To: [redacted]@planet.nl]
From: [redacted]
Sent: Wed 9/30/2020 9:53:48 AM
Subject: FW: Merck's experimental vaccine is given orally for easier use
Received: Wed 9/30/2020 9:53:48 AM

Van: [redacted] <[redacted]@rivm.nl>
Datum: 27 september 2020 om 15:11:34 CEST
Aan: [redacted] <[redacted]@rivm.nl>
Onderwerp: FW: Merck's experimental vaccine is given orally for easier use

Ter info

From: [redacted]) <[redacted]@minvws.nl>
Sent: zondag 27 september 2020 13:34
To: [redacted] <[redacted]@rivm.nl>; [redacted] <[redacted]@rivm.nl>
Cc: [redacted]) <[redacted]@minvws.nl>
Subject: FW: Merck's experimental vaccine is given orally for easier use

Ter informatie: inschatting van mijn [redacted] collega over de MSD Merck kandidaten.
Wellicht nuttig bij het opstellen van een advies.

Groet,
[redacted]

Van: [redacted]@aemps.es <[redacted]@aemps.es>
Verzonden: zaterdag 26 september 2020 13:47
Aan: [redacted]@ec.europa.eu; [redacted]@ec.europa.eu; [redacted]@ec.europa.eu; [redacted]) <[redacted]@minvws.nl>
Onderwerp: RE: Merck's experimental vaccine is given orally for easier use

A few words and thoughts on MSD vaccines

1) Measles Virus Platform.
This is the a measles virus in which the gene that codes for the S protein has been inserted (with some mutations to make it immunogenic but without functions that it would have in SARS-CoV2 virions). This is a replicative virus that will have several rounds of replication in the vaccinated individual (adenovirus do not replicate and express the S protein only in the cell they infect). They use a well-known strain of measles.
Main strengths: (a) MSD is one of the world's largest manufacturers of MMR vaccine (measles, rubella, mumps) so, if the vaccine works, no doubt they can manufacture millions of doses because they have already a working process in place. (b) at a 99.9%, the safety profile is already guaranteed as it should be the same of the measles vaccine that has been supplied in billions of doses. The rest up to 100% is due to lack of data in humans on the effect of incorporating the S protein. This would ensure that they can go very quickly from phase 1 to phase 2, and then to phase 3. Accordingly with their slides, that would mean phase 3 in early 2021 and efficacy data on May-June 2021. (c) only one dose will be needed because it is a replicative vector that will produce a more robust immune response.
Uncertainties: (a) only a few data based on this platform expressing other proteins and no licensed vaccine based on this platform. This raises questions on their immunogenicity and therefore what level of protection is going to confer. Remember that we are all vaccinated against measles and that previous vaccination may reduce the ability of the vaccine to infect cells and reduce the immune response against the S protein (not a problem for the first dose and can be managed by increasing the amount of virus /dose). (b) if they fail with a single dose (see above), they will have to prove the effect of the second dose because after the first dose a powerful immune response against measles would have been generated and that would decrease the effectiveness of the second dose.
Potential milestone to monitor before concluding any agreement: (a) they have to show us experiments in non-human primates both about immunogenicity and challenge; (b) phase 1 in humans (expected by the end this year). The question is how we entertain in the meantime.

2) VSV platform.
The vaccine is a cattle virus (VSV) that does not infect humans. In order to infect humans, the genome is modified, removing the gene for its external protein and inserting the S protein. In this case, unlike the measles platform, the S protein should be functional because the survival of the recombinant VSV virus itself depends on the S proteins full functionality (the same than in the wild type SRAS-CoV2)
Main strengths: (a) this platform has been used to manufacture an Ebola vaccine and therefore there is a relatively extensive safety database.
Uncertainties: (a) They would start Phase 1 at the end of this year, what means that it is a development that is very slow, with no efficacy data, I would say until the end of 2021; (b) the issue of using a wild type S protein raises concerns about safety what explains a relatively lengthy development.
Potential milestone to monitor before concluding any agreement: (a) we need to start with the non-clinical data; even if the non-clinical data is successful, they probably will proceed very slowly through phases 1, 2 and 3 to control a potential safety problem.

I hope this is useful
Best regards, colleagues

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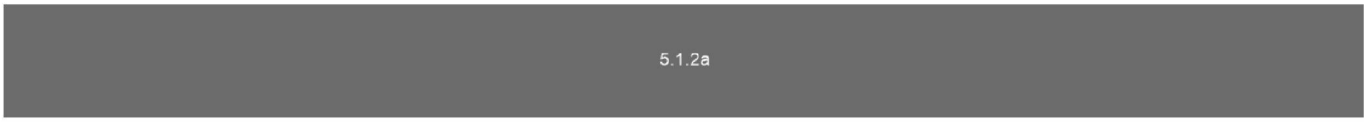
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