CureVac Conference Call, November 10, 2020

Positive Interim Phase 1 Data of CureVac's COVID-19 Vaccine Candidate, CVnCoV

Presenters

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Operator Greetings and welcome to the positive interim Phase 1 data of CureVac's COVID-19 vaccine candidate CVnCoV.

At this time, all participants are in a listen-only mode. A question and answer session will follow the formal presentation. If anyone should require operator assistance during the conference, please press star, zero on your telephone keypad. As a reminder, this conference is being recorded.

I would now like to turn the conference over to your host, Sarah Fakih. Thank you. You may begin.

Sarah Thank you

Good morning, good afternoon, and welcome to our conference call. My name is Sarah Fakih, and I am the Vice President of Investor Relations at CureVac. Please let me introduce today's speakers. On the call with me are Franz-Werner Haas, the Chief Executive Officer of CureVac, Mariola Fotin-Mleczek, our Chief Technology Officer, and Pierre Kemula, the Chief Financial Officer.

Please note that this call is being webcast live and will be archived on the events and presentation section of our home page.

Before we begin a few forward-looking statements. The discussion and responses to your questions on this call reflect management's view as of today, Tuesday, November 10, 2020. We will be making statements and providing responses to your questions that state our intentions, beliefs, expectations, or predictions of the future. These constitute forward-looking statements for the purpose of the safe harbor provision. These statements involve risks and uncertainties that could cause actual results to differ materially from those projected.

CureVac disclaims any intentional obligation to revise any forward-looking statements.

For more information, please refer to our filings with the U.S. Securities and Exchange Commission. I will now turn the call over to Franz.

Franz Thank you, Sarah.

Ladies and gentlemen, a warm welcome to this conference call from all of us here at CureVac. Over the course of this presentation, we will provide you with the most important information from the interim Phase 1 data of our CVnCoV, our lead vaccine candidate to address COVID-19.

Please let me start by reminding you that the main goal of our comprehensive Phase 1 dose-escalation study was to assess safety as well as tolerability and to identify an optimal dose for our vaccine candidates to advance into a pivotal Phase 2b/3 trial with the best balance between tolerability and induced immunogenicity. We have achieved that goal, and I would like to highlight the following interim Phase 1 key outcomes, which we believe enable us to proceed into the next step in the clinical development of CVnCoV.

The interim data from our Phase 1 study shows that our vaccine candidate was able to induce a balanced immune response expressed by a strong induction of binding and neutralizing antibodies, as well as first indications of T cell activation. Based on our unique mechanism of action, I will describe in greater detail at a later point, we found that the quality of our induced immune response was comparable to recovered COVID-19 patients, thereby closely mimicking the immune activation following a natural COVID-19 infection. CVnCoV was generally well tolerated across the tested dose range of 2 to 12µg, with no observed serious adverse events and all other adverse events being transient and manageable.

The data we have collected strongly support our preference for a 12µg dose to advance into a pivotal Phase 2b/3 study and provide clear direction for further clinical development of CVnCoV. I would therefore like to reaffirm that given the necessary regulatory approval, we remain well on track to initiate a pivotal Phase 2b/3 study before the end of this year.

On slide four, you can see a condensed overview of the most important CVnCoV development milestones. Today's data follow our selection of a pre-clinically successful vaccine candidate earlier in 2020, which entered into a Phase 1 study in June of this year. Since March, we are also ramping up our GMP manufacturing for CVnCoV at our GMP III suite. And since then, we have used every manufacturing slot for the production of CVnCoV for our current and all planned clinical trials.

In September of this year, we also entered into a clinical Phase 2a study in Peru and Panama to confirm safety and evaluate the reactogenicity of CVnCoV in older adults, over 60-year-old, and in a geographical environment with a high incidence of COVID-19 infection at the time. We expect to provide initial interim data from this trial before the end of this year.

As I already highlighted, if it is approved by the regulatory authorities, we plan to initiate the pivotal Phase 2b/3 trial before the end of 2020, this year, which, if successful, would enable us to seek regulatory approval for CVnCoV in the first quarter of 2021.

I am now on slide five. To highlight our unique technology approach, which was based on the use of natural non-chemically modified messenger RNA, mRNA. Based on 20 years of experience with mRNA in medical applications, we have built extensive expertise and know-how of mRNA optimization, which allows us to extensively tailor the protein-coding as well as the untranslated regions of our unmodified constructs. Improved translation efficiency and ribosome interaction is a key optimization step that allows highly efficient protein production and forms the core of our ability to induce mRNA activity at very low doses.

Our other key optimization process improves the immunogenicity of our mRNA constructs. This is based on a unique and differentiated mechanism of action, which hinges on the induction of interferon type one signaling. Interferon type one is a key antiviral cytokine that mediates activation of the innate immune system and represents an important component of our own body's natural defense against any viral challenge by also activating T-cell responses. Through this differentiated mechanism of action, we believe our vaccine candidate is able to induce broad and balanced immune activation, including both humoral and cellular immune responses that closely mimics the natural immune response to COVID-19 infection.

Now, I would like to turn the call over to my colleague Mariola, our Chief Technology Officer, who will talk to you through the details and key data from our Phase 1 trial.

Mariola Thank you, Franz.

Moving on to slide six, I would like to give you a brief overview of the setup of our comprehensive Phase 1 clinical trial.

The study, which is still ongoing, assesses the safety, reactogenicity, and immunogenicity of our COVID-19 vaccine candidate, CVnCoV, which encodes for the full-length, pre-fusion stabilized Spike protein. The study has enrolled 261 participants at clinical sites in Germany and Belgium and assesses an intramuscular two vaccination regimen on day one and day 29. Participants in the study will be followed for at least one year after the second vaccination.

We will present to you today's detailed results from the full 2 and 8µg cohorts, as well as the sentinel group that received the 12µg dose consisting of 11 individuals. The latter dose is particularly important because we have selected it as our preferred dose as we move ahead with the clinical development of CVnCoV.

I am now on slide seven to update you on the observed safety and tolerability profile of our vaccine candidate. Shown here at the individual systemic, as well as local symptoms, observed for the 2, 8, and 12µg doses, as well as the placebo groups after the first and second vaccination.

Our vaccine candidate was generally well tolerated and showed no serious adverse events or any other dose-limiting effects. Data for each separate dose group were discussed in detail with an independent Data and Safety Monitoring Board to approve the recruiting of the dose group and clear initiation of the next higher dose. Tolerability profiles were considered to be acceptable across all tested doses.

For the data shown here, we see a dose-dependent increase in adverse events, with the majority of events accumulating around fatigue, headache, muscle pain, or myalgia and chills. Only a few fever events were recorded. All events were transient and rapidly resolved within 24 to 48 hours. It is interesting to note that the placebo group reported mild to moderate fatigue and headache adverse events as well.

Given that the 12µg dose was generally well tolerated, we were recently given approval by the Data and Safety Monitoring Board to also escalate to higher doses and have already initiated the testing of 16 and 20µg dose group. The ongoing dose escalation will not only further assess the safety and tolerability of our vaccine candidate at higher doses but will also allow us to further confirm our selection of a 12µg dose to morph into a pivotal Phase 2b/3 trial.

On slide eight, I would like to give you an overview of the conditions essay and competitor standards we have applied to greater clinical data in our Phase 1 study. Binding and neutralizing antibody immune responses were measured at the certified and experienced lab using two independent and also validated methods. The first method was an ELISA-based assay to detect antibodies binding either to the SARS-CoV-2 spike protein or to the receptor-binding domain of the protein.

The second method was a micro-neutralization assay with a Cytopathic Effect, applying the life human SARS-CoV-2 virus to measure the level of functional neutralizing antibodies. Antibody titers were then compared to the antibodies measured in a group of 67 convalescent individuals. This group of convalescent individuals is a key control group, which defines the standard against which we measure the strength of the immunogenicity induced by our vaccine. It represents a stringent comparison group of high clinical relevance.

All convalescent individuals in our pool were symptomatic, exhibiting multiple symptoms, including fever and shortness of breath. 24% of them were hospitalized. Blood samples were taken between four to eight weeks after the onset of symptoms, representing an optimal time window to provide peak antibody levels.

On slide nine, you can see the data for the spike binding antibodies for the 2, 8, and 12µg dose groups. Following our differentiated mode of action and low dose activity as highlighted earlier by Franz, we are very happy to see strong binding antibody responses in many individuals already at a very low dose of 2µg, which confirms good protein expression already at this low dose. As we move from 2µg into higher doses, binding antibody levels show a clear dose-dependence increase and at 12µg reach the medically relevant level set by the human convalescent sera panel.

On the next slide, you see a similar picture for neutralizing antibodies. Again, we see a very nice dose-response and good titers already at the 2µg dose in many individuals, which further increases at 8µg and reaches the level of our human convalescent sera panel 12µg.

What is particularly important to note is the additional time point of day 57 that we measured for 8µg. Here we are able to show that four weeks after the second vaccination on day 29, we see no decrease in neutralizing antibody levels. Antibody titers remain stable. This is highly encouraging for the longevity of the immune response induced by our vaccine candidate and we are also collecting this data for other dose growths as well.

Slide 11 shows our assessment of how the immune responses induced in vaccinated individuals compares to the immune responses observed in convalescent patients. For this, we looked at the ratios of neutralizing versus binding antibodies in all individuals of both groups. This ratio is highly important because we know that induction of high levels of antibodies that bind but do not have the ability to neutralize can be associated with a potential risk for disease enhancement.

And we were very happy to see that vaccinated individuals showed ratios that confirm good translation from binding into neutralizing antibodies that are very similar to what is seen naturally in infected and recovered patients. This is a clear hint that the immune response induced by our vaccine candidate mimics the natural immune responses we observe in patients who have recovered from COVID-19 infection. This is based on our unique mechanism of action and is further discussed on the next slide.

As Franz mentioned earlier, our technology is defined by the use of unmodified but specifically optimized messenger RNA, which was proven to enable high expression levels of encoded protein, but also to induce interferon type one mediated activation of innate immunity. This mechanism of action was demonstrated in many different animal models, always showing the same picture, good induction of antibodies, T-cell responses, and development of memory B and C cells.

We were able to prove the exact same mechanism of action in humans. You can see on the right-hand side of the slide the induction of interferon type one in humans vaccinated with 2 or 8µg of our COVID-19 vaccine candidate. As with any cytokine, induction needs to stay within a certain range. And it was encouraging to see that at 8µg, the interferon alpha level was up but still remained in the safe window below 15 picograms per milliliter in the blood.

And there are a lot of recent publications showing the importance of interferon type one signaling for the control of COVID-19 infection. These published data show that in patients with impaired interferon type one signaling, control of the disease is much more difficult. Therefore, with our specific mode of action, mimicking the natural immune response to SARS-CoV-2, we think our vaccine has the potential to significantly help control the continued spread of this virus and to potentially provide long-term protection owing to the induction of a memory response. The induction of memory responses after infection in seropositive subjects is shown on the next slide.

I am now on slide 13 to show you the results obtained from a defined population of seropositive study participants. In this study, participants had previously recovered from COVID-19 infection and our aim was to understand whether a vaccination on top of formerly mounted immune responses to COVID-19 is safe and beneficial.

Indeed, we saw that the vaccine was well tolerated in this specific population of seropositive individuals. But the learning from having seropositive individuals included in our trial is the induction of memory responses, which follow the natural of infection.

If you look at this graph, you see that even subjects with low titers, below 40, benefited from 2µg of CVnCoV and developed strong antibody responses that expanded more than 10-fold within only a few days. And this is a sign for good induction of memory responses in these subjects. According to this finding, we are convinced that the strength of a vaccine is not necessarily only reflected in the initial antibody titers but in the ability of the vaccine to induce potent memory responses.

And why we are confident that our vaccine is a good solution? Because based on our mechanism of action, we saw good induction of memory responses in different animal models as well as in our previous human rabies trial.

In the present Phase 1 clinical trial, we also see induction of cytokines important for the development of memory cells. And this is why we are optimistic that with CVnCoV, we will be able to prime people and also induce good memory responses.

Let me now hand the call back over to Franz for a brief summary.

Franz Thank you, Mariola.

Let me quickly summarize today's key takeaways before we move into the question and answer session.

We have achieved our goals to assess safety and identify an optimal dose for our vaccine candidate with the best balance between tolerability and induced immunogenicity to enable us to advance the clinical development with the 12µg dose.

The Phase 1 data confirmed that CVnCoV is well tolerated and demonstrates activity across all tested doses. With our preferred dose of 12µg, which currently represents the lowest mRNA dose in an advanced clinical trial, we plan to move into the pivotal Phase 2b/3 and subsequent regulatory approval processes.

With this, I would like to conclude our presentation and also would like to open the webcast to your questions. Thank you.