Lonza accelerating efforts to make Moderna vaccine

Lonza aims to be making vaccine ingredients by July and have production lines ready by November, some 4-6 weeks ahead of plans. In May, they were enlisted by Moderna for a 10-year manufacturing contract and then selected as a finalist alongside companies such as: AstraZeneca, Merck, Pfizer and Johnson & Johnson for 'Operation Warp Speed' - a US initiative to expedite COVID-19 vaccines to the public.

Moderna is the smallest company among the collection and is rapidly progressing into mid- and late-stage testing with its mRNA candidate.

Lonza aims to speed up completion of 2 commercial production lines for the trial COVID-19 vaccine. Manufacturing could start 4 to 6 weeks earlier than planned if the project is successful.

Last week Moderna's experimental COVID-19 vaccine entered phase II clinical trial and dosed initial participants in a 600-patient study. The Phase III trial begins in July and includes a study of 30,000. The Fast Track designation and the start of the Phase II trial means that mRNA-1273 may be the first vaccine to be approved and launched for the Covid-19 pandemic, as it is the only vaccine that has received FDA approval to initiate a Phase II trial, therefore placing it ahead of all other candidate Covid-19 vaccines in development.

Challenges:

- Hiring staff to operate production lines.
- Possible equipment shortages.
- mRNA technology has yet to be approved in medicine and is unknown territory.

An mRNA facility has a multitude of advantages including being smaller, cheaper and faster to scale up, in comparison to traditional biological production lines. However, ingredients for an mRNA vaccine are also very specialized, requiring production of mRNA and encapsulation inside lipid nanoparticles for delivery to humans.

Finance

- Lonza is financing the first $60-$70 million commercial production line in Visp.
- Moderna is paying for the first U.S. production line, and up to three more at Lonza facilities in Portsmouth and Visp. Moderna recieved $483 million from the U.S. government and $1 billion in new capital.

Combined capacity could produce ingredients for 600 million to 1 billion vaccine doses annually

Moderna is clearly very confident in its ability to develop a Covid-19 vaccine. However, there is also the issue of getting the vaccine to the public in an efficient manner. Upon finding a vaccine, Moderna would face enormous pressure to produce the vaccine as quickly as possible. Lonza is preparing to mitigate these challenges.

Moderna and Lonza Announce Worldwide Collaboration to Manufacture vaccine against COVID-19

Moderna Inc. and Lonza Ltd announced a 10-year strategic collaboration agreement to enable manufacturing on a greater scale of Moderna's mRNA vaccine (mRNA-1273) against the novel coronavirus (SARS-CoV-2) and additional Moderna products in the future.

Under the terms of the agreement, the companies plan to establish manufacturing suites at Lonza's facilities in the United States and Switzerland for the manufacturing of mRNA-1273 at both sites. Initial manufacturing is planned to take place at Lonza's sites in Portsmouth, New Hampshire and Visp, Switzerland (with a 2nd phase planned at its Ibex facility).

Technology transfer is expected to begin in June 2020, and the companies intend to manufacture the first batches of mRNA-1273 at Lonza U.S. in July 2020. Over time, the parties intend to establish additional production suites across Lonza's worldwide facilities, ultimately allowing for the manufacture of material equivalent to up to 1 billion doses of mRNA-1273 per year for use worldwide, assuming the currently expected dose of 50 µg is met. The manufacturing facilities at Lonza complement Moderna's ongoing U.S. manufacturing efforts, which continue to ramp up to prepare for the further clinical development and commercialization of mRNA-1273.

Manufacturing operations at Lonza US are partially covered by Moderna's 'up to' $483M contract with the US Biomedical Advanced Research and Development Authority (BARDA). BARDA agreed to support late-stage clinical development programmes of mRNA-1273.

mRNA-1273 is a novel lipid nanoparticle (LNP)-encapsulated mRNA vaccine encoding for a prefusion stabilized form of the Spike (S) protein. The vaccine candidate is under study in a Phase I open-label, dose-ranging trial of mRNA-1273 (NCT04283461) in males and non-pregnant females, 18 to 55 years old, occurring at Kaiser Permanente Washington Health Research Institute in Seattle.

The 45-patient study is designed to assess the safety and reactogenicity of a 2-dose vaccination schedule of mRNA-1273, given 28 days apart, across 3 dosages in healthy adults. The first patient was dosed in March.

On April 27, Moderna submitted an IND application to the FDA for Phase II and late-stage studies of mRNA-1273. Moderna said it received initial feedback from the FDA on the design of the planned study, which is expected to begin in the second quarter of 2020.

The Phase II trial will be designed to assess the safety, reactogenicity, and immunogenicity of two vaccinations of mRNA-1273 given 28 days apart. Each subject will be assigned to receive placebo, a 50 µg or a 250 µg dose at both vaccinations. Moderna said it intends to enroll 600 healthy participants across two cohorts of adults aged 18-55 years (n=300) and older adults aged 55 years and above (n=300). Participants will be followed for 12 months after the second vaccination.

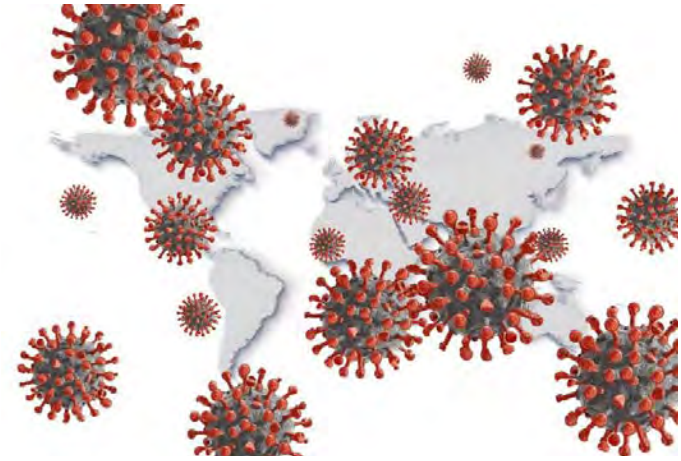
About mRNA-1273

mRNA-1273 is an mRNA vaccine against SARS-CoV-2 encoding for a stabilised form of the Spike (S) protein, which was selected by Moderna in collaboration with investigators from Vaccine Research Center (VRC) at the National Institute of Allergy and Infectious Diseases (NIAID), a part of the NIH.

The potential advantages of an 'mRNA approach' to prophylactic vaccines include: the ability to combine multiple mRNAs into a single vaccine, rapid discovery to respond to emerging pandemic threats and manufacturing agility derived from the platform nature of mRNA vaccine design and production.

Moderna currently has nine development projects in its prophylactic vaccines modality, including:

- Vaccines against respiratory infections
- Respiratory syncytial virus (RSV) vaccine for older adults (mRNA-1777 and mRNA-1172 or V172 with Merck)
- RSV vaccine for young children (mRNA-1345)
- Human metapneumovirus (hMPV) and parainfluenza virus type 3 (PIV3) vaccine (mRNA-1653)
- Novel coronavirus (SARS-CoV-2) vaccine (mRNA-1273)
- Influenza H7N9 (mRNA-1851)



There are already at least 250 therapies and 95 vaccines specific COVID-19 being explored. Dozens of vaccines are starting clinical trials. Many use experimental RNA and DNA technology, which provides the body with instructions to produce its own antibodies against the virus.

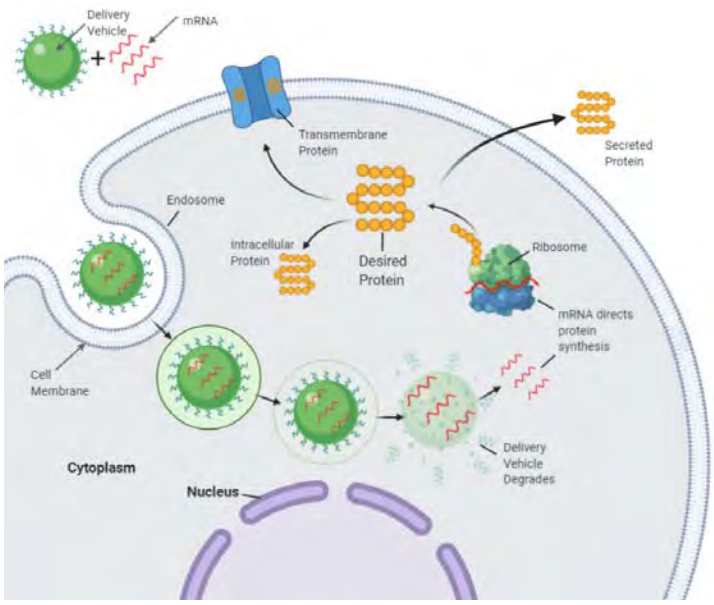
COVID-19 Vaccines, Treatments and Testing

https://evolutionexec.com/COVID-19/treatments/

Global mRNA Vaccine Market

Some key factors driving the growth of the Global mRNA Vaccine Market include: increasing adoption of mRNA vaccine (owing to its higher efficiency), shorter manufacturing times and growing licensing agreements between mRNA vaccine manufacturers.. Furthermore, the excellent ability of mRNA to combine multiple molecules into a single therapeutic has gained significant attention from potential investors and the pharmaceutical industry.

- During the last two decades, there has been broad interest in RNA-based technologies for the development of therapeutic vaccines. Preclinical and clinical trials have shown that mRNA vaccines provide a safe and long-lasting immune response in humans and manufacturing is safe and time-saving. Vaccination with non-viral delivered nucleic acid-based vaccines mimics infection or immunization with live microorganisms and stimulates potent T helper and B cell immune response.
- Recent improvements in mRNA vaccines act to increase protein translation, modulate innate and adaptive immunogenicity and improve delivery.
- mRNA vaccines have elicited potent immunity against infectious disease targets in animal models of influenza virus, Zika virus, rabies virus and others, especially in recent years, using lipid-encapsulated or naked forms of sequence-optimized mRNA.
- Diverse approaches to mRNA cancer vaccines, including dendritic cell vaccines and various types of directly injectable mRNA, have been employed in numerous cancer clinical trials, with some promising results showing antigen-specific T cell responses and prolonged disease-free survival in some cases.
- Therapeutic considerations and challenges include scaling up good manufacturing practice (GMP) production, establishing regulations, further documenting safety and increasing efficacy.



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Conventional vaccines usually contain inactivated disease-causing organisms or proteins made by the pathogen (antigens), which work by mimicking the infectious agent. They stimulate the body's immune response, so it is primed to respond more rapidly and effectively if exposed to the infectious agent in the future.

RNA vaccines use a different approach that takes advantage of the process that cells use to make proteins: cells use DNA as the template to make messenger RNA (mRNA) molecules, which are then translated to build proteins. An RNA vaccine consists of an mRNA strand that codes for a disease-specific antigen. Once the mRNA strand in the vaccine is inside the body's cells, the cells use the genetic information to produce the antigen. This antigen is then displayed on the cell surface, where it is recognised by the immune system.

Vaccines: mRNA-based

Important future directions of research will be to compare and elucidate the immune pathways activated by various mRNA vaccine platforms, to improve current approaches based on these mechanisms and to initiate new clinical trials against additional disease targets.

mRNA-based vaccines are a promising novel platform that are highly flexible, scalable, inexpensive, and cold-chain free. Most importantly, mRNA-based vaccines can fill the gap between emerging pandemic infectious diseases and a bountiful supply of effective vaccines. A variety of preclinical and clinical projects have made enormous strides toward the conceivable application of mRNA vaccines and have suggested that mRNA-based prophylaxis and therapy can be translated to human applications.

mRNA vaccines represent a promising alternative to conventional vaccine approaches because of their high potency, capacity for rapid development and potential for low-cost manufacturing and safe administration.

Vaccines	Advantages	Disadvantages
Viral Vectored Vaccines	Stimulation of innate immune response; induction of T and B cell immune response.	Induction of anti-vector immunity: cell based manufacturing.
DNA Vaccines	Non infectious stimulation of innate immune response, egg and cell free; stable, rapid and scalable production; induction of T and B cell immune response.	Potential integration into human genome; poor immunogenecity in humans.
RNA Vaccines	Non-infectious, non-integrating, natural degredation, egg and cell free, rapid and scalable production; stimulation of innate immune response; induction of T and B cell immune response.	Concerns with instability and low immunogenecity.

Strategic Collaboration

The future of mRNA vaccines is therefore extremely bright, and the clinical data and resources provided by these companies and other institutions are likely to substantially build on and invigorate basic research into mRNA-based therapeutics.

The agreement is one of several partnerships being struck between drugmakers as they rush to bring protection against COVID-19 to the market. AstraZeneca Plc announced an agreement to make an experimental coronavirus vaccine developed by the University of Oxford, eyeing production capacity for 100 million doses by the end of the year.

The pact with Lonza will enable a tenfold increase in manufacturing, which Moderna has already begun, according to a statement.

The smaller players in the race won't be able to produce a vaccine in large quantities on their own.

A partnership between Sanofi and GlaxoSmithKline Plc announced last month brought together a pair of pharmaceutical giants with manufacturing might. Sanofi will test its experimental coronavirus vaccine with Glaxo supplying so-called adjuvants, additional ingredients that improve efficacy and make it easier to produce shots in larger quantities.

Lonza

Lonza has received more than 40 clinical and commercial inquiries regarding projects related to COVID-19. They are focusing efforts on selected key development projects relating to both vaccines and therapeutic treatments. Lonza's expertise is manufacturing, process development and scaling up processes.

Lonza is likely to use its Ibex Solutions model for some of the COVID-19 projects and may accelerate expansion if required. Typically, Ibex Design focused on customers' preclinical and IND needs to Phase I, while Ibex Develop focused on process validation to BLA and commercial supply. The offerings aim to speed up the drug development process by eliminating the need for tech transfers, allowing process optimizations and creating operational efficiencies.

Moderna

Moderna are leveraging the fundamental role that mRNA plays in protein synthesis. They have proprietary technologies to create mRNA sequences that cells recognize as if they were produced in the body. Using mRNA as a drug opens up a breadth of opportunities to treat and prevent disease. mRNA medicines can go inside cells to direct protein production, something not possible with other drug approaches.

Moderna is advancing messenger RNA (mRNA) science to create a new class of transformative medicines for patients. The company's platform builds on continuous advances in basic and applied mRNA science, delivery technology and manufacturing, providing Moderna the capability to pursue in parallel a robust pipeline of new development candidates. Moderna is developing therapeutics and vaccines for infectious diseases, immuno-oncology, rare diseases and cardiovascular diseases, independently and with strategic collaborators.

Related COVID-19 Vaccine Projects

Company	Vaccine	Type	Target
Moderna/ Lonza	mRNA-1273	mRNA vaccine	Sars-CoV-2 spike protein
Arcturus Therapeutics / Catalent	LUNAR-COV19	mRNA vaccine	SARS-CoV-2 coronavirus
Inovio Pharma/Richter-Helm Biologics	INO-4800	DNA Vaccine	coronavirus SARS-CoV-2
Biontech/ Pfizer/Fosun	BNT162a1, b1, b2 & c2	mRNA vaccine	Large spike sequence, or 2 smaller receptor-binding domains
Johnson & Johnson	AdVac® and PER.C6® technology	Adenovirus type 26 vaccine	Sars-CoV-2 spike protein
Sanofi/ Glaxosmithkline	Spike (S) protein COVID-19 antigen (Sanofi)/ AS03 adjuvant technology (GSK)	DNA vaccine	Sars-CoV-2 spike protein
Translate Bio/ Sanofi	MRT platform	mRNA vaccine	SARS-CoV-2 coronavirus
CanSino Biologics	Ad5-nCoV	Adenovirus Type 5 Vector	SARS-CoV-2 spike protein
Shenzhen Geno-Immune Medical Institute	LV-SMENP-DC and pathogen-specific aAPC	lentivirus (disabled HIV) used to deliver viral proteins	SARS-CoV-2 spike protein

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