CUREVAC

Investor news


phase III

approximately 40,000 press release

Per protocol 36,500

June 17, 2021

The Curevac vaccine mRNA decisively failed in the second interim analysis of phase III. (article is not clear if the trial was suspended, and if it failed at the interim for superiority or failed for futility).

Potentially most seriously concerning is that nearly all cases of covid were from a virus mutation, not from SARS-CoV-2

https://www.fiercebiotech.com/biotech/curevac-s-first-gen-covid-19-vaccine-shows-only-47-efficacy-market-value-halved-after-hours?mkt_tok=Mjk0LU1RRi0wNTYAAAF9ufOR0m9eG9azZaEZKhvo0UEKKaBRCvzns8BNxeRnxcdQePAS4p6dIIE1bj_MQc3BcClq1_A0t_Gp4IEkJnG1yGgmjRZgVEtDgLUXw_mfBK52XLCc&mrikid=986425

https://tinyurl.com/nvd63twv

Preliminary data from CureVac's first-generation mRNA candidate vaccine showed that it was only 47% effective at preventing any severity of COVID-19.

The company said late Wednesday that the shot, which the European Commission signed up to buy an initial 225 million doses of late last year, had failed to meet the prespecified measure of statistical success in a phase 2b/3 study.
The 40,000-subject trial, spanning Latin America and Europe and conducted with help from Bayer, will still continue on to a final analysis in "the next few weeks," and the company said the initial data has been delivered to the European Medicines Agency.

The latest results included 134 cases that took place at least two weeks after the vaccine's second dose was administered: 57% of the cases were from so-called variants of concern, while only one was identified as the original SARS-CoV-2 virus.

Press release

June 16, 2021


- Pivotal study conducted in 10 countries in fast changing environment of at least 29 COVID-19 variant strains; original strain almost completely absent
- At second interim analysis, statistical success criteria not met. Favorable safety profile confirmed
- Initial analyses show trend for age and variant dependent efficacy
- Results communicated to EMA, study progressing to final analysis within the next few weeks

TÜBINGEN, Germany / BOSTON, USA – June 16, 2021

CureVac N.V. (Nasdaq: CVAC), a clinical-stage biopharmaceutical company developing a new class of transformative medicines based on messenger ribonucleic acid (“mRNA”), today announced results of the second interim analysis of its international pivotal Phase 2b/3 study in approximatively 40,000 subjects (the HERALD study) of CureVac’s first-generation COVID-19 vaccine candidate, CVnCoV. In the unprecedented context of at least 13 variants circulating within the study population subset assessed at this interim analysis, CVnCoV demonstrated an interim vaccine efficacy of 47% against COVID-19 disease of any severity and did not meet prespecified statistical success criteria. Initial analyses suggest age and strain dependent efficacy. Available data were communicated with the European Medicines Agency (EMA). The Data Safety Monitoring Board (DSMB) confirmed a favorable safety profile for CVnCoV. The study is continuing to the final analysis and the totality of the data will be assessed for the most appropriate regulatory pathway.

In total, 134 Covid-19 cases were assessed in this interim analysis. Out of these cases, 124 were sequenced to identify the variant causing the infection. The outcome confirms that only one single case was attributable to the original SARS-CoV-2 virus. More than half of the cases (57%) were caused by Variants of Concern. Most of the remaining cases were caused by other less characterised variants such as Lambda or C.37, first identified in Peru (21%) and B.1.621, first identified in Colombia (7%). In this context, the interim results suggest efficacy in younger participants but did not allow to conclude on efficacy in the age group above 60.

“While we were hoping for a stronger interim outcome, we recognize that demonstrating high efficacy in this unprecedented broad diversity of variants is challenging. As we are continuing toward the final analysis with a minimum of 80 additional cases, the overall vaccine efficacy may change,” said Dr. Franz-Werner Haas,
Chief Executive Officer of CureVac. “In addition, the variant-rich environment underlines the importance of developing next-generation vaccines as new virus variants continue to emerge.”

The HERALD study, conducted by Curevac in conjunction with Bayer, enrolled approximately 40,000 participants in ten countries in Latin America and Europe. The second interim analysis included 134 cases, occurring at least two weeks after administration of the second dose. To identify strains causing COVID-19 infections within the trial, sequencing of virus variants has so far been performed on 474 COVID-19 cases, of which 124 fulfilled adjudication criteria and were included in the present efficacy analysis.

CureVac remains committed to COVID-19 vaccine development. Beyond CVnCoV, the company develops in partnership with GSK second-generation COVID-19 vaccine candidates. These candidates are based on new mRNA backbones and include potential variants in multivalent vaccine formats as well as combination vaccines for potential protection against multiple infectious diseases in one vaccine. Preclinical data from the first vaccine candidate, CV2CoV, has recently been accepted for publication in Nature Communications. CureVac and GSK expect to progress the second-generation vaccine candidate into clinical testing in the third quarter of 2021, with the goal of introducing the vaccine in 2022, subject to regulatory approval.

CureVac will also host a webcast and conference call on Thursday, June 17, 2021 at 2:00 p.m. CET / 8:00 a.m. EST. The live conference call dial-in details and webcast link can be accessed via the Investor Relations section of the CureVac website at https://www.curevac.com/en/newsroom/events/

Corresponding presentation slides will be posted shortly before the start of the webcast. A replay will be made available on this website after the event.

About CVnCoV

CureVac began development of mRNA-based COVID-19 vaccine candidates in January 2020. The vaccine candidate chosen for first clinical development, CVnCoV, is an optimized, non-chemically modified mRNA, encoding the prefusion stabilized full-length spike protein of the SARS-CoV-2 virus, and formulated within Lipid Nanoparticles (LNPs). Phase 1 and 2a clinical trials of CVnCoV began in June and September 2020, respectively. Phase 1 interim data reported in November 2020 showed that CVnCoV was generally well tolerated across all tested doses and induced strong antibody responses in addition to first indication of T cell activation. The quality of the immune response was comparable to recovered COVID-19 patients, closely mimicking the immune response after natural COVID-19 infection. A pivotal Phase 2b/3, the HERALD study, with a 12µg dose of CVnCoV was initiated in December 2020. In February 2021, CureVac initiated a rolling submission with the European Medicines Agency (EMA) for CVnCoV.

About CureVac

CureVac is a global biopharmaceutical company in the field of messenger RNA (mRNA) technology, with more than 20 years of expertise in developing and optimizing the versatile biological molecule for medical purposes. The principle of CureVac’s proprietary technology is the use of non-chemically modified mRNA as a data carrier to instruct the human body to produce its own proteins capable of fighting a broad range of diseases. Based on its proprietary technology, the Company has built a deep clinical pipeline across the areas of prophylactic vaccines, cancer therapies, antibody therapies, and the treatment of rare diseases. CureVac had its initial public offering on the New York Nasdaq in August 2020. It is headquartered in Tübingen, Germany, and employs more than 700 people at its sites in Tübingen, Frankfurt, and Boston, USA. Further information can be found at www.curevac.com.
Protocol

The Curevac vaccine mRNA decisively failed apparently at the second(2) interim analysis of phase III. Article is not clear if the trial was suspended, and if it failed at the interim for superiority or for futility. Note (below) the trial assessed both superiority and futility.

- Potentially most seriously concerning is that nearly all cases of covid were from a virus mutation, not from SARS-CoV-2

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Table 8 of the clinical trial protocol gives the stopping rules at each interim

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the clinical trial protocol

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CureVac plans to move seamlessly into the phase 3 clinical trial if the data support the larger study. The phase 3 study will recruit 32,500 subjects. CureVac plans to pool data from the phase 2b and 3 portions of the clinical trial.

https://tinyurl.com/y6mukyab


The approach has created a candidate that triggers immune responses at a 12-µg dose, compared to the 100 µg used by Moderna. That will enable CureVac to make more doses of the vaccine. CureVac is also aiming to trigger balanced immune responses

Curevac is starting what appears to be an "adaptive seamless" phase 2b/3. Adaptive seamless are a large class of modern (<25 year old) clinical trial designs that "seamlessly" combine a phase 2 (sometimes called "learning phase") with phase III. The stated objective is to "accelerate clinical trials" aka shorten development time from first in human to marketing authorization and approval

The protocol (below) is thin on details about how the seamless combination is carried out. Typically the clinical trialists distinguish between "operationally seamless" (one protocol with a standard phase 2 and phase 3) and "inferentially seamless" -the phase 2 and phase 3 inferences (hypothesis tests) are combined. The inferentially seamless is "sort of" like a meta-analysis .There are hundreds of technical papers on the combination, better viewed as using "weighted averages of hypothesis tests". A main advantage of the operationally seamless is the IRB reviews and approves the phase 2 and phase 3 at one time, rather than each separately.

Ordinarily phase 2 and phase 3 are conducted completely separately with perhaps a 3 month to 1 year gap between the end of phase 2 and start of the phase 3. In the seamless, the "gap" disappears. the phase II ends (say on Monday ) and phase III starts the next day on Tuesday. The combination of hypothesis tests/inferences is a substantive statistical step and the detailed specifications must be reviewed by FDA.
A substantial part of biostatistical work is "pre specification" of all decisions to be made and extensive computer simulations. The simulations must prove to FDA that "Type I error" is controlled and identify -unforseen- or unexpected outcomes for the trials. once the trial is underway there is no (zero) option for an "oooppssss, we made a mistake, we'll make a quick fixup".

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The benefit is shortening development time by several months to as much as a year. And a further benefit is using phase II data as part of the Phase III trial. The press release below calls it "pooling" but it is not simply a matter of combining the datasets into one combined dataset.

The news has the overview of the seamless part.

CureVac is now putting its approach to the ultimate test. The phase 2b portion of the clinical trial will randomize 4,000 subjects across two age cohorts—18 to 60 years and 61 years and older—to take two doses of CVnCoV or placebo four weeks apart. Around 800 to 1,000 of the participants will be aged 61 years and older.

The phase 2b trial will generate safety, reactogenicity and immunogenicity data to inform the start of the phase 3. Once 1,000 subjects have at least one week of follow-up after the first vaccination, the Data and Safety Monitoring Board will review the data and make a decision on the phase 3.