Webex Meeting WHO, MHO and INTRAVACC
12-06-2020

Proposed Agenda

1. **Short introduction participants of the meeting**
2. Introduction [redacted (10)(2e)]
3. The status of privatization process of Intravacc
4. An explanation of the work of intravacc on three possible Covid vaccines
5. The status of GAP3 development in the labs of Intravacc
6. Any other business and conclusions

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Webex meeting WHO, MOH and Intravacc

Participants from the WHO:

From the Polio Programme:

- (10)(2e)
- (10)(2e)
- (10)(2e)

From the WHO Legal Office:

- (10)(2e) (10)(2e)
- (10)(2e) (10)(2e)

Participants from MoH and Intravacc:

- (10)(2e) (10)(2e) (10)(2e)
- (10)(2e)
- (10)(2e)
- (10)(2e) (10)(2e)

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(10)(2e)

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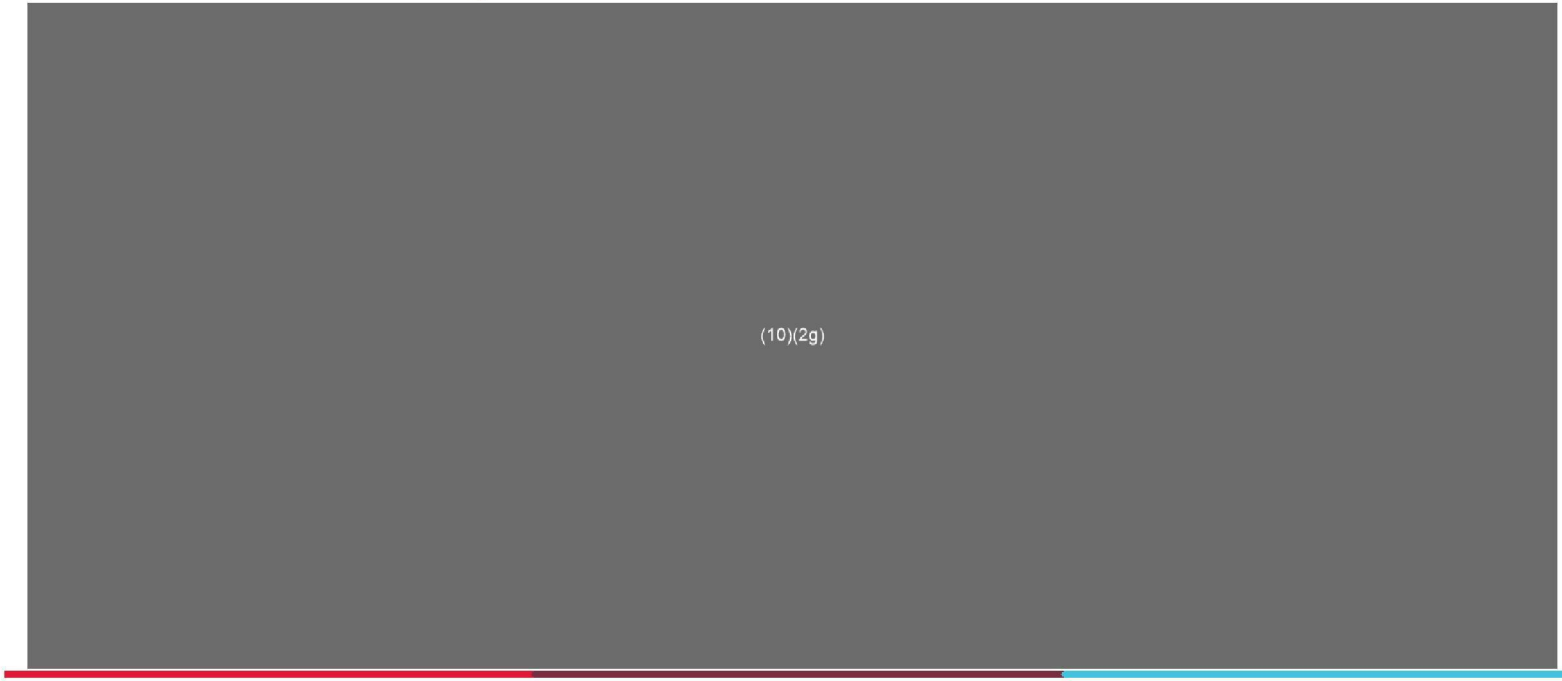
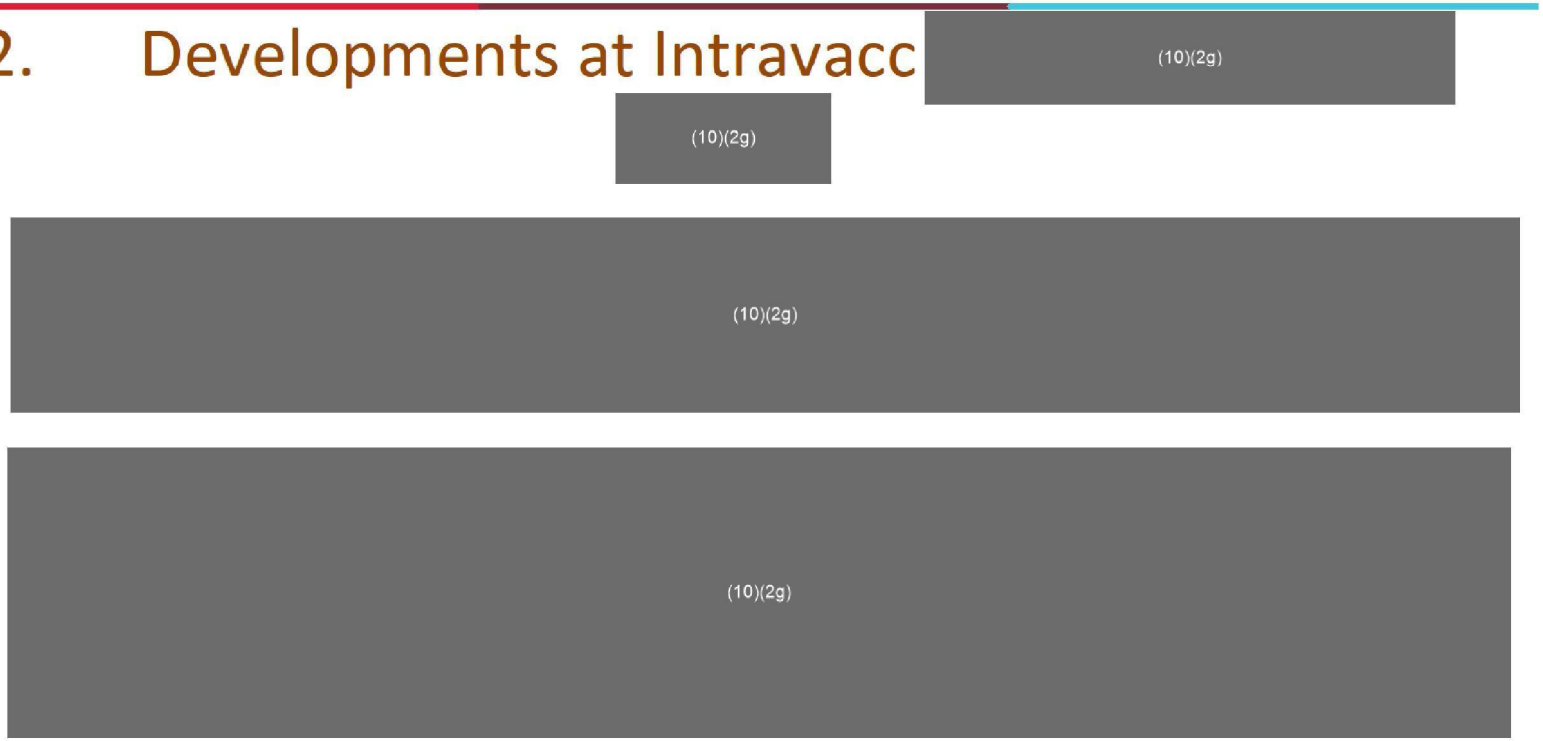
1. Status update on Privatization of Intravacc



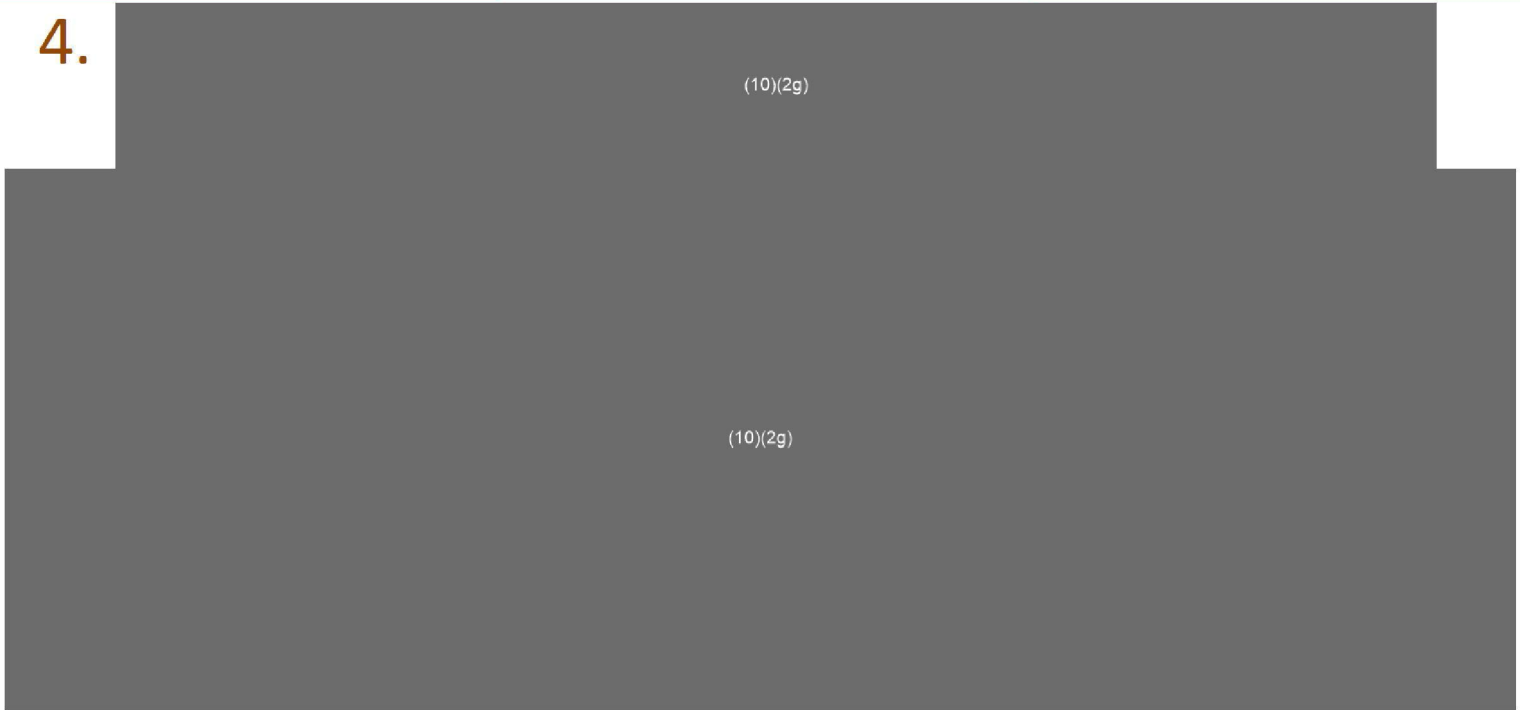
2. Developments at Intravacc



3. Public-Private Collaboration and development of a COVID-19 vaccine

(10)(2g)
2) The intent is that Intravacc will create a valuable partnership together with selected public and private parties with the objective to strengthen the know-how and expertise in the development and production of vaccines;
3) Considering the current worldwide Corona crisis the PPS will in first instance focus on the development of one or more Corona Vaccines together with other Dutch parties. Intravacc is currently developing three vaccine candidates against Covid-19.
4) Through vaccine producers Bilthoven Biologicals ("BBio") and Halix there is access towards at least two other vaccine concepts against Covid-19. This number of vaccine concepts may be further increased by adding more candidates.
(10)(1c)
6) Final objective is to provide access to safe, efficient, effective and affordable vaccines for the people in the Netherlands, Europe and worldwide;
7) In due course Intravacc will have access to its own (pilot) production facilities (Building X, located at the Poonawalla Science Park) and in cooperation with Poonawalla Science Park there are design studies to build new vaccine production facilities in Bilthoven, The Netherlands;
8) Such production facility could be available within 18 month and include two production lines and one filling line;
9) Alternative production capacities are available via the cooperation partner Halix, located in Leiden, the Netherlands and the production facilities of BBio in Bilthoven. By extending the production facilities the expected demand for safe, effective, efficient and fairly priced Corona Vaccine in Europe and worldwide can be covered.
10) The PPS is aiming to work together with international parties. Intravacc is currently already working together with e.g. CEPI, the European Vaccine Initiative etc. Please note that on short term Intravacc will submit a Covid-19 vaccine proposal towards CEPI on behalf of an international consortium;
11) Moreover Intravacc strives to leverage on its international partnerships and contacts as towards the Gates Foundation, International Vaccine Institute ("IVI"), UNICEF, the WHO and the network of vaccine producers in developing countries ("DCVMN")
12) Ultimately, the Public-Private Corporation will constitute more than the joint efforts of developing a Corona Vaccine, but will also reinforce the leadership position of the Netherlands as a contributor to the development and production of vaccines for a wide range of Global Health objectives.

4.



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innovating vaccines

Bilthoven, 12 June 2020

(10)(2e)

Intravacc: A one stop shop for vaccine development

- The only independent vaccine development institute in the Netherlands
- ~40% childhood vaccines are based on Bilthoven technology & know-how
- Services from discovery, pilot production to registration
- The bridge between research scale and large scale GMP manufacturing
- Two of COVID-19 vaccine concepts in development

Institute for **Tra**nslational **Vacc**inology

- Spin-off from RIVM and NVI (2013)
- Proprietary vaccine technology platforms
- 20 patent families
- 140 employees
- State-of-the art laboratory facilities (2000 sqm)
- Two leading concepts for COVID-19 vaccines
  - Vector vaccine (Vero cell platform
  - OMV vaccine (OMV click platform)

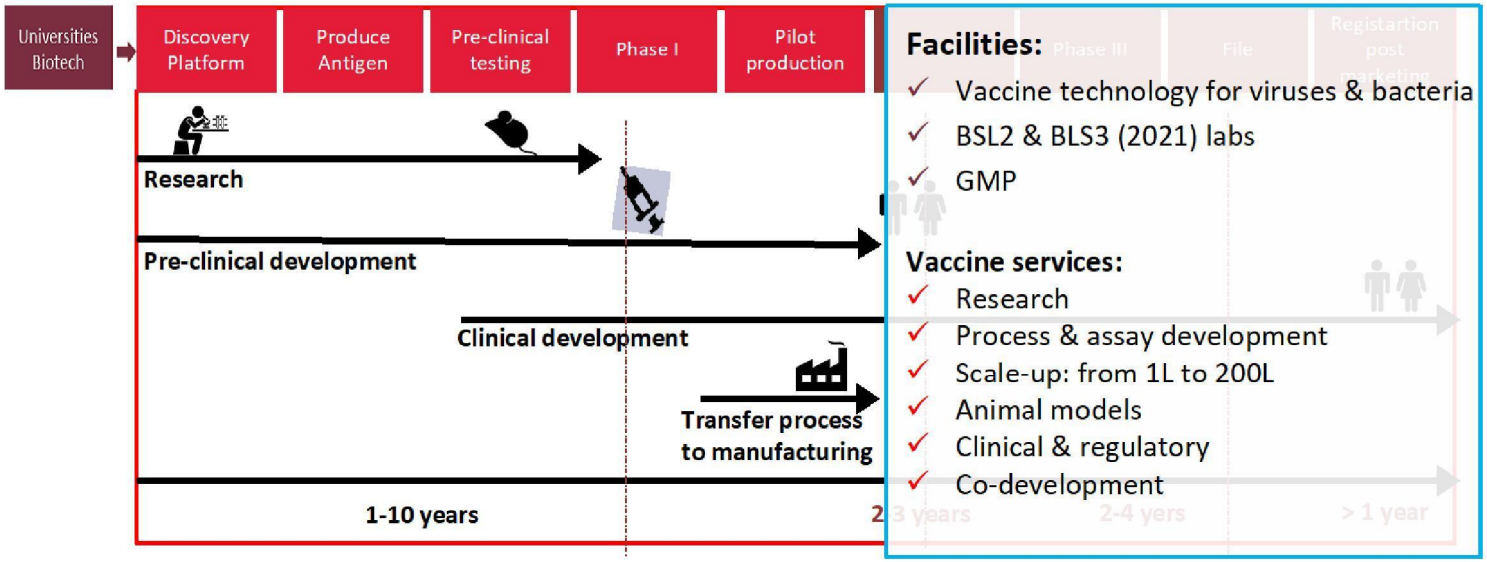
Our Vision

Eradication of human diseases through innovative vaccine technology

Our Mission

To partner with (non) governmental agencies and private entities to help eradicate diseases

Bridging academia and biotech towards pharma



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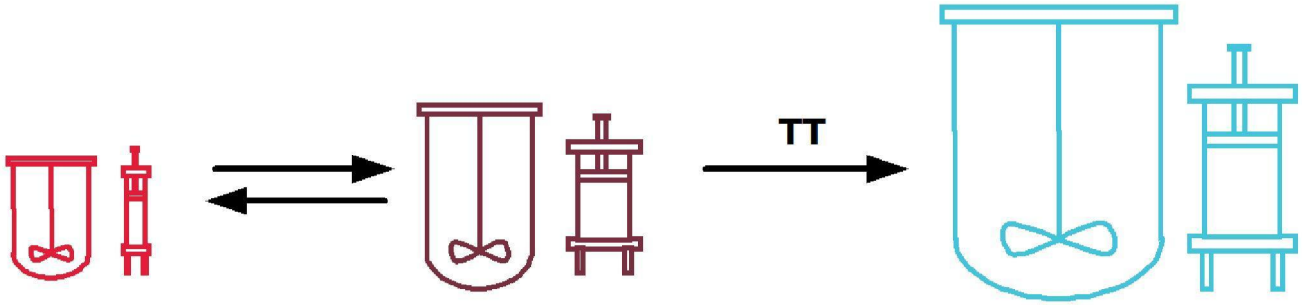
From research to manufacturing



Research
University & Biotech
< 1-5 L

GMP pilot production
Intravacc
5 -200 L

GMP manufacturing
Pharma
>1000 L

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Selected vaccine development achievements

Vero cell platform technology	Breakthrough in upscaling conventional Polio vaccine production. Globally used.
Sabin IPV	Technology transfer to 5 LMIC manufacturers, foreseen production of 60 million doses p.y. (2021)
Influenza vaccine	Technology transferred to multiple vaccine manufacturers
Haemophilus Influenza B	Hib technology transfer 200 million doses produced per year

Global Research Partners and Customers

Connecting public with the healthcare market

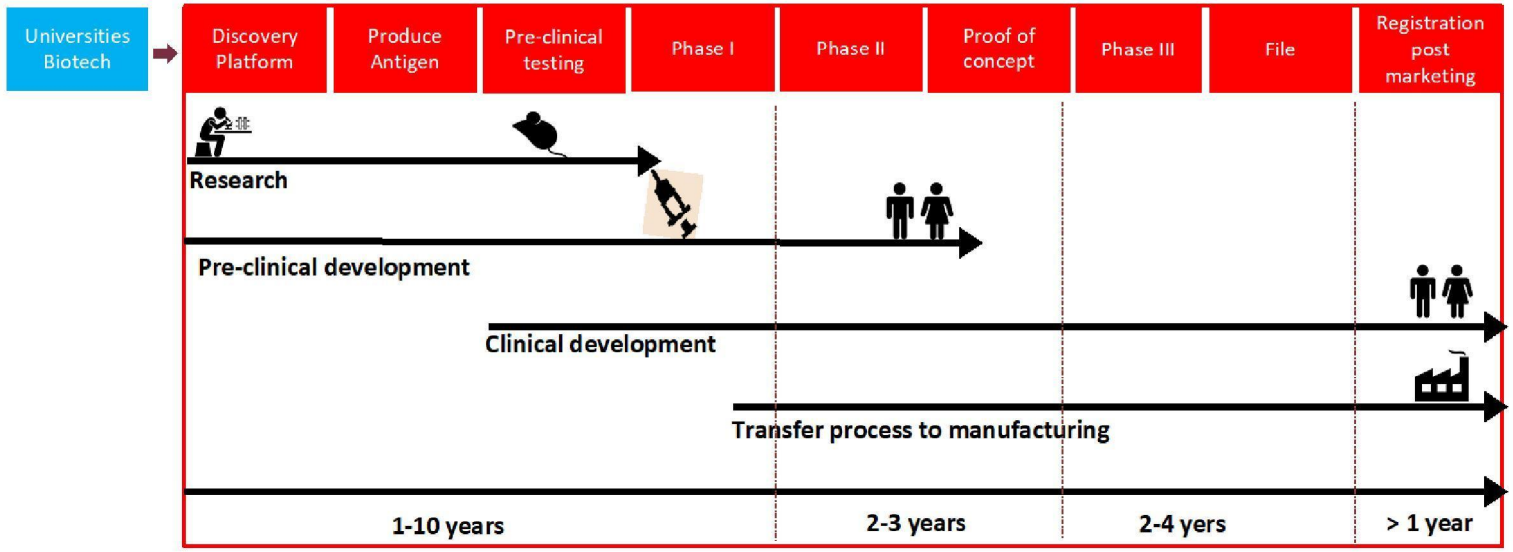
Biotech & Pharma (18)

Governments & NGO's

Universities (17)

Public Health Institutes (12)

Vaccine research and development cycle



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Common cold and vaccines

World-wide 3-5 million severe flu cases per year

- **> 200** virustypes causing flu like symptoms
- **1** approved vaccine on the market for **Influenza**
- All other attempts have failed

Corona pandemic

Emerging Disease

4 Old human viruses

3 Zoonotic viruses

0.5-2%

Mortality rate

~400,000

COVID-19 related deaths YTD

0

Vaccines

No approved drugs

~$140B

Estimated 14B doses at $10/dose

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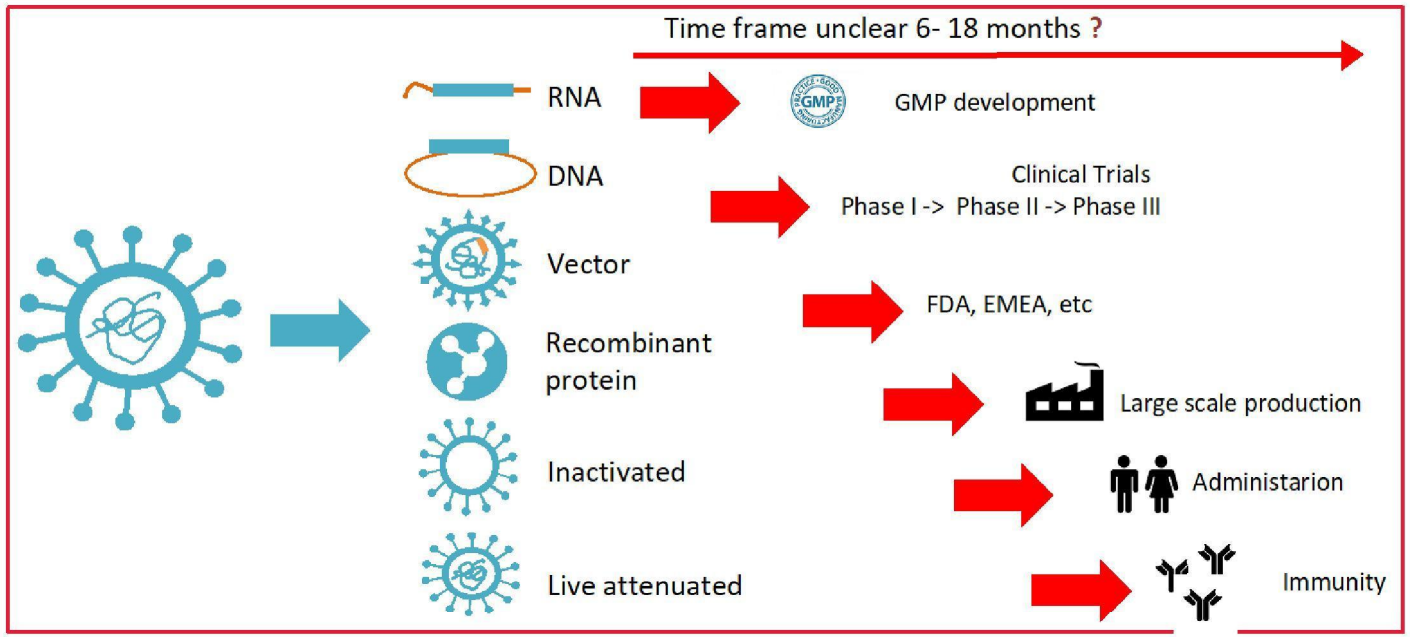
Development of candidate COVID vaccines



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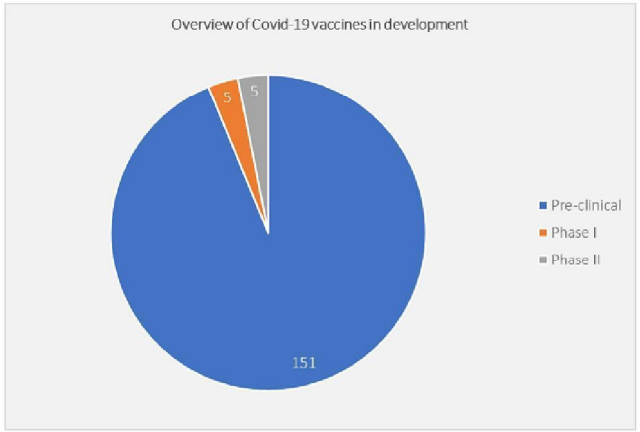
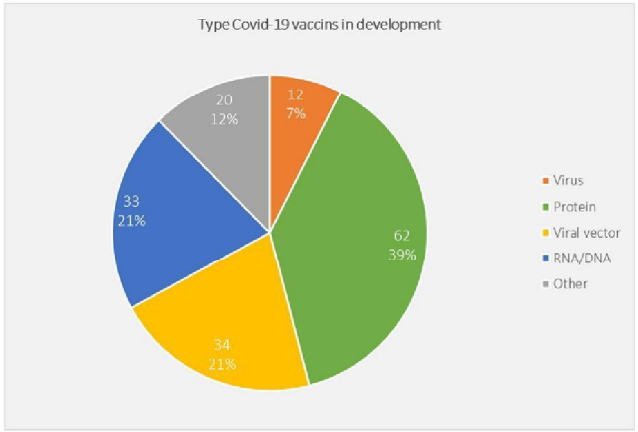
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7136867/

Worldwide response to Covid-19





Source: public resources, status per 9 June 2020

- Out of 160 vaccines, 10 vaccines entered testing in humans (phase I-II)
- From all vaccine candidates approx. 67% is based on live-attenuated, viral vector and protein-based vaccine technology
- Apart from R&D and clinical development, next challenge will be process development, upscaling and large-scale manufacturing

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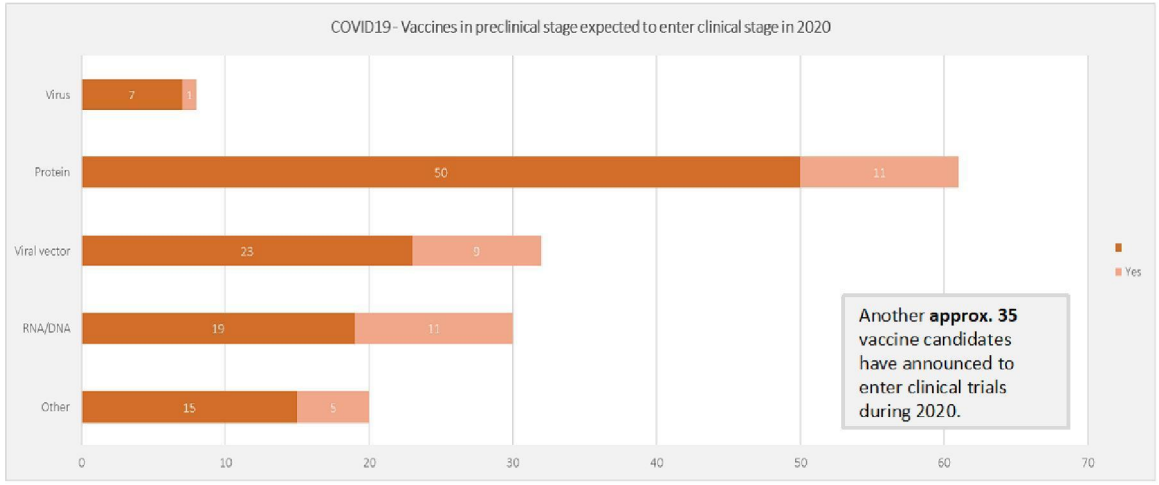
Worldwide response to Covid-19



Source: public resources, status per 9 June 2020

→ Among the vaccine candidates to enter clinical testing in 2020 are:

- (Virus) : Serum Institute of India/Codagenix
- (Protein subunit) : Clover, Sanofi Pasteur/GSK,
- (Viral vector) : Avexis/Novartis, Johnson & Johnson, Vaxart/Emergent, Themis/Merck,
- (mRNA) : CureVac, Sanofi/Translate Bio

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Intravacc COVID-19 vaccine approach

Intravacc COVID-19 vaccine concepts

Emergency vaccines

- Fast timelines
- Prevent mortality and morbidity
- OMV-T-cell peptide based vaccine

Conventional vaccines

- More compressed timelines
- Prevention of disease
- One Vector based vaccine
- One OMV-protein based vaccine

Partners

WAGENINGEN UNIVERSITY & RESEARCH

EpiVax

Sanquin Bloedbank

PEPSCAN

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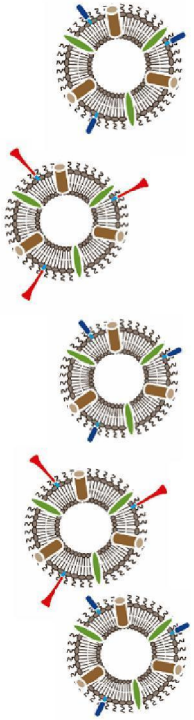
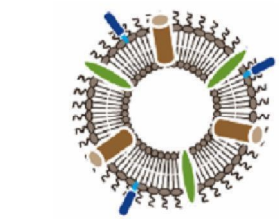
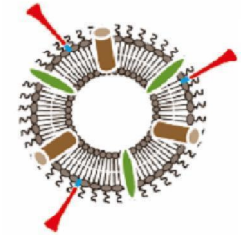
Outer membrane vesicle (OMV) platform



- OMV are produced by bacteria secreting natural vesicles
- OMV have been **proven safe in humans**
- OMV spherical vesicles vary in size from 20-200 nm
- Self adjuvanticity
- Animal studies show induction of strong immune response
- Click-approach for flexible design and fast track
- Scientific & clinical evidence
  - 8 patent applications
  - 84 publications

Corona OMV vaccine concepts





- **Vaccine Platform**
  - Intravacc outer membrane vesicle (OMV) platform
  - Intranasal or injectable application
- **OMV T-cell peptide vaccine**
  - Specific targets are selected that are predicted to
    - ✓ activate T cells in most people
    - ✓ induce very strong immune responses
    - ✓ be widely protective against β-coronaviruses
- **OMV spike protein vaccine**
  - Parts of the protein that may induce harmful- or suppress immune responses eliminated to make the vaccine safe and efficacious
  - Induces an antibody and T cell response

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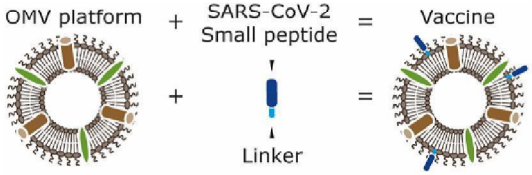
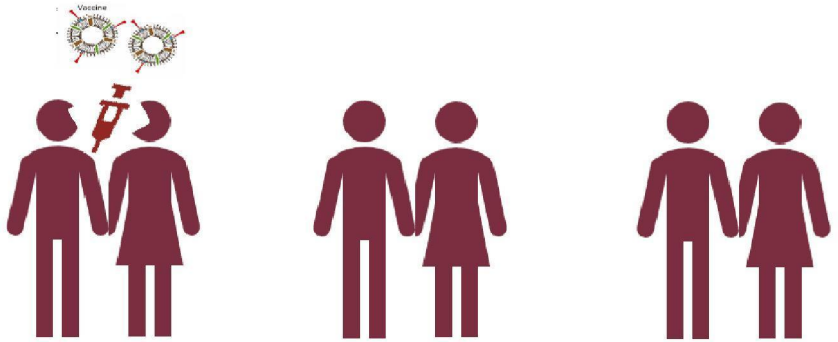
COVID-19 Emergency peptide vaccine

OMV-peptide





Vaccination (by injection)

Innate immune and T-cell activation

No death & severe disease (no IC)

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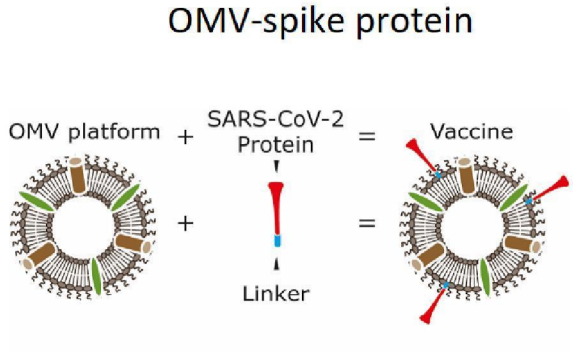
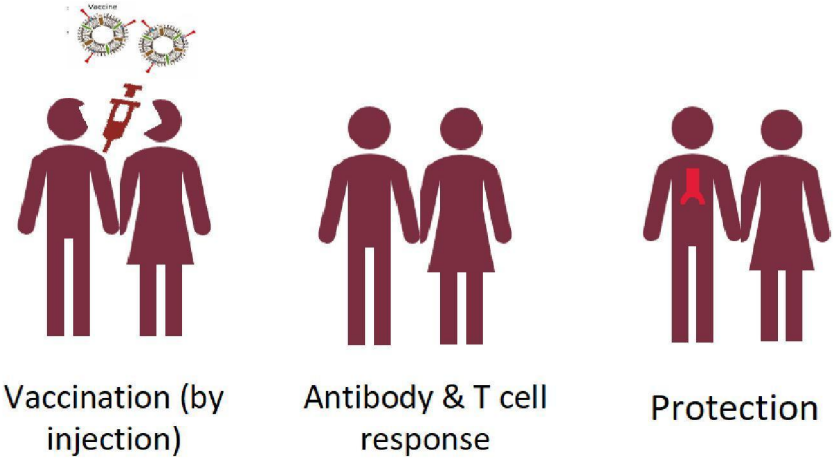
Conventional COVID-19 OMV vaccine





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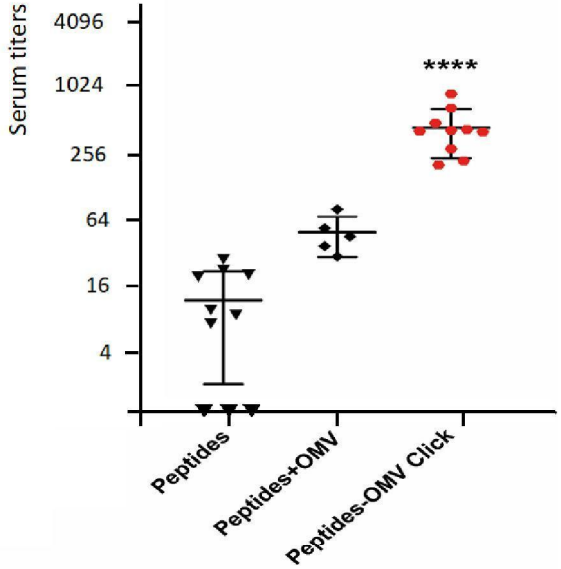
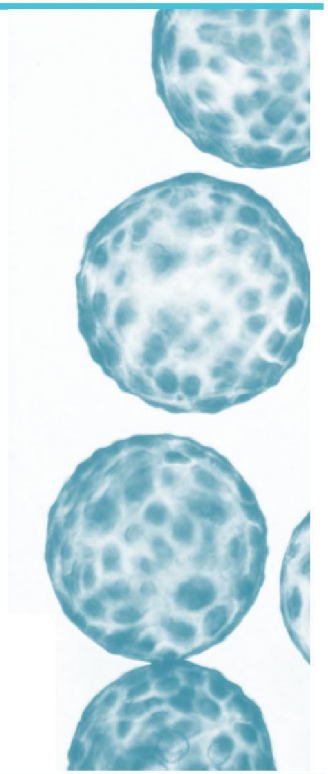
Pre-clinical Click-OMV data

- Successful linking of different type of antigens to OMVs:
  - viral antigens,
  - bacterial antigens
  - Alzheimer antigens
- Prototype Enterovirus 17 OMV vaccine was studied in mice.



Intravacc Vero cell platform technology

- Approved platform for human vaccines like Polio
- Platform for inactivated, live attenuated and vector vaccines
- GMP grade master and working cell banks directly available
- Several Vero cell based vaccines on the market
- Track record in technology transfer
- Scientific & clinical evidence
  - > 2 patents
  - > 32 publications



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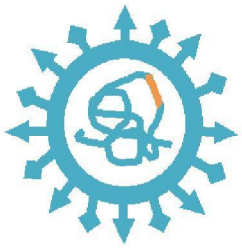
Corona Vector Vaccine



- **Platform**
  - Intravacc Vero cell platform technology
- **Virus vector**
  - A vector virus is used to incorporate genetic material of the corona Spike protein
- **The Vector** : Newcastle disease virus (NCD)
  - NCD is an avian vaccine
  - NCD can replicate in humans but does not cause disease in humans
  - Therapeutic NCD vaccines in development to treat cancer
- **Coronavirus NCD vector vaccine**
  - Nose spray vaccination
  - Strong and broad stimulation of the immune system

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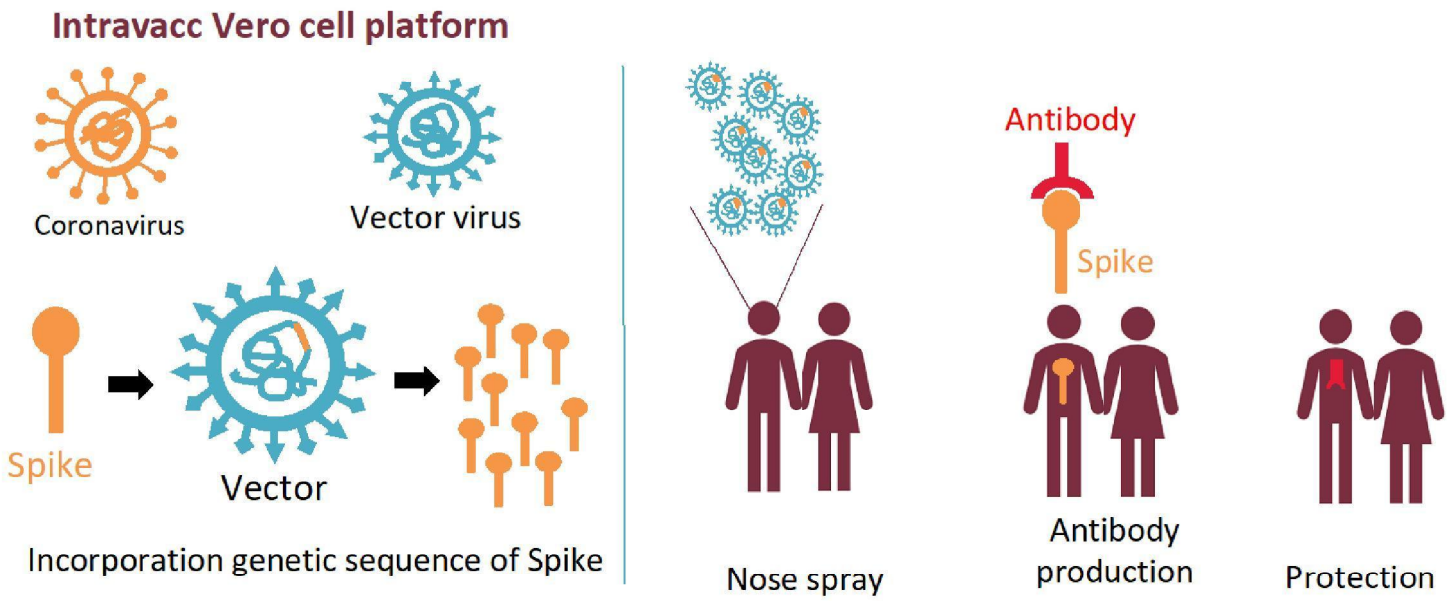
Conventional COVID-19 vector vaccine



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SARS NCD vector vaccine response in primates

PNAS

Newcastle disease virus, a host range-restricted virus, as a vaccine vector for intranasal immunization against emerging pathogens

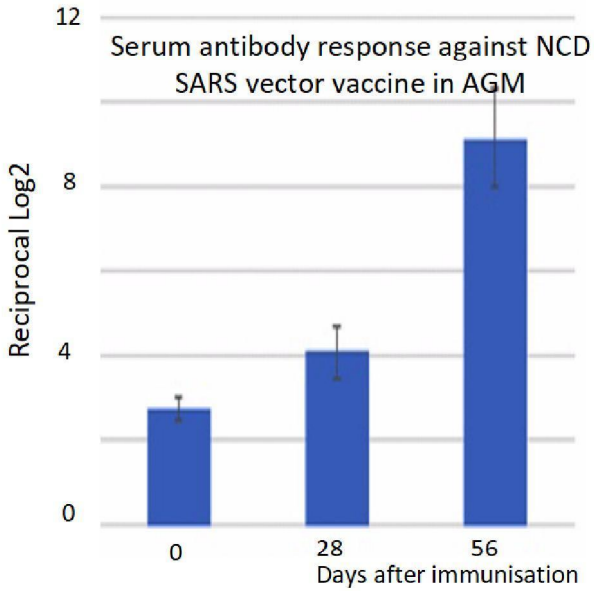
Joshua M. DiNapoli*, Alexander Kotelkin*, Lijuan Yang*, Subbiah Elankumaran†, Brian R. Murphy*, Siba K. Samal†, Peter L. Collins*, and Alexander Bukreyev*‡

*Laboratory of Infectious Diseases, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, MD 20892; and †University of Maryland, College Park, MD 20742

Communicated by Robert M. Chanock, National Institutes of Health, Bethesda, MD, April 24, 2007 (received for review January 22, 2007)

Immunisation of African green monkeys (AGM) with NCD SARS spike vector vaccine

- Immunized at day 0 and day 28
- High neutralizing antibody titers were measured



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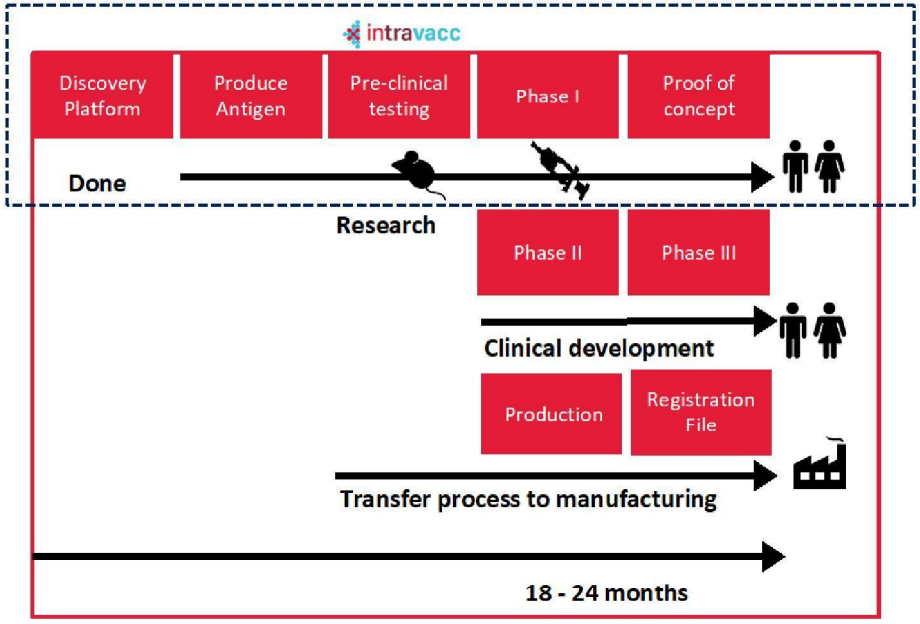
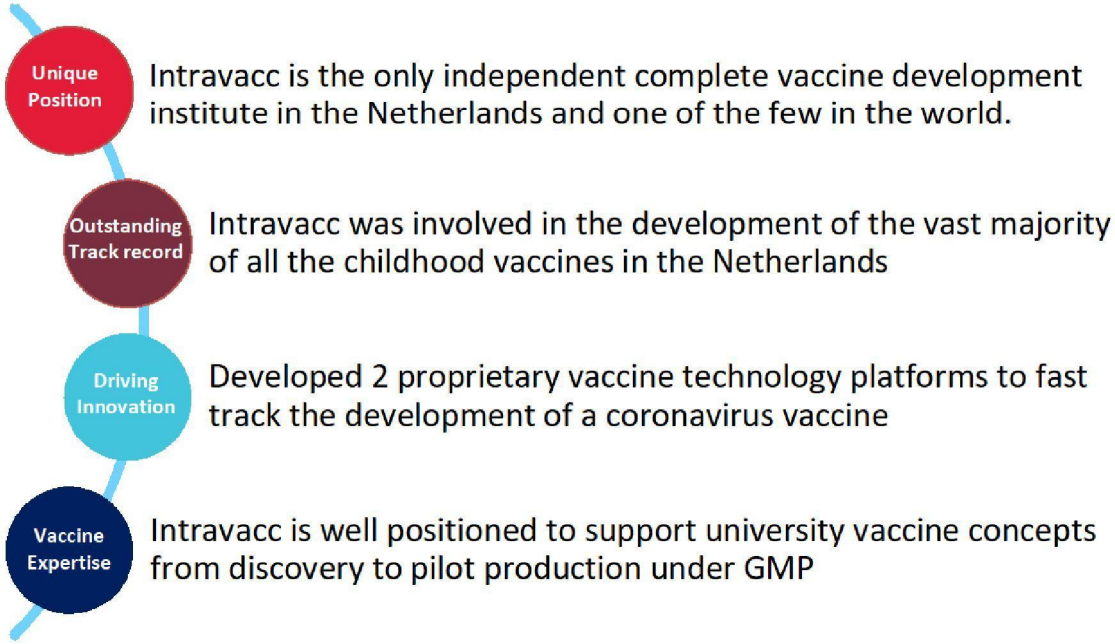
Compressed timelines for COVID 19 vaccine



Intravacc development timelines

Vaccine concept	Time in months
NCD vector	21
OMV protein	14
OMV peptide	9

Summary


Unique Position
Intravacc is the only independent complete vaccine development institute in the Netherlands and one of the few in the world.
Outstanding Track record
Intravacc was involved in the development of the vast majority of all the childhood vaccines in the Netherlands
Driving Innovation
Developed 2 proprietary vaccine technology platforms to fast track the development of a coronavirus vaccine
Vaccine Expertise
Intravacc is well positioned to support university vaccine concepts from discovery to pilot production under GMP

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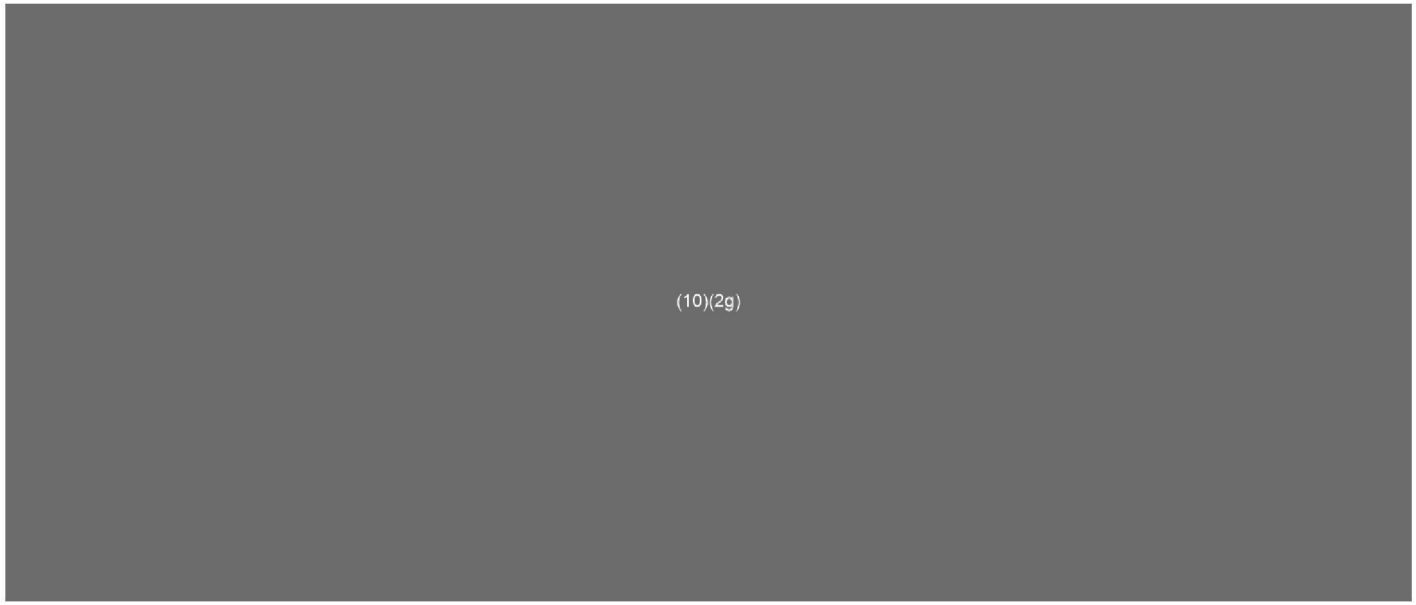

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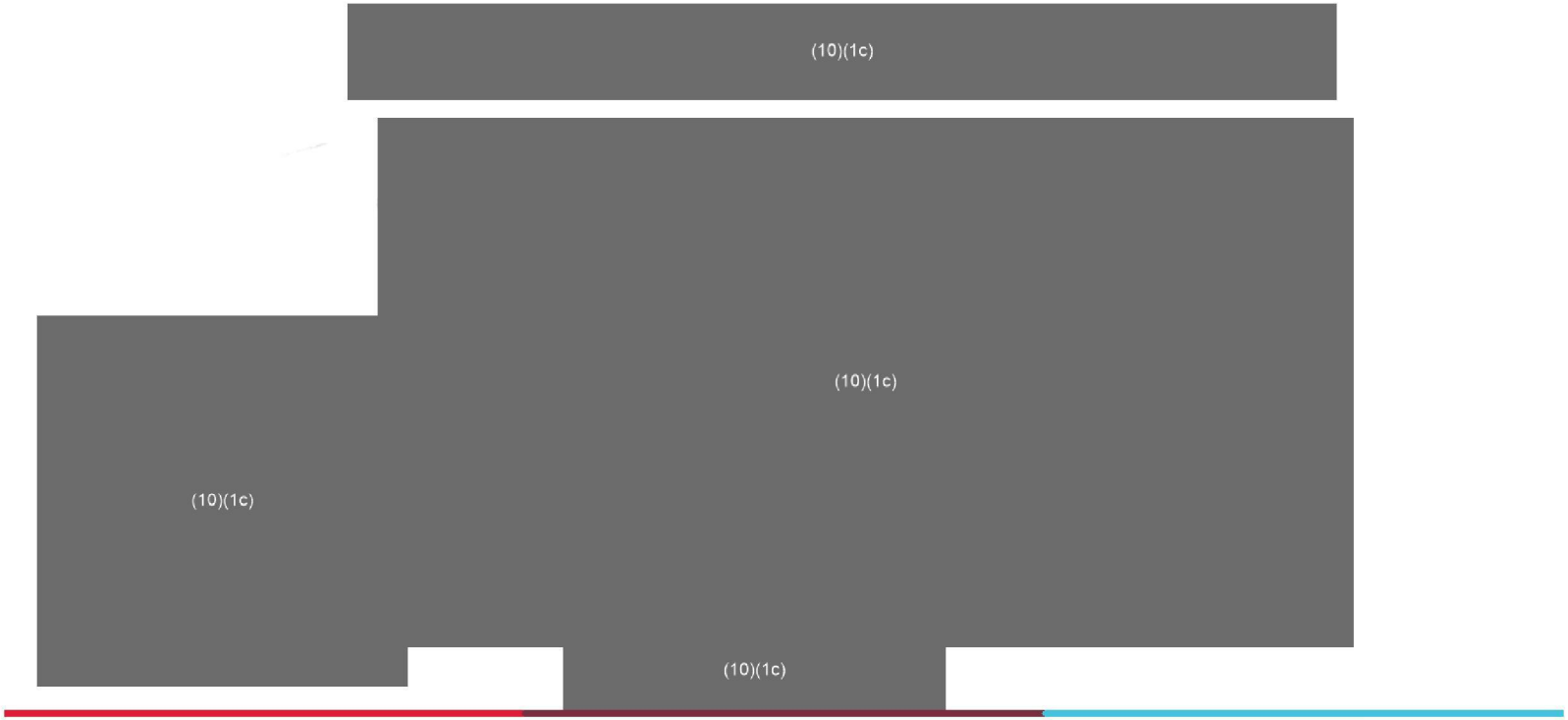

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