Novartis International AG
Novartis Global Communications
CH-4002 Basel
Switzerland

https://www.novartis.com
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MEDIA & INVESTOR RELEASE

Novartis provides update on CAN-COVID trial in hospitalized patients with COVID-19 pneumonia and cytokine release syndrome (CRS)

- *The Phase III trial investigating canakinumab plus standard of care (SoC) did not meet its primary endpoint of a greater chance of patient survival without the need for invasive mechanical ventilation, or its key secondary endpoint of reduced COVID-19 mortality, compared with SoC[1]*

- *Ilaris® (canakinumab) remains an effective treatment option for its approved indications, with a well-characterized safety profile[2,3]. The safety profile of canakinumab plus SoC in CAN-COVID was comparable to placebo plus SoC[1]*

- *Interim Day 29 results will be submitted for peer-reviewed publication to further support the scientific understanding of COVID-19 infection and potential treatments*

- *Novartis further strengthened its pandemic response efforts by collaborating with Molecular Partners to develop two DARPin® therapies for potential use against COVID-19[4]. In addition, a Phase III trial for ruxolitinib in COVID-19 is ongoing, with preliminary results expected by year end[5]*

Basel, November 6, 2020 — Novartis today announced new data from an interim analysis for the randomized, double-blind, placebo-controlled CAN-COVID trial evaluating the efficacy and safety of canakinumab in hospitalized patients with COVID-19 pneumonia and cytokine release syndrome (CRS)[6]. The ongoing trial failed to meet its primary endpoint showing that treatment with canakinumab plus standard of care (SoC) did not demonstrate a significantly greater chance of survival for patients without the need for invasive mechanical ventilation, compared with placebo plus SoC up to Day 29[1]. The trial did not meet its key secondary endpoint of reducing the COVID-19-related death rate during the 4-week period after treatment[1]. The safety profiles of canakinumab plus SoC and placebo plus SoC were comparable[1].

“Though the CAN-COVID trial did not show the patient benefit we were hoping for, it helps improve the scientific understanding of COVID-19 and the role of interleukin-1β inhibition,” said John Tsai, M.D., Head of Global Drug Development and Chief Medical Officer for Novartis. “There’s still an urgent need for effective ways to combat COVID-19 and we will continue to apply our best scientific minds in support of the global pandemic response, including a Phase III trial of ruxolitinib. We’re deeply grateful to the patients who participated and their caregivers, as well as the healthcare professionals and hospital staff who made this research possible while fighting the pandemic on the front line.”

In the trial, the primary endpoint of survival without the need for mechanical ventilation was 88.8% for canakinumab plus SoC vs 85.7% for placebo plus SoC (*P*=0.29)[1]. The key secondary endpoint of COVID-19-related mortality up to 4 weeks was 4.9% for canakinumab plus SoC vs 7.2% for placebo plus SoC (*P*=0.33)[1]. Both the primary and key secondary endpoints trended in favor of canakinumab but did not reach statistical significance[1]. No new safety signals for canakinumab were identified[1].

This interim analysis will be submitted to a peer-reviewed journal in the coming weeks. The CAN-COVID results do not affect any other ongoing trials for canakinumab, including investigations for the treatment of non-small cell lung cancer (NSCLC)[7-9].

As part of its continued efforts to support the global pandemic response, Novartis in October announced a collaboration with Switzerland-based Molecular Partners to develop two DARPin® therapies designed for potential use against COVID-19[4]. In addition, a Phase III trial for ruxolitinib in COVID-19 is ongoing, with preliminary results expected by year end[5].

About CAN-COVID
CAN-COVID is a Phase III, multicenter, randomized, double-blind, placebo-controlled trial to assess the efficacy and safety of canakinumab plus standard of care (SoC) in hospitalized patients with COVID-19 pneumonia and cytokine release syndrome (CRS)[6]. Patients were hypoxic but not requiring intubation or invasive mechanical ventilation[6]. The primary endpoint was to demonstrate the benefit of canakinumab plus SoC vs placebo plus SoC in increasing the chance of survival without the need for invasive mechanical ventilation up to Day 29[6]. The key secondary endpoint was to reduce the COVID-19-related death rate during the 4-week period after trial treatment[6]. The trial enrolled 454 patients at multiple centers across the US, Russia and Europe[1]. Both endpoints were analyzed at Day 29[6]. The average age of trial participants was 58 years old, ranging from 18 to 98 years old[1]. Approximately 30% were Hispanic or Latino, 16% were Black or African American and 4% were Asian[1]. Interim analysis of Day 29 results is available. The trial is ongoing (to Day 127) with full results expected in early 2021[6].

About canakinumab
Canakinumab is biologic medicine used in the treatment of a number of rare, debilitating auto-inflammatory diseases, for which there are limited options available. It is a monoclonal antibody that binds to and neutralizes interleukin-1 beta (IL-1β), blocking its action[2,3,10]. Excessive production of IL-1β plays a prominent role in certain inflammatory diseases and immune responses[11,12]. Canakinumab is an established medicine approved under the trade name Ilaris® in approximately 60 countries including the US, Europe and others. It is indicated for rare conditions including periodic fever syndromes, adult-onset Still's disease (AOSD) and systemic juvenile idiopathic arthritis (SJIA)[2,3]. First approved in 2009, canakinumab has been proven to be highly effective and well tolerated as a treatment option for its approved indications based on previously reported clinical trials[2,3]. As well as being studied in severe COVID-19, canakinumab is also being investigated for the treatment of a number of other diseases involving inflammation, including non-small cell lung cancer (NSCLC)[7-9].

Novartis response to COVID-19 pandemic
Novartis is making multiple contributions to the global effort to combat the COVID-19 pandemic and support the stability of global healthcare systems. The company has committed to donating USD 40 million to support communities around the world impacted by the pandemic. In addition, Novartis is active in several key cross-industry research initiatives, the COVID-19 Therapeutics Accelerator, coordinated by the Bill & Melinda Gates Foundation, Wellcome, and Mastercard as well as a COVID-19 directed partnership supported by the Innovative Medicines Initiative (IMI)[13]. Novartis has also announced a collaboration with Molecular Partners to develop two DARPin® therapies designed for potential use against COVID-19, and the company is separately supporting COVID-19-related clinical investigations of several Novartis medicines[4]. We continue with the Phase III trial for ruxolitinib, another

Novartis medicine, in collaboration with Incyte[5]. Preliminary results from this trial are expected by year end. Two medicines in early stage development are also being investigated focusing on stopping or slowing the body's overactive immune response to COVID-19[14, 15]. In our labs, we have started a collaborative, longer-term drug discovery effort to develop an antiviral molecule to potentially treat all coronaviruses. To sustain access, the Novartis generics and biosimilars division Sandoz became the first company to commit to keeping stable prices for a basket of essential medicines that may help in the treatment of COVID-19 and entered into a partnership with US-based Civica Rx to support stable supply of essential generic hospital medicines. We are making 15 drugs that treat key symptoms of COVID-19 available to low- and lower-middle income countries at zero profit until a vaccine or curative treatment is found. This includes dexamethasone, which is the only medicine shown to decrease mortality so far in severe hospitalized COVID pneumonia[13]. Furthermore, Novartis Gene Therapies entered into a manufacturing agreement with Massachusetts Eye and Ear and Massachusetts General Hospital to produce its novel genetic COVID-19 vaccine candidate called AAVCOVID[16]. More information about the Novartis response to COVID-19 is available at www.Novartis.com/coronavirus

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About Novartis

Novartis is reimagining medicine to improve and extend people's lives. As a leading global medicines company, we use innovative science and digital technologies to create transformative treatments in areas of great medical need. In our quest to find new medicines, we consistently rank among the world's top companies investing in research and development. Novartis products reach nearly 800 million people globally and we are finding innovative ways to expand access to our latest treatments. About 110,000 people of more than 140 nationalities work at Novartis around the world. Find out more at https://www.novartis.com.

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Novartis Media Relations
E-mail: media.relations@novartis.com

Antonio Ligi
Novartis External Communications
+41 61 324 1374
antonio.ligi@novartis.com

Louise Clark
Novartis Pharma Communications
+41 723 3681 (mobile)
louise.clark@novartis.com

Eric Althoff
Novartis US External Communications
+1 646 438 4335
eric.althoff@novartis.com

Novartis Investor Relations
Central investor relations line: +41 61 324 7944
E-mail: investor.relations@novartis.com

Central		North America	
Samir Shah	+41 61 324 7944	Sloan Simpson	+1 862 778 5052
Thomas Hungerbuehler	+41 61 324 8425		
Isabella Zinck	+41 61 324 7188		