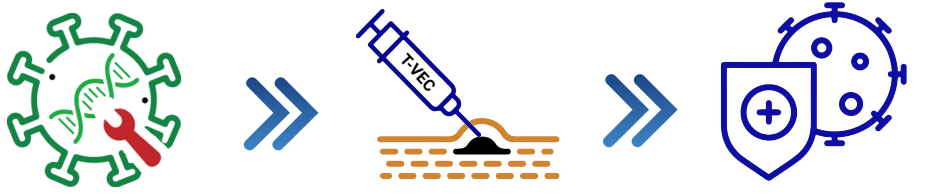


Hamid et al., Cancer Immunology and Immunotherapy (2017)

Oncolytic Viruses Platform: Cancer Vaccines in Development

Currently, there is one **FDA-approved** oncolytic virus immunotherapy – **Talimogene laherpavepvec (T-VEC) owned by Amgen.**

Still, there is active development of oncolytic viruses that would target a wider spectrum of tumours and won't induce the formation of undesired antibodies by the immune system.



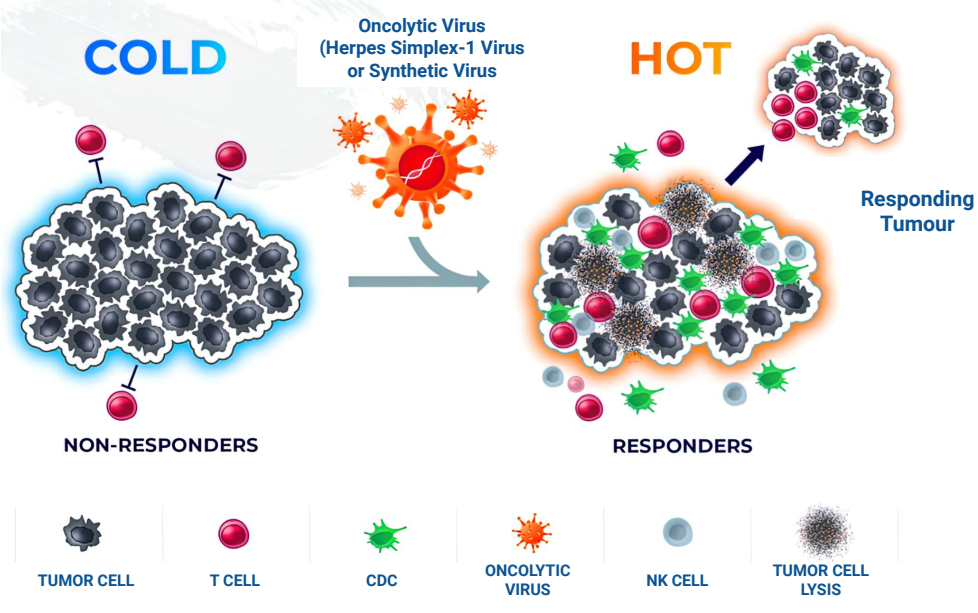
Oncolytic Viruses Cancer Vaccines Development Pipeline

Discovery	Pre-IND	Phase I/II	Phase III

- **ONCR-177 HSV** for intratumoural injections by **Oncorus**
- **CAN-2409 Adenovirus** for prostate cancer by **Candel Therapeutics**
- **OLVI-VEC** for ovarian cancer by **Genelux**
- **ParxOryx** for GBM **by Oryx**

Oncolytic Viruses Platform: Key Players

Oncorus — BioTech company which develops next-generation viral immunotherapies for oncology. Their technology enables immune system to target cold tumours (tumours surrounded by immunosuppressive cells), converting them into hot tumours.



They state that their approach not only activates anti-tumoural immunity but also **stimulates the release** and presentation of a greater number and variety of **neoantigens.**

One more important mechanism is a synthesis of **transgenes,** which influence **tumour microenvironment.**

Sources —Oncorus Technology

Oncolytic Viruses Platform: Key Players

Oncorus is moving into two directions in virotherapy field: Herpes Simplex Virus platform and viral RNA platform. The products of these platforms have different delivery approaches: directly intratumoural through the injection and intravenous, respectively.

oHSV

ONCR-177 is a leading product of this platform, which is an oncolytic virus that should be administered directly into the tumour site; consequently, this induces **immunogenic cancer cell death** and drives lasting and systemic anti-tumour response.

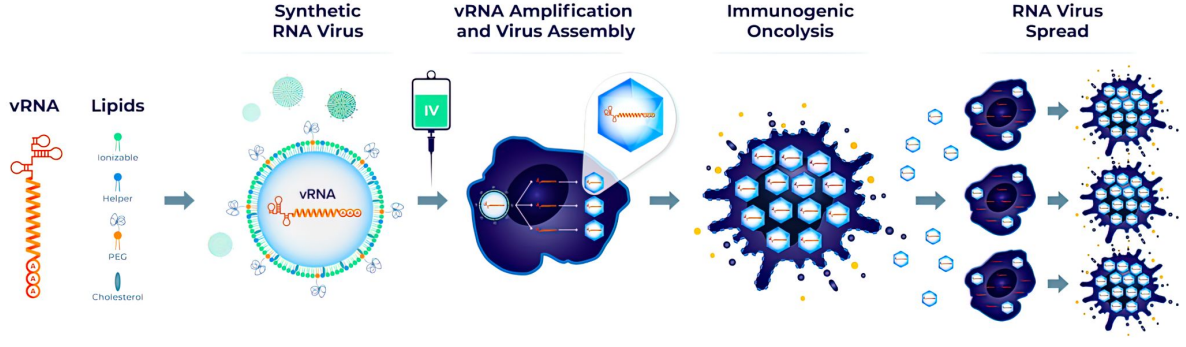
Oncolytic virus brings five immunostimulatory agents:

IL-12, CCL4, FLT3LG, anti-PD-1, and anti-CTLA-4

vRNA

This technology is supposed to be less immunogenic, which should result into a lower nonspecific immune response. Viral RNA is delivered in lipid nanoparticles.

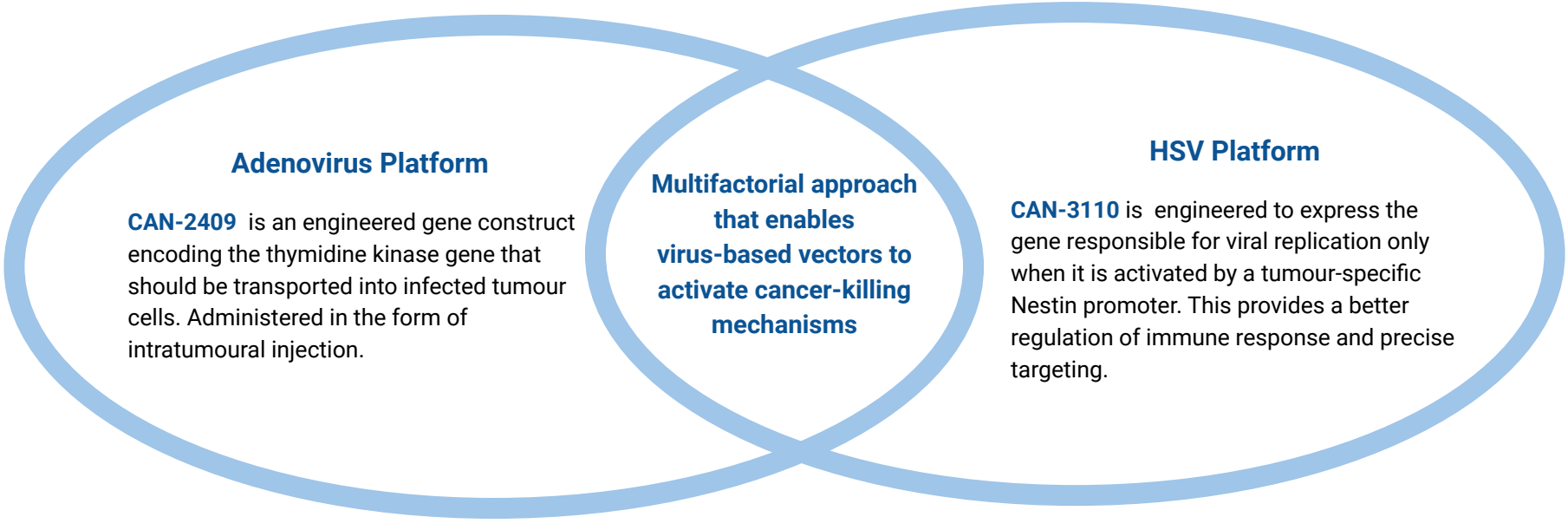
Leading programmes ONCR-021 and ONCR-788 are based on coxsackievirus A21 (CVA21) and Seneca Valley Virus (SVV), respectively.



Sources —Oncorus Technology

Oncolytic Viruses Platform: Key Players

Candel Therapeutics focuses on preventing the recurrence and progression of cancer by applying viral immunotherapy. They aim to reach a low toxicity level ,which is well suited for the treatment of less aggressive or slower growing cancers.



Oncolytic Viruses Platform: Key Players

Genelux is an innovative biopharmaceutical company which develops oncolytic virotherapy and combines it with other cancer vaccine approaches.

Their leading product, **Olvi-Vec,** is currently on the Phase II of clinical trials and is stated to be able to effectively fight multiple cancers (including both solid tumours and blood malignancies). Genelux owns a **Choice Discovery Platform to** develop an extensive library oncolytic viruses strains identified from multiple *in vitro* and *in vivo* selection criteria.

V2ACT (Virus and Vaccine (Neoantigen)-Enhanced Adoptive Cell Therapy) is a unique combinational approach for immunotherapy developed by Genelux.

This immunotherapy is aimed to produce a strong immune response and an outburst of primed cancer neoantigen-specific effector T-cell precursors.

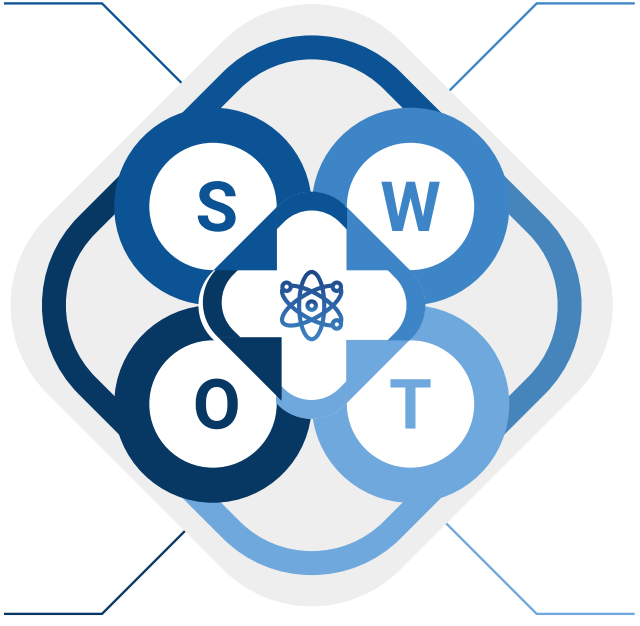
Olvi-Vec Immunotherapy Chemotherapy (platinum) refractory and/or resistant cancers			**Generation Oncolytic Virus**
	Regional (Advantages)	**Intravenous** (Advantages)	**Local** (Advantages)
Ability to target advanced and metastatic diseases	✓	✓	✗
Ability to target cancers without prolonged treatment burden	✓	✓	✗
Ability to target and treat tumours of different sizes	✓	✓	✗
Robust immune activation profile	✓	✓	✗

Sources — Genelux Technology

Oncolytic Viruses Platform: SWOT Analysis

Strengths

- Can reach ‘cold’ tumours and turn them into ‘hot’ tumours;
- Targets both tumour and its microenvironment;
- Creates a strong immune response.



Weaknesses

- Usually causes undesirable immune response with extensive antibodies production, which neutralises the virus;
- Limited number of the antigens that can be targeted;
- Mostly needs to be administered through an injection.

Opportunities

- Can be efficiently improved through combinational therapies;
- Can become the main mechanism of the tumour immunisation if it is not reachable for other therapies.

Threats

- Severe side effects resulted by the viral activity regarding healthy cells;
- Gene-modified viruses injected into a human body might cause some ethical concerns.

Cancer Vaccines Delivery Systems

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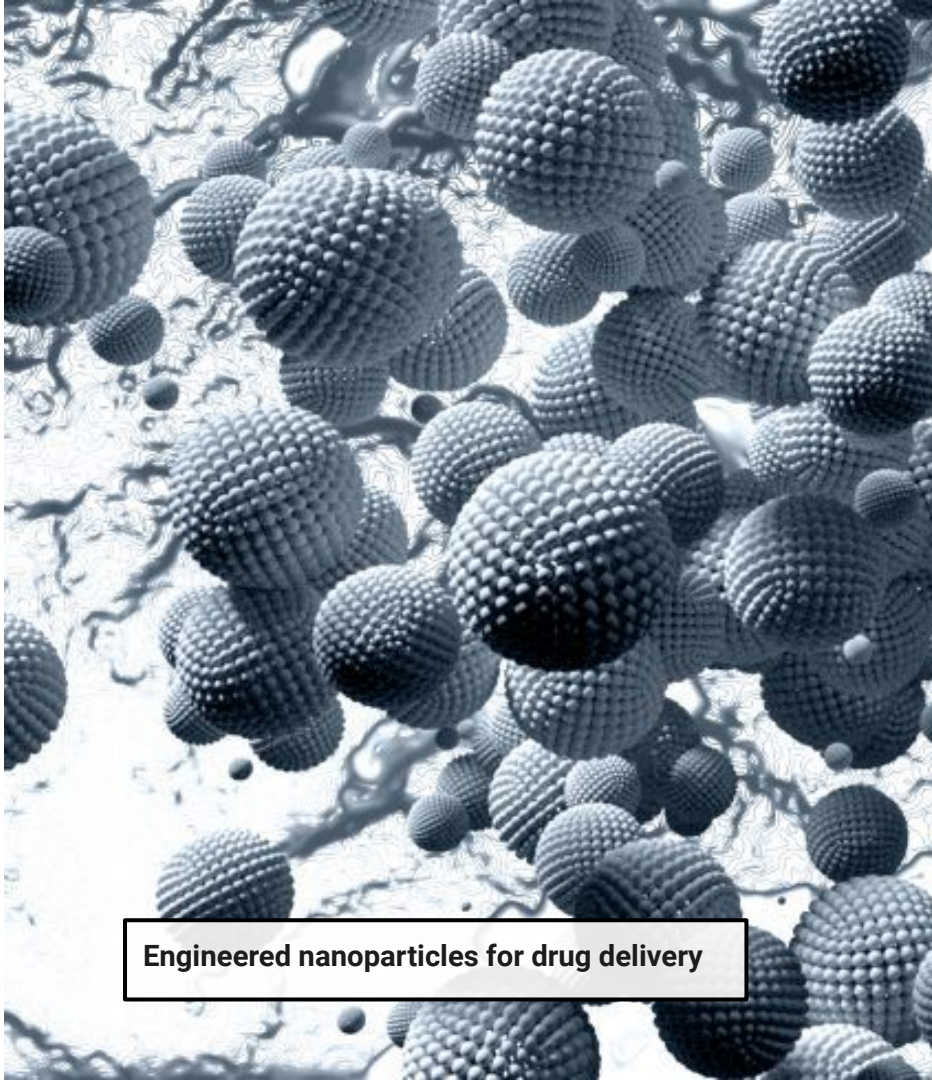


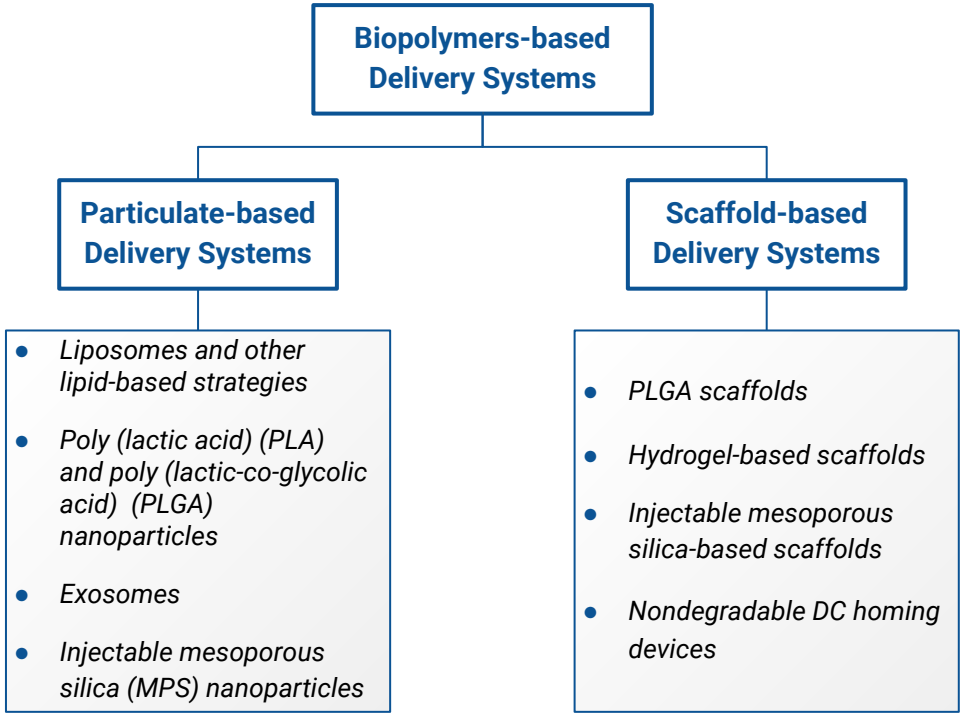
Engineered nanoparticles for drug delivery

The Need of Effective Delivery System

One of the main challenges in modern immunotherapy is **targeting cold tumours**, the subclass of **solid tumours**. Implementing the appropriate delivery system is the primary way to overcome this challenge. Many clinical trials of cancer vaccines fail because of ineffective delivery methods. For example, vaccination using unmodified peptides generated an overall response rate of only 3% due to difficulty activating antigen-presenting cells.

Biopolymers-based delivery systems could enable spatiotemporal presentation to cells and the microenvironment, thus enhancing efficacy and reducing potential adverse effects. Nowadays, the science of biopolymers is rapidly developing, which allows the usage of different biopolymers to overcome various delivery challenges specific to each type of vaccine.

Combining advances in biomaterials with a deeper understanding of cancer immunology is critical for developing a clinically effective cancer vaccine platform.



Sources — Emerging biomaterial-based strategies for personalized therapeutic in situ cancer vaccines

Particulate-based Delivery Systems

Particulate-based approaches have long been utilised to improve therapeutic delivery to particular tissue areas, while minimising off-target and systemic side effects.

Liposomes

Liposomes have a hydrophobic outer layer and a hydrophilic inner core, making them ideal for encapsulating both hydrophobic and hydrophilic medicinal cargo.

✓ Stable
✓ Long depot action at the injection site
✗ Limited loading capacity
✗ Once released, vaccines become impossible to retrieve -> uncontrollable responses

Nanoparticles

Nanoparticles are used for oncotherapeutics delivery because they display target specificity to the tissue of interest, based on size, charge, surface properties ,and dissemination strategy.

✓ Limited off-target accumulation
✗ Limited delivery efficiency
✗ Limited loading capacity
✗ Limited to a cargo of peptides

Exosomes

Exosomes, microvesicles, and apoptotic bodies, which are membrane-bound extracellular vesicles released from the endosomal compartment of most eukaryotic cells, can be used as drug delivery vehicles.

✗ Many manufacturing challenges
✗ New technology which requires more research before trials in humans

MPS Nanoparticles

Mesoporous silica-based approaches aim to address the challenge in high variability in delivery efficacy dependent on cellular interactions by leveraging their well-established drug carrier properties and high versatility in conjunction with other materials.

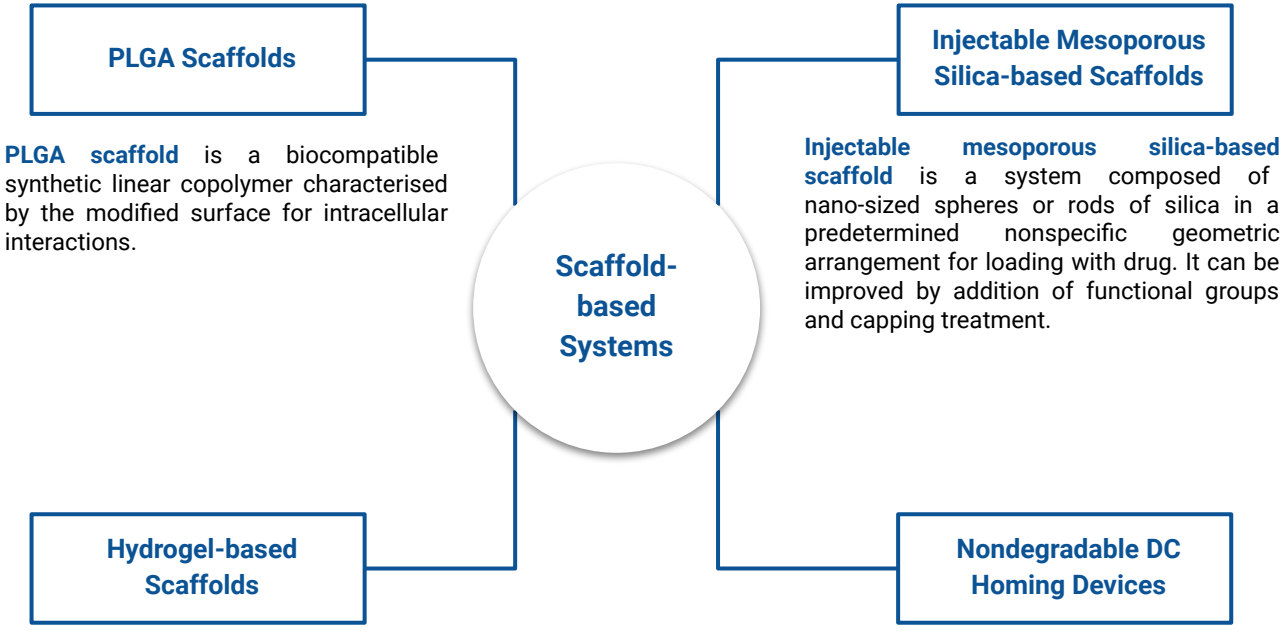
✓ Silica is nontoxic material
✓ Large loading capacity
✗ New technology that requires more research before trials in humans

Sources — Emerging biomaterial-based strategies for personalized therapeutic in situ cancer vaccines

Scaffold-based Delivery Systems

Scaffold-based vaccines are structures intended to initiate anti-tumour immunity locally at the implantation or injection site. For *in situ* cancer vaccines, most deliver stimulatory **adjuvants and antigens** to induce in situ DC homing and subsequent antigen-specific immune activation.

In general, in situ cancer vaccines utilising scaffolds must be designed to address three key criteria. They should be **macroporous, clinically translatable**, and should **release immune potentiating adjuvants.**



Sources — Emerging biomaterial-based strategies for personalized therapeutic in situ cancer vaccines

Companies Applying Advanced Cancer Vaccines Delivery Systems

SilVacx — is a spin-off from Merck AG that specialises on developing novel delivery systems for cancer immunotherapy, including cancer vaccines. SilVacx technology is based on **silicon dioxide nanoparticles**, which can help to make cancer vaccines material delivery in the human body efficient and cost-effective.

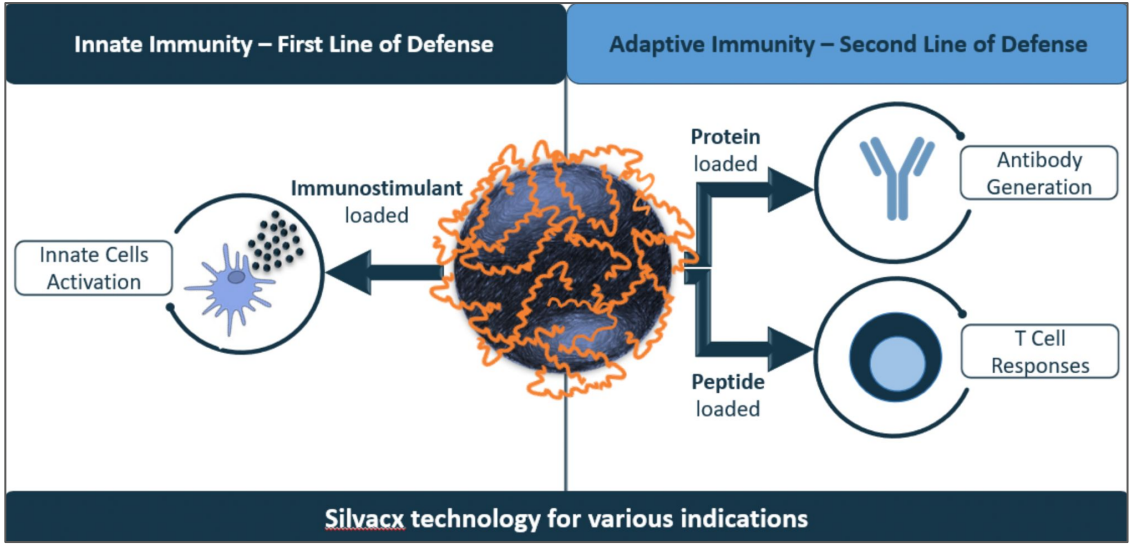
SilVacx project is supported by **Life Science Inkubator GmbH** (LSI), which is the first time LSI supported a research project originating from a pharma company. The platform is mainly oriented for therapeutic cancer vaccines, but it can also be used for preventive vaccines.

Currently, the platform is designed for **neoepitope-based personalised** anti-tumour vaccines and extremely powerful for **HPV** (human papillomavirus) induced cancers.

SilVacx's technology provides

- stimulation of the **innate** immune system
- stimulation of the **adaptive** immune system

Virus-sized particles with a virus-like morphology provide an efficient uptake and processing of antigens by dendritic cells.



Sources — SilVacX

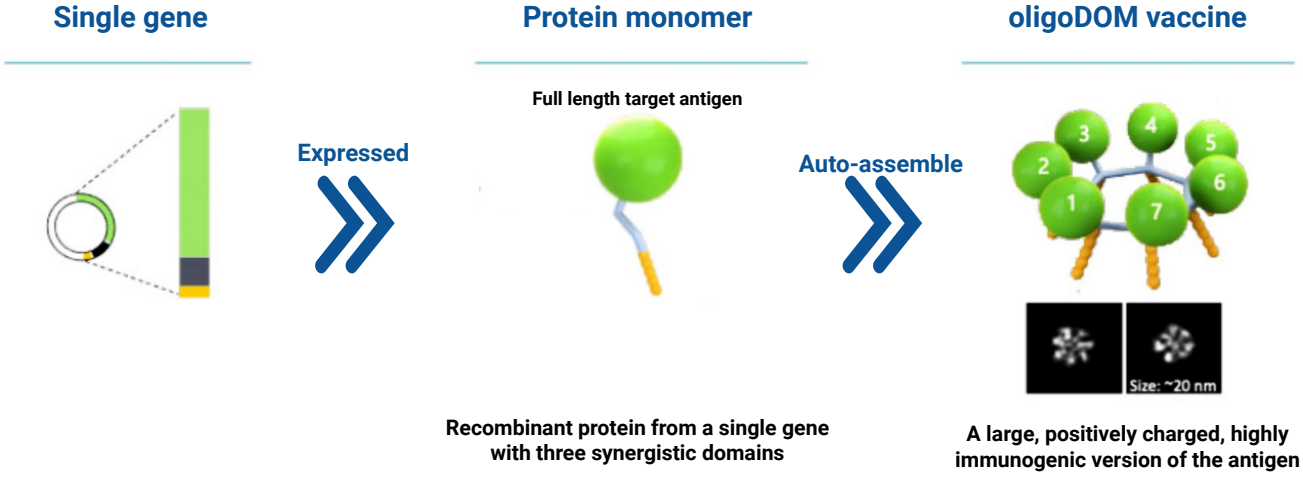
Companies Applying Advanced Cancer Vaccines Delivery Systems

Osivax is a clinical-stage BioTech company that owns a novel proprietary **nanoparticle technology** – **oligoDOM.** This technology can be applied for many types of vaccines, including cancer vaccines.

It is specifically designed to trigger superior T-cell responses, in addition to strong and sustained B-cell responses. In other words, it engages both cytotoxic and memory immune cells.

OligoDOM technology was tested with different antigens, as well as within different vaccine forms. It can be combined with recombinant proteins, or mRNA technology, leading to multiple value generation opportunities.

Currently Osivax is expanding their portfolio to include cancer targets such as **HPV antigen.**



Sources — Osivax Technology

Companies Applying Advanced Cancer Vaccines Delivery Systems

Midatech Pharma is a pharmaceutical company focused on drug delivery technology and its application for various diseases, including cancer.

Midatech owns three drug delivery platforms which enable comprehensive improvement of biodelivery and biodistribution of 'on-market' and pre-approval drugs.

Q-Sphera

proprietary 3D-printing technology that **encapsulates** medicines into **bioresorbable polymer microspheres** with precision characteristics:

- Micro-encapsulation **PLGA polymer** depot system;
- Advanced piezo printing technology;
- Several million microspheres produced per second.

MidaCore

ultra-small **gold nanoparticle** (GNP) drug conjugates.

The small size and multi-functional arrangement of molecules around a gold core underpin MidaCore's ability to improve biodistribution and targeted drug delivery.

MidaSolve

solubilises potent molecules that have minimal solubility at biological pH, extending available routes of administration.

Used for direct-to-tumour delivery.

Sources — Midatech Pharma Technology

Companies Applying Advanced Cancer Vaccines Delivery Systems

Alnylam Pharmaceuticals is a biopharmaceutical company that develops therapy with an RNA interference (RNAi) approach. The company's therapeutic focus areas are genetic medicines, cardio-metabolic, infectious, central nervous system (CNS), and ocular diseases. For delivery of their therapy, Alnylam utilises two delivery platforms – **lipid nanoparticles (LPNs)** and **conjugates**.

Lipid Nanoparticles

- Alnylam has an approved iRNA therapy that utilises LNP-based delivery – **ONPATTRO® (patisiran)**.
- **LNPs** are chemically synthesised **multicomponent lipid formulations** (~100 nm in size) that encapsulate siRNAs and deliver the medicine to the target tissue.
- **LNPs** protect the drug from degradation by **ubiquitous nucleases**.
- **LNPs in ONPATTRO** have an affinity for **apolipoprotein E,** which is expressed on the surface of hepatocytes that allows the accurate delivery of siRNA to the liver.

Conjugates

- **Conjugates** are single chemical entities that have siRNA coupled to target ligands to aid them in finding their way to a particular cell or tissue in the body. The ligand attached to the siRNA has an affinity to the receptor on the target cell, which creates a **'lock and key' system**.
- Alnylam has developed two conjugate approaches to enable targeted delivery to the **liver** and **CNS**.
- The company utilises **GalNAc conjugates** that bind to the **asialoglycoprotein receptor** for targeting the liver, which is abundantly expressed on liver cells (hepatocytes).

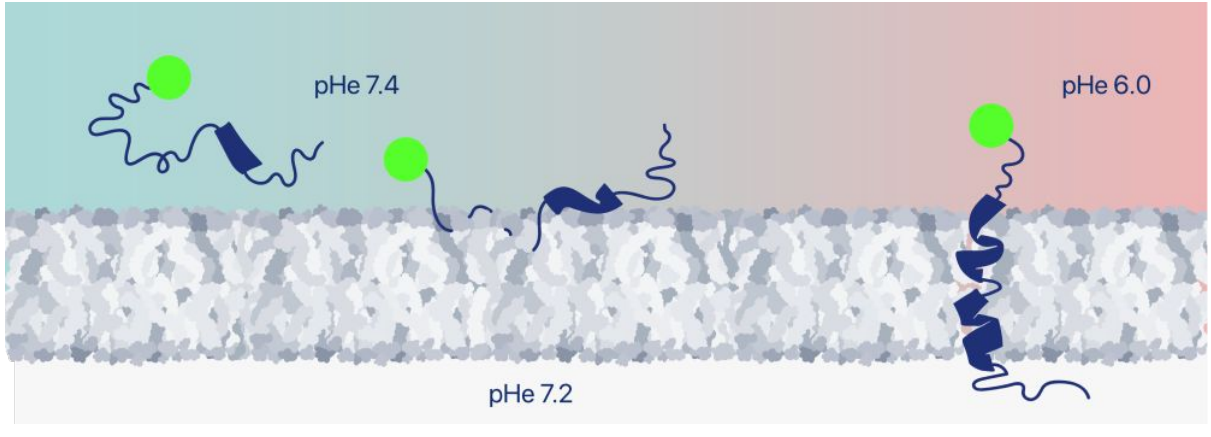
Sources — Alnylam Pharmaceuticals

Companies Applying Advanced Cancer Vaccines Delivery Systems

pHLIP is a company that develops peptide-based targeted delivery platforms to cure cancer, inflammation, and other acidic tissue diseases. Their innovative platform **pHLIP®s** (**pH-Low Insertion Peptides**) is a platform technology of **pH-sensitive peptides** that exploit pH differences between healthy and diseased cells as a biomarker for targeting and delivering therapeutic and imaging agents to cells in acidic diseased tissues.

Molecular Mechanism:

- **pHLIP® peptides sense and target pH at cell surfaces** where the pH is the lowest, thus providing high sensitivity.
- **pHLIP® peptides exploit folding and insertion across the cell membrane**, a cooperative process that gives high specificity.
- **pHLIP® peptides do not target or accumulate in cells with normal surface pH in healthy tissue.**



Sources — Philip Inc.

Companies Applying Advanced Cancer Vaccines Delivery Systems

Codiak Biosciences is a biopharmaceutical company focused on pioneering the development of exosome-based therapeutics. Codiak created the **engEx Platform** that allows us to build and engineer exosomes with unique features, load them with a variety of therapeutic compounds, and guide their tropism to particular target cells. The platform uses exosome-associated proteins – PTGFRN and BASP1 – as scaffolds to direct proteins of interest (targeting ligands and therapeutic molecules) to the surface or the lumen of exosomes.

Exosomes have the potential to be a beneficial therapeutic method due to their capacity to selectively transport a wide range of therapeutic payloads to cells, opening the door to a wide range of possible applications in illnesses that have eluded other treatments.

Targeted Delivery

- Exosome tropism can be designed so they reach specific cell types in the body.
- The targeted delivery enhances drug efficacy and safety.

Immune Silent

- Exosomes are composed of natural human proteins and lipids, making them inherently nonimmunogenic.

Multi-Functional

- Exosomes can be loaded with multiple different types of molecules and can influence their targets in multiple ways.

Key Takeaways and General Conclusions

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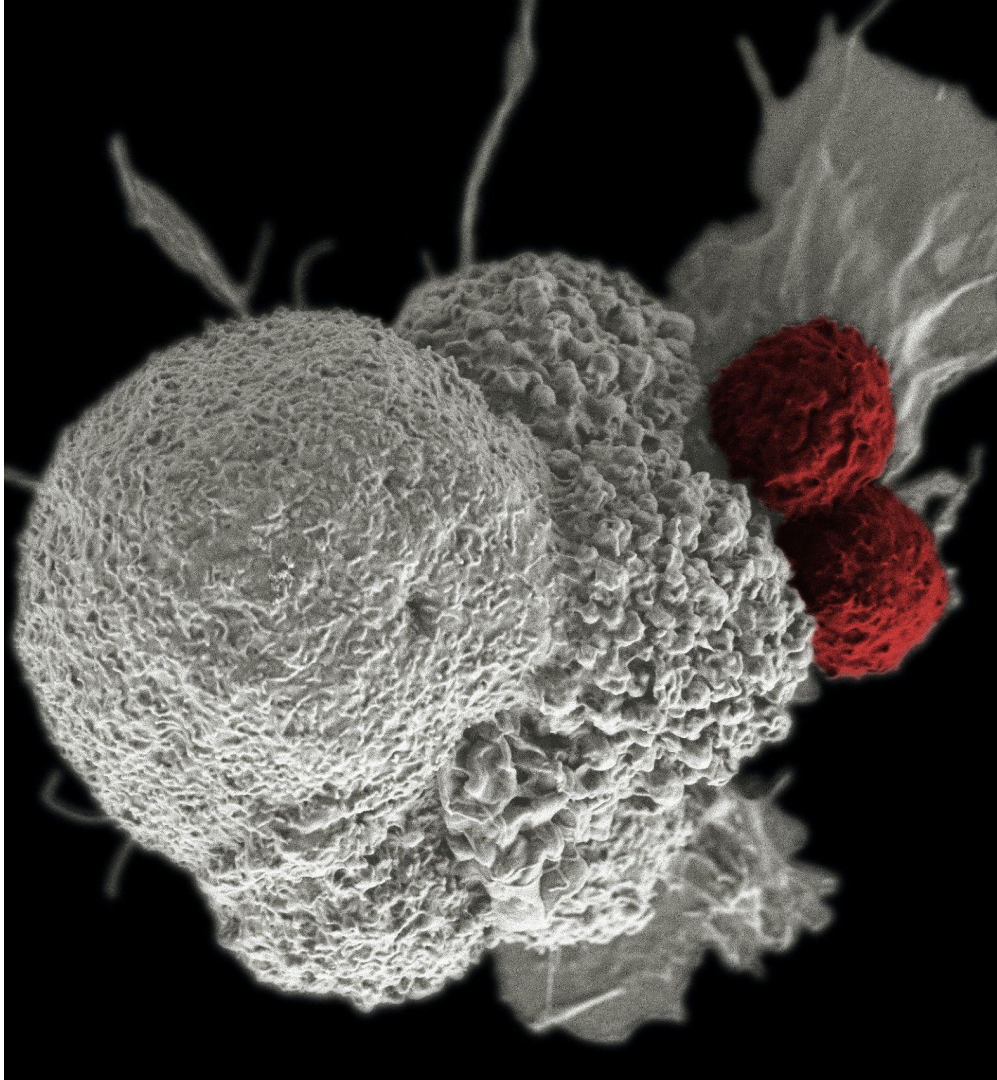
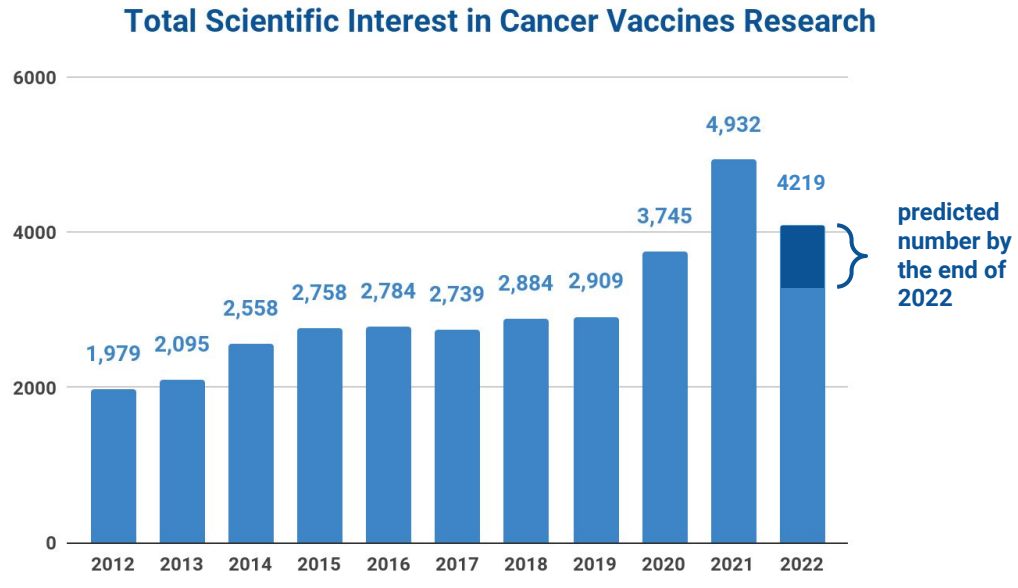


Key Takeaways

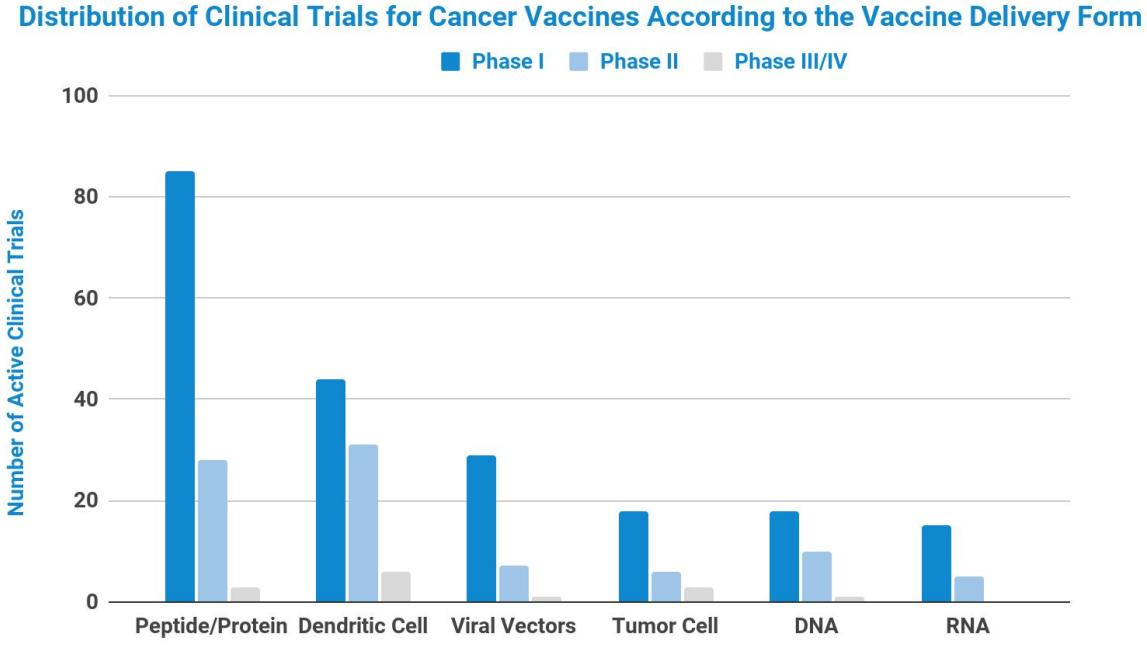


The graph demonstrates the growing number of publications mentioning cancer vaccines by year. Over a decade, the annual publishing grew more than 2.5-fold and is expected to continue increasing. Here, we included all available article types on PubMed.

- The interest in cancer vaccination is continually growing, experiencing an outburst in 2021. This mature field of immunotherapy requires **novel approaches and revitalisation solutions.**
- The most actively developing platform right now is **neoantigens platform,** which we observe from analysing the lead products of big pharmaceutical companies.
- The most **prominent research vectors** in the field of cancer vaccines are aimed at **enhancement of immunogenicity,** while reducing a nontargeted damage of healthy cells, targeting **multiple antigens** and developing an **universal vaccine** for a broad spectrum of malignancies.

Sources — PubMed Database

Key Takeaways



This graph uses the information from clinicaltrials.gov and data provided by Cuzzubo et al. (2021). You can see data that summarise open cancer vaccine trials by trial phase and vaccine type.

- Besides the common tendency of having the highest number of product candidates on the first phases of clinical trials, there is an even distribution of numbers, depending on the delivery form of cancer vaccine.
- Peptide/protein form was represented by over 115 candidates on different stages of clinical trials, being the leading platform for vaccine delivery to the target cells. Dendritic cells appear to be the second leader, with already approved Sipuleucel-T.
- Fewer number of cancer vaccines are delivered in the form of DNA and RNA, which can be due to higher cost of development and younger age of the platform.

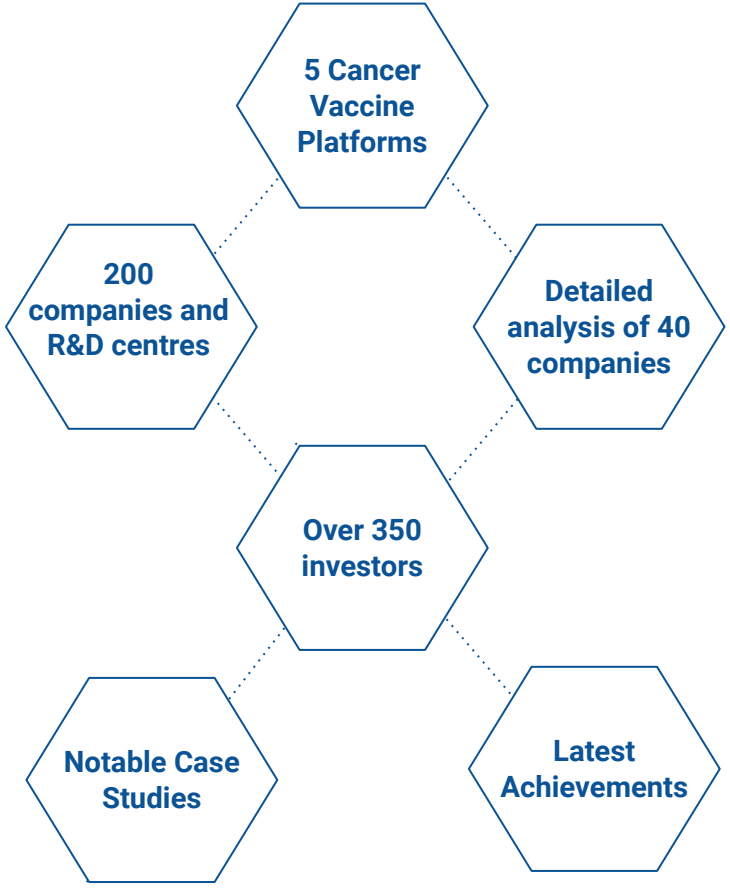
General Conclusions

- We have reviewed five cancer vaccine platforms that are actively developing their products to enter the market of immunotherapy. As a result, we conducted an assessment of more than 200 companies and R&D centres and detailed analysis of more than 40 of them. Besides, we analyzed investments into those companies and found more that 350 investors.

- Identified cancer vaccine platforms have distinguishable features and development timelines, as well as representative companies with the products pipelines. All the reviewed key player companies, in our opinion, possess strong R&D bases, well-developed level of technology and intellectual property, and large total addressable markets for their products.

- We believe that cancer vaccine development is moving into the direction of more specific tumour targeting, while reducing side effects by the novel delivery methods, antigen identification applications, or vaccine preparation process itself.

- Currently, the major attention is paid to neoantigen platform, but it will probably be pushed out by such growing cancer vaccine platform as antigenic essence, which is likely to combine a high specificity, efficiency, and time- and cost-effectiveness.



Overview of Proprietary Analytics by Deep Pharma Intelligence

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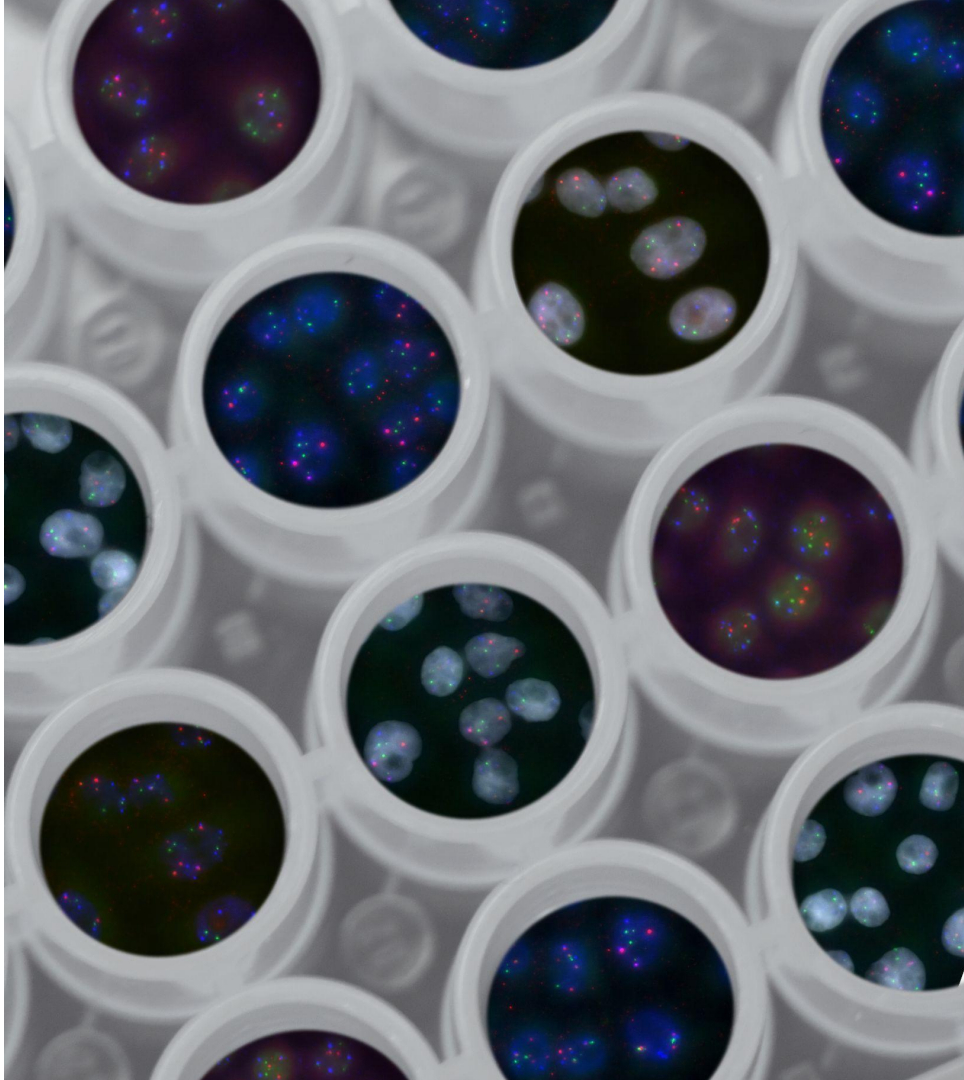


Deep Pharma Intelligence — New Era in Pharma Analytics

Deep Pharma Intelligence (DPI), an analytical subsidiary of Deep Knowledge Group, is a highly specialised think tank in the area of BioTech innovation profiling, market intelligence, and BioTech development advisory. The company is dedicated to producing powerful data mining and visualisation systems, interactive analytics tools, and industry reports, offering deep technical insights, market intelligence, and strategic guidance in the high growth and significant opportunity areas.

DPI is Focusing on Three Key Activities:

Conducting Market Intelligence

Producing regular **open-access** and **proprietary reports** on the emerging topics and trends in the pharmaceutical and healthcare industries. All reports are supported by our back-end analytics systems and tools that allow to receive fresh insights and updates about opportunities and risks.

Creating Big Data Analytical Dashboards

Building a comprehensive **Big Data Analytical Dashboard** (SaaS) as a one-stop-platform for all market and business intelligence operations our customers may need, including profiling thousands of companies, market signals and trends based on tens of millions of constantly updated data points.

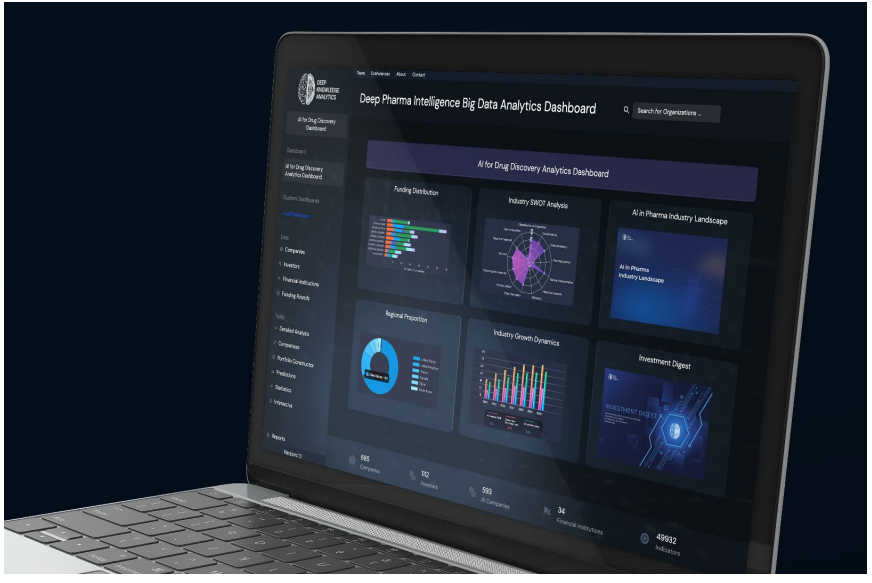
Producing Scientific Content

DPI provides a **full-cycle development of articles, scientific journals, and books**. We are ready to develop a detailed Requirement Specifications document, including layout of the journal, fully designed brand book, with example templates for each chapter.

AI in Drug Discovery Analytical Dashboard

AI in Drug Discovery Analytical Dashboard is a fundamental tool for strategic insights, opportunity evaluation, competitor profiling, and other purposes relevant to Pharma and BioTech decision-makers, life science investors, consulting companies, and regulatory agencies.

600	Companies
1,100	Investors
290	R&D Collaborations
120	Clinical Trials
170	Parameters of Automated SWOT Analysis



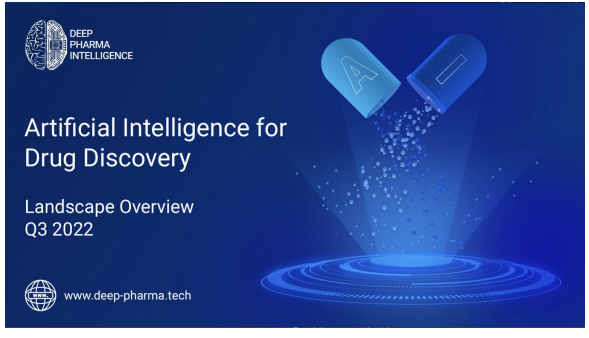
Market Intelligence Focus

- Automated SWOT Analysis
- Stock Price Forecasting
- Interactive Chart Builder
- Automized Competitive Analysis
- Financial Portfolio Constructor
- Matching Tool for Investors

Comprehensive Market Intelligence

Deep Pharma Intelligence's proprietary services include **custom consulting projects based on the specific customer needs,** as well as a collection of preproduced 'ready-to-use' proprietary reports, developed by our research team and covering general trends and specific action ideas and strategy insights related to the most promising business prospects (e.g. new technologies, BioTech start-ups), M&A prospects (e.g. pipeline development targets), and strategic growth ideas (trends profiling, industry overviews, etc.).

Selected Open Access Reports



Artificial Intelligence for Drug Discovery Landscape Overview, Q3 2022 is an analytical report that aims to provide a comprehensive overview of the AI in drug discovery industry, clinical research, and other aspects of pharmaceutical R&D.

Epigenetic Drugs Q2 2022 report aims to provide a comprehensive overview of the current state of the epigenetic drugs market and research. The aim of this report is to provide insights into the diversity of possible epigenetic targets, mechanisms of their action in treating cancer and other diseases.

Landscape of Advanced Technology Companies in Pharmaceutical Industry Q4 2021 is an analytical report providing insights into the expansion of technology developers and vendors in the pharmaceutical space, as well as their increasing role in the pharmaceutical business.

Business Consulting Services

Deep Pharma Intelligence offers a comprehensive range of **consulting services**, including **market and competitor research, technology scouting and due diligence, investment landscape profiling, and comprehensive analytics support for investment decision-making.**

Investment Landscape Profiling

Identifying investment trends in the pharma, BioTech, medicine, healthcare, drug development technological space, investments risk profiling based on risk tolerance, risk capacity, and risk requirements.

Technology Scouting and Due Diligence

Identifying, locating, and evaluating existing or developing technologies, products, services, and emerging trends. The service includes business, science and technology, intellectual property (IP) profiling, and potential assessment.

Market Research

Thorough market assessment within a specific industry in the field of pharma, BioTech, medicine, healthcare, drug development, AI, and others.

Competitor Research

Competitive analysis of companies, technologies, technological sectors, etc. Competitive analysis includes SWOT analysis and competitive profiling.

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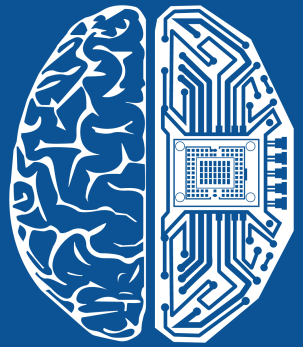

Link to the Report: www.deep-pharma.tech/cancer-vaccines-q4-2022

E-mail: info@deep-pharma.tech | **Website: www.deep-pharma.tech**