Intellectual Property

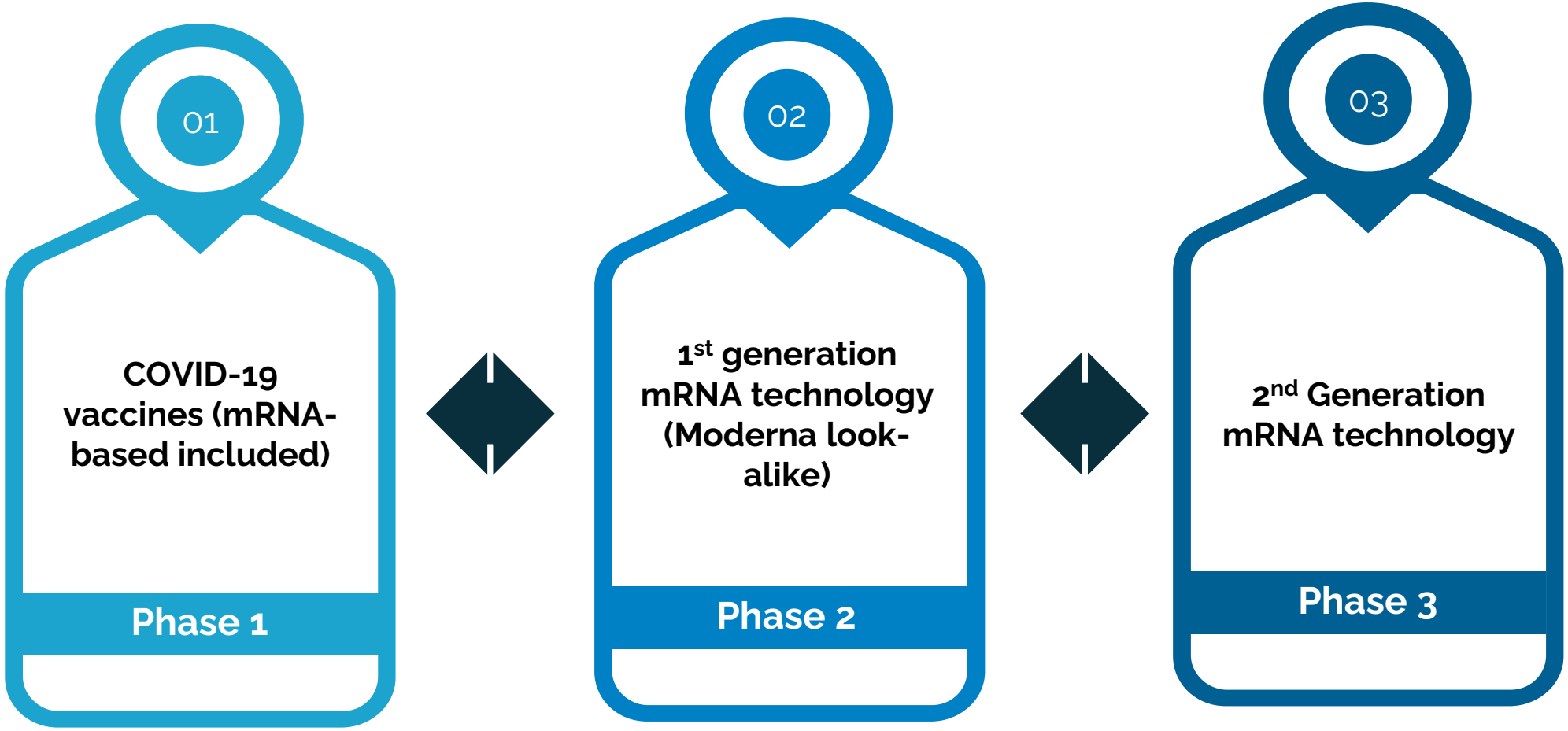
Amina Larbi – MPP, Head of patent Information
Chan Park – MPP, General Counsel

April 18th, 2023 - Face-to-Face meeting , Cape Town, South Africa

Table of content

mRNA Technology Transfer Programme

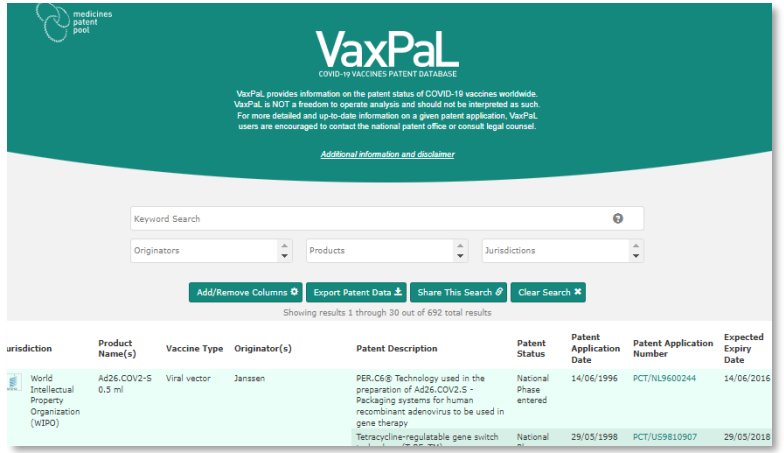
IP landscape strategy



Phase 1: COVID-19 vaccines (mRNA-based included)

VaxPaL, MPP's patent database devoted to COVID-19 vaccines created in June 2021 and released as a searchable DB in Dec 2021 covering vaccines in use or in late development.

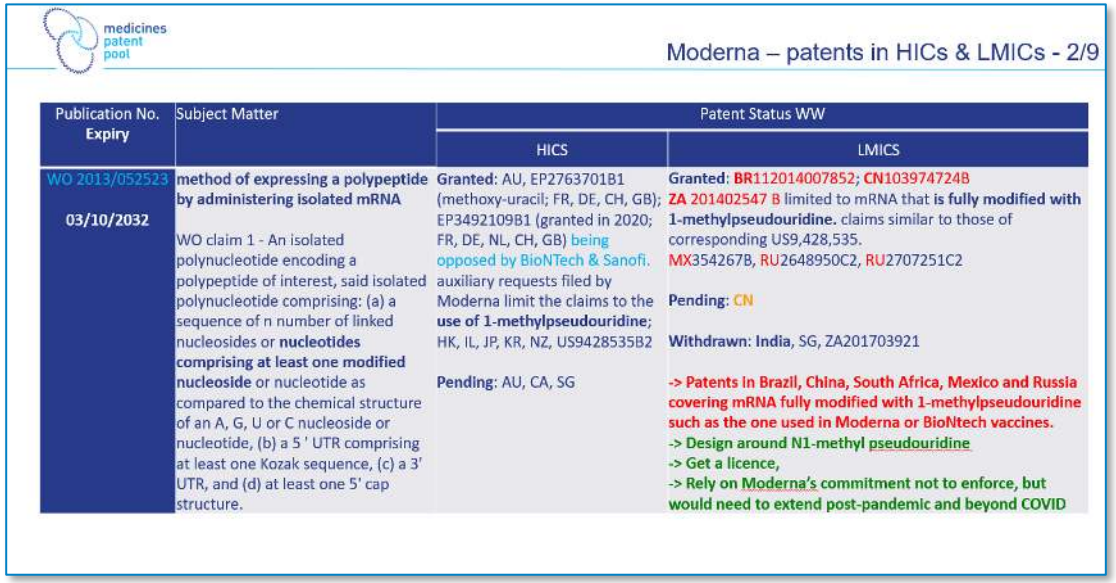
- Comprises patent information on 13 approved or late-stage COVID-19 vaccines.
- Includes 3 vaccines based on mRNA technology: Moderna's Elasomeran/mRNA-1273, Pfizer/BioNtech's Tozinameran/BNT162b2, and CureVAC 's Zorecimeran/CVnCoV- (not approved).
- Includes patents on **underlying technologies.**
- Patent status worldwide.
- Regularly updated.
- Open access : https://www.vaxpal.org/



mRNA Technology Transfer Programme

Phase 2: 1st generation mRNA technology (Moderna look-alike)

- Critical patents for the vaccine manufacturing technology identified.
- Information on patents linked to the vaccine technology under development at Afrigen with status in LMICs monitored and updated.
- **mRNA patent landscape** documents shared with Programme stakeholders (MPP, WHO, PAHO, committees' members), the South African Consortium (Afrigen, Biovac, SAMRC and other research organisations working in the Programme) and the technology recipients.



medicines patent pool

Moderna – patents in HICs & LMICs - 2/9

Publication No. Expiry	Subject Matter	Patent Status WW	
		HICS	LMICS
WO 2013/052523 03/10/2032	**method of expressing a polypeptide by administering isolated mRNA** WO claim 1 - An isolated polynucleotide encoding a polypeptide of interest, said isolated polynucleotide comprising: (a) a sequence of n number of linked nucleosides or **nucleotides comprising at least one modified nucleoside** or nucleotide as compared to the chemical structure of an A, G, U or C nucleoside or nucleotide, (b) a 5 ' UTR comprising at least one Kozak sequence, (c) a 3' UTR, and (d) at least one 5' cap structure.	**Granted**: AU, EP2763701B1 (methoxy-uracil; FR, DE, CH, GB); EP3492109B1 (granted in 2020; FR, DE, NL, CH, GB) being opposed by BioNTech & Sanofi. auxiliary requests filed by Moderna limit the claims to the **use of 1-methylpseudouridine**; HK, IL, JP, KR, NZ, US9428535B2 **Pending**: AU, CA, SG	**Granted**: **BR**112014007852; **CN**103974724B **ZA** 201402547 B limited to mRNA that **is fully modified with 1-methylpseudouridine.** claims similar to those of corresponding US9,428,535. MX354267B, RU2648950C2, RU2707251C2 **Pending**: CN **Withdrawn**: **India**, SG, ZA201703921 **-> Patents in Brazil, China, South Africa, Mexico and Russia covering mRNA fully modified with 1-methylpseudouridine such as the one used in Moderna or BioNtech vaccines.** **-> Design around N1-methyl pseudouridine** **-> Get a licence,** **-> Rely on Moderna's commitment not to enforce, but would need to extend post-pandemic and beyond COVID**

mRNA Technology Transfer Programme

Phase 2: Moderna statements on non-enforcement

Moderna announced intention not to enforce its patents:

October 2020: during the pandemic period and willingness to license its intellectual property for COVID-19 vaccines to others for the post pandemic period.

March 2022: Updated pledge. Non enforcement for COVID-19 vaccines in 92 LMICs and in ZA (not in writing)

In **August 2022,** Moderna sued Pfizer-BioNtech for infringement in the US (asserting 3 patents)

Country name	Country codes (ISO Alpha-2)	mRNA technology recipient	Gavi COVAX AMC-eligible countries and economies
Argentina	AR	Sinergium Biotech	No
Brazil	BR	Bio-Manguinhos	No
Egypt	EG	BioGeneric Pharma S.A.E	Yes
Kenya	KE	BioVax	Yes
Nigeria	NG	Biovaccines Nigeria Limited	Yes
Senegal	SN	Institut Pasteur de Dakar	Yes
Tunisia	TN	Institut Pasteur de Tunis	Yes
Bangladesh	BD	Incepta Vaccine Ltd	Yes
Indonesia	ID	Biofarma	Yes
India	IN	BiologicalE (Bio E)	Yes
Pakistan	PK	National Institute of Health	Yes
Serbia	RS	Institut Torlak	No
South Africa	ZA	Biovac	No
Ukraine	UA	Darnitsa	Yes
Viet Nam	VN	Polyvac	Yes

Phase 2: Moderna-Pfizer litigation and implications for the Programme - 1/2

- Equivalents of the 3 US patents being asserted have been filed in LMICs.
- Scope of the claims in equivalent patents vary widely across jurisdictions.
- The core of Moderna's complaint against Pfizer/BioNTech is the **use of the same 1-methylpseudouridine modificatio**n as the one patented by Moderna.
- The other part of the complaint relates to patents covering broadly **mRNA vaccines against betacoronavirus**.

Countries where Moderna has patents	1-methylpseudouridine	mRNA vaccines against betacoronavirus
Collaborative network partners	South Africa, Brazil, Argentina, and Serbia	Serbia
Other LMICs	Mexico, Russia, Albania, Bulgaria, North Macedonia and Türkiye	Albania, North Macedonia, Bosnia, Montenegro, Morocco and Moldova

Phase 2: Moderna-Pfizer litigation and implications for the Programme - 2/2

In its complaint, Moderna is being consistent with their modified patent pledge:

- not seeking injunction (damages only);
- not seeking damages within the 92 countries;
- seeking damages only as of 8 March 2022, when they changed their patent pledge.

One can reasonably guess that for Covid-19 applications, Moderna will also not seek injunctive relief against network partners.

What we don't know is whether Moderna will seek injunctive relief for 3rd parties' use of 1-methylpseudouridine for applications outside of Covid-19. The risk mitigation mechanisms remain the same (design around, seek voluntary licence).

Phase 2: 1st generation mRNA technology (Moderna look-alike) - **Landscaping main findings**

- Due to existing patents, freedom to operate (FTO) in ZA, CN, BR, RS likely more challenging than other LMICs.
- For newer applications, FTO will depend on claims finally granted in each country.
- Deep patent landscape evaluation to be performed to support network partners in making their own FTO for COVID-19, especially if based in countries not included in the Moderna waiver (i.e. BR, AR, RS, ZA), and in relation to other third-party patents
    - *PAHO hired consultants started complementing the work done so far for AR, BR and other Latin American Countries*
- Monitor newly published applications and on-going litigations

Phase 3: 2nd Generation mRNA technology – **Monitoring of newly published patent applications**

IP landscape strategy redefined to be aligned with the 2nd generation mRNA technology strategy discussions (improved technology, other pathogens beyond COVID-19)

IP search strategy was broadened in scope to account for:

- Formulation based on lipid nanoparticles (especially when including cationic lipids).
- Modified mRNA (at nucleotide, capping, terminal, construct level) for improved expression.
- mRNA vaccines specific for high/medium priority infections.

Monitoring launched in March 2022 with first results in June 2022 and regular monitoring implemented in December 2022.

Phase 3: 2nd Generation mRNA technology – **Monitoring of newly published patent applications**

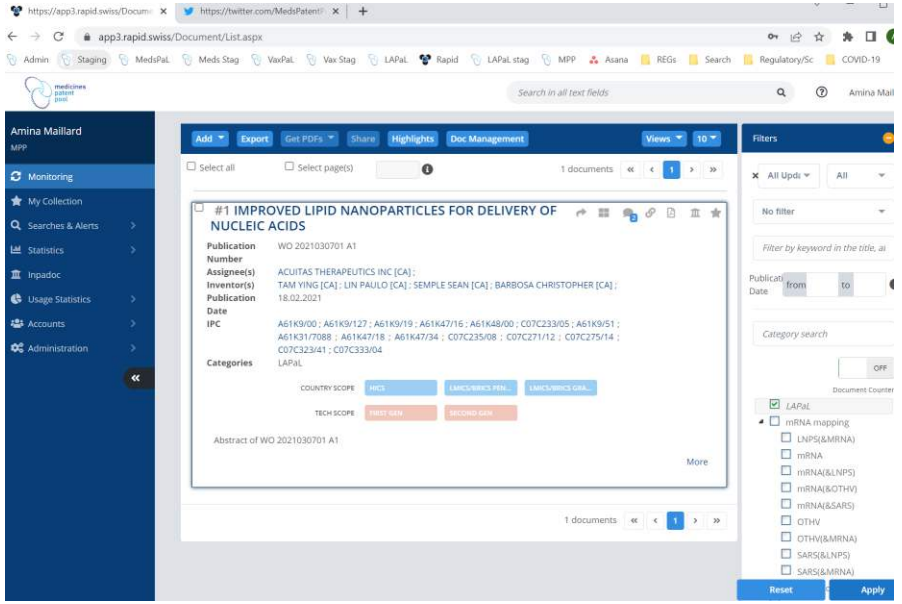
- **June 2022**: **500** patent publications were identified and "broadly" categorised according to technical content.
- The results – **compiled in an Excel sheet** - have been shared with various Programme stakeholders. Publications identified as being relevant to 1st generation vaccines were added to VaxPaL.
- **Oct–Dec 2022**: **217** patent publications added, reviewed and categorised further.

		Rapid Categories					
Pub. Number and Link to Patentscope	Pub. Number	INGREDIENT(S) Lipid Nanoparticles	INGREDIENT(S) RNA/DNA	TARGET(S)	Manufacturing/Analysis/Devices	Administration	Title
WO2022137133	WO2022137133		mRNA optimisation	SARS-Cov-2			RNA VACCINE AGAINST SARS-COV-2 VARIANTS

- **March 2023**: **200** additional patent publications retrieved and being reviewed.
- **File will be made available for download on MPP website**.

Phase 3: 2nd Generation mRNA technology – **Monitoring of newly published patent applications**

- **Rapid** from Centredoc, a tool designed to manage patent and non-patent literature, was selected to manage/share monitoring results (in addition to the Excel sheet).
- Accounts to be created for interested users.
- **Go live planned Q2 2023.**



Please express your interest should you want to have access to this database.

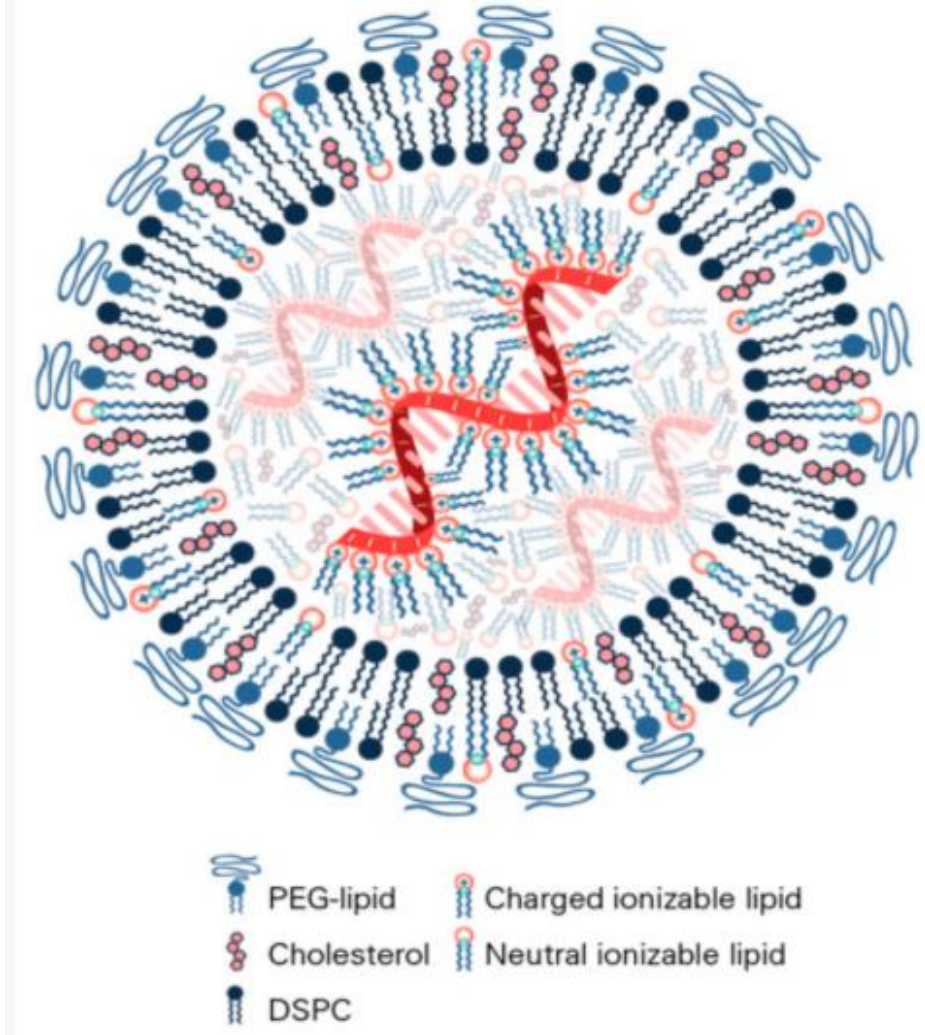
Next steps – Strategy for information sharing/monitoring

- IP Monitoring results:
  - will be shared on MPP website as an .excel file (same content and categorisation as in Rapid).
  - Link from MPP website to Rapid tool with process to request creation of account for interested parties.
- Organise trainings on available tools.
- Establish contacts with IP specialists from each Network Partner.
- Align monitoring scope with research progression/results.
- Supporting the countries participating in the Programme with their FTO assessments.

Table of content

mRNA Technology Transfer Programme

mRNA lipid nanoparticle structure



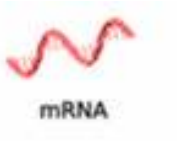
Factors impacting immunogenicity, stability, and subject to intellectual property claims
Sequence, poly-A tails, codon optimization, base modification, capping, self-amplification, etc. Critical to stability and efficacy.
Cationic lipid: Chemical structure (infinite possibilities), molecular ratio. Minor changes to lipid major can impact on stability and efficacy
Non-ionic lipid (e.g. phospholipid) – acyl component, head group, molecular ratio
Cholesterol or derivative – molecular ratio
Conjugated lipid to inhibit aggregation. PEG length, lipid anchor, molecular ratio. May also impact biodistribution / bioavailability.

mRNA Technology Transfer Programme

Drawings adapted from Vaccines 2021, 9, 65. https://doi.org/10.3390/vaccines9010065

University of Pennsylvania

Chemical modification of mRNA to more effectively produce proteins in vivo. Applies to e.g. Moderna and Pfizer/BioNTech vaccines

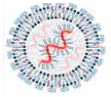


Publication No. **Expiry**	Subject Matter	Patent Status LMICS			Patent status HICS		
		Granted	**Pending**	**Withdrawn**	**Granted**	**Pending**	**Withdrawn**
WO2007024708 **21/08/2026**	Method for inducing a mammalian cell to produce protein using in-vitro synthesized mRNA that comprises Ψ or m<1>Ψ (1-methylpseudouridine	EP2578685B1 (Turkey EP3611266B1 (AL, BA, BG, MK, **RS**, TR)	EP div filed end 2022 (AL, BA, BG, MK, **RS**, TR)		EP (AT, BE, CH, CY, CZ, DE, DK, ES, FI, FR, GB, HU, IE, IT, LI, LT, NL, PL, PT, RO, SE, SK) & US	EP (AT, BE, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, HR)	
WO2014160243 **13/03/2034**	Purified preparation of messenger RNA comprising a 1-methyl-pseudouridine residue				US11060107	US2021292786	

Licences: Pfizer/BioNTech and Moderna licensed Penn technology non-exclusively

Protiva (Tekmira) - Arbutus - Genevant

mRNA lipid nanoparticles. Apply or may apply to Moderna and Pfizer/BioNTech vaccines



Publication No. **Expiry**	Subject Matter	Patent Status LMICS			Patent status HICS		
		Granted	Pending	Withdrawn	Granted	Pending	Withdrawn
WO2004002453 **30/06/2023**	**Process** for producing a lipid vesicle encapsulating a nucleic acid within the lipid vesicle			EP (AL, BG, MK, TR)	AU, CA, JP, EP1519714 (AT, BE, DK, FR, DE, IE, IT, NL, ES, SE, CH, GB); EP2338478 (FR, DE, GB), EP2823809B (FR, DE, GB), ++ US (US 7,901,708) - US9,504,651 challenged by Moderna		
WO2007012191 **27/07/2026**	**Method** of producing a lipid vesicle encapsulating a therapeutic product which includes nucleic acid				AU, CA, EP (FR, DE, IE, LI, SE, CH, GB), JP, US 9,005,654 (exp 25/11/2028)		
WO2009127060 **15/04/2029**	**Lipid nano- particle composition** ((a) a nucleic acid; (b) a cationic lipid … (c) a non-cationic lipid comprising a mixture of a phospholipid and cholesterol …. (d) a conjugated lipid ..)	TR (EP2279254) - Opposed by Moderna and MSD		EP (AL, BA, BG, MK, **RS**) **Rejected**: CN	AU, CA, IL, JP, NZ, EP2279254 (AT, BE, DK, FI, FR, DE, GR, HU, IS, IE, IT, LI, LU, MC, NO, PL, PT, ES, SE, CH, GB) - Opposed by Moderna and MSD, US 8,058,069 and US9,364,435 validity being challenged by Moderna with USPTO Patent Trial and Appeal Board - US8,492,359 - US8,822,668, US11,141,378		
WO2012000104 **30/06/2031**	**Lipid nano-particle composition** (non-lamellar)	**CN**102119217B		**IN**, EP (AL, BA, BG, MK, RS)	US9,404,127 - validity being challenged by Moderna; US9518272, US9006417		

Feb 28, 2022: Arbutus and Genevant filed a complaint against Moderna for infringement of the **US patents in red**
Applicant/Assignee: Protiva Biotherapeutics, Inc/Arbutus Biopharma Corp

Acuitas

Lipids and lipid nanoparticle formulations. ALC-0159 and ALC-0315 lipid are both used in Biontech's BNT162b2 and could have been used in Curevac's CVnCoV

Publication No. **Expiry**	Subject Matter	**Patent Status LMICS**			**Patent status HICS**		
		Granted	**Pending**	**Withdrawn**	**Granted**	**Pending**	**Withdrawn**
W2015199952 **05/06/2035**	Lipids and lipid nanoparticle formulations for delivery of nucleic acids (**ALC-0159** lipid and analogues)	**CN**, EP3766916 (AL, BG, MK, **RS**, TR)	EP div (…)	EP (AL, BA, MA, MK, RS, TR)	AU, EP3160938B1 (AT, BE, FR, DE, IE, IT, LI, LU, NL, ES, CH, GB), CA, HK, JP, IL & US (US9738593B2, US9737619B2, US10106490B2) EP3766916 (AT, BE, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, SM)	EP **div**	EP3160938B1 (HR, CZ, EE, FI, GR, HU, IS, LV, LT, MC, MT, NO, PL, RO, SM, SK, SE)
WO2017075531 **28/10/2036**	**ALC-0315 lipid** and analogues and lipid nanoparticle formulations for delivery of nucleic acids	**CN**, EP3368507 (AL, BG, MK, **RS**, TR)	**CN**, EP div (…)	EP (BA, ME, MA, MD)	AU, US (US10166298B2), JP, EP3368507 (AT, BE, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, SM)	AU, EP (…), CA, IL, HK, JP & US	
WO2018078053 **26/10/2037** Acuitas/Curevac	Lipid nanoparticle comprising cationic lipid (III) or PEG lipid (IV) or cationic lipid (I) or cationic lipid (II) and mRNA compound with **nucleoside unmodification**	EA (AM, AZ, BY, KZ, KY, RU, TJ, TM, RU)	**BR**, **CN**, EP (AL, MK, RS, TR), **IN**, **MX**, SG	EP (BA, ME, MA, MD)	AU	CA, EP (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, SM), IL, JP, KR, SG & US	

BioNtech **non-exclusive licence** from Acuitas Therapeutics, grants use rights relevant to proprietary lipid nanoparticles and formulations used in BNT162b2.

Acuitas **collaboration** with CureVac allowing access to the full patent portfolio and know-how of Acuitas and its lipid technology.

mRNA Technology Transfer Programme

Acuitas - Lipids and lipid nanoparticle formulations

Example of recent patent applications to be monitored

Publication No. **Expiry**	Subject Matter	**Patent Status LMICS**			**Patent status HICS**		
		Granted	**Pending**	**Withdrawn**	**Granted**	**Pending**	**Withdrawn**
WO 2021/030701 **14/08/2040**	Method for delivering a nucleic acid to a primate (Human) by administering a **lipid nanoparticle with specific mean particle diameter between 40 nm to 70 nm** comprising nucleic acid encapsulated within the LNP, cationic lipid, neutral lipid, steroid and polymer-conjugated lipid		**Pending**: **BR**, CN, CO, CR, EC, EG, PE, GE, HN, ID, IN, JO, LK, MY, MX, PE, PH, SV, TH, TR, UA, VN, **ZA2022/01787**, EP (AL, BG, MK, **RS**, TR, BA, ME, KH (Cambodia), MA, MD, **TN**) National phase time limit was 14.02.2022			**Pending**: AE, AU, CA, CL, DE, ES, GB, IL, IT, JP, KW, KR, NZ, OM, PA, QA, SA, SG, EP (AT, BE, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, SM), US National phase time limit 14.02.2022	

Moderna – patents mainly in HICs - 1/3

Publication No. **Expiry**	Subject Matter	Patent Status LMICS			Patent status HICS		
		Granted	**Pending**	**Withdrawn**	**Granted**	**Pending**	**Withdrawn**
WO 2012/045075 **03/10/2031**	**mRNA synthesis using modified nucleotides**	EP3590949 (AL, BG, MK, **RS**, TR)	EP div (…)	EP2622064B1 (AL, BG, MK, RS, SK, TR)	**Granted** : EP2622064B1 (2019; FR, DE, IT, NL, ES & GB), EP3590949 (AT, BE, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, SM)- Opposed by BioNTech & Sanofi, US (US9334328, US9657295, US10064959)	**Pending**: CA, EP div (…)	**Withdrawn**: EP (AT, BE, HR, CY, CZ, DK, EE, FI, DE, HU, IS, IE, LV, LT, LU, MT, MC, MK, NO, PL, PT, RO, SM, SK, SI, SE, CH)
WO 2013/151663 WO 2013/151664 WO 2013/151665 **WO 2013/151666** **WO 2013/151667** WO 2013/151668 WO 2013/151669 WO 2013/151670 WO 2013/151671 WO 2013/151672 WO 2013/151736 **09/03/2033**	**composition comprising lipid nanoparticles comprising mRNA encoding a polypeptide**		EP3501550A1 (WO 2013151665) pending with broad claims (AL, **RS**, TR, BG)		AU, CA, JP & EP (with). AU, CA, EP (with), JP & US. AU, CA, EP (with) & JP. AU, CA, EP (with) & JP. AU, CA, EP (with), JP & US. AU, CA, EP (with) & JP. AU, CA, EP, JP & US. AU, CA, EP & JP. AU, CA, EP & JP. AU, CA, EP & JP. AU, CA, EP, JP & US. Mainly grants in the US		

Moderna – patents mainly in HICs - 2/3

Publication No. **Expiry**	Subject Matter	Patent Status LMICS			Patent status HICS		
		Granted	**Pending**	**Withdrawn**	**Granted**	**Pending**	**Withdrawn**
WO2012135805 **02/04/2032**	**Composition** comprising lipid nanoparticles comprising a cationic lipid, a sterol, and a PEG-lipid, wherein the lipid nanoparticles comprise an mRNA encoding a polypeptide.		**EP2691101** (AL, BG, MK, **RS**, TR) (pending claims relate to pharma comp comprising modified mRNA encoding a POI modified 100% with N1-methyl-pseudouridine, administered intramuscularly)	EP (BA, ME)	AU, JP, US10898574B2 (26.08.2022 Moderna sues Pfizer for infringement)	AU, CA, **EP2691101** (AT, BE, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, SM), JP	AU
WO2014081507 **02/10/2033**	**Methods** for the manufacture and optimization of modified mRNA molecules via optimization of their terminal architecture	EP (AL, MK, **RS**, TR)	EP div (AL, MK, RS, TR)	EP (BA, ME)	AU, JP, US, EP2922554 (at least one miRNA binding site in 3 UTR; AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, SM), opposed in Nov 2021 by patent agent	AU, CA, EP4074834 (div), HK, US, JP	
WO2014164253 **16/03/2034**	Vaccine **composition** comprising lipid nanoparticles comprising mRNA encoding a polypeptide				HK		EP, US
WO2017049245 **16/09/2036**	**Lipid SM-102**	EP3350157B1 (AL, MK, **RS**, TR)	EP3736261 div (AL, MK, RS, TR)	EP (BA, ME, MA, MD)	AU, CA, JP, US9,868,692, EP3350157 (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, SM),	AU, TW, US, EP div	

Moderna – patents mainly in HICs - 3/3

Publication No. **Expiry**	Subject Matter	Patent Status LMICS			Patent status HICS		
		Granted	**Pending**	**Withdrawn**	**Granted**	**Pending**	**Withdrawn**
WO2017070626 **21/10/2036**	**Betacoronavirus mRNA vaccine** (formulated in a cationic lipid nanoparticle)	**EP3718565B2** (AL, MK, **RS**, TR, BA, ME, MA, MD) A betacoronavirus (BetaCoV) messenger RNA (mRNA) vaccine	EP3364983 & EP4011451 (human metapneumovirus (hMPV) mRNA vaccine)	AR	**EP3718565B2** (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, SM); opposed by BioNTech, Sanofi and Pfizer US10,702,600, US10,933,127 - 26.08.2022 Moderna sues Pfizer for infringement	AE, TW, EP3364983 & EP4011451 (human metapneumovirus (hMPV) mRNA vaccine)	
WO2017099823 **10/12/2036**	Lipid nanoparticle **composition** (except PEG-Lipid)	EP3386484 (AL, MK, MT, **RS**, TR, BA, ME, MA, MD)	EP3964200A1 (div)		US, EP3386484 (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, SM)	AU, CA, EP3964200A1 (div), JP & US	

Moderna – patents in HICs & LMICs - 1/6

Scope of claims may vary greatly between countries

Publication No. **Expiry**	Subject Matter	Patent Status LMICS			Patent status HICS		
		Granted	**Pending**	**Withdrawn**	**Granted**	**Pending**	**Withdrawn**
WO2012045082 **03/10/2031**	**Compositions and methods for delivering biological moieties such as modified nucleic acids** into cells to modulate protein expression. Such compositions and methods include the use of modified messenger RNAs, and are useful for production of proteins.	Granted: ZA 201303161B (specific to the production of immunoglobulins, specifically trastuzumab) **ZA** 201403666 B covers kits for production of immunoglobulin proteins, trastuzumab and rituximab. Two independent broad kit claims were granted.		BR, CN, MX, RU	EP (FR, DE, NL), NZ 608972 (production of trastuzumab), US9701965 Europe EP2625189 and EP3431485 relate to A kit and pharmaceutical preparation for production of immunoglobulins. US 9,701,965 B2 granted claims restricted to a method for producing rituximab)		AU, CA, IL, JP (rejected), SG

Granted claims in most countries restricted to immunoglobulins except in ZA due to national patent law. Relevance to be checked with local patent counsels/attorneys.

Moderna – patents in HICs & LMICs - 2/6

Risk mitigation

Publication No. **Expiry**	Subject Matter	**Patent Status LMICS**			**Patent status HICS**		
		Granted	**Pending**	**Withdrawn**	**Granted**	**Pending**	**Withdrawn**
WO 2013052523 **03/10/2032**	**Method of expressing a polypeptide by administering isolated mRNA**	**BR**112014007852; **CN**103974724B **ZA** 201402547B limited to mRNA that is fully modified with 1-methylpseudouridine. claims similar to those of corresponding US9,428,535. MX354267B, RU2648950C2, RU2707251C2 EP3682905 (AL, BG, MK, RO, **RS**, TR)	**CN**, EP4015005 (AL, BG, MK, RO, RS, TR)		AU, EP2763701B1 (methoxy-uracil; FR, DE, CH, GB); EP3492109B1 (granted in 2020; FR, DE, NL, CH, GB) being opposed by BioNTech & Sanofi. auxiliary requests filed by Moderna limit the claims to the **use of 1-methylpseudouridine**; HK, IL, JP, KR, NZ, US9428535B2 **EP3682905** (granted in 2021; 5-methyl-cytidine; +1-methylpseudouridine; being opposed by 10 opponents GSK, Sanofi; Pfizer.....)	AU, CA, SG**, EP4015005** (use of 1-methylpseudouridine)	

Patents in Brazil, China, South Africa, Mexico and Russia covering mRNA fully modified with 1-methylpseudouridine:

-> Design around N1-methyl pseudouridine

-> Get a licence,

-> Rely on Moderna's commitment not to enforce, but would need to extend post-pandemic and beyond COVID

Moderna – patents in HICs & LMICs - 3/6

Scope of claims may vary greatly between countries

Publication No. **Expiry**	Subject Matter	Patent Status LMICS			Patent status HICS		
		Granted	**Pending**	**Withdrawn**	**Granted**	**Pending**	**Withdrawn**
WO2013090648 **14/12/2032**	Method of producing a polypeptide in a mammalian cell or tissue with a formulation comprising a modified mRNA encoding the polypeptide; Pharmaceutical compositions comprising **modified mRNA formulated in LNPs**	RU, **ZA**201403783, EP (AL, BG, MK, **RS**, TR)	**CN**, **ZA** 201503620 A (div of ZA 2014/03783), **ZA** 201503621 A (div of ZA 2014/03783).	**Withdrawn/rejected:** CN, IN, MX. EP (BA, ME)	US (US granted equivalents covers the production of specific proteins), EP2791160 (AT, BE, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO,SE, SI, SK, SM) Opposed in June 2022 (10 opponents, including Pfizer, Sanofi and BioNtech	EP (div), JP (appeal)	AU,CA, HK, IL, KR, SG, NZ

ZA '783 claim 1. A **modified mRNA encoding polypeptide of interest** for use is a method of producing the polypeptide of interest in a mammalian cell or tissue, the method comprising, contacting said mammalian cell or tissue with a formulation comprising a modified mRNA encoding the polypeptide of interest, wherein the **formulation is selected from the group consisting of nanoparticles, poly(lactic-co-glycolic acid) (PLGA) microspheres, lipidoid, lipoplex, liposome, polymers, carbohydrates (including simple sugars), cationic lipids, fibrin gel, fibrin hydrogel, fibrin glue, fibrin sealant, fibrinogen, thrombin, rapidly eliminated lipid nanoparticles (reLNPs) and combinations thereof**.

EP2791160 claim 1. A pharmaceutical composition comprising a **1-methyl-peudouridine**-modified m-RNA encoding a polypeptide of interest, wherein the **mRNA is formulated as a lipid nanoparticle**".

Moderna – patents in HICs & LMICs - 4/6

Scope of claims may vary greatly in time. Pending applications to be monitored to understand final scope and relevance

Publication No. **Expiry**	Subject Matter	Patent Status LMICS			Patent status HICS		
		Granted	**Pending**	**Withdrawn**	**Granted**	**Pending**	**Withdrawn**
WO2015164674 **23/04/2035**	**Nucleic acid compositions**	**RU**2746406 C2 (WO claim granted)	**BR**, **CN**, **IN** (opposed), EP divisionals filed (AL, BG, MK, **RS**, TR, BA, ME, MA)		JP, US, EP3134131 (granted, claims restricted to influenza virus),	AU, CA, EP Divs filed (AT, BE, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, SM)	
WO2020061457 **20/09/2039**	Method of producing a lipid nanoparticle (LNP) encapsulating a nucleic acid which used in the preparation of mRNA-1273 vaccine.		**CN**, EP (AL, BG, MK, **RS**, TR)	EP (BA, ME, KH, MA, MD, TN)		CA, EP (AT, BE, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, SM), JP, US	

Moderna – patents in HICs & LMICs - 5/6

Monitoring in time to understand final geographic scope / patent strength

Publication No. **Expiry**	Subject Matter	Patent Status LMICS			Patent status HICS		
		Granted	**Pending**	**Withdrawn**	**Granted**	**Pending**	**Withdrawn**
WO2021154763 **26/01/2041**	mRNA comprising an open reading frame (ORF) that encodes a **SARS-CoV-2 spike (S) protein** having a double proline stabilizing mutation		CO, DO, MX, PE, PH, TH National phase ddl 28 July 2022	EP (AL, MK, RS, RT, BA, ME, KH, MA, MD, TN), AR, BR, CN, RU, EA End of 2022-Early 2023		AE, TW, NZ National phase ddl 28 July 2022	AU, CA, EP, IL, KR, SA national filing US17/000,215 allowed in Aug 2021, abandoned by failure to pay final fees due to on-going discussions with NIH (**dispute over inventorship**). Claims restricted to a specific mRNA sequence (assumed to cover mRNA-1273)
WO2021222304 **27/04/2041**	SARS-CoV-2 messenger ribonucleic acid (mRNA) vaccine compositions as well as methods of using the vaccines			International application National phase ddl 27 October 2022 - No entry **Third party Obs filed with IPEA**			International application National phase ddl 27 October 2022 - No entry **Third party Obs filed with IPEA**
WO2021159130 **14/05/2041**	SARS-CoV-2 mRNA vaccine compositions as well as methods of using the vaccines			International application National phase ddl 15 November 2022 - No entry			International application National phase ddl 15 November 2022 - No entry

Moderna – patents in HICs & LMICs - 6/6

Monitoring in time to understand final geographic scope / Secondary patents

Publication No. **Expiry**	Subject Matter	Patent Status LMICS			Patent status HICS		
		Granted	**Pending**	**Withdrawn**	**Granted**	**Pending**	**Withdrawn**
WO2021262909 **23/06/2041**	mRNA with extended half-life (optimised 5'-UTR and 3'-UTR sequences)		RU, BR, MX, EP National phase ddl 23 December 2022 – **Countries still being published**			IL, SA, EP, CA, KR, NZ, AU National phase ddl 23 December 2022	
WO2021231963 **14/05/2041**	RNA liquid formulations for high-volume distribution (SARS-COV-2 specific)		**Pending**: EP (AL, MK, RS, RT, BA, ME, KH, MA, MD, TN) National phase ddl 15 November 2022			**Pending**: EP National phase ddl 15 November 2022	

BioNTech patents in HICs & LMICs – 1/3

Publication No. **Expiry**	Subject Matter	Patent Status LMICS			Patent status HICS		
		Granted	**Pending**	**Withdrawn**	**Granted**	**Pending**	**Withdrawn**
WO2007036366 **28/09/2026**	Nucleic acid molecule comprising promoter, transcribable nucleic acid sequence and nucleic acid sequence with at least two copies of a 3'-untranslated region of a human beta-globin gene	EP (BG, TR, AL, BA, HR, MK, RS), IN	IN		AU, CA, EP (AT, BE, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK), HK, JP, US		
WO2016005324 **06/07/2035**	Nucleic acid molecule comprising promoter, transcribable nucleic acid sequence which codes for modified polyadenyl sequence (containing nucleotides other than A nucleotides)	EP3167059 (BG, TR)	EP3594337 (AL, BA, MA, ME, MK, RS, BG, TR)	EP3167059 (AL, BA, MA, ME, MK, RS) ; EP3594337 (MA)	EP3167059 (AT, BE, CZ, DK, FI, FR, DE, GR, HU, IE, IT, NL, PL, RO, SI, SK, ES, SE, CH, GB), JP	AU, CA, EP3594337, US	EP3167059 (HR, CY, EE, IS, LV, LT, LU, MT, MC, NO, SM)
WO2017036889 **24/08/2036**	Method of decreasing immunogenicity of RNA by modifying the nucleotide sequence of the RNA by reducing the uridine (U) content		EP4029522A1 (AL, MK, RS, MA, BG, TR)	EP3341026B1 (AL, BA, ME, MA, MD, MK, RS, MA, BG, TR) EP4029522A1 (BA, ME, MA, MD)	US, **EP3341026B1** (AT, BE, CH, CY, DE, FR, GB, IE, IT, LI, LU) granted on 05.02.2022; third party observations filed anonymously in Dec 2021, NO opp filed.	AU, CA, EP4029522A1	EP3341026B1 (CZ, DK, EE, FI, GR, HR, HU, IS, LV, LT, LV, MC, NL, MT, NO, PL, PT, RO, SM, SK, ES, SE, SI), JP (rejected)

BioNTech patents in HICs & LMICs – 2/3

Monitoring patents from other players and understand relevance

Publication No. **Expiry**	Subject Matter	Patent Status LMICS			Patent status HICS		
		Granted	**Pending**	**Withdrawn**	**Granted**	**Pending**	**Withdrawn**
WO2021213924 **16/04/2041**	Composition or medical preparation comprising RNA encoding an amino acid sequence comprising a **SARS-CoV-2 S** protein, an immunogenic variant thereof, or an immunogenic fragment of the SARS-CoV-2 S protein or the immunogenic variant thereof which covers the Tozinameran (BNT162b2 COVID-19 Vaccine).		EP (AL,BG, MK, RS, TR, BA, M), BR, CN, RU, MX, IN National phase ddl 22 October 2022	EP (KH, MA, MD, TN)	US	AU,CA, IL, JP, EP (AT, BE, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, SM), TW, US National phase ddl 22 October 2022	
WO2021214204 **22/04/2041**	RNA polynucleotides comprising a 5' Cap, a 5' UTR comprising a cap proximal sequence and a sequence encoding a payload.		IN, MX, RU, EP National phase ddl 22 October 2022			AU, CA, IL, KR, EP National phase ddl 22 October 2022	
WO2021213945 **16/04/2041**	Packaging, transportation, and storage of temperature-sensitive materials, such as biological and/or pharmaceutical products		IN, MX, RU, EP, BR, CN National phase ddl 22 October 2022			AU, CA, IL, KR, EP, IL, NZ, JP National phase ddl 22 October 2022	

Table of content

mRNA Technology Transfer Programme

The mRNA Technology Transfer Programme was established to improve health security in LMICs through sustainable, regional production of mRNA vaccines

Objective 1

Establish or enhance **sustainable mRNA vaccine manufacturing capacity** in regions with no or limited capacity

Objective 2

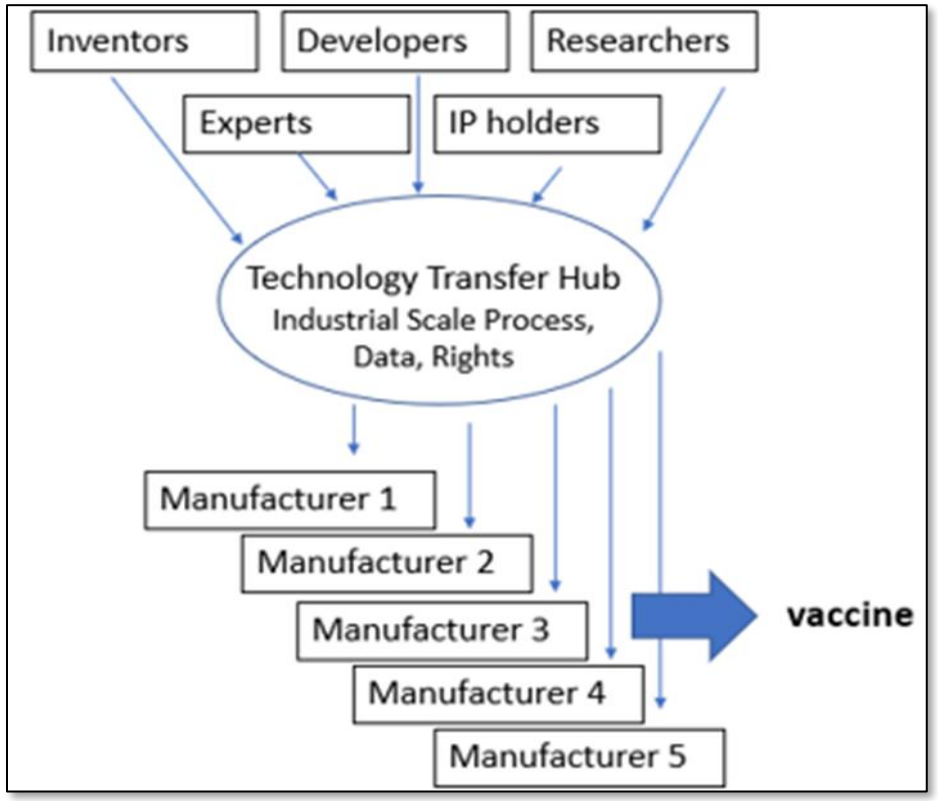
Build human capital for regulation and biomanufacturing in LMICs

The Programme is guided by three key principles:

- Principle 1: ***Equitable access to technologies suitable to respond to pandemics - mRNA technology***
- Principle 2: ***Value and share intellectual property - multilateral technology transfer***
- Principle 3: ***Promote establishment of sustainable capacity to produce mRNA vaccines - coherent policies and adequate investments***

mRNA Technology Transfer Programme

Technology Transfer: “donor & recipient” model



Technology donor

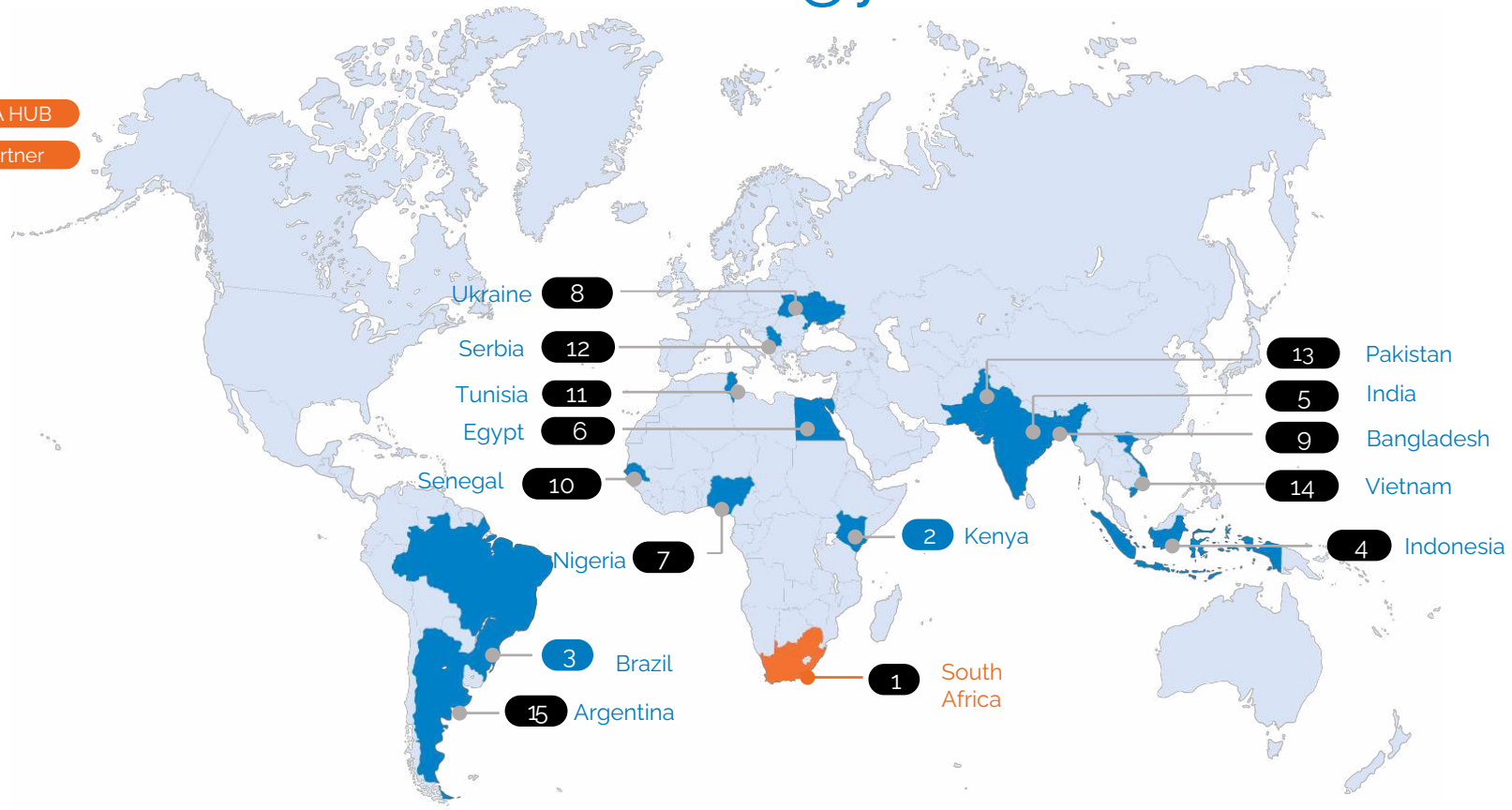
- Develop mRNA technology
- Implement mRNA technology for vaccine(s) production at scale and testing according to GMP
- Serve as training center on mRNA technology for recipients
- Develop technology transfer content
- Assist recipients during technology transfer

Technology recipient

- Develop viable business model incl. required upfront financing
- Establish required infrastructures and workforce to receive mRNA technology
- Receive and execute technology transfer from the Programme according to an agreement signed with MPP
- Implement and scale up/out (if needed) the technology according to own business model and needs

13/15 Partners have signed a Technology Transfer Agreement to receive the technology from the Hub

1. Afrigen — mRNA HUB
2. Biovac — 1st Partner
3. BioVax
4. Bio-Manguinhos
5. Biofarma
6. BiologicalE
7. BioGeneric Pharma
8. Biovaccines Nigeria
9. Darnitsa
10. Incepta Vaccine
11. Institut Pasteur de Dakar
12. Institut Pasteur de Tunis
13. Institut Torlak
14. National Institute of Health
15. Polyvac
16. Sinergium Biotech



- **Status: 13** contracts signed
- **Contract content:** parties obligations, technology transfer packages description, IP and data sharing clauses

Agreements available at: https://medicinespatentpool.org/covid-19/mrna-technology-transfer-hub-programme/agreements

Intellectual property obligations ensure know-how/data sharing

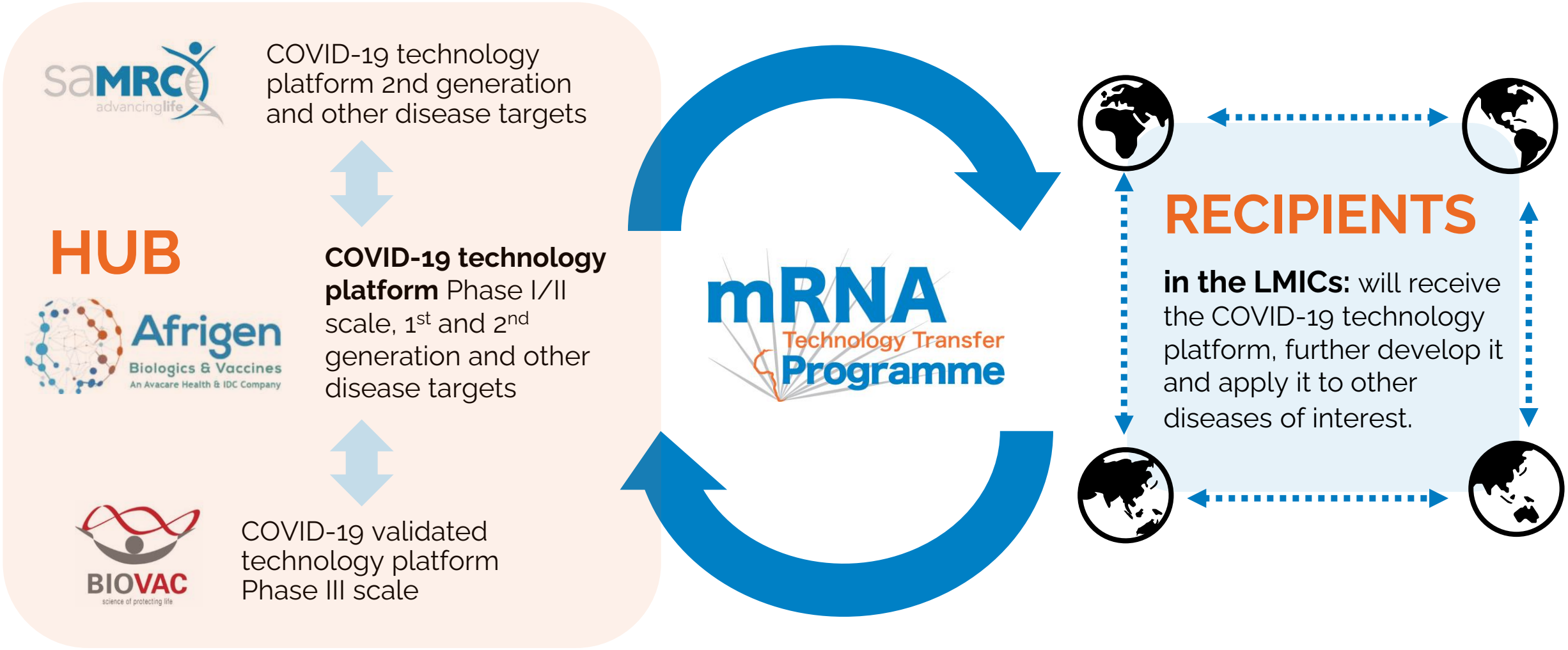
1. **Freedom to Operate (FTO):**

   MPP and WHO will not guarantee FTO at country level but will provide an IP landscape analysis detailed at country level. The confirmation of actual status and scope of patents/claims filed and/or granted in the country is each recipient's responsibility.

2. **MPP grant of licence to Recipient:**
   - MPP grants to each Recipient a non-exclusive licence to technology transfer packages to develop and commercialise "Products" based on the technology
   - MPP agrees to grant to each Recipient non-exclusive licence to any other sublicensable rights that it obtains through other Hub agreements (e.g., through SAMRC grantees – see next slide)

3. **Recipient grant-back to MPP**
   - Each Recipient agrees to grant to MPP a non-exclusive licence to any data or inventions it develops based on the technology transfer to make available to other Recipients
   - To the extent that Third Party IP is used by Recipient, Recipient undertakes to make efforts to make such Third Party IP available to MPP on same or similar terms

Technology and know-how sharing process



Design features/tradeoffs inherent in Hub

Operating in a Competitive IP/R&D environment

- Many third-party players active in mRNA R&D actively staking out IP claims on the mRNA "commons" who are not bound by same terms as Hub agreements
- Is pure "open access" feasible/desirable in such an environment?

Speed and convenience vs Freedom to operate

- Quickest way to develop an mRNA platform may not result in greatest freedom to operate for recipients later on. Strategic decisions to identify potential barriers and evaluate options – e.g., to design around, need to be made early on (e.g., mRNA modification, choice of lipids)

Sustainability vs Access

- Potential tension in ensuring the long-term sustainability of each Partner vs defining equitable access at lowest possible price
- Obligations relating to affordable access that Recipients take on for receiving the technology should be commensurate to the potential benefits they expect to receive from it

mRNA Technology Transfer Hub Programme

Thank you!!