Afrigen
Biologics & Vaccines
An Avacare Health & IDC Company

Global mRNA Technology Transfer and Training Hub

mRNA TECHNOLOGY TRANSFER & TRAINING HUB

The African Growth and Opportunity Act (AGOA)
CIVIL SOCIETY NETWORK

7th ANNUAL AGOA CSO NETWORK SPRING CONFERENCE

THEME

U.S. - Africa Trade and Investment: Current Threats, Challenges, and Opportunities

Presentation overview

mRNA Hub design and objectives

Hub and Spoke model: a global network

The fast changing landscape of vaccine innovation in Africa

Success is not singular

Strengthening Africa's vaccine manufacturing capacity through the South African mRNA technology transfer hub

A need for equity in access to COVID-19 vaccines

Similar to previous pandemics, COVID-19 has underscored (yet further) that gross inequity exists in relation to access to health products, especially vaccines. As of November 22nd, 2021, more than 7.71 billion vaccine doses have been administered globally, but about 74% have gone to high- or upper-middle income countries1; while 7 in 10 people in North America have been vaccinated, only 1 in 10 people have been vaccinated in Africa.

OVERVIEW OF PROJECT STATUS AND SUMMARY OF COMMUNICATIONS TO DATE

2021 — 2022

April 16th

WHO call for EOI to contribute by providing technology or hosting a hub, or

> ***One or more*** *technology transfer hub(s)*
>
> *Will expand to* ***other technologies*** *in the future*

June 21st

French President, SA president & WHO DG **announcing establishment of SA mRNA hub**

> *The* ***first of a long list*** *to come.* ***Other hubs in the pipeline***
>
> *Will launch* ***calls for other technologies****, such as viral vectors and proteins, in coming months*

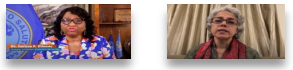
July 7th

Vaccine Manufacturing Working Group

> *Proposed network* ***could include additional hubs (3 to 6 in total)****, ensuring global coverage and training for spokes with different degrees of support*

September 21st

WHO/PAHO announce selection of **Agentina and Brazil** as **spokes** in LatAm



> ***First*** *hub is being set up in South Africa*
>
> *And this* ***will start happening from the beginning of 2022***

November 10-11th

WHO **call for EOI** for additional spokes of SA mRNA and call for EOI to establish **workforce training hub**

> ***Seeking interest from manufacturers elsewhere*** *(i.e. low- or middle-income countries not in PAHO)*
>
> *Provide training on general* ***biomanuf. processes*** *in an industrial-type setting*

February 18-25th

WHO announce selection of **Egypt, Kenya, Nigeria, Senegal, South Africa and Tunisia** and **Bangladesh, Indonesia, Pakistan, Serbia and Vietnam** as spokes

WHO announce establishment of **global biomanufacturing training hub in Republic of Korea**

March 7-9th

Afrigen receives first spokes for training at lab-scale: Argentina & Brazil

Parallel initiative

- ***BioNTech*** *announced plan to develop capacity to produce mRNA Vx in Rwanda Senegal*
- ***Moderna*** *announced ambition to build a mRNA facility in Africa*
- ***NantAfrica*** *announced launch of prod. center in SA*

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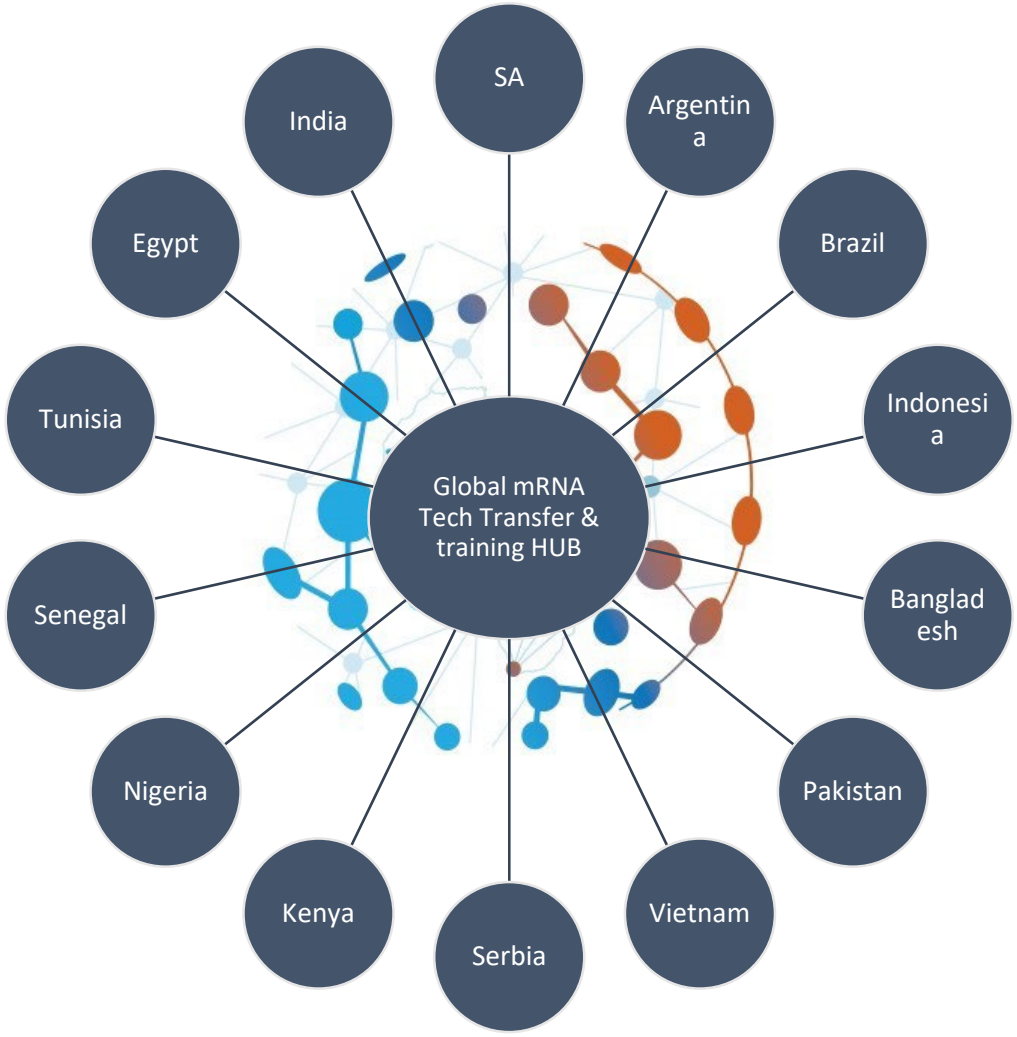
Global mRNA Technology Transfer and Training Hub

"The mRNA technology transfer programme is a global initiative to **improve health and health security** by establishing sustainable, locally owned mRNA manufacturing capabilities **in and for low- and middle-income countries** (LMICs). Its core concept is empowerment.

The hub at Afrigen, in South Africa, will transfer technology for COVID-19 vaccines and other mRNA products to 15-20 "spokes" in LMICs for commercial production creating a mega network of vaccine manufacturing capacity across LMICs. This programme will contribute to future pandemic preparedness in LMICs."

In support of a sustainable initiative the WHO is further supporting the programme through a biomanufacturing workforce training hub, located in South Korea, and regulatory training and strengthening.

mRNA HUB NETWORK OF SPOKES (April 2022)



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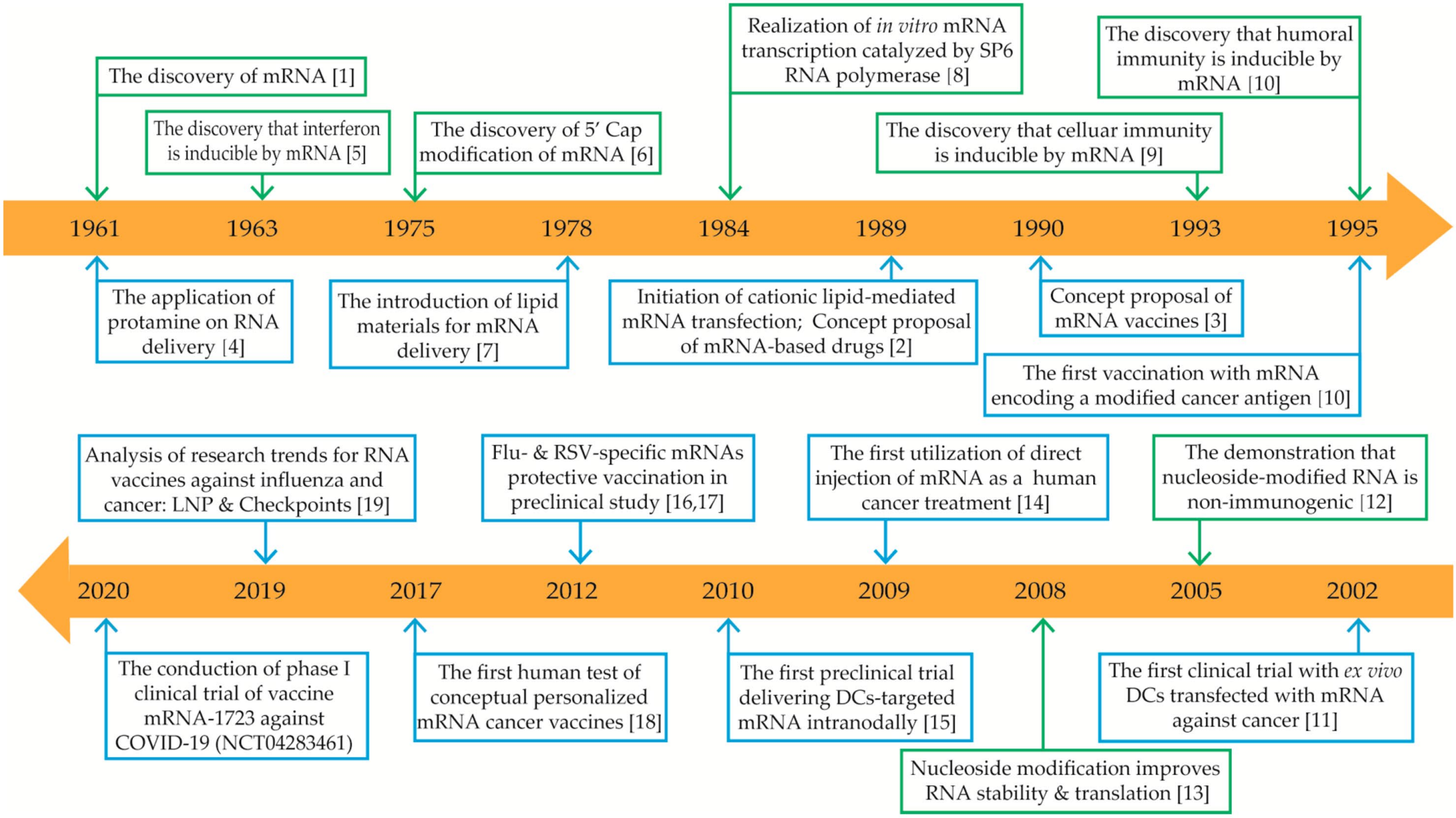
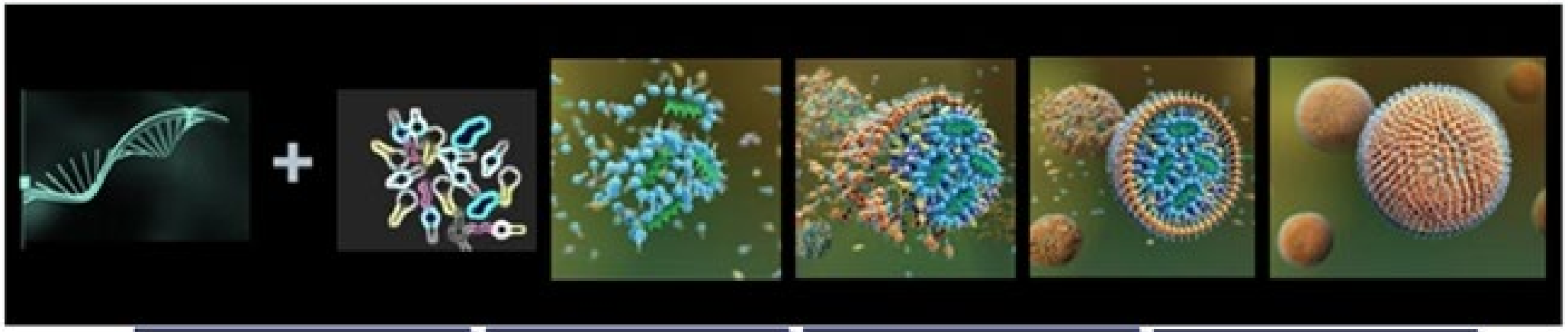
Global mRNA Technology Transfer and Training Hub

Doc No:

mRNA


The discovery of mRNA [1]
The discovery that interferon is inducible by mRNA [5]
The discovery of 5′ Cap modification of mRNA [6]
Realization of *in vitro* mRNA transcription catalyzed by SP6 RNA polymerase [8]
The discovery that celluar immunity is inducible by mRNA [9]
The discovery that humoral immunity is inducible by mRNA [10]
1961
1963
1975
1978
1984
1989
1990
1993
1995
The application of protamine on RNA delivery [4]
The introduction of lipid materials for mRNA delivery [7]
Initiation of cationic lipid-mediated mRNA transfection; Concept proposal of mRNA-based drugs [2]
Concept proposal of mRNA vaccines [3]
The first vaccination with mRNA encoding a modified cancer antigen [10]
Analysis of research trends for RNA vaccines against influenza and cancer: LNP & Checkpoints [19]
Flu- & RSV-specific mRNAs protective vaccination in preclinical study [16,17]
The first utilization of direct injection of mRNA as a human cancer treatment [14]
The demonstration that nucleoside-modified RNA is non-immunogenic [12]
2020
2019
2017
2012
2010
2009
2008
2005
2002
The conduction of phase I clinical trial of vaccine mRNA-1723 against COVID-19 (NCT04283461)
The first human test of conceptual personalized mRNA cancer vaccines [18]
The first preclinical trial delivering DCs-targeted mRNA intranodally [15]
Nucleoside modification improves RNA stability & translation [13]
The first clinical trial with *ex vivo* DCs transfected with mRNA against cancer [11]

mRNA Vaccine Technology



NON-LIVE	SAFETY	IMMUNOGENICITY	MANUFACTURING
• No live pathogens • Sequence specificity • Flexible product design • Well characterized	• RNA does not integrate into the host genome and is degraded once the protein is made	• Induces potent humoral and cell-mediated immune responses • Self-adjuvanting	• *In vitro* transcription • No cell culture • Scalable to large capacity

SANOFI PASTEUR

*severe acute respiratory syndrome coronavirus 2, (SARS-CoV-2)

Doc No:

mRNA Vaccine

Components

mRNA (blueprint of protein)

Production

Faster because mRNA molecules are easier to produce

Process

Components are injected into the arm and serve as instructions for the body to make microbial protein

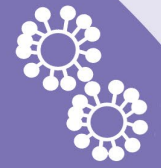
R & D

Antigen determined for immune stimulation

Result

Teaches the body to protect itself against a microbe

Traditional Vaccine



Components

Microbial protein or inactive microbe

Production

Slower and more difficult to produce the right type of protein

Process

Components are made in a lab and injected into the arm to stimulate immune response

Doc No:

THE UNBIASED SCIENCE PODCAST

Pfizer-BioNTech COVID-19 Vaccine

WHAT'S IN IT AND WHY?

Active Ingredient

mRNA encoding the viral spike glycoprotein (S) of SARS-CoV-2

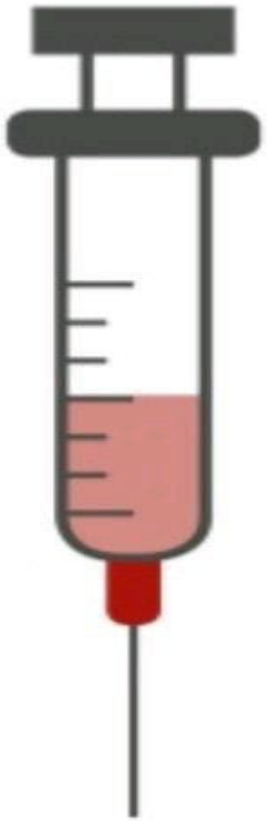
RNA is a template to produce a single specific protein.

In the vaccine, this is the message for our cells to produce the viral protein that will trigger the immune response to the virus.

Salts

4 different salts

These buffer the vaccine to stabilize the pH, so that it matches the pH in our bodies



Lipids

4 different fatty molecules (some with long names)

They form a protective capsule around the RNA.

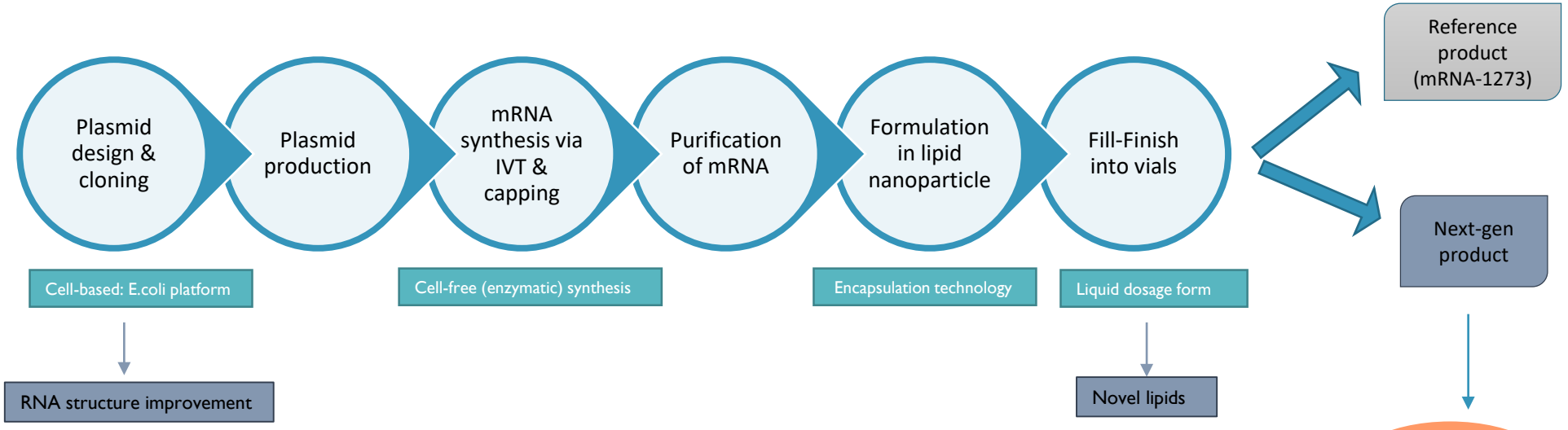
This aids in delivery of the RNA, as well as protects the RNA from degradation (RNA is very unstable).

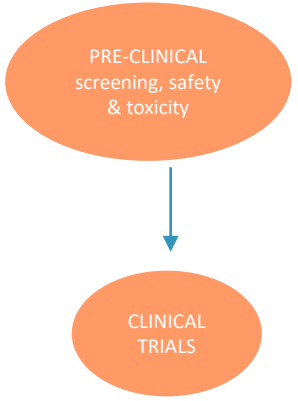
Sugar

Sucrose

This is a cryoprotectant.
It ensures the lipids don't get too sticky at the extremely cold storage temperatures.

GREENFIELDS : mRNA Hub forward innovation process of a mRNA vaccine

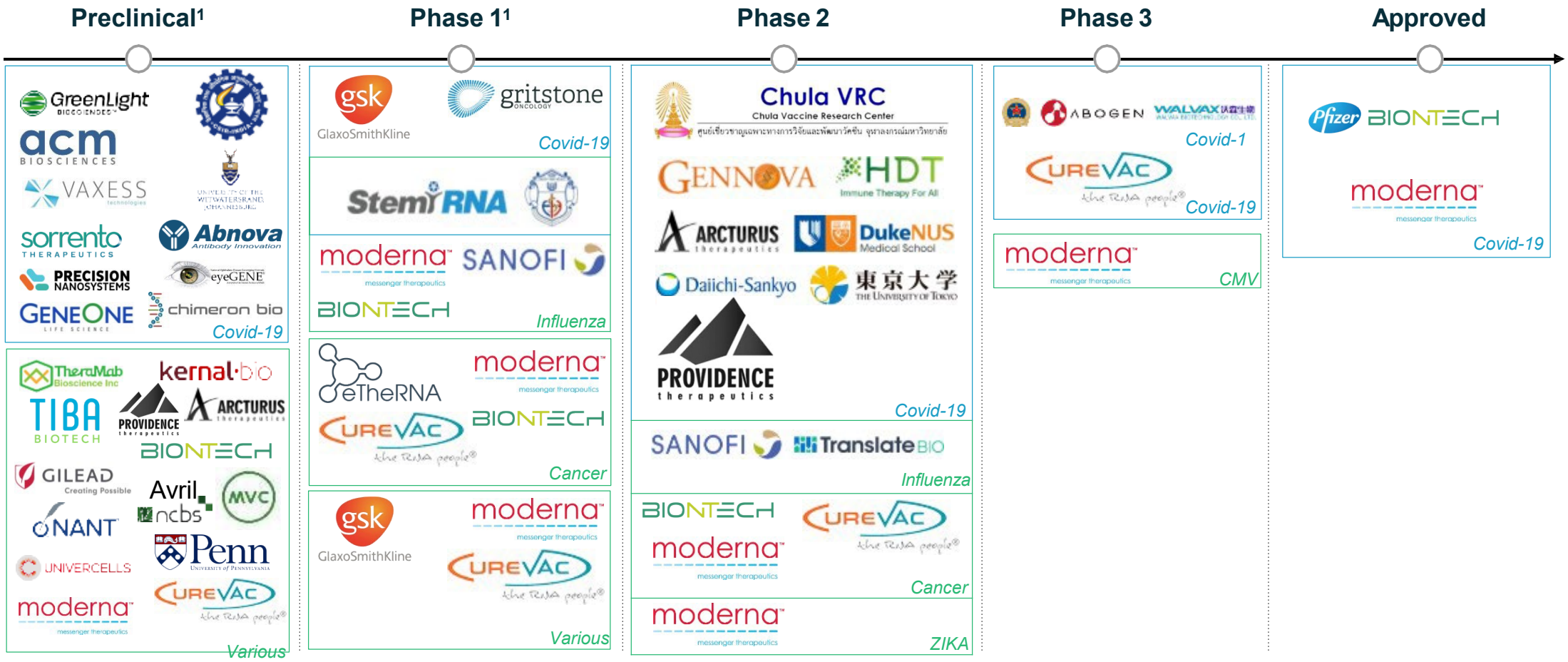




	HUB MEMBERS	SCALE	PLASMID DESIGN & CLONING	PLASMID PRODUCTION	mRNA SYNTHESIS	mRNA PURIFICATION	LNP FORMULATION	FILL/FINISH
PROCESS & PRODUCT DEVELOPMENT	AFRIGEN AGTRU -WITS	µL – mL	✓	✓	✓	✓	✓	
	AFRIGEN CeBER-UCT	mL – 30-50 L	✓	✓				
SCALE-UP	BIOVAC	≥50 L						
TRAINING	VIRTUAL			✓			✓	
	HANDS-ON (small scale)			✓	✓	✓	✓	
	HANDS-ON (Large scale)				✓			

Afrigen Biologics & Vaccines

Lots of players catching up with the leaders – some improved 2nd generation technologies



1. Best view from Adis as of 2021. Note: Overview of mRNA Vaccines by development stage; Imperial College taken out based on clinical results; Various indications in Phase I: Respiratory syncytial virus infections, Metapneumovirus infections, Cytomegalovirus infections, Rabies; Various indications in Preclinical: Influenza, Cancer, Multiple sclerosis, Epstein-Barr virus infections, HIV infections, Nipah virus infections, Lassa fever, Yellow fever. Source: ADIS

SUCCESS IS NOT SINGULAR

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QUO VADIS AFRICA?

60 PERCENT OF VACCINE NEEDS PRODUCED LOCALLY BY 2040!!!

African Union

AFRICA CDC
Centres for Disease Control and Prevention
Safeguarding Africa's Health

PAVM Framework for Action

Doc No:

Overall summary of the continental strategy

1 Potential disease prioritisation

Prioritized 22 diseases…

Vaccine exists *Vaccine does not yet exist*

Legacy				*Expanding*		*Outbreak*	
Diphtheria	Hepatitis B	Measles	Meningococcal	HPV	Pneumococcal	Ebola	Influenza
Whooping Cough	Yellow fever	Typhoid fever		*HIV*	COVID-19	*Chikungunya*	*Lassa fever*
Tetanus	Tuberculosis	Cholera		*Malaria*	Rotavirus	*Rift valley fever*	*Disease X*

… requiring a breadth of technology platforms…

2 Technology focus

Traditional → Innovative

Live attenuated	*Inactivated virus*	*Subunit*	*Virus-like particle*	*Viral vector*	*RNA/DNA*

… along the different steps of the value chain

3 Potential value chain focus

Fill & Finish

Focus on highest volume vaccines (vaccine and modality agnostic) for economies of scale with potential for Africa to become cost-effective vis-à-vis other DCVM

Drug Substance

Expand drug Substance mostly in established platforms where tech transfers are readily available; manufacturing will likely require developing a local raw materials industry

R&D

Create regional R&D hubs to support more efficient manufacturing, improve vaccine characteristics and consider research centers to develop new vaccines for Africa

Doc No:

The ABCs of DIY vaccines: Why tech transfer is a big thing

By **Adèle Sulcas** and **Linda Pretorius** - November 18, 2021

A is for access
B is for building a vaccine
C is for capacity and continuity (REGULATORY KEY)

COVID 19 TSUNAMI – TECHNOLOGY TRANSFER CHANGING LANDSCAPE

Transfer included more upstream process steps (e.g. drug substance)

Since 2020

COVID-19 vaccine

	Algeria	Egypt	Morocco	Senegal	South Africa
African partner	GROUPE SAIDAL	EVAPHARMA; PHARCO VACSERA	Sothema	Institut Pasteur de Dakar	aspen PHARMACARE; BIOVAC
International partner	Sputnik V	sinovac; AstraZeneca	sinovac	Recipharm	UNIVERCELLS; Johnson & Johnson; Pfizer BIONTECH

Before 2020

	PCV vaccine	Hexaxim vaccine	Pentavalent vaccine
	South Africa	South Africa	Egypt
African partner	BIOVAC	BIOVAC	VACSERA
International partner	Pfizer	SANOFI	dpt; gsk; BE Biological E. Limited Celebrating Life Every Day

mRNA Tech Transfer Hub

South Africa

Afrigen Biologics & Vaccines; AFRICA CDC; saMRC advancing life; BIOVAC

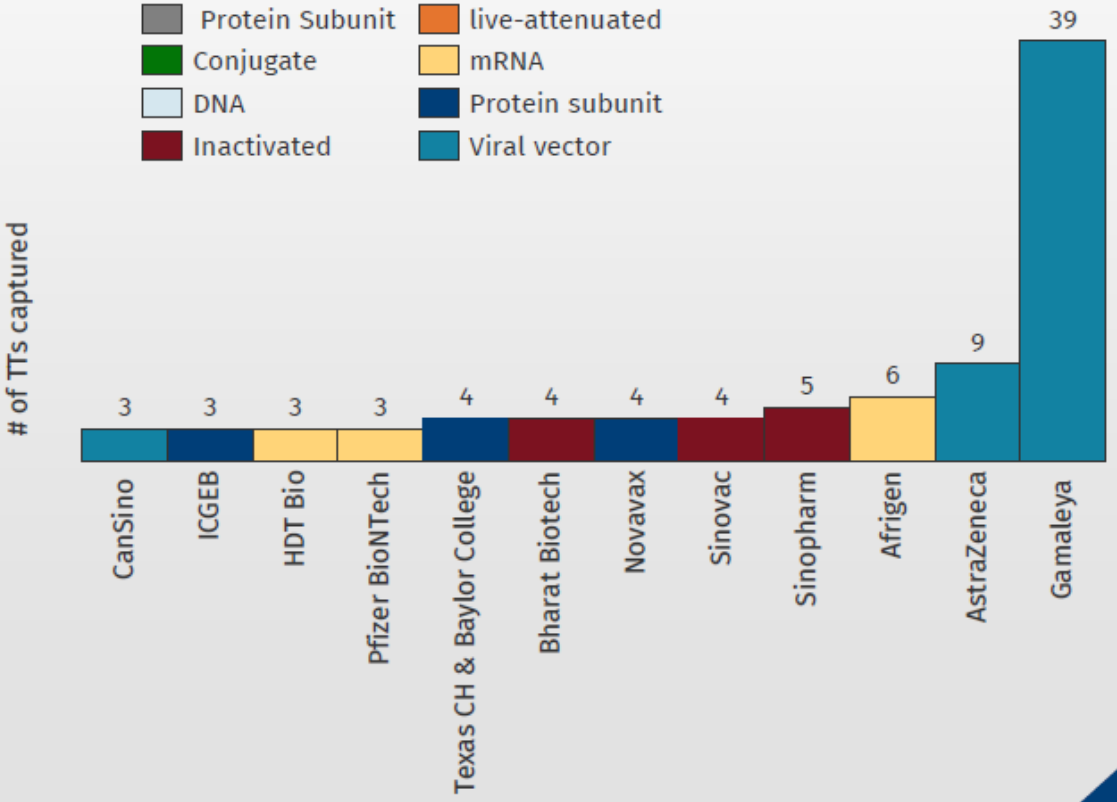
World Health Organization; medicines patent pool

Executive Summary (1/3)

***Tech-transfers*: Viral Vector has been the most transferred vaccine platform for facilitating local vaccine production since the start of the pandemic.**

- 113 Covid-19 vaccine technology transfers have been identified as of March 2022, including 19 transfers to Africa, 51 to Asia, 14 to Latin America, and 9 to the Middle East.
- The Gamaleya Research Institute's Viral Vector and AstraZeneca's Viral Vector have been the most outsourced Covid-19 platforms.
- For fill-finish production and end-to-end production, inactivated and mRNA platforms are also popular.
- African technology transfers have mainly been for fill-finish, Asia for end-to-end production, and the Middle East and Latin America for fill-finish/end-to-end production.

Top 12 identified sources of TTs as at Mar 2022



s: Airfinity (Link); Chart uses data from CHAI's "LVM-Landscape-Baseline-March-01-2022" database of LVM commitments; CHAI staff calculations.

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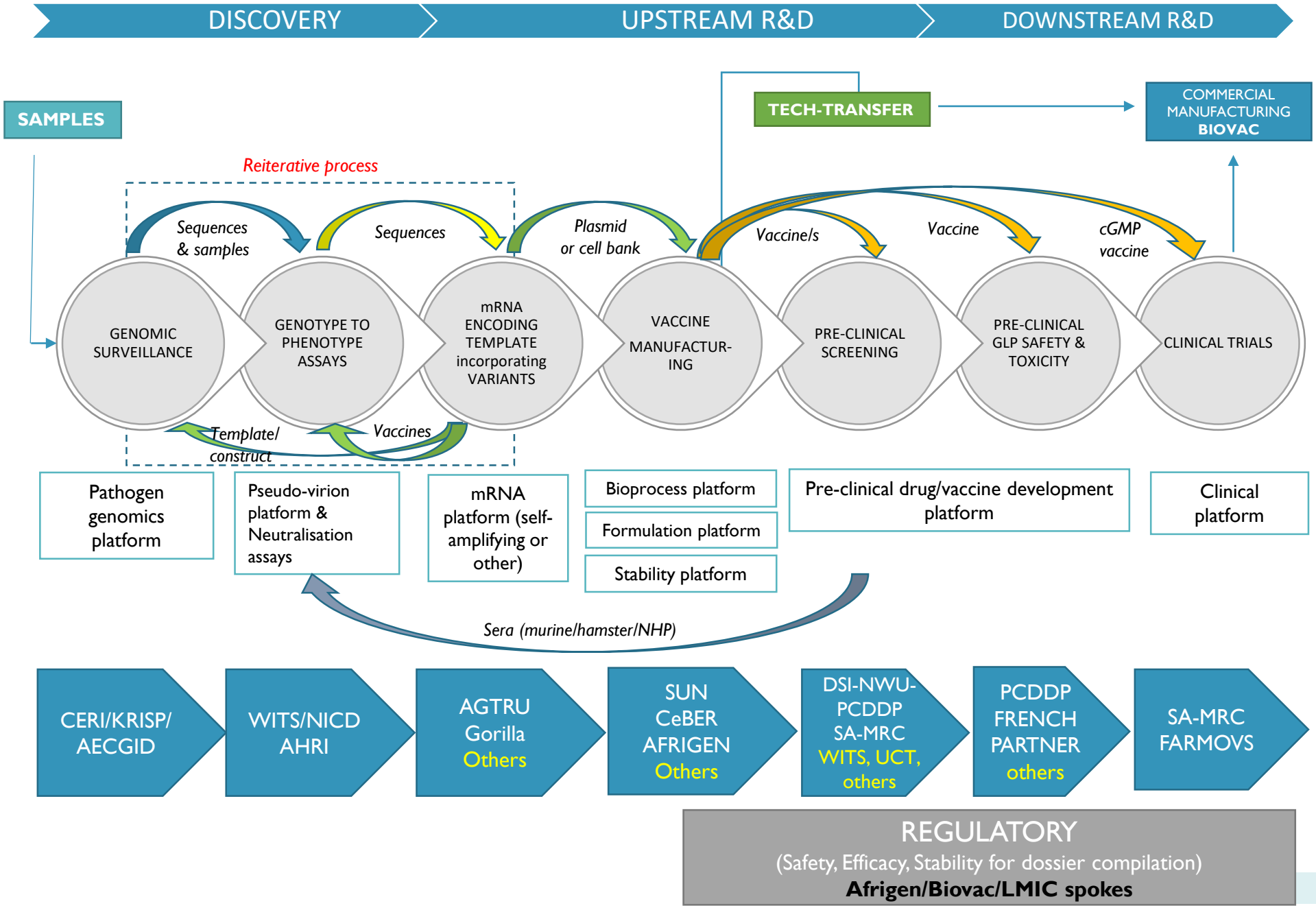
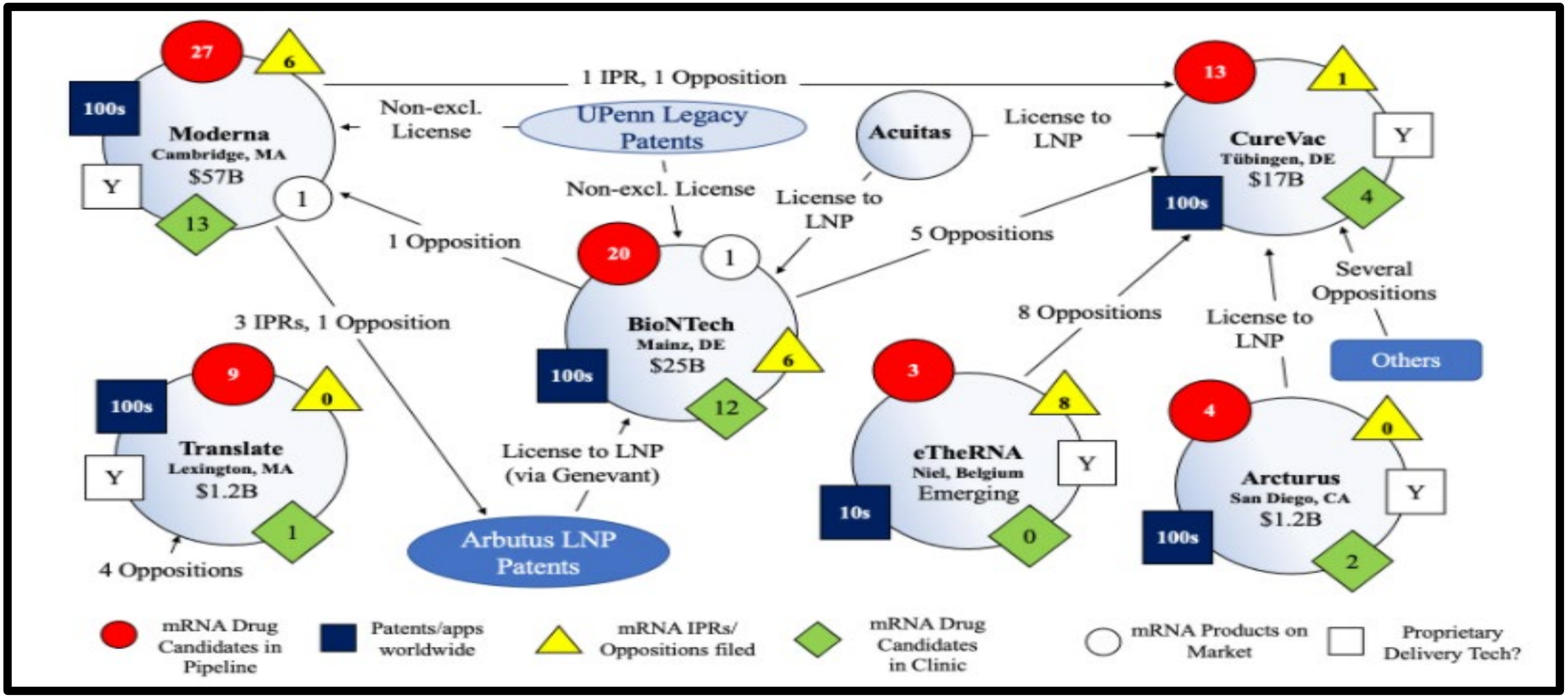

DISCOVERY
UPSTREAM R&D
DOWNSTREAM R&D
SAMPLES
TECH-TRANSFER
COMMERCIAL MANUFACTURING BIOVAC
Reiterative process
Sequences & samples
Sequences
Plasmid or cell bank
Vaccine/s
Vaccine
cGMP vaccine
GENOMIC SURVEILLANCE
GENOTYPE TO PHENOTYPE ASSAYS
mRNA ENCODING TEMPLATE incorporating VARIANTS
VACCINE MANUFACTUR-ING
PRE-CLINICAL SCREENING
PRE-CLINICAL GLP SAFETY & TOXICITY
CLINICAL TRIALS
Template/ construct
Vaccines
Pathogen genomics platform
Pseudo-virion platform & Neutralisation assays
mRNA platform (self-amplifying or other)
Bioprocess platform
Formulation platform
Stability platform
Pre-clinical drug/vaccine development platform
Clinical platform
Sera (murine/hamster/NHP)
CERI/KRISP/ AECGID
WITS/NICD AHRI
AGTRU Gorilla Others
SUN CeBER AFRIGEN Others
DSI-NWU-PCDDP SA-MRC WITS, UCT, others
PCDDP FRENCH PARTNER others
SA-MRC FARMOVS
REGULATORY
(Safety, Efficacy, Stability for dossier compilation)
Afrigen/Biovac/LMIC spokes



SUCCESSFUL VACCINE INNOVATION IN AFRICA WILL REQUIRE IP SYSTEMS REFORM

Increase in launched initiatives with varying tangibility

Tunisia
☆ Announced ambition to establish Vx production unit with Japanese partners

Morocco
★ **Recipharm** F&F capacity development incl. for **mRNA** Vx ($500M investment, **300M** capacity, pledged start in 2023)
☆ **Sothema & Sinopharm** for Covid-19 F&F (60M capacity)
☆ RDIF[1] to fund **Galenica** for production options of Sputnik V

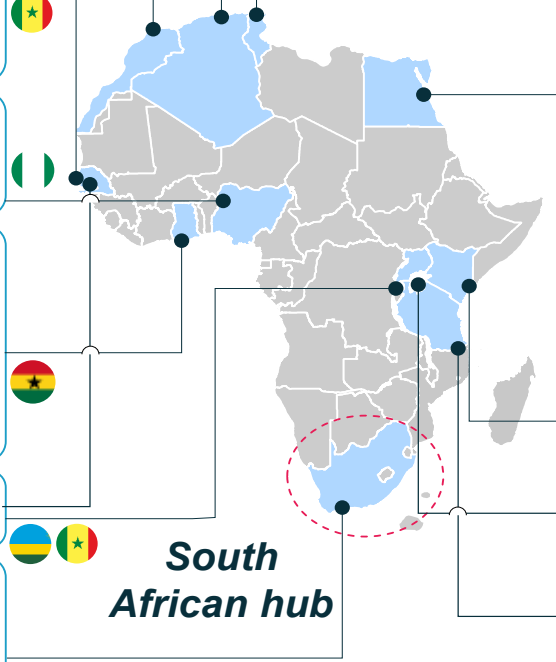
Senegal
★ IFC[2], Univercells and Team Europe funding the building a COVID-19 Vx manufacturing facility, starting with packaging, with **Institut Pasteur de Dakar (IPD)** ($200M+ investment, 300M capacity by end of 2022)
☆ **BMGF**[3] funding **IPD** to develop short-medium-long term strategy as well as set up Delivery Unit and build capacity to contribute to vaccine security on the continent ($5M investment)

Nigeria
☆ Plan to establish a **Biovaccines** F&F facility then move up the value chain ($30M investment, capacity to vaccinate 10M people)
☆ Afreximbank to fund the development of infrastructural facilities like hospitals, vaccine production with **Gateway Pharmaceuticals** ($200M investment in total)

Ghana
☆ Plan to establish a national vaccine institute to develop and manufacture Vx ($20M investment) and to source additional private capital for the project (incl. promoting a viable venture and reaching out to stakeholders like GAVI, CEPI, UNICEF and WHO, as well as Africa Union and European Union)
☆ Government to invest $90M to establish local Vx plants, incl. potentially partnerships with DEK Vaccines to use F&F capabilities or IDT Biologika for Covid-19 Vx, and in the longer term other Vx, incl. EPI-managed or Atlantic LifeSciences to install a F&F plant
☆ Early engagements in the **Phyto-Riker-ASPEN** pharmaceutical partnership (collaboration with J&J)

Rwanda and Senegal
☆ **BioNTech** announced plan to develop capacity to produce upcoming **mRNA**-based vaccines (50M, pledged start in 2022 for Covid-19, then moving to Tuberculosis and Malaria[4]

South Africa
★ **mRNA tech transfer hub**
★ **Aspen & J&J** for Covid-19 F&F ($710M investment, 300M capacity, started in 2021, plan to boost capacity by a further 200M doses)
★ **BioNTech & Biovac** for **mRNA** Covid-19 F&F(100M capacity, start in 2022)
★ Patrick Soon-Shiong launched a production center in SA of Covid-19 2nd generation **mRNA** Vx with his company **NantAfrica and ImmunityBio**, in collaboration with SA CSIR, CERI, SAMRC, and SA universities. Plan to expand in Botswana, Ghana, Kenya and Uganda and work on cancer, TB and HIV (first doses planned in 2022 for CTs)



moderna announced in October 2021 the ambition to build a state-of-the-art **mRNA** facility in Africa (500M doses, from drug substance to F&F), location (country and site) still to be decided

Algeria
★**Saidal & Sinovac** for Covid-19 F&F (200M capacity, started in 2021) then move up the value chain
☆**Saidal** plans to F&F Sputnik V starting Sept 2021 (40M capacity)

Egypt
★**Egy Vac (Vacsera) & Sinovac** for Covid-19 F&F (200M capacity, started in 2021), plan to boost capacity with a new F&F facility (1B capacity, pledged start in November 2021)
☆**Eva Pharma** end-to-end Vx capacity development (pledged start in 2022)
☆RDIF[1] to fund **Minapharm** for production of Sputnik V (40M doses capacity)
☆**Pharco** announced partnerships to produce Sinovac Covid-19 Vx (20-60M pledged start in 2021), and Sputnik V funded by RDIF[2] (25M pledged start in 2021)

Kenya
☆Establishing a F&F facility for COVID-19 Vx then moving up the value chain to set up an end-to-end manufacturing plant (pledged start in 2022)

Uganda
☆Biological Drugs and **mRNA** vaccine facility – private initiative led by **Dei BioPharma**

Tanzania
☆Health Permanent Secretary announced plans to establish local manufacturing of Vx for Covid-19 and other diseases to reduce importation costs

☆ *Announced projects*
★ *Advanced projects*
★ *Advanced projects with COVAX partners*[5]

1. Russian Direct Investment fund 2. International Finance Corporation, a sister organization of World Bank 3. Bill and Melinda Gates Foundation 4. Clinical trials not yet started 5. Confirmed collaborations according to publicly available sources. Note: Other potential plans in Namibia to be defined. Source: Carnegie Endowment for International Peace; Industrie Pharma, Companies websites

CONTRIBUTION AND RECOGNITION

WHO

Medicines Patent Pool (MPP)

University of the Witwatersrand

SA Government DSI

AU and Africa CDC (PAVM)

SAMRC

Biovac

PATH

Independent specialists and advisors

Civil Society Groups

Funders: France, Belgium, Germany, Norway, Canada, South Africa, EC.

Afrigen Team and Shareholders