

FOR RELEASE: Updated Tuesday 9 February 2021

Phase I Trial of Novel COVID-19 Vaccine Candidate in South Africa

University of Cape Town researchers are due to commence a Phase I clinical trial of a hAd5 T-cell-based SARS-CoV-2 vaccine developed by the immunotherapy company, ImmunityBio, Inc. and manufactured by NantKwest, Inc. (NASDAQ: NK) - after approval from the South Africa Health Products Regulatory Authority (SAHPRA) was recently granted. The trial will be conducted at the Wellcome Centre for Infectious Diseases Research in Africa (CIDRI-Africa) Khayelitsha Clinical Research Site.

This Phase I trial (called Pro-VIVA-SA-1) will enroll 35 healthy participants and evaluate the safety and immune responses induced by the vaccine. Phase I trials are not sufficiently sized to address the question of whether the vaccine prevents infection or disease, but are a necessary first step towards Phase II and III trials which can address these questions. While high-income countries are already rolling out safe and effective vaccines, there are a number of reasons why this Phase I trial is critically important in South Africa.

1. Additional target in this vaccine candidate

Vaccines currently being administered internationally are designed to generate immunity against the SARS-CoV-2 Spike (S) protein alone. As already witnessed, the Spike (S) protein is mutation-prone, with variants 501Y.V2 and B.1.1.7 in this Spike (S) protein leading to higher transmissibility, increasing the urgency for a broader range of effective and safe COVID-19 vaccines to be available to the global population. There is also now evidence for certain vaccines that protection against the 501Y.V2 variant is reduced. In light of this, we will likely need alternative or adapted vaccines that are safe and effective against all current and future variants.

An additional protein in the SARS-CoV-2 virus is the Nucleocapsid (N) protein. The Nucleocapsid (N) protein appears to be much more stable over time and therefore has a lower risk of developing mutations that could risk vaccine failure. This Phase I clinical trial will be assessing a vaccine candidate that concurrently exposes the immune system to both the Spike (S) and Nucleocapsid (N) proteins. The dual construct of the hAd5 vaccine candidate has the potential to provide recipients with durable, long-term immunity induced by memory T-cells and memory B cells against SARS-CoV-2, including current and any future variants. This potentially includes immunity against the 501Y.V2 variant, which has been found in patients in South Africa and elsewhere.

"We are excited about the potential of our COVID-19 vaccine candidate, especially how it could solve the growing problem of new variants of the virus that have begun to appear," said Patrick Soon-Shiong, M.D, Chairman and CEO of ImmunityBio. "We're seeing these mutations around the world, causing serious outbreaks already in the UK and in my native South Africa. The mutations are occurring on the 'S' protein of the virus, which is why it's vital to pursue a vaccine that does not rely solely on targeting the S protein. Unlike those antibody-based vaccines, our T-cell-based vaccine candidate is intended to kill the infected cell to prevent the virus from replicating, and could provide long-term memory to recipients that would not be affected by S protein mutations."

President of the South African Medical Research Council Prof Glenda Gray said, "It is exciting for South Africa to partake in this innovative trial. This will be the first COVID-19 vaccine trial in South Africa, and one of only a handful globally, to test a candidate that targets the nucleocapsid as well as the spike protein."

2. A second-generation Adenovirus platform

A recognized constraint of Adenoviral-based vaccines is that they are less effective when a person already has immunity to the vaccine's Adenovirus "carrier" component. Immunity to the Adenovirus is commonly developed in childhood or via the use of other Adenoviral vaccines. However, a unique characteristic of the hAd5 design in this Phase I clinical trial is that it uses a second-generation hAd5 platform that has been shown to overcome preexisting Adenoviral immunity in multiple vaccine trials conducted in the USA. The ability to raise anti-SARS-CoV-2 immune responses even in Adenoviral-immune individuals means that individuals could effectively receive the vaccine multiple times, if necessary in the future.

Further, the ability of this vector to overcome pre-existing Ad5 immunity and still elicit immune responses suggests that the Ad5 vector is relatively undetected by the immune system. This is a necessary reassurance for trialing this particular platform in a high HIV incidence setting like South Africa. The reason for this is that there is a concern that previous Adenovirus vectors may have increased the risk of HIV acquisition in men. This was observed in the STEP and PHAMBILI trials more than a decade ago and was thought to be due to the immune responses elicited to the first-generation Ad5 vector used in those trials. The second-generation vector being used in this Phase I trial has been substantially modified to reduce immune responses to the Ad 5 vector and therefore, in theory, does not pose the same risk. Nonetheless participants will be counselled during the informed consent process and at each visit about potential increased HIV risk and provided with a package of HIV prevention measures, and this will be monitored during the trial.

3. Accessible vaccine candidate for South Africa

“This Phase I trial and the planned development strategy for this vaccine are critical for us in South Africa towards addressing the health and social crisis that COVID-19 has caused in our country and the threat posed by the spread of new variants. ImmunityBio has engaged with government agencies and indicated a commitment to ensuring this vaccine is available in South Africa, should it be shown to be safe and effective. Hence, the importance that we evaluate it here from Phase I trials onwards,” said Prof Graeme Meintjes, Second Chair in the Department of Medicine at the University of Cape Town, lead of CIDRI-Africa’s Clinical Platform and a co-investigator on the trial.

Dr Morena Makhoana, CEO of Biovac said, “A safe and universally effective COVID-19 vaccine that is easily accessible is critical for South Africa at this point in the pandemic. We believe that this Phase I trial is a crucial step for the country in this regard and are eager to see the outcomes of the trial.”

4. Expected timeline

A similar Phase I trial has already completed enrollment of two doses in participants in the USA and preliminary data indicate that the novel candidate has a favorable safety profile.

ImmunityBio and the UCT team of researchers led by Prof. Meintjes have been working in partnership with the South African Biovac Institute and have received authorization from the South African National Department of Agriculture, Forestry and Fisheries to import the vaccine into the country for testing. The study protocol has already been reviewed by the University of Cape Town Human Research Ethics Committee and South African Health Products Regulatory Authority (SAHPRA) and all relevant approvals are in place for this important trial to commence. The trial is expected to start in February 2021. Participants will receive two subcutaneous injections of the vaccine candidate 21 days apart and will be closely monitored for safety outcomes and immune responses generated. The evaluation of this novel COVID-19 vaccine, which has also been designed to be formulated in a room-temperature stable capsule and can be administered sublingually, is a critical step for South Africa in the fight against the pandemic. The plan is to evaluate the capsule and sublingual formulations in a follow-on trial.

Dr Soon-Shiong said: “We have begun clinical trials in the USA testing our room temperature stable oral version of the T-cell vaccine. Based on the encouraging results in the non-human primate studies in which these oral boosts to a subcutaneous prime provided complete protection to a Covid virus challenge, the potential for our second generation T cell vaccine to serve as a “universal boost” to the vaccines to be deployed in South Africa is exciting. We are committed to develop these vaccines in South Africa as well as supporting a manufacturing infrastructure so that the country could be self-sufficient.”

“I’m pleased to study this next-generation adenovirus vaccine platform for COVID-19 at the University of Cape Town. This is the third adenovirus-based COVID-19 vaccine to enter trials in South Africa. Understanding sensitivities related to adeno vaccine platforms in South Africa, we have taken the utmost care in designing our trial,” said Dr. Amy Ward, principal investigator of the Phase I trial.