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Supplementary information

The mRNA vaccine development landscape for infectious diseases

In the format provided by the authors

Data sourcing and analysis
From February 2020 onwards, CEPI has studied the mRNA vaccine development landscape for infectious diseases by using internal and external data sources, including:

- CEPI internal sources: Call for proposal process, direct interaction with mRNA vaccine developers
- Clinical trial databases (ClinicalTrials.gov)
- WHO
- Publicly available literature (PubMed)
- Media and press releases

Our search collected, documented and updated information regarding platform technology, development status, and consortium partners including manufacturing from the available data sources on a weekly basis.

Inclusion criteria. Our search identified and operationalized three data sources:

• Vaccine developers with detailed vaccine development plans recorded through the CEPI Call for proposal process or through personal communication
• Vaccine candidates that have been announced publicly by the product developer, including details on the platform technology and/or current development status
• Vaccine developers which licensed their technology to several partners, which are listed only once.

There are several reasons for the selection of these data sources. First, the CEPI team has been uniquely positioned to outline these data, since CEPI has undertaken the lead role of processing these applications. Second, the criteria of public announcement relate to the retrievability, transparency and reliability of our sources.

This landscape analysis focuses on mRNA vaccines for infectious diseases only.

Exclusion criteria. Vaccine candidates in clinical phases without confirmation of dosing start/trial registration were not listed in the database.

Limitations. Vaccine development programmes described in languages other than English have not been systematically screened. A large amount of publicly available information comes from media sources, which might not be completely reliable. Internal or public information about development status (that is, exploratory, preclinical or later development stage) is not available for some vaccine candidates.

Supplementary Table 1 | **Current pipeline of mRNA platform-based vaccine candidates in clinical development**

Lead organization	mRNA platform	Pathogen	mRNA ID	Phase	Source
Moderna	Modified	SARS-CoV-2	mRNA-1273	Approved	https://www.modernatx.com
		SARS-CoV-2 Beta variant	mRNA-1273.351	Phase 1	
		SARS-CoV-2 Delta variant	mRNA-1273.617	Phase 2	
		SARS-CoV-2 Wild + beta variant	mRNA-1273.211	Phase 2	
		SARS-CoV-2 Omicron variant	mRNA-1273.529	Phase 2	
		SARS-CoV-2 Beta + delta variant	mRNA-1273.213	Phase 2	
		SARS-CoV-2 Next-generation (2-5 °C)	mRNA-1283	Phase 2	
		Flu	mRNA-1010	Phase 2	
		CMV	mRNA-1647	Phase 3	
		EBV	mRNA-1189	Phase 1	
		Paediatric hMPV+PIV3	mRNA-1653	Phase 1	
		RSV	mRNA-1345	Phase 2/3	
		Zika	mRNA-1893	Phase 2	
		HIV	mRNA-1644	Phase 1	
CureVac	Non-modified	SARS-CoV-2*	CVnCoV	Phase 3	https://www.curevac.com
		Rabies	CV7202	Phase 1	
Imperial College	Self-amplifying	SARS-CoV-2*	LNP-nCoV saRNA	Phase 1/2	ISRCTN17072692
Sanofi (TranslateBio)	Non-modified	SARS-CoV-2*	MRT5500	Phase 1/2	NCT04798027
		Flu	MRT5400/5401	Phase 1/2	Source
StemiRNA	Modified	SARS-CoV-2	mRNA Covid-19 vaccine	Phase 1	ChiCTR2100045984
BioNTech/ Pfizer	Modified	SARS-CoV-2	BNT162b2	Approved	https://biontech.de/
		Flu	BNT161	Phase 1	
Arcturus Therapeutics	Self-amplifying	SARS-CoV-2	ARCT-021	Phase 2	https://arcturusrx.com/
		SARS-CoV-2 (variants)	ARCT-154	Phase 3	
Gennova Biopharmaceuticals	Self-amplifying	SARS-CoV-2	HGC019	Phase 2/3	https://hgco19.com/
Daiichi Sankyo/ University of Tokyo	NA	SARS-CoV-2	DS-5670a	Phase 1/2	NCT04821674
Chula/ BioNet Asia	Modified	SARS-CoV-2	ChulaCoV19	Phase 1/2	NCT04566276
Walvax Biotechnology	Modified	SARS-CoV-2	ARCoV	Phase 3	NCT04847102
Elixirgen	Self-amplifying	SARS-CoV-2	EXG-5003	Phase 1/2	https://elixirgentherapeutics.com
Providence Therapeutics	Modified	SARS-CoV-2	PTX-COVID19-B	Phase 2	https://providencetherapeutics.com/
GSK	Self-amplifying	SARS-CoV-2	GSK4184258A	Phase 1	NCT04758962
		Rabies	GSK3903133A	Phase 1	NCT04062669
Gritstone Bio	Self-amplifying	SARS-CoV-2	SAM-LNP-S	Phase 1	https://gritstonebio.com/

*Amended

Supplementary Box 1 | Key challenges for mRNA vaccines

Disease target
• Pathogen and strain coverage — multivalency yet to be established across strains and pathogens

Clinical
• Reactogenicity — unclear safety risk/benefit outside a pandemic setting
• Immunogenicity — some pathogens other than SARS-CoV-2 may require greater cellular response
• Durability —unproven durability of protective immunity

Delivery
• Thermostability —stability at 4°C or ambient temperature in liquid formulation currently not available
• Deployability — syringe and needle intramuscular administration requires skilled personnel

Manufacturing/other
• IP restrictions — uncertain freedom to operate in various countries
• Geographic diversity — production and expertise concentrated in US and EU
• Response time — 10–12 months from sequence to EUA
• Regulatory pathway — traditional efficacy pathway currently required for initial vaccines
• Bottlenecks in availability of raw materials