mRNA patent landscape

19.07.2022

Medicines Patent Pool

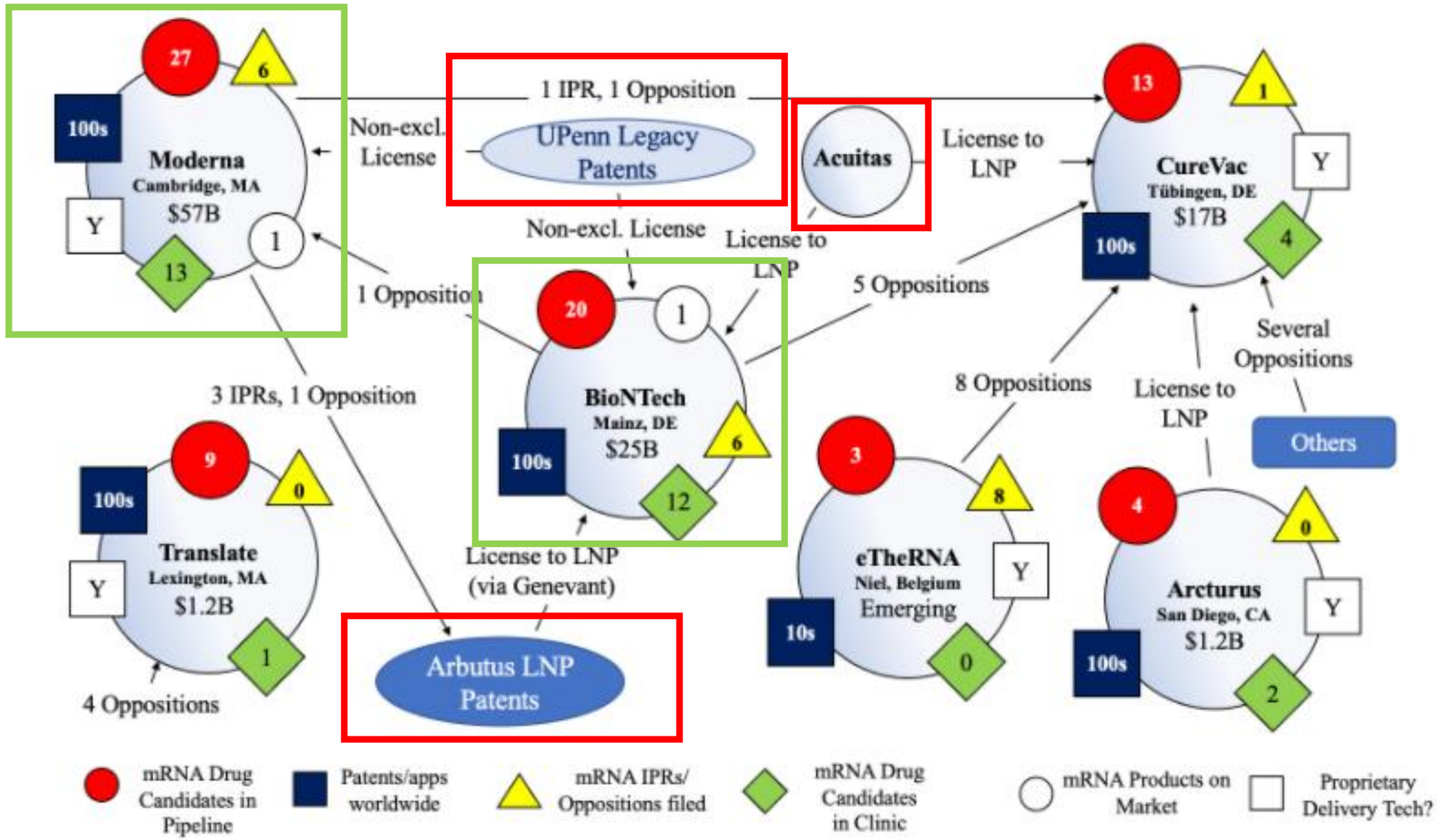
MPP provides herein information on the patent status of mRNA vaccines.

This is not a freedom to operate analysis and should not be interpreted as such. The patent information on mRNA vaccines was compiled for the purpose of providing greater transparency on patents relating to key COVID-19 vaccines and focuses primarily (though not exclusively) on patents filed by the entities that have developed vaccines.

This landscape may not be comprehensive. It may not cover all granted patents or patent applications for a given vaccine, particularly where no patent applications have been made public for the more recent innovations.

Overview of mRNA IP and Competitive Landscape (April 2021)

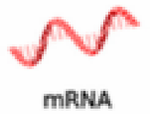
Figure 8: Overview of mRNA IP and Competitive Landscape as of April 2021. N.B. the above overview and other information provided in Parts I, II, and III are in a **constant state of flux and subject to significant ongoing change** (e.g., market capitalization, opposition and IPR filings, regulatory candidates, alliances, etc. are all constantly changing and will continue to do so on an ongoing basis). This is one snapshot as of April 2021.



Source: https://www.jdsupra.com/legalnews/the-mrna-patent-and-competitive-7682620/

University of Pennsylvania - Upenn “legacy patents”

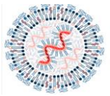
Chemical modification of mRNA to more effectively produce proteins in vivo. Applies to e.g. Moderna and Pfizer/BioNTech vaccines



Publication No. **Expiry**	Applicant/Assignee	Subject Matter	Patent Status WW		Licence(s)
			HICS	LMICS	
WO 2007/024708 **21/08/2026**	The Trustees of the University of Pennsylvania; assigned in the US to the National Institutes Of Health (NIH)	Method for inducing a mammalian cell to produce protein using in-vitro synthesized mRNA that comprises Ψ or m<1>Ψ (1-methylpseudouridine	**Granted**: EP2578685B1 (AT, BE, CH, CY, CZ, DE, DK, ES, FI, FR, GB, HU, IE, IT, LI, LT, NL, PL, PT, RO, SE, SK) & US. **Pending**: EP3611266A1 (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)	**Granted**: EP (TR) **Pending**: EP (AL, BA, BG, MK, RS, TR) **-> Patents/applications in few LMICS**	Pfizer/BioNTech and Moderna licensed Penn technology non-exclusively
WO 2014/160243 **13/03/2034**	The Trustees of the University of Pennsylvania	Purified preparation of messenger RNA comprising a 1-methyl-pseudouridine residue	**Granted**: US11060107 **Pending:** US2021292786	**-> No patents in LMICS**	

Protiva (Tekmira) - **Arbutus** - Genevant

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



Publication No. **Expiry**	Subject Matter	Patent Status WW	
		HICS	LMICS
WO 2004/002453 **30/06/2023**	**Process** for producing a lipid vesicle encapsulating a nucleic acid within the lipid vesicle	**Granted**: 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 **Withdrawn**: EP (CY, CZ, EE, FI, GR, HU, LV, LT, LU, MC, PT, RO, SI, SK)	**Withdrawn**: EP (AL, BG, MK, TR) **-> No patents in LMICS**
WO 2007/012191 **27/07/2026**	**Method** of producing a lipid vesicle encapsulating a therapeutic product which includes nucleic acid	**Granted**: AU, CA, EP (FR, DE, IE, LI, SE, CH, GB, JP, US 9,005,654 (exp 25/11/2028) **Withdrawn**: EP (AT, BE, HR, CY, CZ, DK, EE, FI, GR, IS, IT, LV, LT, LU, MC, NL, PL, PT, RO, SK, SI, ES)	**Withdrawn**: EP (AL, BA, BG, MK, **RS**, TR) **Rejected**: China **-> No patents in LMICS**
WO 2009/127060 **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 ..)	**Granted**: AU, CA, IL, JP, NZ, **EP**2279254 (AT, BE, DK, FI, FR, DE, GR, HU, IS, IE, IT, LI, LU, MC, NO, PL, PT, ES, SE, CH, TR, 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 **Withdrawn**: EP (CY, HR, CZ, EE, LV, LT, MT, RO, SI, SK), SG	**Granted**: CN102119217B **Withdrawn**: **IN**, EP (AL, BA, BG, MK, **RS**) **-> Granted patent in China**
WO 2012/000104 **30/06/2031**	**Lipid nano-particle composition** (non-lamellar)	**Granted**: US9,404,127 - validity being challenged by Moderna; US9518272, US9006417	**-> No patents in LMICS**

On Feb 28, 2022 Arbutus and Genevant filed a complaint against Moderna for infringement of the US patents in red above

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 WW		Licence(s)
		HICS	LMICS	
WO 2015/199952 **05/06/2035**	Lipids and lipid nanoparticle formulations for delivery of nucleic acids (**ALC-0159** lipid and analogues)	**Granted**: AU, EP (AT, BE, FR, DE, IE, IT, LI, LU, NL, ES, CH, GB), CA, HK, JP, IL & US (**US9738593B2**, US9737619B2, US10106490B2 **Pending**: EP **Withdrawn** EP (HR, CZ, EE, FI, GR, HU, IS, LV, LT, MC, MT, NO, PL, RO, SM, SK, SE)	**Granted:** CN **Withdrawn** EP (AL, BA, MA, MK, **RS**, TR) **-> Granted patent in China**	**Biontech** non-exclusive license 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
WO 2017/075531 **28/10/2036**	**ALC-0315 lipid** and analogues and lipid nanoparticle formulations for delivery of nucleic acids	**Granted**: AU, US (**US10166298B2**) **Pending**: AU, EP (…), CA, IL, HK, JP & US	**Granted**: CN **Pending**: CN, EP (…) **-> Granted patent in China**	
WO 2018/078053 **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**	**Pending**: AU, CA, CN, 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), IL, JP, KR, SG & US	**Pending**: **BR**, CN, EA (AM, AZ, BY, KZ, KY, RU, TJ, TM, RU), EP (AL, BG, MK, **RS**, TR), **IN**, MX **-> Pending in many LMICs**	

Acuitas - Lipids and lipid nanoparticle formulations

Example of new patent applications that may become relevant

Publication No. **Expiry**	Applicant/Assignee	Subject Matter	Patent Status WW	
			HICS	LMICS
WO 2021/030701 **14/08/2040**	Acuitas Therapeutics, Inc	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**: AU, CA, SG, GB, IL, AE, ES, DE, IT, KR, NZ, 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) **National phase time limit was 14.02.2022. More applications might still be published**	**Pending**: CO, CR, **BR**, **IN**, PE, GE, MY, EP (AL, BG, MK, **RS**, TR, BA, ME, KH (Cambodia), MA, MD, **TN**), **UA**, ZA2022/01787 **National phase time limit was 14.02.2022. More applications might still be published**

According to the scientific literature (see e.g. L. Schoenmaker, et al. 2021) the mean diameter of LNP's in the current mRNA vaccines such as Moderna and BioNTech varies between **60-100** nm and for more recent candidates (nCoVsaRNA and ARCoV) the average particles size averages of **75 nm** and **89 nm**, respectively.
The Written Opinion of WIPO's International Searching Authority has found that the pending claims **lack novelty and inventive step**, and these will need to be modified/restricted during examination.

-> Scope of granted claims unknown
-> To be monitored to assess relevance with respect to existing and future vaccines

WO2021030701 : CLAIMS AS FILED

1. A method for delivering a nucleic acid to a primate in need thereof, comprising administering a lipid nanoparticle (LNP) to the primate, the LNP comprising:

i) a nucleic acid, or a pharmaceutically acceptable salt thereof, encapsulated within the LNP;

ii) a cationic lipid;

iii) a neutral lipid;

iv) a steroid; and

v) a polymer-conjugated lipid,

wherein a **plurality of the LNPs has a mean particle diameter ranging from 40 nm to 70 nm**.

7. A method for delivering a nucleic acid to a primate in need thereof, comprising administering a lipid nanoparticle (LNP) to the primate, the LNP comprising:

i) a nucleic acid, or a pharmaceutically acceptable salt thereof, encapsulated within the LNP;

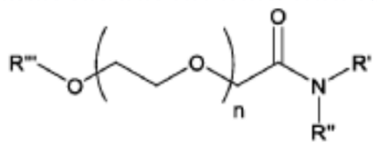
ii) a cationic lipid;

iii) a neutral lipid;

iv) a steroid; and

v) from 2.0 to 3.5 mol percent of a polymer-conjugated lipid based on total mol of lipids in the LNP.

61. A compound having the following structure:



or a salt thereof, wherein: R' and R'' are each independently a saturated alkyl having from 8 to 12 carbon atoms, provided that the total number of carbon atoms collectively in both of R' and R'' is no more than 23;

R''' is H or C1-C6 alkyl; and n is an integer ranging from 30 to 60.

66. A lipid nanoparticle comprising a compound of any one of claims 61-65.

Moderna statement on non-enforcement

October 2020

“Accordingly, while the pandemic continues, Moderna **will not enforce our COVID-19 related patents** against those making vaccines intended to combat the pandemic. Further, to eliminate any perceived IP barriers to vaccine development **during the pandemic period**, upon request we are also willing to license our intellectual property for COVID-19 vaccines to others for the post pandemic period.”

March, 7 2022 - Moderna's Updated Patent Pledge

“… Moderna is now updating its patent pledge to never enforce its patents for COVID-19 vaccines against manufacturers in or for the **92 low- and middle-income countries in the Gavi COVAX Advance Market Commitment** (AMC), provided that the manufactured vaccines are **solely for use in the AMC 92 countries**.

In non-AMC 92 countries, **vaccine supply is no longer a barrier to access**. In these countries, the **Company expects those using Moderna-patented technologies will respect the Company's intellectual property**. Moderna remains willing to license its technology for COVID-19 vaccines to manufacturers in these countries on commercially reasonable terms. Doing so enables Moderna to continue to invest in research to develop new vaccines, prepare for the next pandemic, and meet other pressing areas of unmet medical need. …”

March, 7 2022 – Politico News

“Consistent with this pledge, Moderna will not enforce its patents for COVID-19 vaccines in South Africa against the efforts by Afrigen Biologics and/or the WHO hub targeted at AMC 92 countries,” a Moderna spokesperson said in a statement to POLITICO on Monday.

Moderna – patents mainly in HICs - 1/2

Publication No. **Expiry**	Subject Matter	Patent Status WW	
		HICS	LMICS
WO 2012/045075 **03/10/2031**	**mRNA synthesis using modified nucleotides** EP2622064B1 granted claim 1: A modified messenger RNA comprising a modified nucleotide, said modified nucleotide comprising one or more chemical modifications of a naturally occurring nucleotide, …. and wherein 100% of the corresponding naturally occurring nucleotides have been replaced with: i. 5'-O-(1-thiophosphate)-cytidine and N1-methyl-pseudo-uridine, ii. 5-methyl-cytidine and **N1-methyl-pseudo-uridine**, or iii. 25% N1-methyl-pseudo-uridine and 75%-pseudo-uridine.	**Granted** : EP2622064B1 (2019; FR, DE, IT, NL, ES & GB), US (US9334328, US9657295, US10064959) **Pending**: 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) **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)	**Pending**: EP (AL, BA, BG, MK, **RS**, TR) **Withdrawn**: EP (AL, BG, MK, **RS**, SK, TR) **-> Patent application in Serbia**
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**	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**	**-> No patents in LMICS**

Moderna – patents mainly in HICs - 2/2

Publication No. Expiry	Subject Matter	Patent Status WW	
		HICS	LMICS
WO 2012/135805 **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.	**Granted**: AU, JP, US **Pending**: AU, 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 **Withdrawn**: AU	**Pending**: EP (AL, BG, MK, **RS**, TR) **-> No patents in Hub/Spoke countries. App. pending in Serbia**
WO 2014/081507 **02/10/2033**	**Methods** for the manufacture and optimization of modified mRNA molecules via optimization of their terminal architecture	**Granted**: AU, JP, US, EP (miRNA; 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) **Pending**: AU, CA, EP (div), HK	**Granted**: EP (AL, BG, MK, **RS**, TR) **Pending**: EP div (**RS**…) **Withdrawn**: EP (BA, ME) **-> Patent in Serbia**
WO 2014/164253 **16/03/2034**	Vaccine **composition** comprising lipid nanoparticles comprising mRNA encoding a polypeptide	**Granted**: HK **Withdrawn**: EP, US	**-> No patents in LMICs**
WO 2017/049245 **16/09/2036**	**Lipid SM-102**	**Granted**: AU, CA, JP, US9,868,692, EP3350157 (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), **Pending**: AU, TW, US, EP div	**Granted**: EP (AL, BG, MK, MT, **RS**, TR) **Withdrawn**: EP (BA, ME, MA, MD) **-> Patent in Serbia**
WO 2017/070626 **21/10/2036**	**Betacoronavirus mRNA vaccine** (formulated in a cationic lipid nanoparticle)	**Granted**: US10,702,600, **Pending**: AE, 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	**Pending**: EP (AL, BG, MK, MT, **RS**, TR, BA, ME, MA, MD) **Withdrawn**: **AR** **-> App. pending in Serbia**
WO 2017/099823 **10/12/2036**	lipid nanoparticle **composition** (except PEG-Lipid)	**Granted**: US, EP3386484 (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) **Pending**: AU, CA, EP (div), JP & US	**Granted** EP (AL, BG, MK, MT, **RS**, TR, BA, ME, MA, MD) **-> Patent in Serbia**

Moderna – patents in HICs & LMICs - 1/9

Publication No. **Expiry**	Subject Matter	Patent Status WW	
		HICS	LMICS
WO 2012/045082 **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**: EP (FR, DE, NL), NZ 608972 (production of trastuzumab), US9701965 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) **Withdrawn**: AU, CA, IL, JP (rejected), SG	**Granted**: **ZA** 201303161B (specific to the production of immunoglobulins, specifically trastuzumab) **ZA** 201403666 B covers kits for production of immunoglobulin proteins, trastuzumab and rituximab. Broad independent claims **18** and **20** not granted anywhere else. **Withdrawn**: **BR,** CN, MX, RU **-> Granted claims in most countries restricted to immunoglobulins except in ZA201403666 with two independent broad kit claims (claims 18 and 20)**

Claim 18. A kit for protein production, comprising a first isolated nucleic acid encoding a translatable region encoding a protein, wherein the **first nucleic acid comprises a nucleic acid modification**, wherein the first nucleic acid displays **decreased degradation in a cell into which the first isolated nucleic acid is introduced as compared to nucleic acid not comprising a nucleic acid modification**, and packaging and instructions therefor.

Claim 20. A kit for protein production, comprising **a first isolated nucleic acid encoding a translatable region encoding a protein**, wherein the first nucleic acid **comprises a nucleic acid modification**, wherein the first nucleic **acid is more stable in a cell into which the first isolated nucleic acid is introduced as compared to nucleic acid not comprising a nucleic acid modification**, and packaging and instructions therefor.

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**: **IN**, SG, **ZA**201703921 **-> 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.**

ZA 201402547 B - independent granted claims (amendment 12.06.2017)

1. An isolated mRNA encoding a polypeptide of interest for use in a method of expressing the polypeptide of interest in a mammalian subject, comprising administering to the subject said isolated mRNA, wherein said isolated mRNA comprises:
(a) a sequence of n number of linked nucleosides,
(b) a 5 ' UTR,
(c) a 3' UTR, and
(d) at least one 5' cap structure.

wherein said isolated mRNA is fully modified with 1-methylpseudouridine, wherein said isolated mRNA, when administered to peripheral blood mononuclear cells provides Protein:Cytokine (P:C) ratios of greater than 100 for TNF-alpha and greater than 100 for IFN-alpha after about eighteen or more hours, and wherein said P:C ratios are higher than those of a corresponding mRNA comprising pseudouridine in place of 1-methylpseudouridine.

26. Use of an isolated mRNA encoding a polypeptide of interest in the manufacture of a medicament for use in a method of expressing the polypeptide of interest in a mammalian subject, comprising administering to said subject the medicament, wherein said isolated mRNA comprises:
(a) a sequence of n number of linked nucleosides,
(b) a 5′ UTR,
(c) a 3′ UTR, and
(d) at least one 5′ cap structure,

wherein said isolated mRNA is fully modified with 1-methylpseudouridine, wherein said medicament, when administered to peripheral blood mononuclear cells provides Protein:Cytokine (P:C) ratios of greater than 100 for TNF-alpha and greater than 100 for IFN-alpha after about eighteen or more hours, and wherein said P:C ratios are higher than those of a corresponding medicament having mRNA comprising pseudouridine in place of 1-methylpseudouridine

Moderna – patents in HICs & LMICs - 3/9

Publication No. **Expiry**	Subject Matter	Patent Status WW	
		HICS	LMICS
WO 2013/090648 **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**	**Granted**: 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 **Pending**: EP (div) **Withdrawn**: AU,CA, HK, IL, JP, KR, SG, NZ	**Granted**: EP (AL, BG, MK, **RS**, TR), RU, **ZA 201403783:** broad claims granted relevant to any mRNA vaccine**.** Slight reformulation of the claims of the international application **found to lack inventive step** by WIPO's International Search Authority (few independent claims found novel). **Pending**: CN, **ZA** 201503620 A (div of ZA 2014/03783), **ZA** 201503621 A (div of ZA 2014/03783). **Withdrawn/rejected:** CN, **IN**, MX **-> Claims in South Africa are broad compared to other equivalents. Equivalents in other LMICS rejected. EP and RU restricted to 1-methylpseudouridine.**

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 – ZA 2014/03783

ZA 2014/03783 granted independent claims (total claims :123; amendment 17.10.2014)

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.

55. A formulated modified mRNA encoding a polypeptide of interest for use in a method of producing a pharmacological effect in a primate, the method comprising contacting said primate with a composition comprising the formulated modified mRNA encoding a polypeptide of interest.

64. Use of a modified mRNA encoding polypeptide of interest in the manufacture of a medicament 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.

109. Use of a modified mRNA encoding polypeptide of interest in the manufacture of a medicament 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 the medicament comprising a buffer-formulation comprising the modified mRNA encoding the polypeptide of interest

118. Use of a modified mRNA encoding polypeptide of interest in the manufacture of a medicament for use in a method of producing a pharmacologic effect in a primate comprising contacting said primate with a composition comprising a formulated modified mRNA encoding a polypeptide of interest.

Moderna – patents in HICs & LMICs - 4/9

Publication No. **Expiry**	Subject Matter	Patent Status WW	
		HICS	LMICS
WO 2015/164674 **23/04/2035**	**Nucleic acid compositions** WO claim 1: A nucleic acid vaccine, comprising: one or more RNA polynucleotides having an open reading frame encoding an antigenic polypeptide, formulated in a cationic lipid nanoparticle having a molar ratio of about 20-60% cationic lipid: about 5-25% non-cationic lipid: about 25-55% sterol; and about 0.5-15% PEG-modified lipid.	**Granted**; JP, US, EP3134131 (granted, claims restricted to influenza virus), **Pending**: 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)	**Granted**: RU2746406C2 (WO claim granted) **Pending**: **BR**, CN, EP divisionals filed (AL, BG, MK, **RS**, TR, BA, M , MA), **IN** (pre-grant opposition filed in oct 2021 by Indian Pharmaceutical Alliance) -> broad claims as filed cover e.g. both Moderna and Pfizer/BioNTech and potentially others. Restricted in EP and US however applications with broad claims still pending. -> so far broad claims only granted in Russia. Brazil and China are still pending
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	**Pending**: TW, US International application, National phase ddl 28 July 2022 **Withdrawn**: 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)	**Pending**: **AR** International application, National phase ddl 28 July 2022 **-> SARS-COV-2 specific, recent filing. Complete geo scope not available yet. To be monitored** **-> International Written Opinion found the claims novel and not inventive**

WO2021154763: CLAIMS AS FILED

1. A messenger ribonucleic acid (mRNA) comprising an open reading frame (ORF) that encodes a SARS-CoV-2 spike (S) protein having a double proline stabilizing mutation.

7. A composition comprising a lipid nanoparticle and a messenger RNA (mRNA) comprising an open reading frame (ORF) that encodes a SARS-CoV-2 spike (S) protein having a double proline stabilizing mutation of a wild-type SARS-CoV-2 S protein.

10. A messenger ribonucleic acid (mRNA) comprising an open reading frame (ORF) that comprises a nucleotide sequence having at least 80% identity to the nucleotide sequence of SEQ ID NO: 28 and encodes a polypeptide comprising the amino acid sequence of SEQ ID NO: 29.

20. A composition comprising a lipid nanoparticle and a messenger RNA (mRNA) comprising an open reading frame (ORF) that comprises a nucleotide sequence having at least 80% identity to the nucleotide sequence of SEQ ID NO: 28 and encodes a polypeptide comprising the amino acid sequence of SEQ ID NO: 29.

24. A messenger ribonucleic acid (mRNA) comprising an open reading frame (ORF) that comprises a nucleotide sequence having at least 80% identity to the nucleotide sequence of any one of SEQ ID NOs 3, 7, 10, 13, 16, 19, 22, 25, 31, 48, 50, 52, 54, 56, 61, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, or 106.

37. A method comprising administering to a subject a messenger ribonucleic acid (mRNA) comprising an open reading frame (ORF) that encodes a SARS-CoV-2 spike (S) protein antigen having a double proline stabilizing mutation in an amount effective to induce a neutralizing antibody response against SARS-CoV-2 in the subject.

46. An immunizing composition comprising:

(a) a first ribonucleic acid (RNA) comprising an open reading frame (ORF) that encodes a coronaviruss antigen capable of inducing an immune response, such as a neutralizing antibody response, to a SARS-CoV-2; and

(b) a second ribonucleic acid (RNA) comprising an open reading frame (ORF) that encodes a coronavirus antigen capable of inducing an immune response, such as a neutralizing antibody response, to a SARS-CoV-2, wherein the ORF of the first RNA is different from the ORF of the second RNA.

Moderna – patents in HICs & LMICs - 5/9

Publication No. Expiry	Subject Matter	Patent Status WW	
		HICS	LMICS
WO 2020/061457 **20/09/2039**	Method of producing a lipid nanoparticle (LNP) encapsulating a nucleic acid which used in the preparation of mRNA-1273 vaccine.	**Pending**: 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 National phase entered in March 2021	**Pending**: CN, EP (AL, BG, MK, **RS**, TR) **-> Broad claims as filed. Pending in Serbia**

-> Scope of granted claims unknown. To be monitored

-> Not SARS-COV-2 specific

-> The Written Opinion of WIPO's International Searching Authority has found that the pending claims lack novelty and inventive step, and these will need to be modified/restricted during examination

WO2020061457 - CLAIMS AS FILED (153 CLAIMS)

1. A method of producing a lipid nanoparticle (LNP) composition, the method comprising: i) mixing an aqueous buffer solution and an organic solution, thereby forming a lipid nanoparticle (LNP) formulation comprising a lipid nanoparticle (LNP) encapsulating a nucleic acid; and

ii) processing the lipid nanoparticle (LNP) formulation, thereby forming the lipid nanoparticle composition;

wherein the organic solution comprises an organic solvent-soluble nucleic acid and an ionizable lipid in an organic solvent; and

wherein the organic solvent-soluble nucleic acid comprises a hydrophobic organic cation.

Written Opinion of WIPO/PCT International Searching Authority

Box No. V	Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step and industrial applicability; citations and explanations supporting such statement		
1. Statement:			
Novelty [N]	Claims		YES
	Claims	1-153	NO
Inventive step [IS]	Claims		YES
	Claims	1-153	NO
Industrial applicability [IA]	Claims	1-153	YES
	Claims		NO

Moderna – patents in HICs & LMICs - 6/9

Publication No. **Expiry**	Subject Matter	Patent Status WW	
		HICS	LMICS
WO 2021/222304 **27/04/2041**	SARS-CoV-2 messenger ribonucleic acid (mRNA) vaccine compositions as well as methods of using the vaccines	**Pending**: International application National phase ddl **27 October 2022**	**Pending**: International application National phase ddl **27 October 2022**

-> SARS-COV-2 specific. Recent filing. Geo scope not available yet. To be monitored

-> The Written Opinion of WIPO's International Searching Authority has found the majority of claims novel but not inventive.

Moderna – WO 2021/222304

WO2021/222304 CLAIMS AS FILED (42 CLAIMS)

1. A composition comprising:

50 mg - 250 mg of a messenger ribonucleic acid (mRNA) comprising an open reading frame (ORF) that encodes a SARS-CoV-2 prefusion stabilized spike (S) protein; and

a lipid nanoparticle comprising a mixture of lipids that comprises an ionizable cationic lipid, a non-cationic lipid, a sterol, and a PEG-modified lipid.

25. A method comprising administering to a human subject the composition of any one of the preceding claims to induce in the subject a neutralizing antibody response against SARS-CoV-2.

29. A method comprising administering to a human subject a composition comprising

50 mg of a messenger ribonucleic acid (mRNA) comprising an open reading frame (ORF) that encodes a SARS-CoV-2 prefusion stabilized spike (S) protein; and

a lipid nanoparticle comprising a mixture of lipids that comprises an ionizable cationic lipid, a non-cationic lipid, a sterol, and a PEG-modified lipid.

Written Opinion of WIPO/PCT International Searching Authority

Box No. V	Reasoned statement under Rule 43bis.1[a][i] with regard to novelty, inventive step and industrial applicability; citations and explanations supporting such statement		
1. Statement:			
Novelty [N]	Claims	1-11, 25-28, 32-42	YES
	Claims		NO
Inventive step [IS]	Claims		YES
	Claims	1-11, 25-28, 32-42	NO
Industrial applicability [IA]	Claims	1-11, 25-28, 32-42	YES
	Claims		NO

Moderna – patents in HICs & LMICs - 7/9

Publication No. **Expiry**	Subject Matter	Patent Status WW	
		HICS	LMICS
WO 2021/159130 **14/05/2041**	SARS-CoV-2 mRNA vaccine compositions as well as methods of using the vaccines ***ModernaTx Inc. AND The U.S. Department of Health & Human Services National***	**Pending**: International application National phase ddl **15 November 2022**	**Pending**: International application National phase ddl **15 November 2022**

-> SARS-COV-2 specific. Recent filing. Geo scope not available yet. To be monitored

-> The Written Opinion of WIPO's International Searching Authority has found the majority of claims novel but not inventive.

Moderna – WO 2021/262909

WO2021159130 - CLAIMS AS FILED (38 CLAIMS)

1. A method comprising administering to a human subject a composition comprising a messenger ribonucleic acid (mRNA) comprising an open reading frame (ORF) that encodes a SARS-CoV-2 prefusion stabilized Spike (S) protein, wherein the mRNA is formulated in a lipid nanoparticle, and wherein the composition is administered in an effective amount to induce in the subject a neutralizing antibody response to SARS-CoV-2 S protein, wherein the effective amount is a 25 mg or 100 mg dose.

30. A composition comprising a 25 mg dose of an mRNA of any one of the preceding claims formulated in a lipid nanoparticle, wherein the geometric mean titer (GMT) of anti-SARS-CoV-2 S protein IgG antibodies produced in a human subject at Day 15 or Day 29 post-administration of the composition at Day 1 is at least 1 log higher than the GMT of antibodies produced in convalescent subjects who were infected with SARS-CoV-2.

38. A method comprising administering to a subject a composition comprising a messenger ribonucleic acid (mRNA) comprising an open reading frame (ORF) that encodes a SARS-CoV-2 antigen comprising the amino acid sequence of SEQ ID NO: 8 in an effective amount to elicit high levels of neutralizing antibodies that increase between week 2 and week 4 post administration of the composition.

Written Opinion of WIPO/PCT International Searching Authority

Box No. V	Reasoned statement under Rule 43bis.1[a][i] with regard to novelty, inven step and industrial applicability; citations and explanations supporting s statement		
1. Statement:			
Novelty [N]	Claims	1-29, 32-38	YES
	Claims	30, 31	NO
Inventive step [IS]	Claims		YES
	Claims	1-38	NO
Industrial applicability [IA]	Claims	1-38	YES
	Claims		NO

Moderna – patents in HICs & LMICs - 8/9

Publication No. **Expiry**	Subject Matter	Patent Status WW	
		HICS	LMICS
WO 2021/262909 **23/06/2041**	mRNA with extended half-life (optimised 5'-UTR and 3'-UTR sequences)	**Pending**: International application National phase ddl 23 December 2022	**Pending**: International application National phase ddl 23 December 2022

-> Used in elasomeran but not SARS-COV-2 specific. Recent filing. Geo scope not available yet. To be monitored

-> The Written Opinion of WIPO's International Searching Authority has found 3 claims (70, 71, 73) out of 127 to be novel and inventive

Moderna – WO 2021/262909

WO2021262909 - CLAIMS AS FILED (127 CLAIMS)

1. A polynucleotide encoding a polypeptide (e.g., mRNA), wherein the polynucleotide comprises:

(a) a 5'-UTR comprising the sequence of SEQ ID NO: 1 or a variant or fragment thereof; (b) a coding region comprising a stop element (e.g., as described herein); and

(c) a 3'-UTR (e.g., as described herein).

70. The polynucleotide of any one of claims 58-69, wherein the 3' UTR comprises a fragment of SEQ ID NO: 11, e.g., a 5 nucleotide (nt), 10 nt, 15 nt, 20 nt, 25 nt, 30 nt, 35 nt, 40 nt, 45 nt, 50 nt, 55 nt, 60 nt, 65 nt, or 70 nt fragment of SEQ ID NO: 11.

71. The polynucleotide of any one of claims 58-70, wherein the 3' UTR comprises 15-25 nt fragment comprising a 60 nt fragment of SEQ ID NO: 11.

73. The polynucleotide of any one of claims 58-71, wherein the 3' UTR comprises the sequence of SEQ ID NO: 11 or a fragment thereof (e.g., a fragment that lacks the first one, two, three, four, five, six, or more nucleotides of SEQ ID NO: 11).

Written Opinion of WIPO/PCT International Searching Authority

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to nov industrial applicability; citations and explanations supporting such statemen

1. Statement

Novelty (N)	Yes:	Claims	70, 71, 73
	No:	Claims	1, 3-19, 21-69, 74-127
Inventive step (IS)	Yes:	Claims	70, 71, 73
	No:	Claims	1, 3-19, 21-69, 74-127
Industrial applicability (IA)	Yes:	Claims	1, 3-19, 21-71, 73-127
	No:	Claims	

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<211> 75
<212> RNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic oligonucleotide"

<400> 1
ggaaaucgca aaauuugcuc uucgcguuag auuucuuuua guuuucucgc aacuagcaag 60

cuuuuuguuc ucgcc 75

Moderna – patents in HICs & LMICs - 9/9

Publication No. **Expiry**	Subject Matter	Patent Status WW	
		HICS	LMICS
WO 2021/231963 **14/05/2041**	RNA liquid formulations for high-volume distribution.	**Pending**: International application National phase ddl **15 November 2022**	**Pending**: International application National phase ddl **15 November 2022**

-> Secondary patents covering other aspects such as distribution
-> SARS-COV-2 specific
-> The Written Opinion of WIPO's International Searching Authority has found 3the claims novel but not inventive
-> Geo scope not available yet. To be monitored

WO2021231963 - CLAIMS AS FILED (55 CLAIMS)

1. An article, comprising:

a liquid pharmaceutical composition comprising RNA formulated in a lipid nanoparticle, liposome, or lipoplex; and

a label, suggesting an amount of the liquid pharmaceutical composition to be administered to a subject;

wherein the article has a shelf-life of at least three months when stored at a temperature of greater than 0 °C and less than or equal to 10 °C;

wherein the amount is greater than or equal to (1 + the fraction of the RNA that would degrade in the liquid pharmaceutical composition over the shelf-life of the article) x (an individual dose of the liquid pharmaceutical composition); and

wherein the RNA encodes an infectious disease antigen, wherein the infectious disease is caused by or associated with Severe Acute Respiratory Syndrome (SARS-CoV-2).

8. An article, comprising: a liquid pharmaceutical composition comprising an RNA encoding an antigen formulated in a lipid carrier housed in a container; wherein the container comprises a total amount of RNA and wherein the total amount of RNA includes 40%-95% intact RNA and 5%-60% RNA that is less than full length RNA; and wherein the RNA encodes an infectious disease antigen, wherein the infectious disease is caused by or associated with Severe Acute Respiratory Syndrome (SARS-CoV-2).

23. A pharmaceutical composition comprising mRNA encapsulated in a lipid nanoparticle, wherein the composition comprises a total amount of intact mRNA that is greater than an effective amount of intact mRNA, wherein the composition comprises at least the effective amount of the intact mRNA after storage of the composition for a period of time; and wherein the mRNA encodes an infectious disease antigen, wherein the infectious disease is caused by or associated with Severe Acute Respiratory Syndrome (SARS-CoV-2).

BioNTech patents in HICs & LMICs – 1/3

Publication No. **Expiry**	Applicant/Assignee	Subject Matter	Patent Status WW	
			HICS	LMICS
WO 2007/036366 **28/09/2026**	BioNTech SE	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	**Granted**: 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 **Pending**: CA	**Granted**: EP (BG, TR, AL, BA, HR, MK, **RS**), **IN** **Pending**: **IN**
WO 2016/005324 **06/07/2035**	BioNTech RNA Pharmaceuticals GmbH; Tron-Translational Oncology Mainz	Nucleic acid molecule comprising promoter, transcribable nucleic acid sequence which codes for modified polyadenyl sequence (containing nucleotides other than A nucleotides)	**Granted**: EP3167059 (AT, BE, CZ, DK, FI, FR, DE, GR, HU, IE, IT, NL, PL, RO, SI, SK, ES, SE, CH, GB), JP **Pending**: AU, CA, EP3594337, US **Withdrawn**: EP3167059 (HR, CY, EE, IS, LV, LT, LU, MT, MC, NO, SM)	**Granted**: EP3167059 (BG, TR) **Withdrawn**: EP3167059 (AL, BA, MA, MK, **RS**)
WO 2017/036889 **24/08/2036**	BioNTech RNA Pharmaceuticals GmbH	Method of decreasing immunogenicity of RNA by modifying the nucleotide sequence of the RNA by reducing the uridine (U) content	**Granted**: US, 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) granted on 05.02.2022; third party observations filed anonymously in Dec 2021. **Pending**: AU, CA **Withdrawn** : EP (MA, MD), JP (rejected)	**Withdrawn** : EP (AL, BA, ME, MA, MD, MK, **RS**, MA, BG, TR)

-> No patents or applications found in most LMICs, except for one family in India and Serbia

BioNTech patents in HICs & LMICs – 2/3

Publication No. **Expiry**	Applicant/Assignee	Subject Matter	Patent Status WW	
			HICS	LMICS
WO 2021/213924 **16/04/2041**	BioNTech SE	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).	**Pending**: 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 **Pending**: International application National phase ddl **22 October 2022** **Third party obs filed in EP by Médecins du monde**	**Pending**: CN, EP (AL, BG, MK, **RS**, TR, BA, ME, KH, MA, MD, **TN**). **Pending**: International application National phase ddl **22 October 2022**
WO 2021/214204 **22/04/2041**	BioNTech SE	RNA polynucleotides comprising a 5' Cap, a 5' UTR comprising a cap proximal sequence and a sequence encoding a payload.	**Pending**: International application National phase ddl **22 October 2022**	**Pending**: International application National phase ddl **22 October 2022**

-> Broad claims as filed.
-> Scope of granted claims unknown. To be monitored
-> WO 2021/213924 is specific to SARS-COV-2 whereas WO 2021/214204 might be relevant to other vaccines
-> Same priority applications claims (same complex patent family)

WO2021213924 - CLAIMS AS FILED (73 CLAIMS)

1. A 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.

3. The composition or medical preparation of claims 1 or 2, wherein the 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 is encoded by a coding sequence which is codon-optimized and/or the G/C content of which is increased compared to wild type coding sequence, wherein the codon-optimization and/or the increase in the G/C content preferably does not change the sequence of the encoded amino acid sequence.

4. The composition or medical preparation of any one of claims 1 to 3, wherein

(i) the RNA encoding 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 comprises the nucleotide sequence of nucleotides 979 to 1584 of SEQ ID NO: 2, 8 or 9, a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of nucleotides 979 to 1584 of SEQ ID NO: 2, 8 or 9, or a fragment of the nucleotide sequence of nucleotides 979 to 1584 of SEQ ID NO: 2, 8 or 9, or the nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of nucleotides 979 to 1584 of SEQ ID NO: 2, 8 or 9; and/or ….

Written Opinion of WIPO/PCT International Searching Authority

Box No. V	Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step and industrial applicability; citations and explanations supporting such statement		
1. Statement:			
Novelty [N]	Claims	3, 7, 8, 11-18, 30-32, 34, 35, 37-73	YES
	Claims	1, 2, 4-6, 9, 10, 19-29, 33, 36	NO
Inventive step [IS]	Claims		YES
	Claims	1-73	NO
Industrial applicability [IA]	Claims	1-73	YES
	Claims		NO

WO2021214204 - CLAIMS AS FILED (147 CLAIMS)

What is claimed is:

1. A composition or medical preparation comprising an RNA polynucleotide comprising:

a 5' cap comprising a Cap1 structure; a cap proximal sequence comprising positions +1, +2, +3, +4, and +5 of the RNA polynucleotide; and a sequence encoding a payload, wherein:

(i) the Cap1 structure comprises m7G(5')ppp(5')(2'OMeN_1)pN_2, wherein N_1 is position +1 of the RNA polynucleotide, and N_2 is position +2 of the RNA polynucleotide, and wherein N_1 and N_2 are each independently chosen from: A, C, G, or U; and

(ii) the cap proximal sequence comprises N_1 and N_2 of the Cap1 structure, and:

(a) a sequence selected from the group consisting of: $A_3A_4X_5$ (SEQ ID NO: 1); $C_3A_4X_5$ (SEQ ID NO: 2); $A_3C_4A_5$ (SEQ ID NO: 3) and $A_3U_4G_5$ (SEQ ID NO: 4); or

(b) a sequence comprising: $X_3Y_4X_5$ (SEQ ID NO: 7);

wherein X_3 (nucleotide X at position +3 in SEQ ID NO: 7) or X_5 (nucleotide X at position +5 in SEQ ID NO: 1 or SEQ ID NO: 2) is each independently chosen from A, G, C, or U; and

wherein Y_4 (nucleotide Y at position +4 in SEQ ID NO: 7) is not C.

Written Opinion of WIPO/PCT International Searching Authority

Box No. V	Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step and industrial applicability; citations and explanations supporting such statement		
1. Statement:			
Novelty (N)	Claims	3-7, 14, 15, 17-19, 25-28, 30-40, 42-51, 63-76, 88-97, 112, 121, 122, 127, 128, 130-132, 140, 141	YES
	Claims	1, 2, 8-13, 16, 20-24, 29, 41, 52-62, 77-87, 98-111, 113-120, 123-126, 129, 133-139, 142-147	NO
Inventive step (IS)	Claims	14, 15, 140, 141	YES
	Claims	1-13, 16-139, 142-147	NO
Industrial applicability (IA)	Claims	1-147	YES
	Claims		NO

BioNTech patents in HICs & LMICs – 3/3

Publication No. **Expiry**	Applicant/Assignee	Subject Matter	Patent Status WW	
			HICS	LMICS
WO 2021/213945 **16/04/2041**	BioNTech SE	Packaging, transportation, and storage of temperature-sensitive materials, such as biological and/or pharmaceutical products	**Pending**: International application National phase ddl **22 October 2022**	**Pending**: International application National phase ddl **22 October 2022**

-> Secondary patents covering other aspects such as distribution
-> Broad claims as filed.
-> Scope of granted claims unknown. To be monitored
-> Not SARS-COV-2 specific

WO2021213945 - CLAIMS AS FILED (88 CLAIMS)

1. A kit comprising: a) a primary container; b) a payload container; c) at least one tray placed within the payload container; and d) a dry ice container; wherein the at least one tray has dimensions A x B x H, where A is about 228 to about 233 mm, B is about 228 to about 233 mm, and H is about 38 to about 46 mm.

22. A container system comprising: a) a primary container; b) a payload container that is configured to receive at least one tray; and c) a dry ice container; wherein the at least one tray has dimensions A x B x H, where A is about 228 to about 233 mm, B is about 228 to about 233 mm, and H is about 38 to about 46 mm.

51. A payload container having dimensions of about 229 mm x 229 mm x 229 mm, wherein at least 5 trays are placed within the payload container, and wherein each tray contains at least 100 vials of temperature-sensitive material.

54. A tray configured for carrying temperature-sensitive material, wherein the tray has dimensions A x B x H, where A is about 228 to about 233 mm, B is about 228 to about 233 mm, and H is about 38 to about 46 mm.

72. A kit comprising (a) a composition comprising a lipid nanoparticle encapsulated mRNA; and (b) a temperature monitoring system.

76. A kit comprising (a) a composition comprising a lipid nanoparticle encapsulated mRNA; and (b) a light sensor.

81. A method of shipping and/or storing a composition comprising shipping and/or storing a lipid nanoparticle encapsulated mRNA wherein the composition is filled into a glass vial or syringe; wherein the glass vial or syringe comprises at least one dose.

Written Opinion of WIPO/PCT International Searching Authority

Box No. V	Reasoned statement under Rule 43bis.1[a][i] with regard to novelty, inventive step industrial applicability; citations and explanations supporting such statement		
I. Statement:			
Novelty [N]	Claims	1-53, 55-58	YES
	Claims	54	NO
Inventive step [IS]	Claims		YES
	Claims	1-58	NO
Industrial applicability [IA]	Claims	1-58	YES
	Claims		NO

Summary table 1/4

Comp.	Patents	Brazil	Argentina	India	China	South Africa	Relevant vaccines
Arbutus	LNP compositions **WO2009127060**	-	-	Withdrawn	Granted (Broad claims)	-	All vaccines
Acuitas	ALC-0159 lipid and analogues **WO2015199952**	-	-	-	Granted	-	Pfizer/BioNTech, specific element
Acuitas	ALC-0315 lipid and analogues **WO201707553**	-	-	-	Granted	-	Pfizer/BioNTech
Acuitas/ Curevac	LNP specific lipids (nucleoside unmodified) **WO2018078053**	Pending	-			-	Curevac AG
Acuitas	LNP specific mean particle diameter **WO2021030701** – NP ddl 14.02.2022	International phase - Monitor	-	International phase - Monitor	International phase - Monitor	International phase - Monitor	ALL vaccines with specific mean diameter of LNPs

Summary table 2/4

Comp.	Patents	Brazil	Argentina	India	China	South Africa	Relevant vaccines
BioNTech	mRNA with 2 copies of beta globin 3'-UTR **WO2007036366**	-	-	Granted	-	-	Pfizer/BioNTech Not SARS-CoV-2 specific
BioNTech	Composition or medical preparation comprising RNA encoding an amino acid sequence comprising a SARS-CoV-2 S protein **WO 2021/213924**	International phase National phase ddl **22 October 2022** -Monitor	-	International phase ddl **22 October 2022** -Monitor	International phase National phase ddl **22 October 2022** -Monitor	International phase National phase ddl **22 October 2022** -Monitor	Pfizer/BioNTech SARS-CoV-2
BioNTech	RNA polynucleotides comprising a 5' Cap, a 5' UTR comprising a cap proximal sequence and a sequence encoding a payload. **WO 2021/214204**	International phase National phase ddl **22 October 2022** -Monitor	-	International phase National phase ddl **22 October 2022** -Monitor	International phase National phase ddl **22 October 2022** -Monitor	International phase National phase ddl **22 October 2022** -Monitor	Pfizer/BioNTech and others Not SARS-CoV-2 specific
BioNTech	Packaging, transportation, and storage **WO 2021/213945**	International phase National phase ddl **22 October 2022** -Monitor		International phase National phase ddl **22 October 2022** -Monitor	International phase National phase ddl **22 October 2022** -Monitor	International phase National phase ddl **22 October 2022** -Monitor	Pfizer/BioNTech and others Not SARS-CoV-2 specific

Summary table - 3/4

Comp.	Patents	Brazil	Argentina	India	China	South Africa	Relevant vaccines
Moderna	Compos. and delivery methods **WO2012045082**	Withdrawn	-	-	Withdrawn	Granted ZA201403666B	All vaccines
Moderna	expressing a polypeptide by administering isolated mRNA **WO2013052523**	Granted	-	Withdrawn	Granted	Granted - ZA 201402547 B (similar claims as equivalents)	Moderna, BioNTech (all vaccines using 1-methylpseudouridine)
Moderna	Production of a polypeptide in a mammalian cell **WO2013090648**	-	-	Withdrawn	Withdrawn	Granted ZA 201403783 B (pending: **ZA** 201503620 A (div of ZA 2014/03783), **ZA** 201503621 A (div of ZA 2014/03783). Broad claims	Moderna, BioNTech (all vaccines using modified nucleoside)
Moderna	Nucleic acid compositions **WO2015164674**	Pending	-	Pending	Pending	-	Moderna and others
Moderna	mRNA comprising an open reading frame that encodes a SARS-CoV-2 spike- **WO2021154763**	International phase National phase ddl **28 July 2022**	Pending	International phase National phase ddl **28 July 2022**	InInternational phase National phase ddl **28 July 2022**	International phase National phase ddl **28 July 2022**	Moderna and others

Summary table - 4/4

Comp.	Patents	Brazil	Argentina	India	China	South Africa	Relevant vaccines
Moderna	Method of producing a lipid nanoparticle (LNP) encapsulating a nucleic acid which used in the preparation of mRNA-1273 vaccine. **WO2020/061457**	-	-	-	Pending - Monitor	-	Moderna and others Not SARS-COV-2 specific
Moderna	SARS-CoV-2 mRNA vaccine compositions as well as methods of using the vaccines **WO 2021/222304**	International phase ddl 27 October 2022	-	International phase ddl 27 October 2022	International phase ddl 27 October 2022	International phase ddl 27 October 2022	Moderna SARS-COV-2 specific
ModernaTx Inc. The U.S. Dept of Health & Human Services National	SARS-CoV-2 mRNA vaccine compositions as well as methods of using the vaccines **WO 2021/159130**	International phase ddl 15 November 2022	-	International phase ddl 15 November 2022	International phase ddl 15 November 2022	International phase ddl 15 November 2022	Moderna SARS-COV-2 specific
Moderna	mRNA with extended half-life (optimised 5'-UTR and 3'-UTR sequences) **WO 2021/262909**	International phase ddl 23 December 2022	-	International phase ddl 23 December 2022	International phase ddl 23 December 2022	International phase ddl 23 December 2022	Moderna, Not SARS-COV-2 specific
Moderna	Packaging, transportation, and storage of temperature-sensitive materials, such as biological and/or pharmaceutical products **WO 2021/213945**	International phase ddl 27 October 2022	-	International phase ddl 27 October 2022	International phase ddl 27 October 2022	International phase ddl 27 October 2022	Moderna, SARS-COV-2 specific

Concluding remarks

- Patent situation may vary greatly between countries due to different filing strategies, and difference in national laws, regulations and examination that may lead to patents with different scopes
- A valid broad patent may be difficult to design/around. Licensing or a commitment not to enforce may be options
- If designing around a patent is a possibility, the technical and regulatory impact of doing so would need to be assessed
- Many national legislations provide mechanisms for challenging the validity of a patent or a patent application. Such mechanisms may vary greatly between countries. For example, in South Africa, opposition to the grant of a patent is not provided for, however revocation of a granted patent could be applied for with the Registrar of Patents
- The patent situation is constantly changing and should be monitored closely, preferably by local patent agents in countries of interest
- MPP will be monitoring newly published international applications (known companies in the field as well as newcomers). Over time this will also include 2nd generation COVID-19 vaccines and mRNA vaccines for other priority diseases. This will support the hub and spokes to assess their freedom-to-operate in relevant countries
- Updated patent status in www.vaxpal.org

THANK YOU

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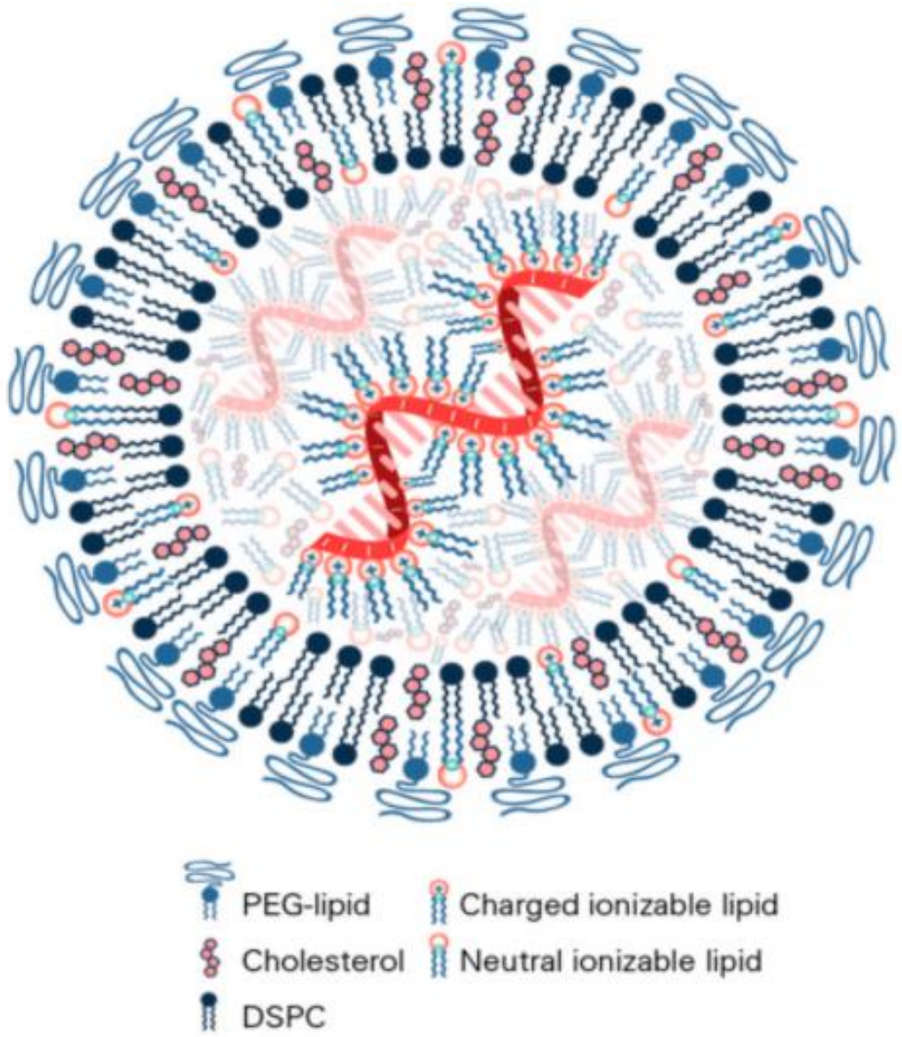
Additional slides

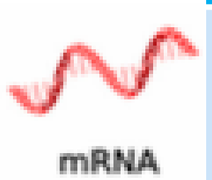
Recipients of mRNA technology from the WHO mRNA technology transfer hub

Country	ISO Alpha-2 country codes	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	tbd*	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

*legal entity under identification in cooperation with Aga Khan Development Network (AKDN). WHO website accessed on 19.07.2022
https://www.who.int/initiatives/the-mrna-vaccine-technology-transfer-hub/recipients-of-mrna-technology-from-the-who-mrna-technology-transfer-hub
https://www.gavi.org/news/media-room/92-low-middle-income-economies-eligible-access-covid-19-vaccines-gavi-covax-amc

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.

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

Arbutus LNP patents - IP rights assignment

Protiva (Tekmira) - Arbutus - Roivant - Genevant

Year	Agreement Type	Licensor/ Assingor	Licensee(s)/ Assignee	Description/comments/Notes	License URL
2009	Patent assignment	Inventors	Protiva c/o Tekmira	Assignment from the inventors to Protiva Biotherapeutics, INC., C/O Tekmira Pharmaceuticals Corp	Link
2018, Jan	Patent assignment	Protiva c/o Tekmira	Arbutus	Arbutus Biopharma Corporation	Link
2018, Feb	Agreement	Arbutus	Acuitas	Arbutus Settles Litigation, Terminating Acuitas' Rights to LNP Technology The settlement stipulates that the four non-exclusive viral vaccine sublicenses previously granted to Moderna are the only sublicenses to survive. These four sublicenses, previously granted by Acuitas to Moderna under the pre-April 15, 2010 Arbutus LNP patent families, are each limited to a specific viral target. **Moderna has no other rights to Arbutus' broad suite of LNP intellectual property.**	Link
2018, April	Licence	Arbutus (+Roivant)	Genevant Sciences	Arbutus together with Roivant launched Genevant Sciences. **Arbutus has licensed exclusive rights to its LNP and ligand conjugate delivery platforms to Genevant** for RNA-based applications outside of Hepatitis B virus.	Link
2018, July	Strategic partnership	Genevant Sciences	BioNTech	BioNTech and Genevant Sciences Sign Strategic mRNA-Focused Partnership in Rare Diseases Genevant and BioNTech will share all future costs and profits for these programs on a 50/50 basis. The companies aim to initiate clinical development in 2020.	Link