LifeLink Ventures

CORONAVIRUS – NEWSLETTER IV

17th March 2021

Brief summary

- There are currently **4 vaccines** (Pfizer, Moderna, AstraZeneca and Johnson & Johnson) approved by USA regulators (FDA) or EU regulators (EMA) and **1 vaccine** approved by Russian regulators (RMH).
- Brazilian (Anvisa) and Chinese regulators (NMPA) have approved a **6th vaccine** (SinoVac) and a **7th vaccine candidate** (NovaVax) with strong positive clinical data is likely to be approved in the upcoming months.
- The companies and organisations whom have created the vaccines described in this newsletter have reported a high clinical effectiveness at preventing severe Covid-19 and moderate to high effectiveness at preventing less severe symptomatic Covid-19.
- These vaccines **do not lead to changes in our own DNA** and there is no data supporting this claim.

Clinical Efficacy (from published literature or company press release)

- SinoVac data is based on a phase 3 clinical trial held in Brazil.
- NovaVax and Sputnik V results are **preliminary**.
- Russia regulatory agencies and governing bodies allowed Sputnik V to be dosed in individuals prior to publication of their interim phase 3 efficacy clinical trial.

Company	Efficacy	Participants	Covid-19 Definition*	Storage	Agency Approvals
Pfizer	95%	36.000	PCR+ with 1 symptom	-80 C	FDA, EMA
Moderna	96%	30.000	PCR+ with 2 symptom	-20 C	FDA, EMA
AstraZeneca	62%	10.000	PCR+ with 1 symptom	4 C	EMA, Anvisa
J & J	66%	20.000	PCR+ with 2 minor or 1 worse symptom	4 C	FDA
Sputnik V	91%	22.000	PCR+ with undisclosed symptom(s)	4 C	RMH, (EMA evaluation ongoing)
SinoVac	50%	13.000	PCR+ with undisclosed symptom(s)	4 C	Anvisa, NMPA
NovaVax	89%	30.000	PCR+ and symptomatic	4 C	To be determined

*__Note:__ each company has a pre-defined list of symptoms to categorize clinical trial participants as having acquired Covid-19. Because the lists across companies are not identical the efficacy results are not necessarily 100% comparable.

Common adverse effects and dosing

- **Side effects:** all of the vaccines below have mild adverse effects relative to the disease Covid-19. However, the adenovirus vaccines are generally less associated with moderate to severe fatigue than the mRNA vaccines. Individuals with allergies are commonly monitored for allergic reactions to mRNA vaccination.

Status	Company	Vaccine Type	Delivery	Doses	Time to 2nd Dose	Common Adverse Effects
Approved	Pfizer	mRNA	Lipid nanoparticle	2	21 days	moderate to severe fatigue / fever
Approved	Moderna	mRNA	Lipid nanoparticle	2	28 days	moderate to severe fatigue / fever
Approved	AstraZeneca	DNA	Adenovirus	2	3-28 weeks*	mild to moderate fatigue / fever
Approved	J & J	DNA	Adenovirus	1	NA	mild to moderate fatigue / fever
Approved	Sputnik V	DNA	Adenovirus	2	21 days	mild to moderate fatigue / fever
Approved	SinoVac	Inactive virus	SARS-CoV2	2	28 days	mild to moderate fatigue / fever
TBD	NovaVax	Protein	Lipid nanoparticle	2	21 days	currently unreported

***Note:** AstraZeneca experienced scheduling problems during their clinical trial and while 86% of the individuals received their second dose 4 to 12 weeks after the first dose, these complications may have skewed the efficacy down. Additionally, some EU countries are pausing administration of AstraZenecta´s vaccine due to a possible association with blood clotting (37 cases out of 17million people vaccinated in the EU alone) while the WHO evaluates the data.

Efficacy at scale as demonstrated by Israel (from Pfizer press release)

- In Dec 2020 Israel launched a national vaccination program and by Feb 2021 the Israel Ministry of Health reported that over 75% of the population had been vaccinated with the Pfizer vaccine.
- The Israel Ministry of Health surveilled the population between Jan and Mar 2021 and reported a **97% efficacy against symptomatic and severe Covid-19**. The analysis reported a **94% effectiveness against asymptotic spread** of Covid-19 suggesting that vaccination against SARS-CoV-2 may effectively prevent asymptotic viral shedding.
- At the time of analysis the **UK variant** (b.1.1.7) was dominant (80% of tested individuals).

Investment / research and development cost

- In 2020 the US government initiated a public-private partnership (Operation Warp Speed) that pumped more than **10 billion dollars** into private companies to develop and manufacture Covid-19 vaccines.
- It is important to note the rapid approval of Covid-19 vaccines is the result of scientific ingenuity and an **unprecedented amount of capital investment**.

Company	Investment (million USD)	Vaccine Status
Moderna	2500	Approved
AstraZeneca	1200	Approved
J & J	1500	Approved
NovaVax	1600	Phase 3 trial
Merck	38	Terminated
Sanofi / GSK	2100	Phase 2 trial

While it has taken decades to generate an effective Ebola vaccine, in a single year more than 5 effective Covid-19 vaccines have been developed. Given the fact that the capital investment in Ebola is on the order of low 100s of millions (100x less than Covid-19), it is no surprise Covid-19 vaccines were generated so rapidly.

New variants and other unknowns

- It is not completely clear how new variants (including those identified in California and Brazil) will affect the efficacy of the current generation of Covid-19 vaccines.
- J & J have reported 68% and 64% efficacy against **California** (D614G) and **Brazil** (P.2) **variants**, respectively.
- NovaVax reported 86% efficacy against the **UK variant** and 60% efficacy against the **South African** (b.1.315) **variant**.
- SinoVac´s Brazilian partner (Butantan biomedical centre) have reported the vaccine is similarly effective against the **UK and South African variant** and will soon report the efficacy against the Brazilian variant.
- It is currently **undetermined exactly how long vaccine protection will last**.

Vaccine technology

- SARS-CoV2 viruses use an external protein named "**spike**" to physically infect cells and cause the disease Covid-19. Spike alone is known to mount an immune response capable of destroying viruses.
- To preemptively train your immune system, Covid-19 vaccines either use spike protein alone (delivered by lipid nanoparticles or adenovirus) or an inactivated non-replicating SARS-CoV2 virus to initiate an immune response.
- **All of the technologies used for Covid-19 vaccines discussed have been described as clinically safe by various regulatory agencies.** While the Pfizer and Moderna vaccines represent the first approvals for RNA vaccines, the technology itself has been previously shown to be safe in a clinical setting for other diseases. However, lacking efficacy (not safety) prevented approval of those specific products.

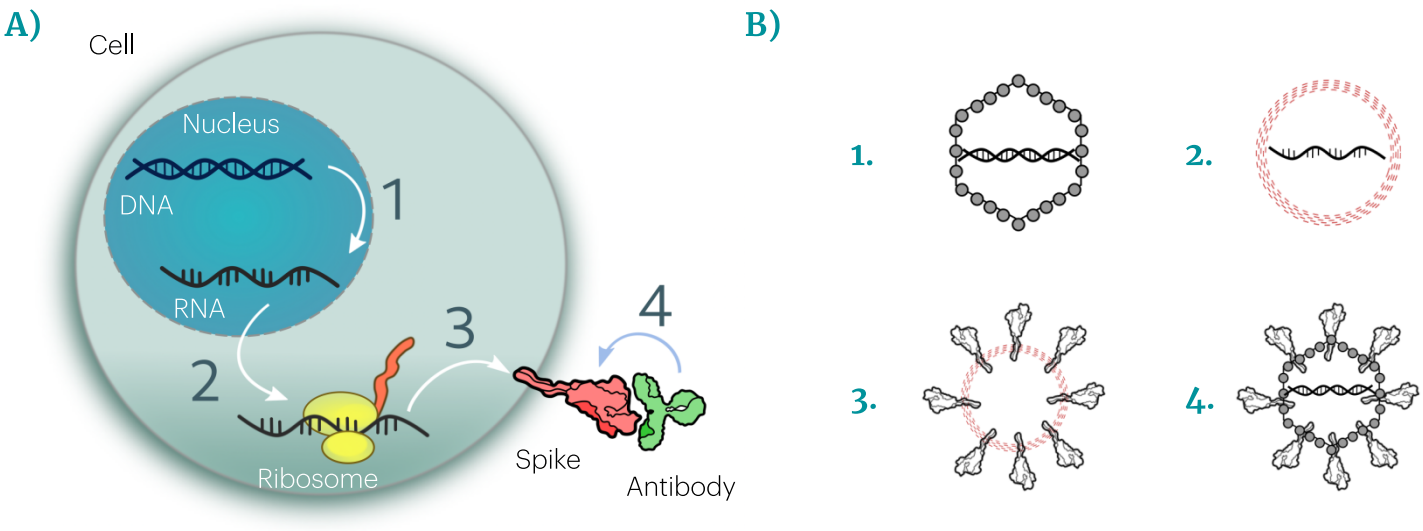

Figure 1: Various vaccine technologies

A) Cells produce proteins by transcribing genetic information from DNA into RNA (1), transporting the RNA to the ribosome (2) then translating RNA into functional protein (3). Vaccines instruct cells to generate **spike protein** by delivering therapeutic DNA, RNA or protein into this cellular pathway. Spike protein then stimulates the production of antibodies (4) and the immune response used to destroy viruses.

B) The four types of technologies used for Covid-19 vaccines: (1.) adenovirus containing DNA, (2.) lipid nanoparticle containing RNA, (3.) lipid nanoparticle containing protein, (4.) inactivated SARS-CoV2.

Reliable sources of information:

- World Health Organisation
- Centers for Disease Control and Prevention
- US Food & Drug Administration
- European Centre for Disease Prevention and Control
- European Medicines Agency

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