COVID-19 Vaccines: The Light at the End of the Tunnel

REGIONS ASSET MANAGEMENT

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The 2020 COVID-19 pandemic disrupted lives and economies all over the world. Stay at home orders and business closures were the norm for part of the year. Vaccines were considered the key to getting back to our pre-pandemic lives. In recent years, vaccine development has taken at least 3-4 years. However, due to the urgency of this pandemic, pharmaceutical and biotech companies used multiple approaches and conducted overlapping trials to reduce vaccine development time. Operation Warp Speed, a public private partnership was launched to help coordinate and accelerate this development. As a result of these efforts, the first COVID-19 vaccine developed by **Pfizer (PFE)/BioNTech (BNTX)** was granted Emergency Use Authorization (EUA) by the FDA on December 11, 2020[1]. This was followed by approval of another vaccine developed by **Moderna (MRNA)** which was granted Emergency Use Authorization (EUA) by the FDA on December 18, 2020[2]. This has been the fastest ever vaccine development.

COVID-19 Vaccines

To date, there are over 100 COVID-19 vaccine candidates in development. Of these, vaccines developed by PFE/BNTX and MRNA have already been approved in the U.S. and EU. The **AstraZeneca (AZN)/Oxford University** vaccine has been approved in the U.K. and India. Vaccines developed in China and Russia have also been approved in several countries. Vaccines developed by **Johnson and Johnson (JNJ), Novavax (NVAX)** and **Sanofi (SNY)** are in phase III trials (Table 1).

Table 1. COVID-19 Vaccines

Company	Method of Development	Doses Required	Status
PFE/BNTX	mRNA	2	Approved in the U.S and EU
MRNA	mRNA	2	Approved in the U.S and EU
AZN/Oxford University	Viral vector	2	Approved in U.K. and India
Gamaleya Research Institute (Russia)	Viral vector	2	Approved in Russia, Belarus, Argentina
Sinopharm (China)	Viral vector	2	Approved in China, UAE, Bahrain, Thailand
JNJ	Viral vector	1	Phase III
SNY	Viral vector	2	Phase III
NVAX	Nanoparticle	2	Phase III

Both PFE/BNTX and MRNA vaccines have been developed using the mRNA technology. This is the first time a vaccine has been developed using this technology. Both vaccines need a booster shot within 3-4 weeks in order to achieve maximum effectiveness. Distribution of these vaccines is challenging, especially the PFE/BNTX vaccine, due to extreme cold storage requirements. JNJ, AZN/Oxford, Sanofi are using traditional methods (viral vectors) for development and do not have stringent cold storage requirements. The JNJ vaccine is the only single dose vaccine. NVAX is also using new technology (nanoparticle) to develop its vaccine (Table 1).

It is important to note that clinical trial data has shown that the vaccines are effective in the prevention of symptomatic or severe COVID-19[3]. However, it is not clear if these vaccines prevent asymptomatic or mild COVID-19 or the transmission of the virus. Initial data from MRNA vaccine study indicated some reduction in asymptomatic infections. Complete data about asymptomatic infections and transmission will be available over the next few months. Also, both the vaccines have been approved for use in adults and children ages 16 years and older. Both PFE/BNTX and MRNA are conducting trials targeting children between 12 and 16 years. This data should be available by end of 2Q2021.

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Vaccine Efficacy

Table 2. Vaccine Efficacy

Company	Efficacy of COVID-19	Comments
PFE/BNTX	95%	94% in adults over 65, 52% efficacy after first dose
MRNA	95%	In all age groups
Gamaleya Research Institute (Russia)	92%	Data has not been made public
AZN	70%	62% for two full doses, 90% for half dose followed by full dose
Sinopharm (China)	79%	Data has not been made public

The efficacy of a vaccine is determined by the magnitude and type of immune response it can generate and is therefore dependent on the antigen protein (the spike protein for COVID-19) that is used to elicit the response which can vary between individuals. Ideally a vaccine should have 100% efficacy. However, due to various factors like the number of different strains of the pathogen and host immune response, most vaccines cannot achieve 100% efficacy. A vaccine with over 80-85% efficacy is considered a highly effective vaccine. Both the PFE/BNTX and MRNA vaccines have achieved over 90% efficacy in phase III trials. Efficacy of the AZN/Oxford University vaccine has ranged from 62-90%. There has been a lot of controversy about this efficacy range as different protocols used in the two phase III trials. In one trial, the first dose was only half the intended dose and the second dose was the full dose concentration. This vaccination protocol resulted in 90% efficacy. In the other phase III trial, where two full doses were given, the efficacy was 62%. Due to differences in protocol, AZN/Oxford University are conducting another phase III trial in the U.S. The Russian developed Sputnik V vaccine is claiming 92% efficacy; however, trial data has not been made public. Similarly, the Chinese vaccine claims to have 79% efficacy and trial data has not been made public (Table 2).

Vaccination Time Frame

In most countries, vaccination against COVID-19 is being managed by the respective governments which have made purchase agreements with various companies for vaccine supplies.

Vaccination time frame is currently limited by manufacturing capacity. Manufacturing bottlenecks during December 2020 resulted in limited supplies of vaccine doses from both the companies. As manufacturing ramps up in 2021, PFE/BNTX expect to manufacture 1.2B doses by end of 2021. MRNA expects to have 100 -125MM doses of its vaccine available globally in 1Q2021 and at least 600MM doses by the end of 2021. Both AZN and NVAX expect to manufacture up to 3B doses each in 2021. JNJ and GSK/SNY expect to manufacture about 1B doses in 2021 (Table 3).

In the U.S., PFE/BNTX and MRNA vaccines are the only vaccines that have been granted the Emergency Use Authorization (EUA) by the FDA. The Center for Disease Control (CDC) has recommended that front line health care workers and elderly population in nursing homes have first priority for vaccinations (phase 1a)[4]. These started in mid-December 2020. The next group to be vaccinated will be front line essential workers like teachers, police, firefighters, manufacturing workers, food and agricultural workers, grocery store workers, as well as people above 75 years old (phase 1b). Vaccination of the general population will begin after all these groups have been fully vaccinated. This is expected in the late spring or end of 2Q2021. By 2Q2021, several other COVID-19 vaccines will likely be granted EUA by the FDA. This will further improve vaccine availability.

Table 3. 2021 Vaccine Manufacturing Capacity

Company	2021 Worldwide Manufacturing Capacity
PFE/BNTX	1.2B
MRNA	600MM -1B
AZN	2-3B
JNJ	Over 1B
SNY	Up to 1B

Herd Immunity

Herd Immunity is viewed as resistance of a community to the spread of an infectious agent and is achieved when a large percent of population in that community has been vaccinated. The threshold of vaccinated population that is needed for developing herd immunity depends on the efficacy of the vaccine. Since both PFE/BNTX and MRNA vaccines have high efficacy, public health officials expect that herd immunity can be achieved if at least

70% of the population is vaccinated. Analysts expect enough vaccine doses to vaccinate about 70% of the population by Fall 2021.

A significant factor in achieving herd immunity is the willingness of people to get vaccinated. Given the speed of development and use of new technologies, there has been a lot of disinformation and skepticism about COVID-19 vaccines, especially on social media. As a result, only 62% of people surveyed in September 2020 were willing to get vaccinated. However, this has now increased to 71%. As more vaccines get approved, it is possible that the willingness to get vaccinated will further improve.

Virus Mutations

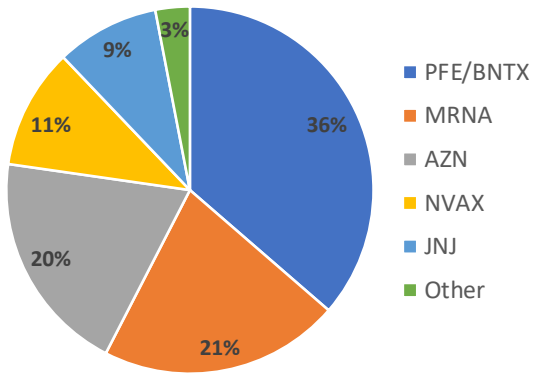
Most viruses develop mutations in order to evade the host immune response and improve their chances of infection and survival. As a result, mutations are a fairly common occurrence. Therefore, the new mutations in the SARS- Cov-2 that were initially identified in the U.K. are not surprising. All of the 17 mutations in the U.K. variant have been mapped to the spike protein that the virus uses to attach to the human cell receptor. So far, it appears that the mutated virus is not more virulent than the original virus, however, it does appear to be more transmissible. Due to the rapid spread of this variant, on January 4, 2021, U.K. imposed its third national lockdown. Another virus variant that has been identified in South Africa also has a mutation in its spike protein. That mutation appears to improve the virus's binding ability. A third spike protein mutation identified in the U.S. appears to allow the virus to replicate more efficiently in the upper respiratory tract compared to the lower tract of mice. This could potentially allow for increased transmission by coughing or sneezing.

The spike protein is also the protein that has been used to develop COVID-19 vaccines. So far, COVID-19 vaccines appear to be effective against all the variants. As the mutations are appearing on the spike protein, it is possible that the effectiveness of the current vaccines may decline over time. Therefore, it is very important to achieve herd immunity as soon as possible.

Investment Scenarios

Based on vaccine availability, pricing and estimates from various sources, we think that COVID-19 vaccine sales in 2021 may reach about $33B and may be split between the top five vaccine producers (Figure 1). We believe PFE/BNTX may get the highest revenue of about $12B, followed by MRNA with $7B, AZN with $6.5B, NVAX with $3.5B and JNJ with $3B. After a blockbuster 2021, we estimate sales to fall every year and reach about $6B in 2025, if a booster shot is required every three years.

Figure 1: 2021 COVID Vaccine Estimated Sales (Billions)



The average price for PFE/BNTX vaccine for developed countries is $39 for two doses. The estimated cost for manufacturing two doses of PFE/BNTX vaccine is about $15. This does not include distribution cost which is quite significant due to extreme cold storage requirements. Finally, along with milestone development payments, PFE will also make royalty payments based on vaccine sales to its partner BNTX. Therefore, while it is expected to generate $12B revenue in 2021 (about 25% of total revenue), COVID-19 vaccine is not expected to be very profitable for PFE.

Its partner BNTX is likely to benefit significantly more from this vaccine. It may generate about $4B revenue in 2021. Its 2021 revenue may increase over 1000% (y/y) from $620MM in 2020 to approximately $7B. It will likely turn profitable in 2021.

MRNA expects to price its vaccine at $10 -$50 per dose. In the U.S., it is priced at $15 per dose and in the EU at $18 per dose. Like BNTX, MRNA will see a significant benefit from its COVID-19 vaccine and may generate about $7B in 2021. This will likely be about 90% of its total 2021 revenue. Its 2021 revenue is may increase over 1400% (y/y) from $530MM in 2020 to approximately $8B. It will likely become profitable in 2021.

As this has been the first time that a successful product has been developed using mRNA technology, this

vaccine has also validated the (mRNA) research platform and will boost product pipelines for both BNTX and MRNA.

Another biotech company that could possibly benefit from its COVID-19 vaccine is NVAX. NVAX is using nanoparticle technology to develop its COVID-19 vaccine. Nanoparticle technology is also a new technology with no approved products. In phase II trials, its vaccine produced the highest immune response. It is currently in phase III trials. If approved, NVAX may see a significant benefit from its COVID-19 vaccine and may generate about $3.5B in 2021. This may be about 86% of its total 2021 revenue. Its 2021 revenue may increase over 640% (y/y) from $543MM in 2020 to approximately $4B. It will likely turn profitable in 2021.

Recently, NVAX also got positive results for its flu vaccine and is in the process of applying for FDA approval. NVAX is also exploring developing of a combination flu and COVID0-19 vaccine. If successful, this could be used for booster shots.

AZN and JNJ have stated that they will be pricing their vaccines at cost for this pandemic (about $4 -$10 per dose).

Summary

The COVID-19 pandemic had a major impact on our lives and caused a lot of hardship. Vaccines were considered the key to putting the pandemic behind us. Due to a concerted effort by the healthcare industry and the government, several COVID-19 vaccines were approved in December 2020. More vaccines are expected to be approved in 2021. Manufacturing capacity is also expected to be ramped up. As a result, herd immunity may be achievable by Fall 2021. COVID-19 vaccine sales of about $33B are expected to be split between the first five developers. Among these, the large pharmaceutical companies are expected to make very little or no profit from their COVID-19 vaccines whereas the three biotech companies are expected to reap significant revenues and profits from their vaccines.

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