REGENERON

Regeneron's REGN-COV2 Antibody Cocktail Reduced Viral Levels and Improved Symptoms in Non-Hospitalized COVID-19 Patients

September 29, 2020

TARRYTOWN, N.Y., Sept. 29, 2020 /PRNewswire/ --

Greatest improvements in patients who had not mounted their own effective immune response prior to treatment

Plan rapidly to discuss results with regulatory authorities

Regeneron to host investor and media webcast to discuss results at 4:30 pm ET today

Regeneron Pharmaceuticals, Inc. (NASDAQ: REGN) today announced the first data from a descriptive analysis of a seamless Phase 1/2/3 trial of its investigational antibody cocktail REGN-COV2 showing it reduced viral load and the time to alleviate symptoms in non-hospitalized patients with COVID-19. REGN-COV2 also showed positive trends in reducing medical visits. The ongoing, randomized, double-blind trial measures the effect of adding REGN-COV2 to usual standard-of-care, compared to adding placebo to standard-of-care.

This trial is part of a larger program that also includes studies of REGN-COV2 for the treatment of hospitalized patients, and for prevention of infection in people who have been exposed to COVID-19 patients.

"After months of incredibly hard work by our talented team, we are extremely gratified to see that Regeneron's antibody cocktail REGN-COV2 rapidly reduced viral load and associated symptoms in infected COVID-19 patients," said George D. Yancopoulos, M.D., Ph.D., President and Chief Scientific Officer of Regeneron. "The greatest treatment benefit was in patients who had not mounted their own effective immune response, suggesting that REGN-COV2 could provide a therapeutic substitute for the naturally-occurring immune response. These patients were less likely to clear the virus on their own, and were at greater risk for prolonged symptoms. We are highly encouraged by the robust and consistent nature of these initial data, as well as the emerging well-tolerated safety profile, and we have begun discussing our findings with regulatory authorities while continuing our ongoing trials. In addition to having positive implications for REGN-COV2 trials and those of other antibody therapies, these data also support the promise of vaccines targeting the SARS-CoV-2 spike protein."

The descriptive analysis included the first 275 patients enrolled in the trial and was designed to evaluate anti-viral activity with REGN-COV2 and identify patients most likely to benefit from treatment; the next cohort, which could be used to rapidly and prospectively confirm these results, has already been enrolled. Patients in the trial were randomized 1:1:1 to receive a one-time infusion of 8 grams of REGN-COV2 (high dose), 2.4 grams of REGN-COV2 (low dose) or placebo. All patients entering the trial had laboratory-confirmed COVID-19 that was being treated in the outpatient setting. Patients were prospectively characterized prior to treatment by serology tests to see if they had already generated antiviral antibodies on their own and were classified as seronegative (no measurable antiviral antibodies) or seropositive (measurable antiviral antibodies). Approximately 45% of patients were seropositive, 41% were seronegative and 14% were categorized as "other" due to unclear or unknown serology status.

Key data findings include:
Note that since this analysis was considered descriptive, all p-values are nominal.

- As hypothesized, patients in the study consisted of two different populations: those who had already mounted an effective immune response, and those whose immune response was not yet adequate. These populations could be identified serologically by the presence (seropositive) or absence (seronegative) of SARS-CoV-2 antibodies, and/or by high viral loads at baseline.
- **Serological status highly correlated with baseline viral load (p<0.0001).** Seropositive patients had much lower levels of virus at baseline, and rapidly achieved viral loads approaching lowest levels quantifiable (LLQ), even without treatment. In contrast, seronegative patients had substantially higher viral levels at baseline, and cleared virus more slowly in the absence of treatment.
- **Serological status at baseline also predicted how rapidly patients had alleviation of their COVID-19 clinical symptoms.** In the untreated (placebo) patients, seropositive patients had a median time to alleviation of symptoms of 7 days, compared to seronegative patients who had a median time to alleviation of symptoms of 13 days.
- **REGN-COV2 rapidly reduced viral load through Day 7 in seronegative patients (key virologic endpoint).** The mean time-weighted-average change from baseline nasopharyngeal (NP) viral load through Day 7 in the seronegative group was a 0.60 log10 copies/mL greater reduction (p=0.03) in patients treated with high dose, and a 0.51 log10 copies/mL greater reduction (p=0.06) in patients treated with low dose, compared to placebo. In the overall population, there was a 0.51 log10 copies/mL greater reduction (p=0.0049) in patients treated with high dose, and a 0.23 log10 copies/mL greater reduction (p= 0.20) in patients treated with low dose, compared to placebo.
- **Patients with increasingly higher baseline viral levels had correspondingly greater reductions in viral load at Day 7 with REGN-COV2 treatment.** The mean log10 copies/mL reduction in viral load compared to placebo were as follows:
  - Viral load higher than 10^5 copies/mL: high dose (-0.93); low dose (-0.86) (p=0.03 for both); approximately 50-60% reduction compared to placebo

- Viral load higher than 10^6 copies/mL: high dose (-1.55); low dose (-1.65) (p<0.002 for both); approximately 95% reduction compared to placebo
- Viral load higher than 10^7 copies/mL: high dose (-1.79); low dose (-2.00) (p$\leq$0.0015 for both); approximately 99% reduction compared to placebo
- **Patients who were seronegative and/or had higher baseline viral levels also had greater benefits in terms of symptom alleviation**. Among seronegative patients, median time to symptom alleviation (defined as symptoms becoming mild or absent) was 13 days in placebo, 8 days in high dose (p=0.22), and 6 days in low dose (p=0.09). Patients with increasing viral loads at baseline had correspondingly increasing benefit in time to symptom alleviation.
- **There were a small number of medically-attended visits given that most non-hospitalized patients recover well at home**. Patients in the seronegative group were at higher risk of medically-attended visits: 10 of the 12 medically-attended visits (defined as hospitalizations, or emergency room, urgent care or telemedicine visits for COVID-19) occurred in patients who were seronegative at baseline. In the seronegative group, 15.2% of placebo-treated patients, 7.7% of patients treated with high dose and 4.9% of patients treated with low dose required additional medical visits.
- **Both doses were well-tolerated.** Infusion reactions were seen in 4 patients (2 on placebo and 2 on REGN-COV2). Serious adverse events occurred in 2 placebo patients, 1 low dose patient and no high dose patients. There were no deaths in the trial.

More than 2,000 people have been enrolled across the overall REGN-COV2 development program, and no unexpected safety findings have been reported by the Independent Data Monitoring Committee.

"Thank you to the global investigators, sites and patients who continue to work with us to conduct REGN-COV2 trials, especially given the unique challenges posed by the pandemic," said David Weinreich, M.D., Senior Vice President and Head of Global Clinical Development at Regeneron. "We plan rapidly to submit detailed results from this analysis for publication in order to share insights with the public health and medical communities. Regeneron continues to enroll patients in this trial and all other ongoing late-stage trials evaluating REGN-COV2."

Additional Trial Background
Among the first 275 patients, approximately 56% were Hispanic, 13% were African American and 64% had one or more underlying risk factors for severe COVID-19, including obesity (more than 40%). On average, patients were 44 years of age. In total, 49% of participants were male and 51% were female.

At least 1,300 patients will be recruited into the Phase 2/3 portion of the outpatient trial overall. Patients will be followed for 29 days, with viral shedding in the upper respiratory tract assessed approximately every 2-3 days in the Phase 2 portion of the trial and clinical endpoints assessed via investigator and patient-reported data throughout.

In addition to this trial in non-hospitalized patients, REGN-COV2 is currently being studied in a Phase 2/3 clinical trial for the treatment of COVID-19 in hospitalized patients, the Phase 3 open-label RECOVERY trial of hospitalized patients in the UK and a Phase 3 trial for the prevention of COVID-19 in household contacts of infected individuals. Recruitment in all 4 trials is ongoing.

Investor and Media Webcast Information
Regeneron will host a conference call and simultaneous webcast to share updates on REGN-COV2 today September 29, 2020 at 4:30 pm ET. To access the call, dial (888) 660-6127 (U.S.) or (973) 890-8355 (International). A link to the webcast may be accessed from the "Investors and Media" page of Regeneron's website at www.regeneron.com. A replay of the conference call and webcast will be archived on the Company's website and will be available for at least 30 days.

About REGN-COV2
REGN-COV2 is a combination of two monoclonal antibodies (REGN10933 and REGN10987) and was designed specifically to block infectivity of SARS-CoV-2, the virus that causes COVID-19.

To develop REGN-COV2, Regeneron scientists evaluated thousands of fully-human antibodies produced by the company's *VelocImmune*® mice, which have been genetically modified to have a human immune system, as well as antibodies identified from humans who have recovered from COVID-19. The two potent, virus-neutralizing antibodies that form REGN-COV2 bind non-competitively to the critical receptor binding domain of the virus's spike protein, which diminishes the ability of mutant viruses to escape treatment and protects against spike variants that have arisen in the human population, as detailed in *Science*. Preclinical studies have shown that REGN-COV2 reduced the amount of virus and associated damage in the lungs of non-human primates.

REGN-COV2's development and manufacturing has been funded in part with federal funds from the Biomedical Advanced Research and Development Authority (BARDA), part of the Office of the Assistant Secretary for Preparedness and Response at the U.S. Department of Health and Human Services under OT number: HHSO100201700020C. Regeneron has recently partnered with Roche to increase the global supply of REGN-COV2. If REGN-COV2 proves safe and effective in clinical trials and regulatory approvals are granted, Regeneron will manufacture and distribute it in the U.S. and Roche will develop, manufacture and distribute it outside the U.S.

About Regeneron
Regeneron (NASDAQ: REGN) is a leading biotechnology company that invents life-transforming medicines for people with serious diseases. Founded and led for over 30 years by physician-scientists, our unique ability to repeatedly and consistently translate science into medicine has led to seven FDA-approved treatments and numerous product candidates in development, all of which were homegrown in our laboratories. Our medicines and pipeline are designed to help patients with eye diseases, allergic and inflammatory diseases, cancer, cardiovascular and metabolic diseases, pain, infectious diseases and rare diseases.

Regeneron is accelerating and improving the traditional drug development process through our proprietary *VelociSuite* technologies, such as *VelocImmune*®*,* which uses unique genetically-humanized mice to produce optimized fully-human antibodies and bispecific antibodies, and through

ambitious research initiatives such as the Regeneron Genetics Center, which is conducting one of the largest genetics sequencing efforts in the world.

For additional information about the company, please visit www.regeneron.com or follow @Regeneron on Twitter.

Contacts:

Media Relations
Alexandra Bowie
Tel: +1 (914) 847-3407
alexandra.bowie@regeneron.com

Investor Relations
Mark Hudson
Tel: +1 (914) 847-3482
mark.hudson@regeneron.com

C View original content:http://www.prnewswire.com/news-releases/regenerons-regn-cov2-antibody-cocktail-reduced-viral-levels-and-improved-symptoms-in-non-hospitalized-covid-19-patients-301140336.html

SOURCE Regeneron Pharmaceuticals, Inc.