Salvagene GROUP

Business Unit: SARS-CoV-2 Task Force
Keynote: #44

November 2020

Salvagene Vaccine & Medication Advisory Board: Still too soon for individual recommendations on vaccination.

Dear Premium Customers,

Unfortunately, it is still too soon for us to be making individual recommendations on vaccination. This is mainly because we do not recommend that our clients volunteer to be among the first 1-2 million recipients of any particular vaccine, as experience has shown that this is the stage at which adjustments to dosage take place and any unwanted side-effects generally manifest themselves.

Even with the three most advanced vaccines, significantly fewer samples have been tested in Phase 3 than would be the case in standard approval procedure.

Currently, 48 of the more than 100 vaccine projects worldwide are in clinical development, and ten of the most credible have reached Phase 3. These ten are also the projects that we have been following most closely since the beginning, i.e. since May.

As early as spring, we predicted that they would be the most successful in producing a viable outcome. As we have already mentioned on several previous occasions, these include the vaccine developed by BioNTech in partnership with manufacturer Pfizer, which has reported an efficacy of 95%. An application for emergency approval has been filed with the FDA, and we expect the go-ahead to be given approximately three weeks from now. Documentation has also been submitted to the European regulatory authority, EMA. This vaccine is mRNA-based (see Keynote 38). The advantage is that vaccines of this type can be produced relatively easily in large quantities. However, they require cooling to much lower temperatures than vector-based vaccines. The BioNTech vaccine can be stored at refrigerator temperatures for five days, but during transport, temperatures of at least minus 70 degrees Celsius are required. This presents a major problem. There are therefore a number of factors that we have to take into consideration in advising our clients: whether their own immune system profile is a good match for the BioNTech/Pfizer vaccine; whether it is even available in the country where the client lives; and the way in which it is to be administered locally. The logistics are a headache, and there is also the question of who is in charge of the vaccination program. There is currently no hard and fast rule in this area, neither in North America nor in Europe. There is also a debate about which of the priority groups is first in line for vaccination and about the criteria for and monitoring of distribution. In Europe, it is not yet clear whether these matters will be decided by the family doctor or by the vaccination centers that are currently being set up around the world.

Moderna is also mRNA-based, and its efficacy rate is more or less the same at 94.5%. It has the same advantage as all mRNA-based drugs. However, there is also a risk that unforeseen, long-term epigenetic changes may occur – even though the manufacturers may deny this – and that there could be unpredictable consequences. The advantage over vector-based vaccines, however, is that fewer side effects are to be expected in the short term. In our opinion, the Moderna vaccine can be distributed more easily. Here too, the logistics are associated with

temperatures well below freezing, but the product can be stored at refrigerator temperature for 20-30 days, which is significantly longer than the BioNTech version. It can therefore be assumed that the BioNtech/Pfizer vaccine will be administered more in vaccination centers, while the Moderna vaccine will also be made available via general practitioners. Here too, we expect an application for emergency approval in the next 2-3 weeks. This means that we can expect the time lag between Moderna and BioNtech/Pfizer to continue. The European regulatory authority has also initiated an accelerated approval procedure.

The AstraZeneca project has already been at number three in our charts for some months now. It has been trialed in various countries, albeit with a number of temporary halts along the way. Dosage plays a role here. With the right strength, i.e. only 50% of volume on the first shot and full volume on the second, 90% efficacy can be achieved. This vaccine is the leader in the vector-based segment of the market. Discussions with the FDA are expected to start in the next few days and they are also in contact with the authorities in the UK and Europe. We expect the AstraZeneca vaccine to become available from mid-January onwards in Europe and mid or late January in the USA. The big advantage is that storage of up to six months at refrigerator temperatures is possible. This brings huge benefits in terms of transport and distribution. We assume that some countries will want to involve family doctors' practices, as handling is much easier there. We consider the risk of short-term side-effects to be much greater than with mRNA-based vaccines. On the other hand, we are reasonably confident that there will be no long-term damage. We also consider this project to be suitable for older people (65+), as the above-mentioned side-effects were significantly lower in the clinical phase.

There is another mRNA project, namely the one being undertaken by the German company CureVac, and we expect that the logistic problems arising from extremely low storage temperatures will be less pronounced. We consider this project to be the best of all mRNA-based vaccines. Unfortunately, we estimate that it will not

be available in the USA and Europe until mid or late February at the earliest, and thus only at the end of the anticipated third wave.

There is also another vector-based project from Johnson & Johnson. Here too, there have been some stops during the trials, and so we expect the rollout of this product in the USA and EU in February or March at the earliest.

There are several projects originating from China. The most interesting one for us has been the one being done by Sinovac because its clinical phase has been characterized by transparency, just like the one of BioNTech. It has also gone through Phase 3 in various countries such as Indonesia, Turkey and Brazil, especially during the period when Brazil was being ravaged by the pandemic. We consider the data to be very impressive. Emergency approval has already been given by the Chinese government and provisional approval by the Brazilian federal state of Sao Paulo.

Sinopharm is also worth a mention. We have already reported on Sinopharm and Sinovac in great detail, and we think these two are the best to emerge from China. Sinopharm has even gone so far as to have two different vaccine projects running in Phase 3, and we suspect that almost one million people may already have been vaccinated. As far as we know, the data comes mainly from Argentina, Morocco, Bahrain and Peru. Again, the figures are very impressive and give hope that the pandemic will be under control worldwide, but especially in Asia, in the course of 2021. In addition to the recommendations and projects mentioned above, we are also evaluating whether and when we can recommend an alternative solution for our Premium clients. Sputnik from Russia is definitely not in the frame, since no clear results from Phase 3 have been published yet. Although we are monitoring this project very closely, we will not be making any recommendation for the time being.

We assume that, as discussed in our last Keynote, we will be able to make individual recommendations on vaccination starting in around 4-6 weeks. As we have often said before, this depends not only on the vaccine and its advantages and disadvantages as well as its availability, but also on our own analyses and profiles as tested within the scope of our Covid-19 Immunization Program. We will be advising clients who have a Covid19 Risk Factor of less than 0.8 and a Cytokine Risk Factor of less than 0.9 to wait. This is because their immune system, especially the NK cells, the T-helper cells and the Memory T cells which are needed for immune defense in the event of a SARS-CoV2 infection, are already optimized in such a way that none of the vaccines listed here would likely be advantageous but only affect the fourth pillar, namely antibody production. It therefore comes down to an individual assessment of whether the benefit is really greater than the risk of short-term or long-term side-effects. In the case of our Premium client segment, we believe that there is still the alternative strategy of making the missing antibodies accessible to an optimized immune system by means of antibody therapy. There are a number of projects in this area which, unfortunately, have not yet reached maturation. Foremost among them is the Regeneron project, an antibody therapy that offers a therapeutic option in the event that an individual has already become infected. From our point of view, it is not suitable for preventive application, because of the cross-reactions which could be triggered by the two antibodies that Regeneron uses.

We will keep you up to date in the coming weeks, quite possibly on a daily basis. We will send notifications via push messaging on our Salvagene Premium App. Premium clients who have not yet downloaded it are urged to do so without delay.

SALVAGENE HQ
Université Paris Sorbonne
125 Rue Saint-Jacques, 75005 Paris

SALVAGENE UK
52 Grosvenor Gardens • SW1W 0AU London UF
Tel: 0044 20 3287 0644

SALVAGENE USA
101 Avenue of the Americas, 8th floor • 10013 New York
Tel: +1 646 583 0370

info@salvagene.com • www.salvagene.com