



PATENT MONITOR

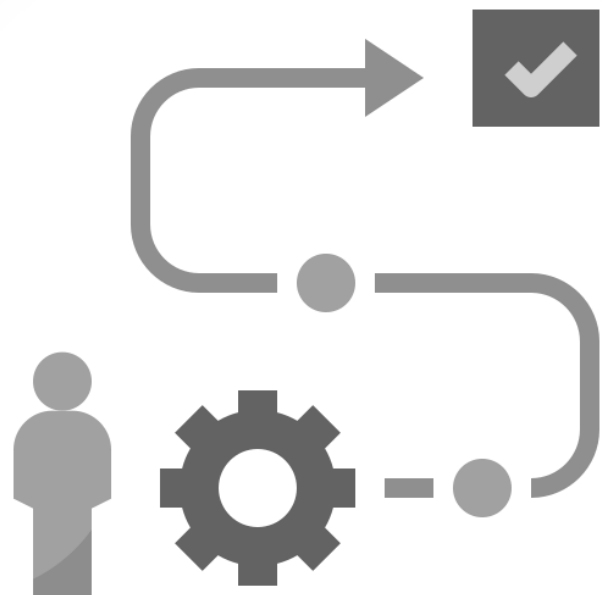
Therapeutic mRNA

Quarterly Report

Q4 2022

TABLE OF CONTENTS

<u>INTRODUCTION & METHODOLOGY</u>	<u>3</u>	<u>NOTICEABLE IP PLAYERS</u>	<u>27</u>
<u>KEY FACTS</u>	<u>8</u>	<u>Summary</u>	<u>28</u>
<u>QUARTER OVERVIEW</u>	<u>14</u>	<u>Main IP players</u>	<u>29</u>
<u>Main IP players overview</u>	<u>15</u>	<u>Newcomers</u>	<u>35</u>
<u>Technological segment overview</u>	<u>16</u>	<u>Established companies</u>	<u>36</u>
<u>Application segment overview</u>	<u>17</u>	<u>Startup</u>	<u>39</u>
<u>Technological vs. application segments overview</u>	<u>18</u>	<u>Academics</u>	<u>41</u>
<u>New patent families</u>	<u>19</u>	<u>NOTICEABLE PATENTS</u>	<u>44</u>
<u>New granted patent families</u>	<u>20</u>	<u>Identification of noticeable patents</u>	<u>45</u>
<u>Abandoned or expired patents</u>	<u>21</u>	<u>New patent families</u>	<u>46</u>
<u>Collaboration</u>	<u>22</u>	<u>New granted patents</u>	<u>50</u>
<u>IP transfer</u>	<u>23</u>	<u>ANNEX</u>	<u>55</u>
<u>US litigation</u>	<u>24</u>	<u>Access to IP analysts</u>	<u>56</u>
<u>New EP opposition</u>	<u>25</u>	<u>Terminology for patent analysis</u>	<u>57</u>
<u>EP opposition new final decision</u>	<u>26</u>	<u>CONTACT</u>	<u>58</u>



INTRODUCTION & METHODOLOGY

PATENT MONITOR

Take advantage of periodic updates on IP activities

CONTENTS

Quarterly IP database (Excel file)

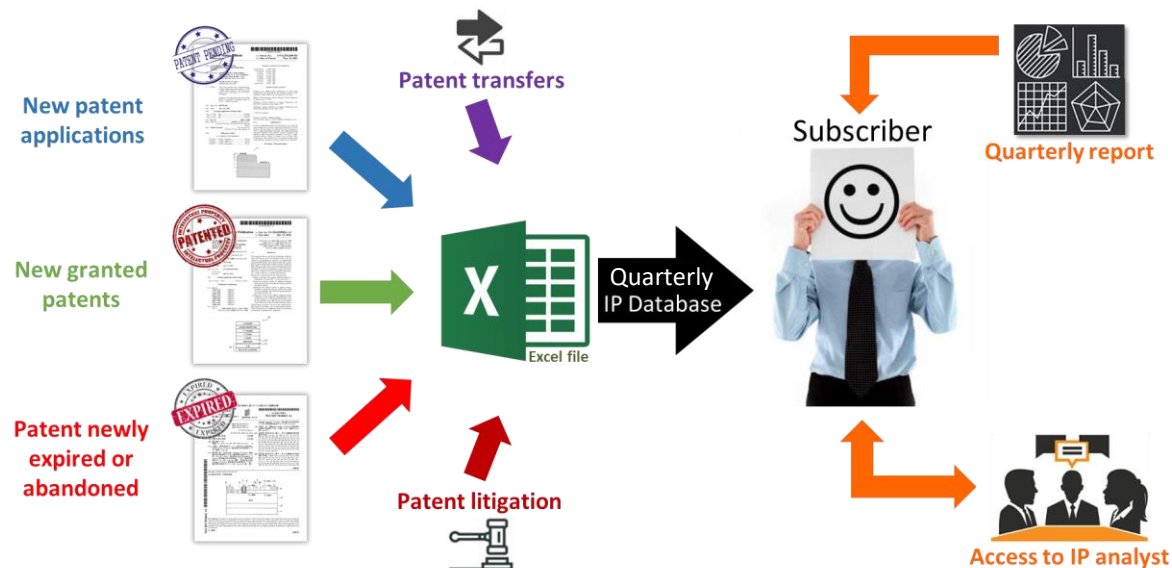
- New patent applications
- Patent newly granted
- Patents expired or abandoned
- Transfer of IP rights (re-assignment, licensing)
- Patent litigations and oppositions
- Patents categorized by technological segment and by applications

Quarterly IP report (PDF slide deck)

- Key fact & figures of the quarter
- Graphs and comments covering the patent landscape evolutions
- A close look at the key IP players, newcomers, and key patented technologies

Access to IP analyst (100h per year)

- Q&A session and discussion with our IP analysts regarding the quarterly report results, trends, analyses, specific patented technologies or companies' patent portfolios in the field of RF front end modules and components.



WHY YOU SHOULD SUBSCRIBE

- ✓ Track your **competitors**, partners or clients
- ✓ Identify **newcomers** to your technology field
- ✓ Early detect **opportunities** and risks for your business strategy
- ✓ Be ahead of **technology trends**
- ✓ Identify emerging research areas and **cutting-edge technology** developments
- ✓ Mitigate patent **infringement risks**
- ✓ Take advantage of **free technologies**

QUARTERLY REPORT

Contents

On a quarterly basis, this report will provide the IP trends over the last three months, with a close look to key IP players and key patented technologies.

- Main patent applicants, their notable patent filings and technologies.
- New entrants and their patents.
- Technology trends and notable patented technical solutions.
- Key patents newly granted, their owners and claimed inventions.
- Main IP right transfers (reassignments, licensing agreements).
- Key patents newly expired or abandoned, their owners and their potential market impact.
- Noteworthy news on patent litigation and opposition, plaintiffs and defendants, patents and products involved.

Q4 2022 KEY FACTS
Key facts overview
In Q4 2022 report you will find:
125 NEW PATENT APPLICATIONS (US EP JP KR)
32 NEWLY GRANTED PATENTS (US EP JP KR)
7 ABANDONED OR EXPIRED PATENTS
0 PATENT TRANSFERS

Q4 2022 Overview
Technological segment overview
Q4 2022 IP ACTIVITY PER TECHNOLOGICAL SEGMENT
Q4 2022 Overview
Technological vs. application segments overview

Q4 2022 MODERNA
SEGMENTS
New patent families granted
Patents expired or abandoned

Q4 2022 NOTICEABLE NEW PATENT APPLICATIONS
Main Players
ASSUMES TITLE SEGMENT SUMMARY OF THE INVENTION

Q4 2022 NOTICEABLE PLAYERS
Identification of noticeable players
In Q4 2022, 111 players, 68 industrial and 43 academics were identified. Most noticeable players are listed in the figure below and detailed in the following table.

MAIN IP PLAYERS	NEWCOMERS	ACADEMICS
moderna	NANOVIATION	Stanford University
moderna	Therion	Penn
moderna	Chimeron bio	
moderna	Celanese	
moderna	LEON	
moderna	Inventage Lab	
moderna	nference	
moderna	maple	
moderna	chromosomed	
moderna	Elanco	
moderna	Abnova	

QUARTERLY REPORT

Quarterly IP database

Patent No.	Title	Filing	Priority	Publ.	Expir.	Legal	Inventor	Assignee	Segments
US20220100001	Novel mRNA vaccine	2021-01-15	2021-01-15	2022-01-15	2041-01-15	PENDING	John Doe	ABC Corp	X
US20220100002	Novel mRNA vaccine	2021-02-20	2021-02-20	2022-02-20	2042-02-20	PENDING	Jane Smith	DEF Inc	X

Segments
(a X indicates a patent family belonging to the segment)

Patent segmentation &
Technological segmentation (mRNA design, modifications, carrier, etc.)
&
Segmentation by application (Prophylactic vaccine, Therapeutic vaccine, Therapeutic drugs), and by pathology (infectious disease, oncology, genetic disease, etc.)

Patent information

Numbers, dates, assignees, title, abstract, claims, hyperlink to updated online database (legal status, original documents etc.)

- Excel worksheet listing the latest **patent litigation & opposition**
- Excel worksheet listing the **changes in ownership** during the past quarter
- Excel worksheet listing the **patents expired or abandoned** during the past quarter
- Excel worksheet listing the **patents newly granted** during the past quarter
- Excel worksheet listing the **new patent families (inventions)** published during the past quarter

METHODOLOGY

Segment definition

Patent families were manually segmented according to their legal status and legal events, as well as their technological features and applications. A patent family can belong to multiple technical or application segments. Each segment is defined as follows:

LEGAL STATUS

New publication

Patent family published for the 1st time in WO, US, EP, JP or KR during the quarter

New Granted

Patent family granted for the 1st time in US, EP, JP or KR during the quarter

Abandoned or expired

All patents expired, rejected or revoked during the quarter

LEGAL EVENT

Patent litigation & opposition

It covers US litigation and European Opposition.

Note : are also extracted from the whole corpus:

IP collaboration (*i.e.*, filed by different entities), and

Transfer of IP rights when data are available (this kind of information are often kept secret)

TECHNICAL SEGMENTATION

mRNAs Design

Conventional mRNA: linear mRNA

sa-mRNA: Self Amplifying RNA (cis & trans)

Circ RNA: circular RNA

mRNA Modification

Carriers

LNP: lipid nanoparticle

Emulsion (CNE): cationic nano emulsion

Liposome

Extracellular vesicle (EV): this segment comprises exosome, micro vesicles, cell-derived vesicle, etc.

Polymeric NP: nanoparticle comprising polymeric compounds

Peptide NP: nanoparticle comprising peptidic compounds

VLP: virus like particle

Inorganic nanoparticle

Bacteria-derived particle

Other: comprise all few represented delivery platform

Targeted delivery

Manufacturing & Device

Storing & Preservation

APPLICATION SEGMENTATION

Therapeutic Approaches

Prophylactic vaccine

Therapeutic vaccine

Therapeutic drugs

Pathology

Infectious disease

Oncology

Genetic disease

Metabolic disorder

Nervous disorder

Blood disorder

Immune disorder

Wound healing

Fibrotic disease

Veterinary

Other (cosmetology application, etc.)

Note: Are excluded mRNA for gene editing approaches (e.g., mRNA encoding a Cas nuclease)



Technical and applicative segment will be adapted over time according to the technological evolution of therapeutic mRNAs

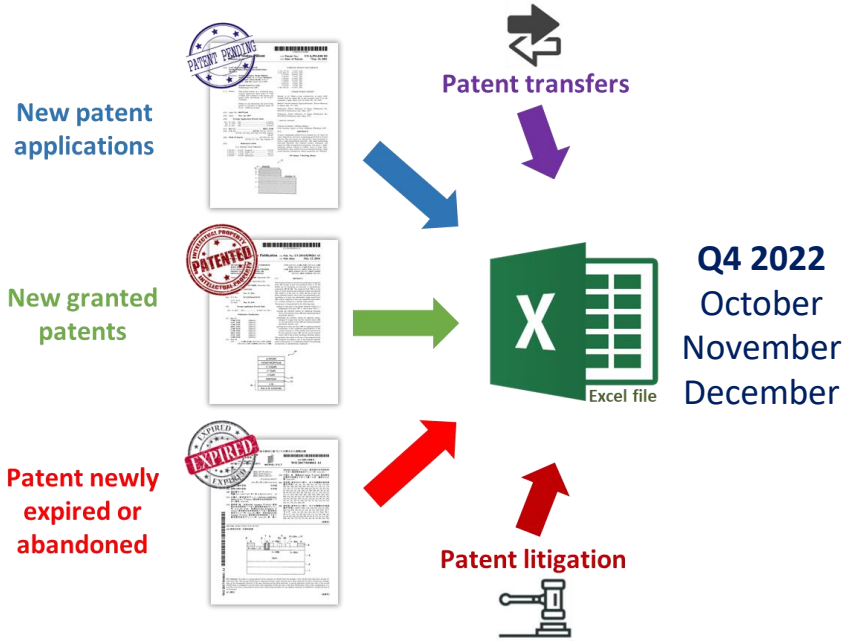









KEY FACTS

Q4 2022 KEY FACTS

Key facts overview

In Q4 2022 report you will find:



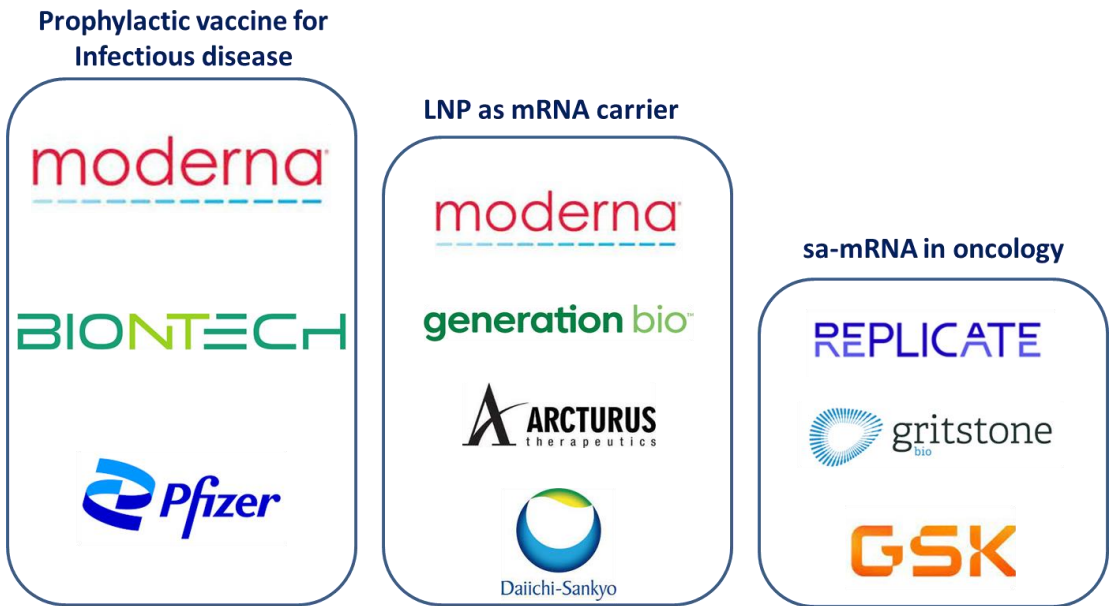
-  **125 New patent applications (US EP JP KR)**
32 Newly granted patents (US EP JP KR)
7 Abandoned or Expired patents
0 Patent transfer
-  **9 IP collaborations identified (patent co-filings)**
-  **8 Patent oppositions (EP)**
0 IP litigation (US)
-  **4 Main industrial IP players selected & analyzed**
-  **9 Newcomers and 6 New startup firms identified**
-  **2 Active academics selected & analyzed**
-  **11 Noticeable new patent families**
11 Noticeable granted patents



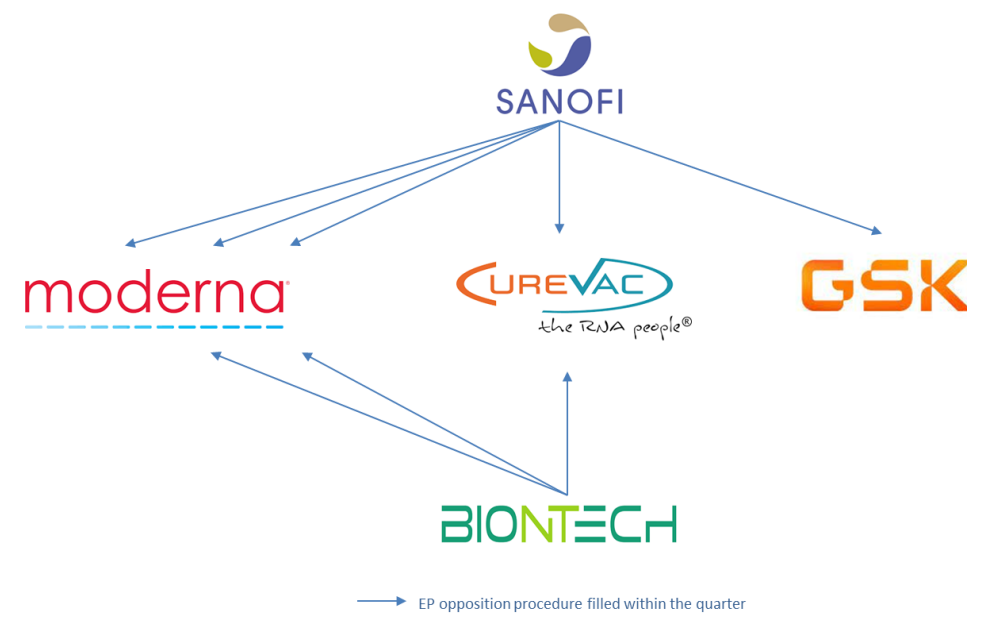
Q4 2022 KEY FACTS

Most active IP players

Q4 2022 is characterized by dynamism in **3 major technology approaches**: prophylactic vaccines for infectious diseases (ID) and Lipid nanoparticles (LNP) as mRNA carriers, which are still the leading therapeutic mRNA strategy driven by **MODERNA**'s portfolio, and to a lesser extent, self amplifying mRNA (sa-mRNA) for oncology driven by **REPLICATE BIOSCIENCE**. Moreover, during Q4 2022, **8 opposition procedures** were filed at the EPO, including **five against MODERNA's EP patents**. Main opponent are **SANOFI** (against MODERNA, GSK, and CUREVAC patents) and **BIONTECH** (against MODERNA and CUREVAC patents). **No new US litigation was found this quarter**.



Main players & technology approaches





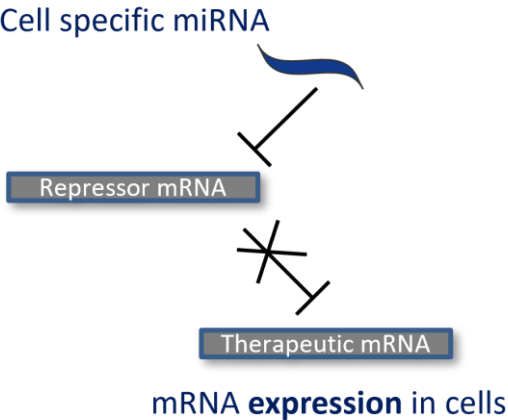
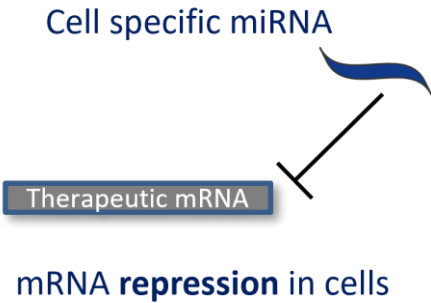
Opposition procedures filed at the EPO

Q4 2022 KEY FACTS

MODERNA & CUREVAC still in a race

Q4 2022 shows that **MODERNA** and **CUREVAC** are developing similar topics with different strategies:

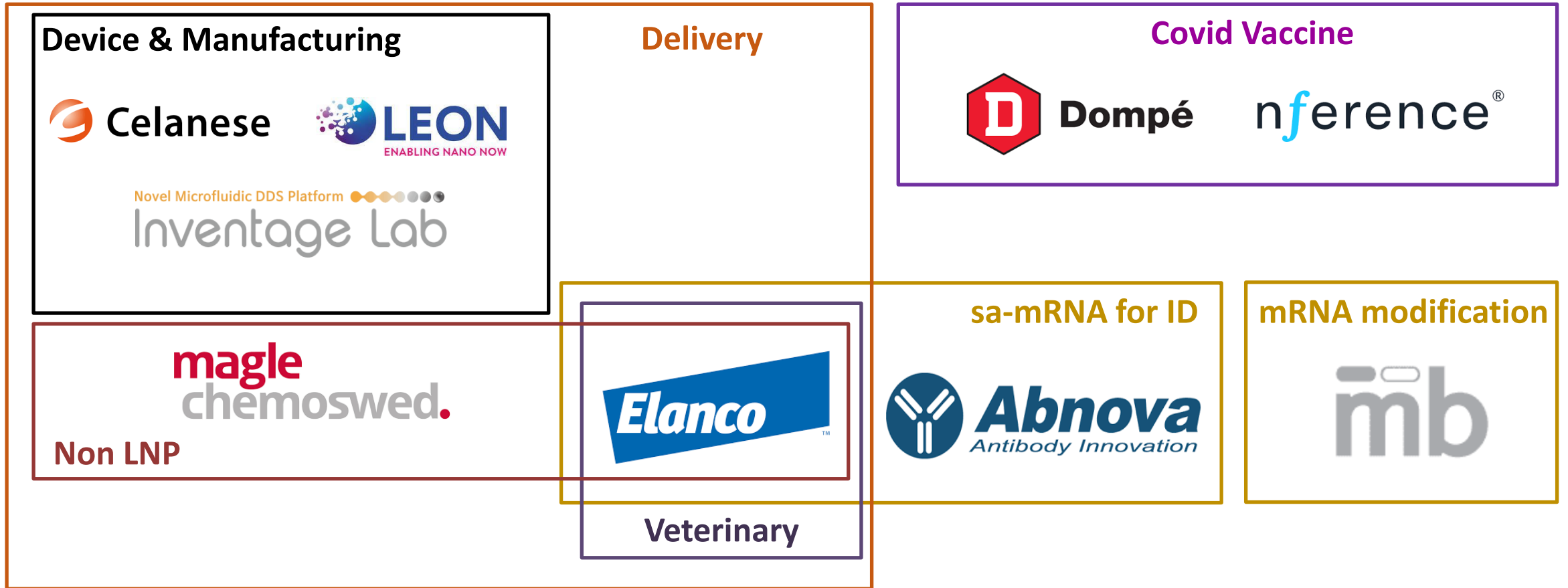
- **Vaccine for zoonotic disease**, with different filing strategies between both (independent patents or broader international application to be divided). Currently, CUREVAC has a stronger position with 3 US granted patents for 3 different zoonotic diseases.
- Use of **miRNA regulation for targeted delivery**, with opposite strategies. MODERNA uses the miRNA sequence to repress a repressor, resulting in an activated expression of the therapeutic mRNA in cells wherein the corresponding miRNA is expressed. Conversely, CUREVAC's miRNA sequence is used to repress the therapeutic mRNA in cells wherein the corresponding miRNA is expressed.

		
ZOONOTIC DISEASE	<p>One PCT application claiming vaccine for Lassa, Nipah, Hendra, or MERS-CoV (WO2018/170347). This PCT application was extended to US and EP, resulting in:</p> <p>Granted US for Nipah virus (US11497807)</p> <p>Pending EP for Nipah or Hendra virus (EP3595676, link to EPO register)</p>	<p>3 independent granted US patents:</p> <p>COVID19 (US11471525)</p> <p>Nipah Virus (US11524066)</p> <p>Lassa virus (US11464847)</p>
miRNA REGULATION FOR TARGETED DELIVERY	<p>WO2022/266083 New publication</p> <p>Schematic representation:</p>  <p style="text-align: center;">mRNA expression in cells</p>	<p>WO2022/233880 New publication</p> <p>Schematic representation:</p>  <p style="text-align: center;">mRNA repression in cells</p>

Q4 2022 KEY FACTS

Established companies enter in the field

In Q4 2022, **9 established companies** has published their **first patent family related to therapeutic mRNA**. Interestingly, most of them describe delivery-related innovations, devices or manufacturing processes, or non-LNP carriers. Two describe Covid-19 vaccines, two describe sa-mRNA, and one describes RNA modification. **ELANCO is the most noticeable newcomer**, as this company is a veterinary company—a domain underrepresented in therapeutic mRNA—that produces sa-mRNA encapsulated into a non-LNP delivery system (see figure below).



Q4 2022 KEY FACTS

New startup firms identified

In Q4 2022, **six new companies developing therapeutic mRNA have published their first patent application**. The innovative tendency towards LNP development and alternative RNA designs is confirmed by the technologies developed by these new startups. Indeed, four of them are focused on LNP for mRNA delivery (NANOVATION, THERNA, RENAGADE, and WEST GENE BIOPHARMA), and two are focused on alternative designs for mRNA (CHIMERON BIO, which develops sa-mRNA, and CIRCODE, which develops Circ RNA), as illustrated in the figure below. These new companies were all founded in North America or Asia; none of them are from the European area.

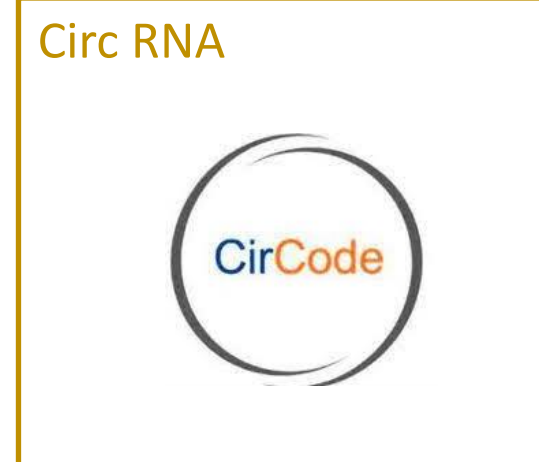
LNP

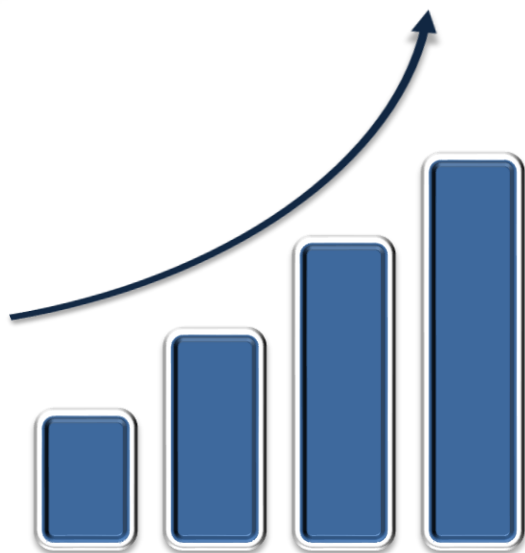


sa-mRNA



Circ RNA



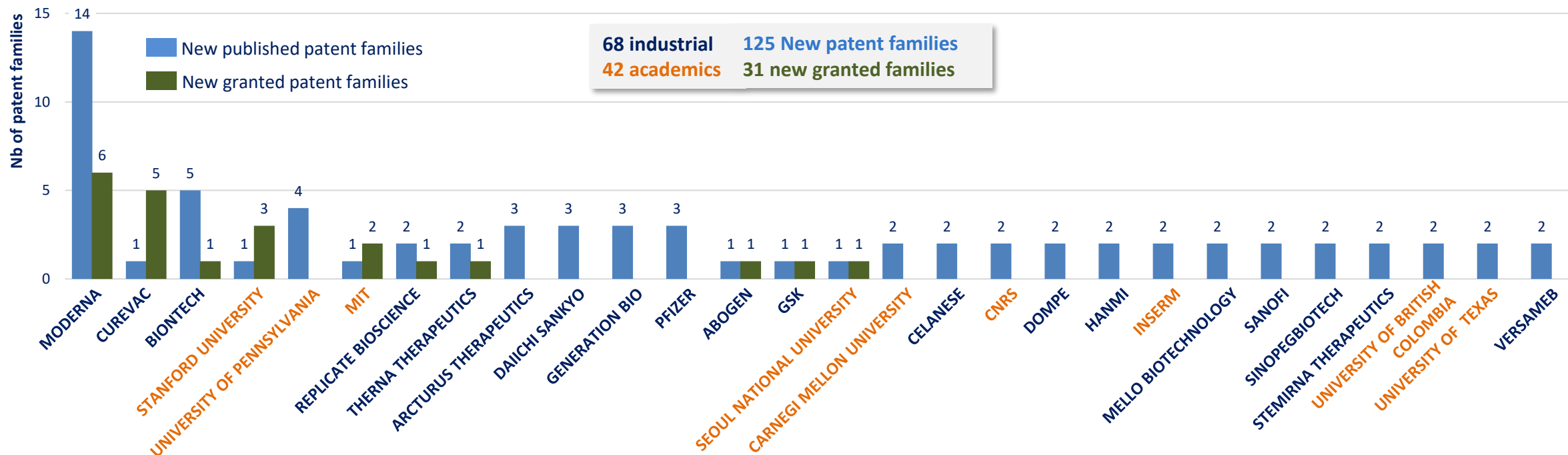


QUARTER OVERVIEW

Q4 2022 Overview

Main IP players overview

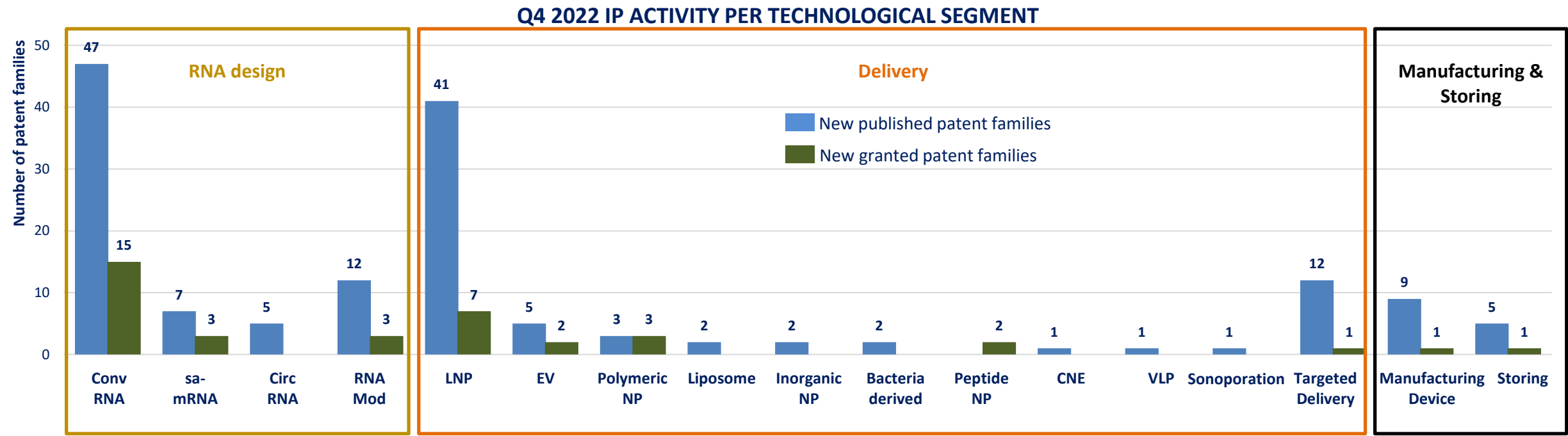
Q4 2022 IP ACTIVITY PER MAIN PLAYERS



- The **28 players** represented in the figure above, consisting of 19 industrial entities and 9 academic ones, are responsible for **60% of the patenting activity**.
- **MODERNA leads the quarter** with approximately 10% of the new published patent applications (14 out of 125) and around 20% of the new granted patent families (6 out of 32).
- BIONTECH, PFIZER, PENN, ARCTURUS, DAIICHI SANKYO, and GENERATION BIO each have three or more new patent applications, while CUREVAC, STANFORD UNIVERSITY, and MIT have reinforced their portfolios with more than two newly granted patent families.
- BIONTECH and CUREVAC show an opposite dynamic between new patent families and newly granted patent families.
- US academics (STANFORD, PENN, MIT, CARNEGIE MELLON UNIVERSITY, UNIVERSITY OF BRITISH COLUMBIA, and UNIVERSITY OF TEXAS) lead the quarter compared to other academics.
- In terms of geographical distribution of industrial players, 34 are from North America, 19 from Asia, and 15 from the European area.

Q4 2022 Overview

Technological segment overview



Note: the numbers represent the number of patent families. A patent family can belong to multiple segments.

- mRNA Design:** Conventional mRNA remains the main design, but alternative designs are increasing with 12 new patent families related to sa-mRNA and circular RNA. For example, REPLICATE BIOSCIENCE owns a new patent family granted as the first publication on sa-mRNA for cancer vaccine.
- mRNA Modifications:** Half of the new patent families rely on UTR modifications for mRNA stabilization. Notable strategies are disclosed in patent families describing the use of new untranslated sequences for mRNA translation efficiency (stem loop designed by MELLO BIOTECH) or cell targeting (use of miRNA recognizing sequences by MODERNA and CUREVAC).
- Delivery:** LNP nanoparticles are still overrepresented. Recent delivery strategies include **extracellular vesicles** derived from cells such as red blood cells (CARMINE THERAPEUTICS) or megakaryocytes (STRM BIO), and **dendrimer-based polymeric nanoparticles** described in two new patent families (TIBA BIOTECH & PENN) and one newly granted patent family (MIT).
- Targeted Delivery:** This is a challenge of interest, as illustrated by the 12 new patent families related to this feature, with a broad spectrum of targets (*i.e.*, mucosa, pancreas, lung, liver, cardiomyocyte, etc.).
- Manufacturing & Storing Challenges:** LNP manufacturing is overrepresented with three new patent families (BIONTECH, NUTCRACKER & MODERNA), as well as stabilization/storing solutions for LNP-based formulations with all five new patent families (from MODERNA or BIONTECH).

Q4 2022 Overview

Application segment overview

The fight against the SARS-CoV-2 pandemic is still driving patenting activity in Q4 2022:

- Among 36 new patent families related to infectious diseases, 22 are for prophylactic vaccines against the coronavirus, as 2 newly granted patent families.
- Ongoing interest in vaccines for other zoonotic diseases (Nipah virus, Lassa virus, and Henipavirus) is also represented with 3 newly granted patent families.

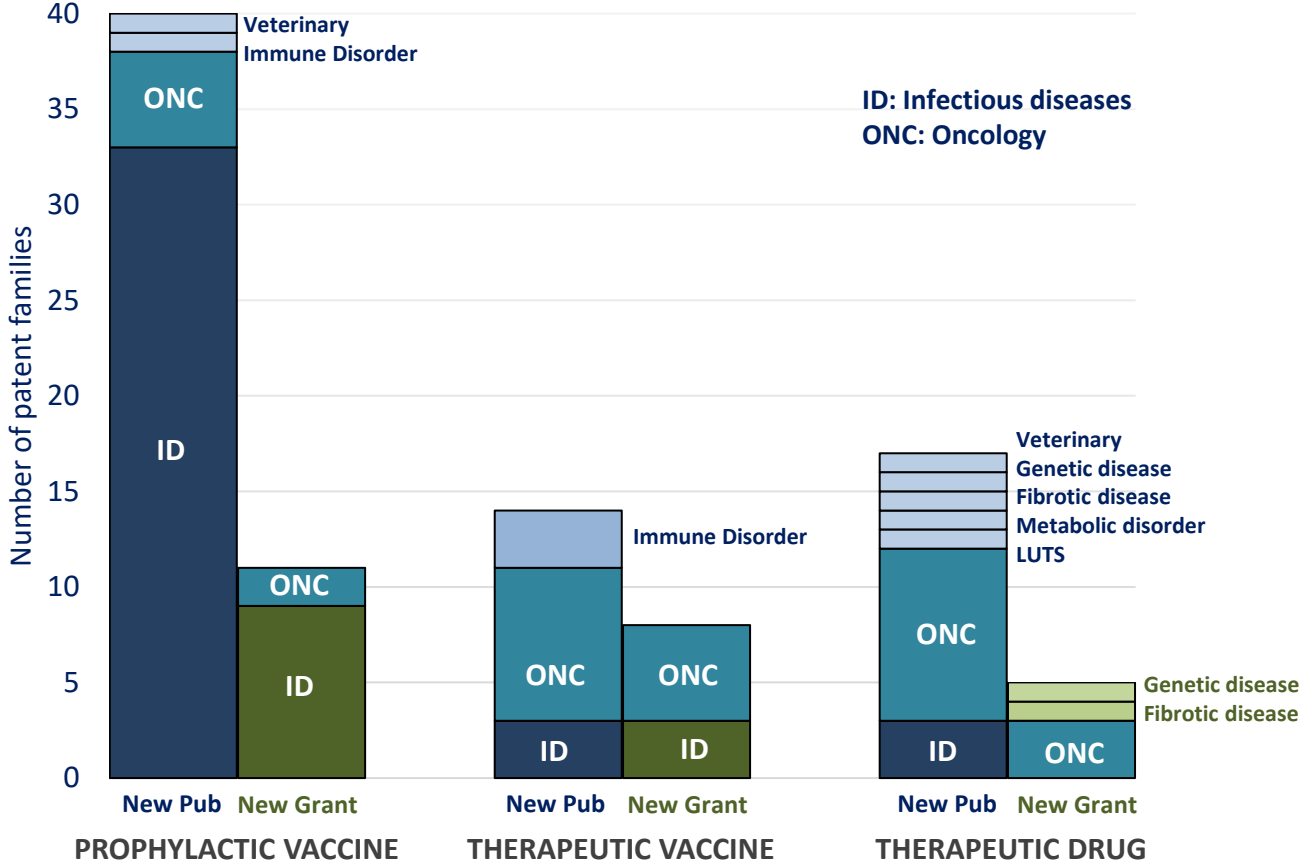
Therapeutic vaccines are still primarily being developed to fight cancer:

- Seven new patent applications describing mRNA encoding cancer-specific antigens and four newly granted patent families.
- Additionally, therapeutic vaccines are being developed to induce immune tolerance in subjects with **autoimmune diseases**, such as rheumatoid arthritis or type 1 diabetes (three new patent families).

Increasing applications are represented in mRNA encoding therapeutic drugs:

- 22 new patent families published and four newly granted this quarter.
- Nine of these patents are related to **oncology** and involve using mRNA to elicit an immune response.
- Six are related to various applications such as **genetic diseases** like Fanconi anemia (newly published) or ciliary dyskinesia (newly granted), **fibrotic diseases**, **metabolic disorders** such as methylmalonic acidemia (newly published), and Low Urinary Tract Syndrome (LUTS).
- One is for **veterinary** applications, with an attenuated bacterium as a delivery platform for sa-mRNA (ELANCO).

Q4 2022 IP ACTIVITY BY TYPE & APPLICATION



Q4 2022 Overview

Technological vs. application segments overview

SEGMENTS	NEW PENDING PATENT APPLICATIONS													NEW GRANTED PATENTS									
	All	Therapeutic approach			Pathologies									All	Therapeutic approach				Pathologies				
		Proph Vaccine	Therap Vaccine	Therap Drug	ID	ONC	Genetic Disease	Immune disorder	Cardio Vasc dis	Vet	Fibrotic disease	Metabo. Disease	Other		Proph Vaccine	Therap Vaccine	Therap Drug	ID	ONC	Genetic Disease	Fibrotic disease	Other	
Conv mRNA	47	27	7	10	28	12		3			1	1	1	15	9	2	5	9	4	1	1	1	
SA mRNA	7	5	1	1	4	1				1				3		3		1	2				
Circ mRNA	5			2	1									0									
mRNA modification	12	1	1	2	1	1					1			3	1	1	1	1	2				
LNP	41	4	1	3	5	5		1	1					7	1	1	1	1	2				
Extracellular vesicle	5	1	2	2		1	1							2			1		1				
Polymeric NP	3	1			1									3			1						
Peptide NP	0													2									
Liposome	2			2		2								0									
Inorganic NP	2													0									
Bacteria derived	2	2	1	1						1				0									
CNE	1			1										0									
VLP	1	1			1									0									
Other carrier	1													0									
Targeted delivery	9			1	1	1		1	1					1									
Manufacturing & Device	9	1	1		1	1		1						1									
Storing & Preservation	5													1	1	1							

Note: the numbers represent the number of patent families. A patent family can belong to multiple segments.

- For new patent families and newly granted patents, **mRNA therapeutics design is still dominated by conventional mRNA** as the choice of **LNP as a carrier for any therapeutic approach**, regardless of the therapeutic application. Indeed, more than half of the 41 new patent applications related to LNP describe specific lipid compounds (13) or improved LNP for delivery efficiency, mRNA stabilization, etc. (13), without a specific application for such delivery systems. **Targeted delivery** in new pending patent publications concerns a broad spectrum of targets, comprising the myeloid compartment, crossing the blood-brain barrier, mucosa, pancreas, lung, stem cells, liver, non-liver organs, cardiomyocytes, and mRNA constructs for cell-specific expression. This targeted delivery is not limited to a specific application in the targeted organ/tissue.
- Incoming dynamics are new patent families disclosing **sa-mRNA** mainly focused on prophylactic vaccine development for treating **infectious diseases**. Moreover, sa-mRNA for treating cancer is well represented in new granted patents covering sa-mRNA.

Q4 2022 OVERVIEW

New patent families

ASSIGNEE	Nb of patent families	Conv mRNA	SA mRNA	mRNA modification	LNP	Polymeric NP	Liposome	CNE	Other carrier	Targeted Delivery	Manufacturing Method & device	Storing & Preservation	Prophylactic Vaccine	Therapeutic Vaccine	Therapeutic Drug	Infectious Disease	Oncology	Other pathology
All Players	125	47	7	12	41	3	2	1	1	12	9	5	36	12	22	36	20	1
MODERNA	14	9			4					2	1	3	7		2	8		
BIONTECH	4	2			1						1	2	1	1		1	1	
PENN	4	1			2	1				1			1			1		
PFIZER	3	3											3			3		
GENERATION BIO	3				3													
ARCTURUS THERAPEUTICS	3				3													
DAIICHI SANKYO	3	3			3								3			3	2	
HANMI PHARMACEUTICAL	2			2														
TERNA THERAPEUTICS	2				2													
VERSAMEB	2	2													2		1	1
SANOFI	2	1			1								1			1		
CNRS	2	1						1					1		1	1		
INSERM	2	1						1					1		1	1		
CARNEGIE MELLON UNIV	2				2					2								
MELLO BIOTECH	2	1		1							1		1	1		1	1	
UNIV OF BRITISH COLUMBIA	2		1		1								1			1		
REPLICATE BIOSCIENCE	2		2											1				1
DOMPE	2	2											2			2		
STEMIRNA THERAPEUTICS	2	1			1								1			1		
UNIVERSITY OF TEXAS	2	1							1						1	1		
SINOPEG BIOTECH	2						2								2			2
CELANESE	2										2							

- In Q4 2022, **MODERNA** leads the patenting activity and drive the development of **conventional mRNA in prophylactic vaccines against infectious diseases**.
- With a lower volume, **BIONTECH's** patenting activity covers the same areas as MODERNA, plus therapeutic vaccines for oncology, while **PFIZER** stays focused on prophylactic vaccines for infectious diseases.
- GENERATION BIO** and **ARCTURUS THERAPEUTICS** develop their portfolios with patent applications only related to LNPs (cationic lipids and peptide-lipid conjugates for LNP formulation), while **DAIICHI SANKYO** filed patent applications related to **therapeutic formulations into LNP**.
- Asian companies are well represented (among players with more than two new patent applications), with Korean companies such as **HANMI PHARMACEUTICAL** and **TERNA THERAPEUTICS**; Chinese companies such as **STEMIRNA THERAPEUTICS** and **SINOPEG BIOTECH**, and the Taiwanese company **MELLO BIOTECH**.
- The newcomer **CELANESE** (established Italian company) develops an implantable device for naked or encapsulated mRNA delivery.

Q4 2022 OVERVIEW

New granted patent families

Assignee	Nb of patent families	Conv mRNA	SA mRNA	mRNA modification	LNP	Polymeric NP	Extracellular vesicle	Peptide NP	Targeted Delivery	Manufacturing Method & device	Storing & Preservation	Prophylactic Vaccine	Therapeutic Vaccine	Therapeutic Drug	Infectious Disease	Oncology	Genetic Disease	Fibrotic disease	Other pathology
All Players	31	15	3	3	7	3	2	2	1	1	1	10	7	7	10	8	1	1	1
MODERNA	6	4		1	3							2		1	2	1			
CUREVAC	5	4			1	1		1				3		1	3			1	
STANFORD UNIVERSITY	3					1	1			1				1		1			
MIT	2				1	1							1	1		1			
REPLICATE BIOSCIENCE	1		1										1			1			
GRITSTONE BIO	1		1										1			1			
GSK	1		1										1		1				
ABION	1	1		1								1	1		1	1			
SEOUL NATIONAL UNIV	1	1		1								1	1		1	1			
ACCANIS BIOTECH F & E	1	1		1										1		1			
ABOGEN	1	1										1			1				
TRANSCRIPTX	1	1												1			1		
CN USA BIOTECH HOLDINGS	1	1										1			1				
SPHCC	1	1										1			1				
BIONTECH	1	1										1	1		1	1			
TRON	1	1										1	1		1	1			
UNIVERSITY OF GOTTINGEN	1	1												1					1
TERNA THERAPEUTICS	1				1														
ACUITAS THERAPEUTICS	1				1														
UNIV OF SOUTH FLORIDA	1							1											
WUSL	1							1											
BWH	1								1										
EVOX THERAPEUTICS	1						1												
INTEGREON GLOBAL	1										1	1	1						

- In Q4 2022, **MODERNA** and **CUREVAC** have strengthened their IP position the most in similar domains: vaccines against zoonotic diseases (COVID-19, Nipah Virus, and Lassa virus for both), therapeutic drugs (cancer therapy and fibrotic disease, respectively), and carrier formulations (LNP or lipidoid with cationic peptide or polymer, respectively).
- Players in the sa-mRNA field have also reinforced their position, such as **REPLICATE BIOSCIENCE** and **GRITSTONE BIO** for oncology applications, and **GSK** for infectious disease (papilloma virus).
- Non-LNP carriers are mainly owned by academics (University of South Florida; WUSL, Washington University in St. Louis; BWH, Brigham & Women's Hospital) and one industrial, **EVOX THERAPEUTICS**.
- **INTEGREON GLOBAL**, a packaging solutions provider in life sciences, develops its cold-chain packaging product with a patent related to vaccine mRNA shipment.



Q4 2022 OVERVIEW

Abandoned or expired patents

DEAD PATENTS	ASSIGNEES	STATUS	SEGMENTS									
			Conv RNA	sa-mRNA	RNA modification	LNP	Manuf. & Device	Prophylactic vaccine	Therapeutic vaccine	Infectious disease	Oncology	
US9433669B2 US9433670B2 US9155788B2	CUREVAC	EXPIRED	X					X		X		X
AU2013242405B2 US10080809B2	CUREVAC	LAPSED (failure to pay maintenance fees)	X		X							
US8007781B2	JOHN HOPKINS UNIV	EXPIRED		X						X	X	X
US6890554B2	LIFE TECHNOLOGY	EXPIRED	X				X		X			

Note: Abandoned or expired patent are grouped in the table by patent family

- In Q4 2022, **CUREVAC** is the player that has lost the most assets this quarter, with five patents expired or lapsed from two patent families. The patent family related to mRNA for therapeutic vaccine to fight cancer, comprising three expired US patents (US9433669, US9433670, and US9155788), is **now fully expired** (or revoked). The second patent family covered UTR modifications for mRNA stabilization (a 5'TOP UTR), comprising AU2013242405 and US10080809, appears to have lapsed in all territories due to failure to pay **maintenance fees**. Nevertheless, it cannot be excluded in some territories that the lapsed patent might be reinstated/restored by paying an additional fee plus the maintenance fee (depending on each national procedure).
- LIFE TECHNOLOGY** has one US patent that expired this quarter. This patent relates to LNP comprising cationic lipids to deliver nucleic acid therapeutics (including mRNA).
- JOHN HOPKINS UNIVERSITY** has one US patent that expired this quarter. This patent relates to sa-mRNA for therapeutic vaccine.



If a patent is dead (expired or abandoned), is it possible to make the formerly patented product?

An expired patent cannot be asserted against competitors; however, other live patents may still cover different parts, features, or combinations described in the expired patent. In some countries, a lapsed patent can be reinstated/restored by paying an additional fee plus the maintenance fee and providing evidence that the delay or non-payment of the maintenance fee within the prescribed period was unintentional.

Q4 2022 OVERVIEW

IP Collaborations



These tables show new collaborations that have led to the co-filing of new patent applications involving at least one industrial entity:

- The collaboration between **BIONTECH** and **GENENTECH** (from **ROCHE**) has released its fifth patent family related to the development of mRNA cancer vaccines targeting neoantigens. This collaboration is a result of BIONTECH's worldwide strategic collaboration with Genentech, which was released in 2016.
- Despite limited information being available on **MAXIRNA**, patent-related data shows that one-third of its portfolio is in collaboration with Shanghai Cell Therapy Group (a provider of a cellular diagnosis center combining cellular research and treatment services), all related to mRNA modification and/or manufacturing.
- **TORSKAL**, a French company founded in 2015 focused on green nanotechnology, is collaborating with French academics to develop gold nanoparticles functionalized with peptides derived from the spike protein of SARS-CoV-2 to produce a vaccine. TORSKAL designs disruptive gold nanoparticles for cancer therapy using green chemistry.
- **NIBEC**'s collaboration with Seoul National University relates to cell-penetrating peptides. Such peptides belong to one of NIBEC's key technologies for its delivery platform.
- Two industrial-academic Japanese collaborations were identified this quarter: **DAIICHI SANKYO** and **NIHON UNIVERSITY** with the **UNIVERSITY OF THE RYŪKYŪS** for the development of a prophylactic vaccine against HTLV virus (etiological agent of adult T-cell leukemia and lymphoma), and **SOGO PHARMACEUTICAL** and **SHIZUOKA UNIVERSITY** for the development of nanoparticles.

INDUSTRIAL APPLICANTS	TITLE	SEGMENTS	ORIGINAL DOCUMENT
BIONTECH / GENENTECH / ROCHE	Methods of inducing neoepitope-specific t cells with a PD1 axis binding antagonist and an RNA vaccine	Conventional mRNA / Therapeutic Vaccine Oncology	US20220378910
MAXIRNA / SHANGHAI CELL THERAPY GROUP	RNA-modifying chimeric protein and application thereof	RNA Modification	WO2022214065

INDUSTRIAL APPLICANTS	ACADEMIC APPLICANTS	TITLE	SEGMENTS	ORIGINAL DOCUMENT
TORSKAL	CNRS / INSERM / IRD / UNIVERSITE DE LA REUNION	Peptides derived from the spike protein of SARS-CoV-2 and uses thereof for diagnosis and vaccine purposes	Conventional mRNA / Prophylactic vaccine/ Infectious disease	WO2022/263451
DAIICHI SANKYO	NIBIOHN UNIVERSITY OF THE RYUKYUS	HTLV-1 nucleic acid lipid particle vaccine	Conventional mRNA / Prophylactic vaccine/ Infectious disease / Oncology	WO2022/244801
NIBEC	SEOUL NATIONAL UNIVERSITY	Nanoparticle comprising peptide-lipid conjugate for delivering oligonucleotide into target cell and pharmaceutical composition comprising same	LNP / Therapeutic Drug / Oncology	WO2022/260480
SOGO PHARMACEUTICAL	SHIZUOKA UNIVERSITY	Lipid and composition	LNP / Organ Targeting	WO2022/215758



**No patents related to therapeutics mRNA have been reassigned (transferred)
in Q4 2022**



Q4 2022 OVERVIEW

Main US IP Litigation filed or closed

No US IP Litigation related to therapeutics mRNA have been filed or closed in Q4 2022



Q4 2022 OVERVIEW

New EP oppositions

This table shows the new oppositions filed at the EPO against therapeutic mRNA-related patents. A hyperlink to the EPO register is provided to enable tracking of the opposition procedure. Note: Third-party observations during the examination process are not included in this monitoring activity.

ASSIGNEE	PATENT NUMBER	TITLE	OPPONENT	LINK TO EPO REGISTER
MODERNA	EP3590949	Ribonucleic acids containing n1-methyl-pseudouracils and uses thereof	BIONTECH SANOFI STRAW MAN*	Link
MODERNA	EP3718565	Respiratory virus vaccines	BIONTECH SANOFI STRAW MAN*	Link
MODERNA	EP2922554	Terminally modified RNA	STRAW MAN*	Link
MODERNA	EP3394030	Compounds and compositions for intracellular delivery of agents	STRAW MAN*	Link
MODERNA	EP3134131	Nucleic acid vaccines	CLS SEQIRUS SANOFI STRAW MAN*	Link
GSK	EP2611461	Pegylated liposomes for delivery of immunogen-encoding RNA	SANOFI STRAW MAN* STRAW MAN* STRAW MAN*	Link
CUREVAC	EP3283125	Lyophilization of RNA	SANOFI BIONTECH	Link
UNIV. DE BORDEAUX / CNRS / INSTITUT POLYTECHNIQUE DE BORDEAUX / ENS / INSERM / UNIV. DE PARIS	EP3621596	Tablets comprising nucleic acid vectors	STRAW MAN*	Link

* Note: STRAW MAN indicates opposition filed by companies acting as a front for other parties to conceal their identities.

- **MODERNA's portfolio was strongly opposed** this quarter with five patents involved in such procedures. In opposition to three of MODERNA's patents (EP3718565, EP2922554, and EP3134131), an opposition was filed on behalf of the same patent law firm (Wither & Rogers), which might suggest the same entity behind these opposition procedures.
- **SANOFI is highly active as an opponent** with 5 new oppositions this quarter against MODERNA and CURVAC patents.



Q4 2022 OVERVIEW

EP opposition new final decisions

The following table summarizes decisions of the Opposition Division of the EPO released this quarter. These decisions apply to all states designated in the European patent. There are three possible outcomes at the end of the proceedings:

- the opposition is rejected, and the patent is maintained as granted;
- the patent is maintained in an amended form, with a new patent specification published; or
- the patent is revoked.

Caution: As with any other final decision of first-instance divisions, decisions by the Opposition Division can be appealed within two months from the date of notification of the decision; depending on the notification date, they may be appealed in the next quarter.

ASSIGNEE	PATENT NUMBER	TITLE	OPPONENT(S)	OPPOSITION RESULTS (notification date)	LINK TO EPO REGISTER
CUREVAC	EP3319622	Method for producing RNA molecule compositions	BIONTECH	EP REVOCKED (15/12/2022)	Link
CUREVAC	EP3292873	Combination of vaccination and inhibition of the pd-1 pathway	MERCK BIONTECH ETHERNA PFIZER STRAW MAN STRAW MAN	EP REVOCKED (22/12/2022)	Link
CUREVAC	EP3062798	Modified RNA with decreased immunostimulatory properties	STRAW MAN STRAW MAN	REJECTION OF THE OPPOSITION (10/11/2022) APPEAL FILED (21/12/2022)	Link

* Note: STRAW MAN indicates opposition filed by companies acting as a front for other parties to conceal their identities

Decisions of the Opposition Division all relate to CURVAC's portfolio. Two of its European patents were revoked, but these decisions can be appealed in the next quarter. One of its European patents was maintained as granted, but this decision has been appealed.



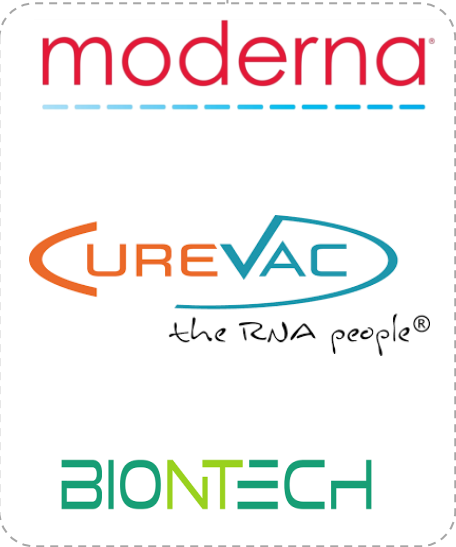
NOTICEABLE IP PLAYERS

Q4 2022 NOTICEABLE IP PLAYERS

Identification of noticeable players

In Q4 2022, **68 industrials** and **42 academics** were identified. Most noticeable players are listed in the figure below and detailed in the following slides.

MAIN IP PLAYERS
Most active industrial players



NEWCOMERS
Startup that published their 1st patent application or established company that published their 1st patent application in the topic



ACADEMICS
Most active academic players



Main IP players

	Q4 2022	SEGMENTS								
		CONV RNA	mRNA MODIF.	LNP	MANUF.	STORING	PROPH. VACCINE	THERAP. DRUGS	INFECTIOUS DISEASE	ONCOLOGY
New patent families (inventions)	14	9	0	4	1	3	7	2	8	0
Patent families newly granted	6	4	1	3	0	0	2	1	2	1
Patents expired or abandoned	0	-		-	-	-	-		-	-

Note: The numbers represent the number of patent families. A patent family can belong to multiple segments.

In Q4 2022, **MODERNA** is the IP player that has enlarged and strengthened its patent portfolio the most. With 14 new applications and 6 new granted inventions, the company is by far the most active player. The 14 new patent families are mainly related to prophylactic vaccination and mRNA delivery.

- **Prophylactic vaccine for infectious disease** related new patent families (7):

Inventions related to mRNA vaccines for Covid-19 have been described in [WO2022/266012](#) (a spike protein with a substitution of D428N, introducing an N-glycosylation site), and in [WO2022/266010](#) (a spike protein with increased flexibility). These patent families feature mRNA improvements of Spikevax® (mRNA-1273).

Inventions related to mRNA vaccines for seasonal flu have been described in [WO2022/245888](#) (mRNAs encoding combinations of antigens from multiple seasonal influenza strains).

Additionally, inventions related to combinational vaccines have been described in [WO2022/221440](#) (two mRNAs encoding antigens from Covid-19 and flu, in a safety clinical trial [NCT05375838](#)) and in [WO2022/221335](#) (three mRNAs encoding antigens from Covid-19, flu and RSV).

Inventions related to vaccination for other infectious diseases have been described in [WO2022/221359](#) (Epstein-Barr virus vaccine, associated with clinical trial [NCT05164094](#)) and in [WO2022/221336](#) (RSV vaccine, associated with clinical trial [NCT05127434](#)).

- **mRNA delivery:** Four new patent families related to LNP delivery have been described in the following patents: [WO2022/232585](#), [WO2022/226318](#), [WO2022/226277](#) and [WO2022/212191](#). Lyophilization methods and stabilized formulations are described in the first two patents, while the third patent describes LNP for mucosal targeted delivery. Moreover, [WO2022/266083](#) describes the targeted delivery of therapeutic mRNA in combination with a repressor encoded mRNA under the control of specific microRNAs.

MODERNA has bolstered its patent portfolio in the same technical field with two newly granted patent families that protect **prophylactic vaccines for infectious diseases** ([US11497807](#), for **Nipah virus**, and [US11464848](#) for **RSV vaccine**), as well as two newly granted patents protecting **lipid compounds for LNP** ([EP3596041](#) and [US11524023](#)).

Note: the numbers represent the number of **patent families**. A patent family can belong to multiple segments.



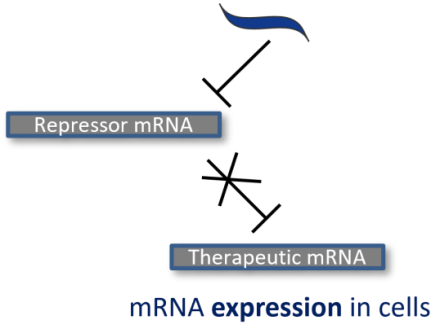
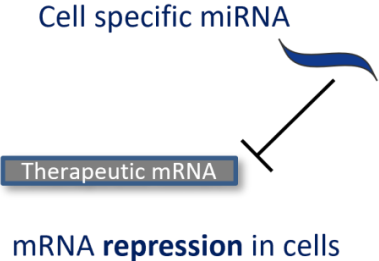
	Q4 2022	SEGMENTS												
		CONV. RNA	RNA MODIF.	LNP	POLYLERIC NP	PEPTIDE NP	TARGETED DELIVERY	MANUF.	PROPH. VACCINE	THERAP. VACCINE	THERAP. DRUG	INFECTIOUS DISEASE	ONCOLOGY	FIBROTIC DISEASE
New patent families (inventions)	1	1	1	0	0	0	1	0	0	0	0	0	0	0
Patent families newly granted	5	4	0	1	1	1	0	0	3	0	1	3	0	1
Patents expired or abandoned	5	5	2	0	0	0	0	3	0	3	0	0	3	0

- This quarter, CUREVAC published a new patent application related to **targeted mRNA expression**. The patent application describes the modification of mRNA by inserting miRNA binding sequences, which will reduce the expression of the therapeutic mRNA in undesired organs or tissues ([WO2022/233880](#)).
- By Q4 2022, CUREVAC had made significant strides in strengthening its IP position, with five newly granted patent families encompassing three **vaccine treatments for zoonotic diseases**: COVID19 ([US11471525](#)), Nipah Virus ([US11524066](#)), and Lassa virus ([US11464847](#)); one **therapeutic drug** approach for fibrotic diseases; and a hybrid carrier system (Lipidoid including cationic peptide or polymer respectively).
- In November, CUREVAC presented **preliminary data of their oncology candidate, CV8102**. This single-stranded non-coding RNA was designed to activate both innate and adaptive immunity. Results from the completed Phase 1 expansion study in patients with PD-1 refractory melanoma confirmed CV8102 to have a robust safety profile as a single agent and in combination with anti-PD-1 antibodies. The company also stated that further clinical development of CV8102 would only be pursued in combination with a defined mRNA cancer vaccine.
- In Q4 2022, **CUREVAC** was the player that experienced the **greatest asset loss** this quarter with five patents expired or lapsed from two patent families: [US9433669](#), [US9433670](#), and [US9155788](#) related to mRNA for therapeutic vaccines to fight cancer, and [AU2013242405](#) and [US10080809](#) covering UTR modification for mRNA stabilization (see dedicated [section](#) for more detail).

MODERNA and CUREVAC are both developing similar topics, but using different strategies:

Vaccine for zoonotic disease: MODERNA and CUREVAC have different filing strategies for developing a vaccine for zoonotic diseases, such as independent patent or broader international applications that are divided. Currently, CUREVAC holds a stronger position with three US patents granted for three different zoonotic diseases.

miRNA regulation for targeted delivery: In MODERNA's invention, the therapeutic mRNA is expressed in cells expressing a specific miRNA. Indeed, in the construction comprising a therapeutic mRNA and a mRNA encoding a repressor of therapeutic mRNA, the expression of a miRNA results in the repression of the repressor. On the other hand, in CUREVAC's invention, the therapeutic mRNA is expressed in cells that do not express a specific miRNA because the expression of a miRNA results in the repression of the therapeutic mRNA (see figure below).

		
ZOONOTIC DISEASE	<p>1 PCT claiming vaccine for Lassa, Nipah, Hendra, or MERS-CoV (WO2018/170347). This PCT application was extended to US and EP, resulting in: Granted US for Nipah virus (US11497807) Pending EP for Nipah or Hendra virus (EP3595676, link to EPO register)</p>	<p>3 independent granted US patents: COVID19 (US11471525) Nipah Virus (US11524066) Lassa virus (US11464847)</p>
miRNA REGULATION FOR TARGETED DELIVERY	<p style="text-align: center;">WO2022/266083 Schematic representation</p>  <p style="text-align: center;">mRNA expression in cells</p>	<p style="text-align: center;">WO2022/233880 Schematic representation</p>  <p style="text-align: center;">mRNA repression in cells</p>

Note: the numbers represent the number of patent families. A patent family can belong to multiple segments.

	Q4 2022	SEGMENTS							
		CONV. RNA	LNP	MANUFACTURING	STORING	PROPHILACTIC VACCINE	THERAPEUTIC VACCINE	INFECTIOUS DISEASE	ONCOLOGY
New patent families (inventions)	4	2	1	1	2	1	1	1	1
Patent families newly granted	1	1	1	0	0	1	1	1	1
Patents expired or abandoned	0	-	-	-	-	-	-	-	-

- This quarter is marked by the publication of the US patent application pertaining to the clinical trial [NCT03289962](#) for BNT122 ([US20220378910](#)). This cancer vaccine, developed in collaboration with ROCHE's GENENTECH, is an **individualized mRNA cancer vaccine** containing up to 20 patient-specific tumor neoantigens associated with a PD-1 inhibitor. BNT122 is currently being evaluated in a Phase 2 trial as a first-line therapy in conjunction with MERCK's pembrolizumab, a PD-1 inhibitor. Data from a Phase 1 solid tumor trial previously demonstrated the induction of neoantigen-specific T cell responses, a tolerable safety profile, and early evidence of clinical activity.
- BIONTECH is one of the ten players developing technological innovations in the manufacturing or storage of mRNA therapeutics this quarter, with two newly published patent families: [WO2022/218891](#) and [WO2022/218503](#). These patents relate to buffer systems that **prevent two detrimental mechanisms: LNP fragmentation and the formation of a stable RNA fold** (also known as "light migrating species"). These mechanisms can limit the stability of therapeutic mRNA products in pharmaceutical practices that operate at temperatures between 2-20°C.
- In Q4 2022, BIONTECH strengthened its IP position with the grant of the US patent [US11471522](#). This patent belongs to a family of patents with currently EP, JP, AU, and CA members, all still under examination process. This US patent protects **immunostimulatory RNA (isRNA) molecules that act as adjuvants** and/or immunostimulatory agents to enhance host immune responses when associated with an antigen from cancer or infectious disease. Such isRNA are derived from an Influenza A virus nucleoprotein-encoding RNA molecule, and, as disclosed in the description, can be associated with mRNA vaccines.
- Additionally, this quarter BIONTECH is initiating **two new Phase 1 clinical trials** for mRNA-based vaccines targeting [Malaria](#), [COVID-19 and Influenza](#), as well as a [Herpes virus vaccine](#). Furthermore, they are developing **new manufacturing facilities** in [Australia](#) and [Singapore](#), and have entered into a global [collaboration with RYVU THERAPEUTICS](#) (based in Poland) to develop and commercialize immuno-modulatory small molecule candidates.

Note: the numbers represent the number of patent families. A patent family can belong to multiple segments.

	Q4 2022	SEGMENTS		
		sa-mRNA	THERAP. VACCINE	ONCOLOGY
New patent families (inventions)	2	2	1	1
Patent families newly granted	1	1	1	1
Patents expired or abandoned	0	-	-	-

- In Q1 2022, **REPLICATE BIOSCIENCE** was identified as a **startup** after the publication of its first patent application related to **sa-mRNA for prophylactic vaccination** against infectious diseases. Then, in Q4 2022, they published two new patent families related to sa-mRNA:
 - [US11510975](#), which was granted as the first publication, relates to **sa-mRNA for a cancer vaccine**. This sa-mRNA encodes a hormone and signaling pathway checkpoint (the ESR1/HER2/HER3/PI3K combination), and its expression elicits an immune response against cancerous cells.
 - [WO2022/226019](#) relates to an alphavirus vector containing a universal cloning adaptation used as an **RNA-based expression platform**.
- Currently, REPLICATE's candidates in the preclinical stage include RBI-1000 for breast cancer, RBI-2000 for solid tumors, and RBI-4000 for infectious disease. In the discovery stage, its pipeline consists of RBI-3000 for lung cancer, RBI-8000 for inflammatory/autoimmune diseases, and RBI-5000 for infectious diseases.

Newcomers

Q4 2022 NEWCOMERS

Established companies

In Q4 2022, nine established companies published their first patent families related to therapeutic mRNA. Interestingly, **most of them described delivery-related innovations**, devices, manufacturing processes, or non-LNP carriers, while two described a Covid-19 vaccine, two described sa-mRNA, and one described RNA modification. **ELANCO was the most noteworthy of the newcomers**, as the company is a veterinary one, a domain underrepresented in therapeutic mRNA. It produces sa-mRNA encapsulated into a non-LNP delivery system (see figure below). Further information on the Q4 2022 newcomers is provided in the following slides.



Q4 2022 NEWCOMERS

Established companies

COMPANY	COMPANY DETAILS	PATENT APPLICATION NUMBER & TITLE	SEGMENT(S)
ABNOVA	ABNOVA, a Taiwanese company founded in 2002, specializes in antibody manufacturing, instrumentation for cell isolation, in vitro diagnostics, and more recently, drug development (immunotherapy). In 2021, the company developed a COVID-19 SAM RBD (receptor-binding domain) formulated in lipid nanoparticle (LNP), which generates a higher antibody titer response than mRNA. This was detailed in a new patent family.	US20220395571 mRNA vaccine and method of inducing antigen-specific immune responses in individuals	<ul style="list-style-type: none"> • sa-mRNA • Proph. vaccine • ID
CELANESE	CELANESE Corporation, formerly known as Hoechst Celanese, is a leading American technology and specialty materials company headquartered in Irving, Texas. They specialize in controlled release dosage forms, such as their VitalDose® technology brand composed of Ethylene-vinyl acetate copolymers (EVA).	WO2022/212302 Implantable medical device for the delivery of a nucleic acid WO2022/212300 Implantable medical device for the delivery of nucleic acid-encapsulated particles	<ul style="list-style-type: none"> • Device
MELLO	MELLO BIOTECH is a Taiwanese company that specializes in biotechnology and medical beauty care. Its portfolio includes, for example, short hairpin RNA (shRNA) that inhibit the production of skin melanin and hyaluronidase, as well as MicroRNAs for the treatment of Alzheimer's disease.	US20220396798 Novel mRNA composition and production method for use in anti-viral and anti-cancer vaccines	<ul style="list-style-type: none"> • RNA modifications • Prophylactic & therapeutic vaccine • ID and oncology
DOMPE	DOMPÉ is an Italian bio-pharmaceutical company with a biotech unit focused on rare diseases, such as ophthalmology. Their R&D department is supported by EXSCALATE, an in-house structure-based virtual screening platform that utilizes powerful supercomputing and artificial intelligence platforms.	WO2022/238585 Novel protein and nucleic acid sequences for covid-19 vaccines WO2022/207860 Combination therapy for covid-19 vaccination	<ul style="list-style-type: none"> • Prophylactic vaccine • Infectious disease
INVENTAGE LAB	INVENTAGE LAB is a South Korean company founded in 2015 with a focus on developing a microfluidics-based drug delivery system. Their IVL-GeneFluidic® platform is specifically designed to encapsulate mRNA.	KR10-2022-0145788 Method for producing nano lipid particle and an apparatus for producing the same	<ul style="list-style-type: none"> • LNP • Manufacturing
LEON NANODRUGS	LEON NANODRUGS is a German company specializing in the encapsulation of biomolecules. Using their proprietary nano technology platform, Leon is capable of continuously manufacturing SMART nanoparticles, ranging from surface-stabilized polymers to lipid nanoparticles (LNPs) and liposomes.	WO2022/234050 Methods for producing nanoparticle dispersions	<ul style="list-style-type: none"> • Manufacturing

Q4 2022 NEWCOMERS

Established companies

COMPANY	COMPANY DETAILS	PATENT APPLICATION NUMBER & TITLE	SEGMENT(S)
NREFERENCE	NREFERENCE is an American company established in 2013. They have created a unique AI-powered software platform, called nSights, and partner with medical centers to transform the otherwise unstructured data stored in EMRs into powerful solutions. These solutions allow researchers to explore and develop personalized diagnostics and treatments for patients.	WO2022/251101 Compositions and methods related to surge-associated sars-cov-2 mutants	<ul style="list-style-type: none"> • Prof. vaccine • ID
MAGLE CHEMOSWED	MÄGLE CHEMOSWED is a Swedish contract development and manufacturing organization that was established in 2017, following the acquisition of Chemoswed by Magle Life Sciences. The company provides services to the pharmaceutical and medical device industry, leveraging its core technology of microporous polysaccharide microspheres derived from purified plant starch, which are naturally bio-absorbable and biodegradable.	WO2022/255931 A pharmaceutically acceptable aqueous gel composition for mRNA delivery	<ul style="list-style-type: none"> • Inorganic nanoparticle
ELANCO	ELANCO is an American pharmaceutical company that produces medicines and vaccinations for pets and livestock. Until 2019, it was a subsidiary of Eli Lilly and Company, before being divested.	WO2022/271976 Attenuated salmonella, vaccines, and delivery platform	<ul style="list-style-type: none"> • sa-mRNA • Bacteria derived delivery • Proph. Vaccine & Therapeutic drug • Veterinary

Q4 2022 NEWCOMERS

New startup firms

In Q4 2022, **six new companies** developing therapeutic mRNA had published their 1st patent applications. The trend towards **LNP development** and **alternative RNA designs** is confirmed by the technologies developed by these startups. Out of the six, **four focus on LNP for mRNA delivery (NANOVATION, THERNA, RENAGADE, and WEST GENE BIOPHARMA)**, and **two specialize in alternative designs for mRNA (CHIMERON BIO, which develops sa-mRNA, and CIRCODE, which develops CircRNA)**, as illustrated in the figure below. All of these new companies were founded in North America or Asia; none of them originate from the European region. The following slide provides a summary of the Q4 2022 newcomers.

LNP



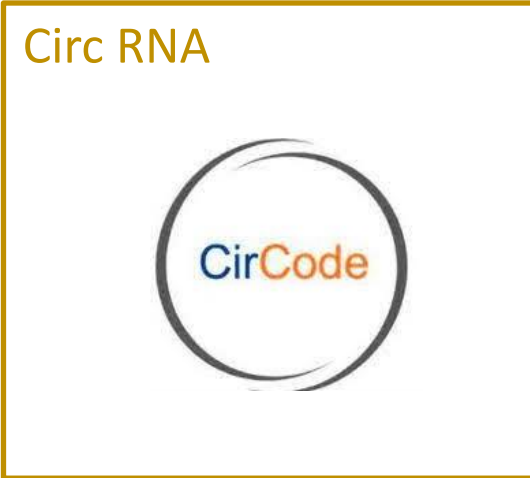
The LNP section contains four logos: NANOVATION therapeutics (blue text with a dotted 'O'), THERNA THERAPEUTICS (red and black), WestGene BIOPHARMA 威斯津生物 (green and black), and ReNAGADE THERAPEUTICS (blue and white on a dark background).

sa-mRNA



The sa-mRNA section contains one logo: chimeron bio An RNA Company, featuring a stylized DNA double helix with A, G, C, T bases.

Circ RNA



The Circ RNA section contains one logo: CirCode, featuring a circular graphic with the text 'CirCode' inside.

Q4 2022 NEWCOMERS

New startup firms - Summary table

COMPANY	COMPANY DETAILS	PATENT APPLICATION NUMBER & TITLE	SEGMENT(S)
NANOVATION THERAPEUTICS	NANOVATION THERAPEUTICS is a Canadian company founded in 2020. NANOVATION is an early-stage gene therapy company developing cutting-edge platform technologies that utilize LNP for the delivery of nucleic acids to various tissues. The company's platform consists of in-house synthetic organic chemistry, mRNA synthesis, and formulation in LNP.	WO2022/246571 Mc3-type lipids and use thereof in the preparation of lipid nanoparticles	• LNP
THERNA THERAPEUTICS	THERNA Therapeutics is a South Korean company founded in 2020. They specialize in the development of LNP technology for the delivery of therapeutic RNA, siRNA, and mRNA oligonucleotide therapeutics.	WO2022/270941 Lipid nanoparticles and method for preparing same KR10-2465349 (Granted) Novel ionizable lipids and lipid nanoparticles comprising thereof	• LNP
RENAGADE THERAPEUTICS	RENAGADE THERAPEUTICS, a US startup founded in 2021, is focused on developing RNA therapeutics. Currently, there is limited information available about this new company.	WO2022/251665 Lipid nanoparticles and methods of use thereof	• LNP
WESTGENE BIOPHARMA	WESTGENE BIOPHARMA, founded in mid-2021 by a team of academicians from West China Hospital of Sichuan University, is a Chinese company. In December, they successfully completed their Series A Round, raising \$21 million to further their portfolio of nearly 20 mRNA candidates, with their lead COVID-19 vaccine being the main focus.	WO2022/218295 Ionizable lipids and compositions for nucleic acid delivery	• LNP
CHIMERON BIO	CHIMERON BIO is a US-based company founded in 2015. Their pipeline consists of oncology-related RNA drugs designed to activate the immune system through upregulation of tumor neoantigens (CarT cell approach), and a nanoparticle technology known as “ChaESAR” – Chimera Encased Self Amplifying RNA – to create novel RNA drugs. The vaccine described in their first patent family is still in pre-clinical development. However, CHIMERON BIO recently entered into an agreement with the NIAID, a federal agency, for pre-clinical assessment of their sa-mRNA COVID-19 Vaccine in April 2022.	WO2022/261355 Self-amplifying RNA-based VLP vaccines	<ul style="list-style-type: none"> • sa-mRNA • VLP • Proph. vaccine • ID
CIRCODE	CIRCODE is a Chinese company founded in 2021, specializing in the development of therapeutic drugs and vaccines through circular mRNA.	WO2022/247943 Constructs and methods for preparing circular RNAs and use thereof	<ul style="list-style-type: none"> • Circ RNA • Manufacturing

Main Academics

Q4 2022 MAIN ACADEMICS

Stanford University



Stanford University owns three newly granted patent families and one newly published patent family. None of them have been co-filed in collaboration with other universities or companies, and four different teams from Stanford University are responsible for these inventions. The areas of interest of these teams are **RNA manufacturing**, **delivery for cancer treatment**, and **circular mRNA**. The main information is summarized in the following table.

	PATENT NUMBER	PATENT DETAILS	INVENTOR	SEGMENT(S)
NEW GRANT	US11492611	Status: Granted as second publication (2022-11-08) Title: Systems and methods for producing RNA constructs with increased translation and stability Associated Scientific publication: Leppek et al., 2022, Nature Communications	Barna Maria Leppek Kathrin Byeon Gun Woo	<ul style="list-style-type: none"> Manufacturing
	US11517530	Status: Granted as second publication (2022-12-06) Title: Therapeutic agents specifically delivered by exosomes for cancer treatment Associated Scientific publication: Wang et al., 2018, Molecular Cancer Therapeutics	Wang Jing-hung Forterre Alexis Matin A C Delcayre Alain	<ul style="list-style-type: none"> Extracellular vesicle Therapeutic drug Oncology
	JP7179715	Status: Granted (2022-11-29) Title: Immolative cell-penetrating complexes for nucleic acid delivery	Levy Ronald Haabeth Ole Audun Werner Benner Nancy Near Katherine Waymouth Robert M Wender Paul Vargas Jessica R Blake Tim R Mckinlay Colin	<ul style="list-style-type: none"> Polymeric nanoparticle
NEW PUBLICATION	WO2022/271965	Status: 1 st publication (2022-12-29) Title: Compositions and methods for improved protein translation from recombinant circular RNAs	Chen Robert Chang Howard Y Chen Chun-kan	<ul style="list-style-type: none"> Circular RNA

Q4 2022 MAIN ACADEMICS

PENN – University of Pennsylvania

University of Pennsylvania (PENN) owns four newly-published patent families. None of them have been co-filed in collaboration with other universities or companies, and regarding inventorship, two different teams in PENN are at the origin of these inventions. The [Weissman Lab](#) (pioneer in mRNA vaccine development), led by Dr. Drew Weissman, is at the origin of three new patent families, all related to **RNA delivery with LNP or polymeric nanoparticles**. Main information is summarized in the following table.

	PATENT NUMBER	PATENT DETAILS	INVENTOR	SEGMENT(S)
NEW PUBLICATION	WO2022/232552	Status: 1 st publication (2022-11-03) Title: Lipid nanoparticle therapeutics that evade the immune response	Parhiz Hamideh Weissman Drew	<ul style="list-style-type: none"> LNP
	WO2022/232514	Status: 1 st publication (2022-11-03) Title: Compositions and methods for targeting lipid nanoparticle therapeutics to stem cells	Parhiz Hamideh Weissman Drew	<ul style="list-style-type: none"> LNP Targeted delivery
	WO2022/251191	Status: 1 st publication (2022-12-01) Title: Compositions and methods for targeting lipid nanoparticle therapeutics to stem cells Associated scientific publication: Zhang et al., 2022, J. Am. Soc	Percec Virgil Weissman Drew Zhang Dapeng Atochina-vasserman Elena Maurya Devendra Xiao Qi	<ul style="list-style-type: none"> Polymeric nanoparticle
	WO2022/212659	Status: 1 st publication (2022-10-06) Title: Multi-genic mRNA vaccine compositions and methods of use	Eberwine James Pardi Norbert Kim Hyunbum Bartfai Tamas Sul Jai-yoon	<ul style="list-style-type: none"> Prophylactic vaccine Infectious disease



NOTICEABLE PATENTS

Q4 2022 NOTICEABLE PATENTS

Identification of noticeable patents

In Q4 2022, **125 new patent applications** and **31 newly granted patent families** were identified. Based on manual screening, the most noteworthy patent families from main players, newcomers, and academics were identified. Noteworthy patent families can be defined differently depending on whether they are new patent families or newly granted patents:

NEW PATENT FAMILIES

Patent families from main players that enforce their leadership positions, as well as patent families from newcomers that describe an original invention in highly active or incoming segments.

In **Q4 2022**, patent families from **BIONTECH**, **MODERNA**, and **CUREVAC** were selected; patent families from newcomers related to **mRNA delivery strategies** and **alternative mRNA designs** were also selected.

NEW GRANTED PATENT FAMILIES

Patent family granted for the first time in the US, EP, KR, or JP that offers broad protection or strengthens an assignee's portfolio.

In **Q4 2022**, patent families were selected from **BIONTECH**, **MODERNA**, and **CUREVAC** related to prophylactic **vaccines for infectious diseases**; from **MODERNA**, **CUREVAC**, **STANFORD UNIVERSITY**, and **REPLICATE BIOSCIENCES** related to **therapeutic vaccines and therapeutic drugs**; and from **MODERNA**, **CUREVAC**, **EVOX THERAPEUTICS**, and **BRIGHAM & WOMEN'S HOSPITAL** related to **mRNA delivery**.

New patent families

Q4 2022 NOTICEABLE NEW PATENT FAMILIES

Main Players

ASSIGNEE - TITLE	SEGMENT	SUMMARY OF THE INVENTION
BIONTECH & GENENTECH US20220378910 Methods of inducing neopeptide-specific t cells with a pd-1 axis binding antagonist and an RNA vaccine	<ul style="list-style-type: none"> Conventional mRNA Therapeutic Vaccine Oncology 	This invention provides methods for inducing neopeptide-specific CD8+ T cells in an individual or for inducing trafficking of neopeptide-specific CD8+ T cells to a tumor in an individual using an RNA vaccine or using an RNA vaccine in combination with a PD-1 axis binding antagonist. Furthermore, this patent application also provides PD-1 axis binding antagonists and RNA vaccines that include one or more polynucleotides encoding one or more neopeptides resulting from cancer-specific somatic mutations present in a tumor specimen obtained from the individual, for use in methods of inducing neopeptide-specific CD8+ T cells in an individual or for inducing trafficking of neopeptide-specific CD8+ T cells to a tumor in an individual. <i>Note: this invention relates to clinical trial NCT03289962</i>
BIONTECH WO2022/218891 RNA compositions comprising a buffer substance and methods for preparing, storing and using the same	<ul style="list-style-type: none"> Storing 	The invention relates to an RNA composition and a method for storing mRNA. This composition comprises a buffer substance with triethanolamine (TEA) and its protonated form. This buffer allows for the preparation of an mRNA composition that is stable and can be stored in liquid form.
BIONTECH WO2022/218503 LNP compositions comprising RNA and methods for preparing, storing and using the same	<ul style="list-style-type: none"> Manufacturing method Storing 	The description of this patent application comprises RNA-LNP compositions, methods for preparing and storing such compositions, and the use of such compositions in therapy. In particular, this invention relates to the use of Tris and its protonated form, instead of PBS , in a composition comprising LNPs, to inhibit the formation of a very stable folded form of RNA . Furthermore, by simply lowering the concentration of the buffer substance in a composition wherein the LNPs comprise a cationically ionizable lipid and RNA, it is possible to obtain an RNA-LNP composition having improved RNA integrity after a freeze-thaw cycle .
CUREVAC WO2022/233880 Improved nucleic acid sequence for cell type specific expression	<ul style="list-style-type: none"> mRNA modification Targeted delivery 	The objective of this invention is to limit the accumulation of therapeutic mRNA in unintended organs or tissues , particularly the liver or kidneys. By adding specific miRNA binding sequences , specific to unwanted organs, before the 5'UTR of the therapeutic mRNA, a significant reduction in its expression in those organs can be achieved.
MODERNA WO2022/266083 Engineered polynucleotides for cell-type or microenvironment-specific expression	<ul style="list-style-type: none"> Targeted delivery 	The objective of this invention is to control the expression of a therapeutic mRNA (first polynucleotide) by using a second mRNA encoding a repressor protein (e.g., L7Ae) comprising a miRNA sequence. With this construction, the therapeutic mRNA will be selectively expressed in cells expressing the mRNAs.

Q4 2022 NOTICEABLE NEW PATENT FAMILIES

Newcomers in delivery

ASSIGNEE - TITLE	SEGMENT	SUMMARY OF THE INVENTION
GENERATION BIO WO2022/261101 ApoE and ApoB modified lipid nanoparticle compositions and uses thereof	<ul style="list-style-type: none">• LNP	The objective of this invention is to enhance intracellular uptake of LNP carrying nucleic acid therapeutics (mRNA or DNA). The proposed solution is to functionalize the LNPs with apolipoprotein E or B (ApoE or ApoB) that will be recognized by the LDL receptor prior to LDL receptor-mediated endocytosis. These LNPs can especially allow nucleic acid therapeutics delivery to the retinal pigment epithelial (RPE) cells and/or photoreceptor cells, as described in the experimental part (mRNA encoding GFP in vivo).
ANIMATUS BIOSCIENCE WO2022/216536 Selective expression of mRNAs in cardiomyocytes without cardiac fibroblast stimulation	<ul style="list-style-type: none">• LNP• Targeted delivery	The objective of this invention is to target mRNA expression in cardiomyocytes without cardiac fibroblast stimulation. Indeed, after an injury, activation of cardiac fibroblasts results in ensuing fibrosis. ANIMATUS BIOSCIENCE develops aptamers that selectively bind to cardiomyocytes prior to endocytosis . These aptamers are then coupled to LNP. The written opinion of the international searching authority states that the whole set of claims are novel and involve an inventive step, suggesting a positive examination process in patent offices.
CARMINE THERAPEUTIC WO2022/211740 Extracellular vesicles loaded with at least two different nucleic acids	<ul style="list-style-type: none">• Extracellular vesicle	The objective of the invention is to develop red blood cell extracellular vesicles (RBCEV) , as an alternative to classical delivery systems. RBCEV described in this patent application can be loaded with two or more nucleic acid cargoes.

Q4 2022 NOTICEABLE NEW PATENT FAMILIES

Newcomers in alternative RNA design

ASSIGNEE - TITLE	SEGMENT	SUMMARY OF THE INVENTION
ELANCO WO2022/271976 Attenuated salmonella, vaccines, and delivery platform	<ul style="list-style-type: none"> sa-mRNA Bacteria-based delivery Prophylactic vaccine Veterinary 	The objective of this invention is to develop an improved delivery platform and system, including suitable vectors and nucleic acid-based systems for rapid and effective expression of heterologous proteins or genes of interest. The use of an attenuated bacteria presents numerous advantages, such as readily internalization by dendritic cells and macrophages and stimulation of a broad immune response. Attenuated bacteria are obtained by mutation in survival factors (<i>e.g.</i> , <i>phoPQ</i> , <i>ompR-envZ</i> , <i>ssrAB</i> , <i>SPI2</i> , <i>sifA</i> , <i>sseJ</i> , <i>sopF</i> , <i>SPI13</i> , <i>sitABCD</i> , <i>feoABC</i> , <i>mgtRBC</i> , <i>sspH2</i> , <i>paba</i> , <i>pabb</i> , <i>asd</i> , and <i>aroA</i>). This mutation results in an increased sensitivity of the bacteria to intracellular lysis, thus facilitating the payload release.
CHIMERON BIO WO2022/261355 Self-amplifying RNA-based VLP vaccines	<ul style="list-style-type: none"> sa-mRNA VLP Prophylactic vaccine Infectious disease 	This patent application describes a self-amplifying SARS-CoV-2 vaccine , comprising an mRNA encoding Spike protein and a virus-like particle (VLP) containing a retroviral gag protein and a fusogenic envelope protein. The experimental part describes an in-vivo study in mice to determine the generation of neutralizing antibodies against SARS-CoV-2 using the VLP-mRNA combination. The vaccine described in this patent family is still in pre-clinical development. Nevertheless, CHIMERON BIO recently (April 2021) entered into an agreement with the NIAID, a federal agency, for pre-clinical assessment of its self-amplifying COVID-19 Vaccine (Press release).
CIRCODE WO2022/247943 Constructs and methods for preparing circular RNAs and use thereof	<ul style="list-style-type: none"> Circ RNA Manufacturing 	The objective of this invention is to develop an efficient alternative to RNA circularization . This is achieved by using a group II intron (a large class of self-catalytic ribozymes) to obtain a head-to-tail circular RNA through ribozyme-catalyzed RNA splicing.

New granted patents

Q4 2022 NOTICEABLE NEW GRANTED PATENTS

Prophylactic vaccine for ID

ASSIGNEE - TITLE	SEGMENT	FAMILY MEMBER(S)	INDEPENDANT GRANTED CLAIM(S)
MODERNA US11497807 Zoonotic disease RNA vaccines	<ul style="list-style-type: none"> Proph vaccine ID 	Pending in EP, US	1. A composition comprising: (a) a messenger ribonucleic acid (mRNA) comprising an open reading frame (ORF) encoding a fusion protein, wherein the fusion protein comprises a Nipah virus F protein and a Nipah virus G protein; and (b) a lipid nanoparticle, wherein the lipid nanoparticle comprises 45-55 mol % ionizable lipid, 5-25 mol % neutral lipid, 35-45 mol % sterol, and 0.5-5 mol % polyethylene glycol (PEG)-modified lipid, wherein the ionizable lipid is a compound of Formula (I): <div style="text-align: center;"> </div> and wherein R1 is R''M'R' or C520 alkenyl; R2 and R3 are each independently selected from C114 alkyl and C214 alkenyl; R4 is -(CH2) _n Q, wherein Q is OH and n is selected from 3, 4, and 5; M and M' are each independently —OC(O)— or —C(O)O—; R5, R6, and R7 are each H; R' is a linear C112 alkyl, or C112 alkyl substituted with C69 alkyl; R'' is C314 alkyl; mis selected from 5, 6, 7, 8, 9, 10, ii, 12, and 13.
CUREVAC US11524066 Henipavirus vaccine	<ul style="list-style-type: none"> Proph vaccine ID 	Pending in EP	1. A method of treating or preventing a disorder, wherein the method comprises applying or administering to a subject in need thereof an effective amount of a composition comprising a RNA comprising at least one coding sequence encoding a Nipah virus fusion protein F: (a) at least about 95% identical to the sequence of SEQ ID NO: 1 and wherein the Nipah virus fusion protein F is encoded by a RNA coding sequence at least about 95% identical to SEQ ID NO: 53; or (b) at least about 95% identical to the sequence of SEQ ID NO: 573 and wherein the Nipah virus fusion protein F is encoded by a RNA coding sequence at least about 95% identical to SEQ ID NO: 625. <i>Note: SEQ ID NO: 1 and 53 correspond to amino acid or nucleic acid sequence of Nipah virus antigen (F-protein) and SEQ ID NO: 573 and 625 correspond to amino acid or nucleic acid sequence of truncated Nipah virus antigen (F-protein lacking its endogenous secretory signal peptide (FdelSS))</i>
BIONTECH - TRON US11471522 Methods and compositions for stimulating immune response	<ul style="list-style-type: none"> Conv mRNA Therap Vaccine Proph vaccine 	Pending in EP, JP, AU, CA	1. A method for stimulating an immune response in a subject comprising providing to the subject at least one antigen and providing an immunostimulatory RNA molecule, the immunostimulatory RNA molecule comprising (i) a sequence selected from the group consisting of the sequence of SEQ ID NO: 1, the sequence of SEQ ID NO: 2, and the sequence of SEQ ID NO: 5, and, wherein said immunostimulatory RNA molecule optionally further comprises the sequence of SEQ ID NO: 3 or the sequence of SEQ ID NO: 4; or (ii) a sequence selected from the group consisting of the sequence of SEQ ID NO: 6, the sequence of SEQ ID NO: 7, the sequence of SEQ ID NO: 8, the sequence of SEQ ID NO: 9, the sequence of SEQ ID NO: 10, and the sequence of SEQ ID NO: 11. <i>Note: SEQ ID NO: 1, 2, 5-11 derive from influenza nucleoprotein and SEQ ID NO: 3-4 are small immunostimulatory sequence (6/11 nucleotides)</i>

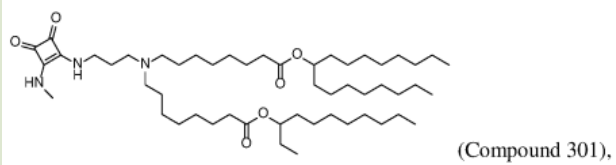
Q4 2022 NOTICEABLE NEW GRANTED PATENTS

Therapeutic Vaccine & Drug

ASSIGNEE - TITLE	SEGMENT	OTHER FAMILY MEMBER(S)	INDEPENDANT GRANTED CLAIM(S)
MODERNA EP3458083 Polynucleotides encoding interleukin-12 (il12) and uses thereof	<ul style="list-style-type: none"> Therapeutic drug Oncology 	KR10-2469450 (Granted in Q4 2022) and pending in KR, RU BR, JP, MX, AU, CN IL, CA	<ol style="list-style-type: none"> A composition for use in a method of reducing the size of a tumor or inhibiting growth of a tumor in a subject in need thereof, wherein (a) the composition comprises an mRNA encoding an IL-12 polypeptide, wherein the mRNA comprises an open reading frame ("ORF") encoding an interleukin 12 p40 subunit ("IL12B") polypeptide and an interleukin 12 p35 subunit ("IL12A") polypeptide, (b) the mRNA is formulated as a lipid nanoparticle that comprises a cationic lipid, a phospholipid, a sterol, and a PEG-modified lipid, and (c) the method comprises administering to the subject an effective amount of said composition intratumorally.
CUREVAC US11464836 RNA for treatment or prophylaxis of a liver disease	<ul style="list-style-type: none"> Therapeutic drug Fibrotic disease 	Pending in EP, JP and CN	<ol style="list-style-type: none"> RNA comprising at least one coding sequence, 10 wherein the coding sequence encodes at least one peptide or protein selected from the group consisting of an extracellular matrix protease, CCAAT/enhancer-binding protein alpha (CEBPA), TNF-related apoptosis15 inducing ligand (TRAIL), hepatocyte nuclear factor 4 alpha (HNF4A), fibroblast growth factor 21 (FGF21), opioid growth factor receptor-like 1 (OGFRL1), Relaxin 1 (RLN1), Relaxin 2 (RLN2) and Relaxin 3 (RLN3), or a fragment or a variant of any of these 20 peptides or proteins, for use in the treatment or prophylaxis of a liver disease.
STANFORD UNIVERSITY US11517530 Therapeutic agents specifically delivered by exosomes for cancer treatment	<ul style="list-style-type: none"> Therapeutic drug Oncology Extracellular vesicle 	-	<ol style="list-style-type: none"> A composition comprising an extracellular-receptortargeted exosome presenting a targeting moiety on its surface, wherein the exosome comprises: 50 (a) a chimeric protein comprising: i) a lactadherin leader sequence (LS) for migration to the exosome surface, ii) a targeting moiety having high aflinity for an extracellular receptor overexpressed in a disease, iii) a lactadherin C1-C2 domain, and iv) an epitope tag for purification; and (b) an active agent included in the exosome, wherein the active agent is a functional mRNA encoding ChrR.
REPLICATE BIOSCIENCE US11510975 Compositions and methods for inducing esr1, pi3k, her2, and her3 immune responses	<ul style="list-style-type: none"> sa-mRNA Therap Vaccine Oncology 	-	<ol style="list-style-type: none"> A nucleic acid construct comprising a nucleic acid sequence encoding a modified Eastern Equine Encephalitis virus (EEEV) genome or self-replicating RNA (srRNA), wherein at least a portion of the nucleic acid sequence encoding the viral structural proteins of the modified EEEV genome or srRNA has been replaced by a coding sequence for a polypeptide construct comprising: a) a coding sequence for estrogen receptor 1 (ESR1) or a variant thereof; b) a coding sequence for P13K or a variant thereof; c) a coding sequence for HER2 or a variant thereof and d) a coding sequence for HER3 or a variant thereof.

Q4 2022 NOTICEABLE NEW GRANTED PATENTS

Delivery

ASSIGNEE - TITLE	SEGMENT	FAMILY MEMBER(S)	INDEPENDANT GRANTED CLAIM(S)
MODERNA US11524023 Lipid nanoparticle compositions and methods of formulating the same	<ul style="list-style-type: none"> LNP 	Pending in WO, EP, TW	1. A compound being Compound 301: <div style="text-align: right;">  <p>(Compound 301),</p> </div> or a salt or isomer thereof.
EVOX THERAPEUTICS JP7149925 Metabolic drug loading of EVs	<ul style="list-style-type: none"> Extracellular Vesicle 	Pending in US, EP, CN, AU, SG, CA (WO2018/011128)	1. Method for metabolically loading pharmaceutical drugs into extracellular vesicles (EVs), comprising culturing the EV supply cell in the presence of conjugates containing said pharmaceutical drug coupled to a metabolite, wherein said metabolite is a C18 fatty acid, cholesterol, palmitic acid, myristic acid, phospholipid, vitamin B7, vitamin B9, vitamin E, or combinations thereof. <i>Note: English machine translation from Japanese claims</i>
BRIGHAM & WOMENS HOSPITAL US11518787 Methods and compositions for delivery of agents across the blood-brain barrier	<ul style="list-style-type: none"> Targeted delivery 	Pending in WO, JP, EP, US, CN, CA,	1. An adeno-associated virus (AAV) vector comprising an AAV capsid, wherein the AAV capsid comprises a peptide insert of up to 21 amino acids, and wherein the peptide insert peptide insert comprises 5-7 amino acids of TVSALFK (SEQ ID NO: 8). <i>Note: SEQ ID NO:8 is an artificial sequence that enhance permeation of agents into cells and across the blood brain barrier.</i>

Q4 2022 NOTICEABLE NEW GRANTED PATENTS

Delivery

ASSIGNEE - TITLE	SEGMENT	FAMILY MEMBER(S)	INDEPENDANT GRANTED CLAIM(S)
<p>CUREVAC US11478552 Hybrid carriers for nucleic acid cargo</p>	<ul style="list-style-type: none"> • Polymeric NP • Peptidic NP 	Pending in IN, JP, RU, AU, EP, MX, KR, BR, CN, SG, CA	<p>1. A method of prophylaxis, treatment, and/or amelioration of a disease or disorder in a patient in need thereof comprising administering to the patient a safe and effective amount of a composition comprising a plurality of nanoparticles, wherein each nanoparticle of the plurality of nanoparticles comprises:</p> <p>(a) a cationic peptide or cationic polymer;</p> <p>(b) a cationic or permanent cationic lipidoid compound; and</p> <p>(c) a nucleic acid compound; wherein the cationic or permanent cationic lipidoid compound comprises two or three moieties of formula IIa and/or formula IIb: $[-N(R1)-CH_2-CH(R5)-R_2]$ (formula IIa) $[-N^+(R3)(R4)-CH_2-CH(R5)-R_2]$ (formula IIb) wherein independently for each individual moiety of formula IIa or formula IIb R1 is selected from hydrogen or C1-C4-alkyl, R2 is selected from linear or branched, saturated or unsaturated C6-C16 hydrocarbyl chain, R3 and R4 are selected from C1-C4-alkyl, and R5 is selected from hydrogen or hydroxyl; and wherein the cationic peptide or cationic polymer is a compound according to formula $L^1-P^1-[P-]_n-P^3-L^2$ (formula IV) wherein P is a cationic moiety having at least one $-SH$ group capable of forming a disulfide linkage, or a disulfide-linked multimer thereof, wherein moiety P is selected from a polymer moiety having a molecular weight from about 0.5 kDa to about 30 kDa, or a peptide moiety composed of 3 to 100 amino acids, wherein at least 10% of the total number of amino acids of the peptide moiety represent basic amino acids selected from Arg, Lys, His and/or Orn; P³ is optional; P¹ and P³ are independently selected, each representing a linear or branched hydrophilic polymer chain selected from the group consisting of polyethylene glycol (PEG), poly-N-(2-hydroxypropyl)methacrylamide, poly-2-(methacryloyloxy)ethyl phosphorylcholines, poly(hydroxyalkyl L-asparagine), poly(2-(methacryloyloxy)ethyl phosphorylcholine), hydroxyethylstarch and poly(hydroxyalkyl L-glutamine), wherein the polymer chain exhibits a molecular weight from about 1 kDa to about 100 kDa, and wherein each of P¹ and P³ is linked with a moiety P through a disulfide linkage;</p> <p>L¹ and L² are optional ligands and independently selected from the group consisting of RGD, an RGD peptide, transferrin, folate, a signal peptide, a localization signal, a nuclear localization signal (NLS), an antibody, a cell penetrating peptide, a trans-activator of transcription (TAT), a ligand of a receptor, a cytokine, a hormone, a growth factor, a carbohydrate, a mannose, a galactose, an N-acetylgalactosamine, a synthetic ligand, an inhibitor of a receptor, an antagonist of a receptor, and a RGD peptidomimetic analogue;</p> <p>n is an integer selected from 1 to about 50; and wherein, if n is greater than 1, each moiety P is linked with another moiety P through a disulfide linkage.</p>



ANNEX

Take advantage of direct interaction with our analysts by phone call and/or email

Q&A session and open discussion with our IP analysts (100h a year).

Asking for questions and/or requesting for specific patent search on company or technology.



Contact: contact@knowmade.fr

Examples:

- Could you tell me more about the patent portfolio of this company?
- What is exactly the invention claimed in these patents?
- Can you give me the patents filed by this company on these specific technologies?
- Can you shortly analyze the patents of this new entrant?
- What are the patents issued in Japan and Korea for this application?
- Please give me more details about this patent litigation.
- We want to file a new patent, can you help us to assess the prior-art in this field?
- I would like to invalidate these patents, could you do a prior-art search?
- Can you help me to identify in patents the technical solutions to solve this issue?
- I would like to assess my freedom of operating in USA, can you give me the granted US patents covering this technology?
- I am looking for free technologies I could use safely without infringing valid IP rights, can you give me newly expired patents related to this technology?

Terminologies for Patent Analysis (1/2)

Patent Applicant, Patent Assignee

An applicant is a person or organization (*e.g.*, company, university, etc.) who/which has filed a patent application. An assignee is a person or organization (*e.g.*, company, university, etc.) who/which holds patent rights. Patent applications may have more than one applicant/assignee.

Patent Family

A patent family is a set of applications or publications related to the same invention (different countries) and claiming the same priority(ies). All members of a patent family, except American continuation-in-part, share all their priorities.

Priority Date

The priority date is defined as the date on which the first patent application disclosing the invention was filed (up to 12 months before the filing of the application). The patent document is made available to the public about 18 months after the priority date (except if early publication is requested).

Priority Number

A priority number is the filing number of a priority document. The priority number is made up of a country code (two letters), the year of filing (two or four digits) and a serial number (variable, maximum seven digits).

Publication Date

The publication date is the date on which the patent application is published and is made available to the public, therefore entering into the state of the art.

First publication date

First publication date is defined as the earliest patent publication date disclosing the invention (herein “year of first publication”). The date or year of publication of a patent family must always read as the date or year of first publication.

Publication Number

The publication number is the number assigned to a patent application for the publication. Publication numbers are generally made up of a country code (two letters) and a serial number (variable, one to twelve digits).

Terminologies for Patent Analysis (2/2)

Citations

A citation is a reference made to a prior art document that is considered relevant to determine the patentability of a given invention. Citations are made by the applicant or by the office examiner during the examination of the patent application.

WO and EP Patent Applications

International (WO) and European (EP) patent applications are administered by the [World Intellectual Property Organization \(WIPO\)](#) and the [European Patent Office \(EPO\)](#), respectively.

- WO applications designate Contracting parties (official or non-official countries) of the Patent Cooperation Treaty (PCT) through their national or regional systems and will have the same effect as national or regional patent applications in each designated state or region, leading to a granted patent in each state or region. In this report, patent families are often designated by their funding PCT member. Entering into national phase of a PCT application can be checked on [WIPO's Patentscope database](#).

EP applications are regional patent applications and may lead to granted EP patents upon validation in one or more designated Contracting States of the European Patent Convention (EPC) (*i.e.* 'bundle' of individual national patents). An EP granted patent can also be validated in Morocco, the Republic of Moldova, Tunisia and Cambodia and/or extended in Bosnia-Herzegovina, and Montenegro upon payment of an additional fee.

Legal Status of the Patent Document (patent or patent application)

Granted: Enforceable patent issued by a patent office after an examination process of a patent application.

Pending: Patent pending is the term used to describe a patent application that has been filed with the patent office, but has not yet been issued as a granted patent. Hence, the scope of protection of a pending application, or whether a patent will even be granted, is unknown.

Abandoned/Lapsed: A patent or patent application that is not enforceable anymore because the applicant withdrew his patent application, failed to respond to an office action during the examination, or did not pay the maintenance fees. Typical office status for Lapsed could be "abandoned", "lapsed", "withdrawn", "surrendered", etc.

Expired: A granted patent that is no longer in force as it has reached its maximum duration (in most countries: 20 years from the filing date, provided CCP or paediatric extension).

Rejected/Revoked: A patent or patent application that is not enforceable before the end of the normal term for patentability-related reasons.

- The status "rejected" mainly refers to a pre-grant patent application for which a grant decision has been denied (*e.g.*, due to a lack of patentability of the invention).
- The status "revoked" mainly refers to a formerly granted patent that have been later cancelled by an office (*e.g.*, following an Opposition, a Post Grant Review or an Inter Partes Review) or a court. Typical office status for "Revoked" could be "suspended", "interrupted", "cancelled", "revoked", "refused", etc.

International Patent Classification (IPC)

The technical content of patent documents is classified in accordance with the International Patent Classification (IPC). The publishing office assigns an IPC symbol valid at the time of publication of the patent application. The complete IPC can be found on the website of the World Intellectual Property Organization (WIPO - <http://www.wipo.int/ipcpub>).



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