Salvagene GROUP

Business Unit: SARS-CoV-2 Task Force
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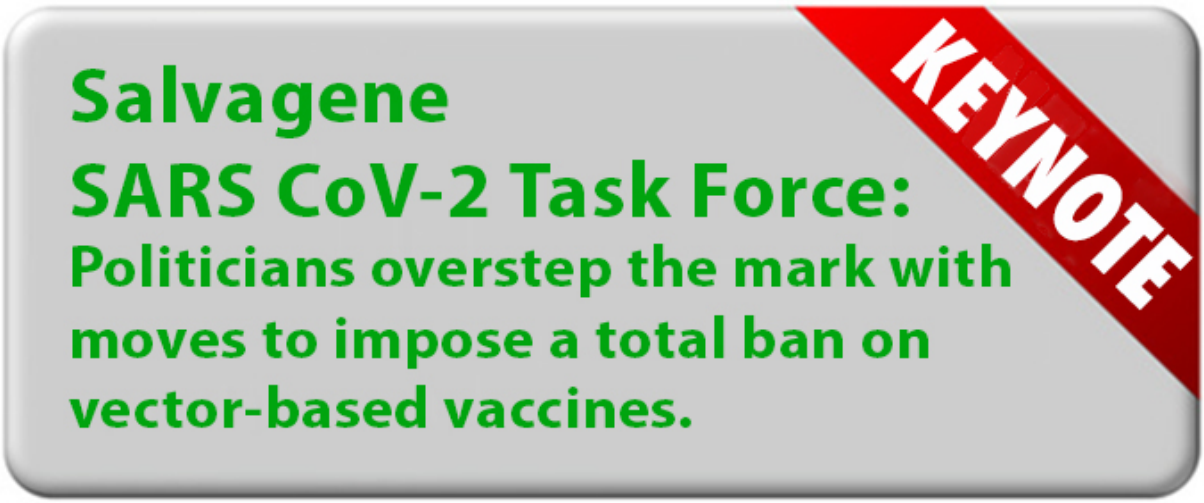

Dear Premium Customers,

We think that the lobbying power of the various pharmaceutical manufacturers – especially in Washington, Brussels and Amsterdam – will prove strong enough to ensure the continued deployment of vector-based vaccines. The industry is able to make a convincing case that these vaccines are needed, especially in Third World countries. Firstly, because AstraZeneca is a very cheap vaccine to store and secondly because only a single dose of Johnson & Johnson has to be administered. These vaccines are therefore a good solution for countries with poor infrastructure.

We consider calls for a complete halt to the use of vector-based vaccines to be over the top, because we see a continuing role for them in combating the pandemic. Especially with their significantly

stronger activation of the interferon system compared to the mRNA vaccines and, in the case of AstraZeneca, the production of T-helper cells, these vaccines offer an enormous advantage for certain population groups. This is especially true for recipients whose interferon system is relatively weak, in particular those in the older age bracket. Conversely, the benefit here becomes a liability for younger people because of the risk that their interferon system might overreact and produce unwanted side-effects.

With mRNA vaccines, we see the disadvantage that the interferon system is not activated enough in older people and the response to an infection is therefore too weak. Where vector-based vaccines are used for certain age groups, however, it is desirable that these should employ two distinct vectors in order to preclude vector immunity. Furthermore, only human adenoviruses should be used. In other words, neither AstraZeneca nor Johnson & Johnson currently fulfill these conditions. We address the problem of vector-based vaccines for different age groups explicitly elsewhere.

We already wrote at length about the core problem of vector-based vaccines in our last two Keynotes. This is such a burning topic and there is such a divergence of information out there – some of which we believe to be plain wrong – that we consider it necessary to provide a further update. The latest development is that thousands of doctors and patients around the world have now been alerted to the risk of thrombosis and the number of reported cases has proliferated. However, many of these cases have nothing to do with the vaccine, so it is very difficult to filter out the ones that occur as a direct result of a recent inoculation. We have already indicated the overall mechanism whereby vector-based vaccines might lead to thrombosis, but at the same time, the details of cause and effect have not yet been ascertained. What we know so far is that there is a structure that binds to a protein in the blood called platelet factor 4 (Pf4). This changes the protein, which in turn leads to it suddenly being misinterpreted as a foreign substance by the immune system. Some people already have autoantibodies that bind to this protein. A comparable mechanism is known to occur with the anticoagulant drug heparin, with a very similar immune

reaction being observed, namely heparin-induced thrombocytopenia (HIT for short) as reported in our previous Keynote. This structure likewise comes from the adenovirus.

There are two possible explanations: either it is the surface of the virus or it is the genetic material of the pathogens. We know from the surface that it is negatively charged and this seems to favor binding to Pf4. The genetic material of the adenoviruses has the same property. Because most of the vectors never enter a cell, their DNA can also be found outside cells, for example as a result of a virus bursting. And with regard to HIT, it is well known that this negative charge is an important factor in molecules binding to Pf4 (platelet factor 4). We think that these complications only occur if an individual meets certain criteria. There may be a rare genetic predisposition that causes the immune system to respond in this way. We are already conducting research in this direction, but in the meantime, we assume that the corresponding antibodies are already in the blood because the body has already produced them in the past against another pathogen with very similar antigens. It is amazing how quickly this side-effect develops, often within the second week. If the immune system were to be confronted with this antigen for the first time, you would expect symptoms to become apparent much later – after three weeks or so. And you would also find some kind of antibodies in the blood. This means that the affected individual would have to have been in contact with something beforehand for the defense cells to form exactly the same antibodies. That something could be a completely harmless substance.

And in one area, we have already made a find. Scientists at Greifswald looking into HIT have already found clear indications that a previous inflammation of the oral gums can provoke the reaction. This in turn suggests that bacterial infections may play a role. The connection with a genetic predisposition, as with most autoimmune diseases, is a topic that we will be examining in greater depth over the coming weeks. There must always be a coincidence of two aspects, namely a genetic predisposition and the corresponding trigger.

Normally, the immune system keeps problematic antibodies in check. Vaccination would then cause the body's own control mechanisms to break down. **This is where the problem arises: because the body is flooded with excessively high doses of antigens, an originally harmless immune response can be transformed into a dangerous one.**

One syringe-full of AstraZeneca or Johnson & Johnson vaccine contains 50 billion adenoviruses. Such local concentrations are not reached with the common cold. The same goes for HIT: thrombosis does not occur in individuals who are given just a few shots of heparin and wear compression stockings to reduce the risk of thrombosis. These are more likely to be people who have received much larger doses during long operations.

Genetic molecules with negatively charged surfaces that potentially trigger autoimmune processes are also present in mRNA vaccines. One of the guiding principles here at Salvagene is that the danger of side-effects is always proportional to the size of the dose. In this case, the mRNA vaccines use much lower doses – BioNTech 30 micrograms and Moderna 100 micrograms – and in any case the DNA molecules of the adenoviruses are much larger than these molecules. This lowers the necessary dose considerably.

In those countries where the third vector-based vaccine – Sputnik V – is being administered, we have to point out that this is unfortunately being done with relatively little oversight. From tests that we have conducted, we know that this vaccine contains twice as many viruses as the AstraZeneca and Johnson & Johnson, namely hundreds of billions. We therefore assume that there is also considerable potential for problems here.

With regard to AstraZeneca and the aforementioned vector-based problem, there is the added complication that this vaccine contains

a chimpanzee-derived adenovirus. In many countries, especially in Europe, where the AstraZeneca vaccine was administered as a first shot, the second dose was subsequently not given. Some experts have claimed that, if no side-effects occurred during the administration of the first dose, they are highly unlikely to crop up after a second. We consider this assertion to be not only wrong but also irresponsible, because the relevant autoantibodies can still be present in the immune system. Consequently, the probability is even higher that the autoimmune reaction will then be significantly increased after a second jab. The solution that we envisage and are working on in our laboratory is to measure in advance the autoantibodies already present in the blood of individuals prior to first vaccination. In this way, we should be able to ascertain whether it is appropriate to exclude a vector-based vaccine individually and from the outset. This also makes sense in the long term, because we expect that the uncertainties surrounding vaccination will continue to be an issue for quite some time. Our proposal is that family doctors should be given extra training to help them decide when and with which vaccine a patient should be immunized after appropriate counselling and pre-testing.

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