Novartis International AG
Novartis Global Communications
CH-4002 Basel
Switzerland

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

Novartis and Molecular Partners report positive topline data from Phase 2 study for ensovibep (MP0420), a DARPin antiviral therapeutic for COVID-19

- *Topline results from the randomized EMPATHY Part A study in acute COVID-19 ambulatory patients comparing single intravenous doses of ensovibep, a DARPin antiviral therapeutic candidate vs. placebo, met the primary endpoint of viral load reduction over eight days*

- *The secondary endpoint of hospitalization and/or ER visits related to COVID-19, or death showed an overall 78% reduction in risk of events across ensovibep arms compared to placebo*

- *A total of 407 patients were recruited in the Phase 2 study and ensovibep was safe and well-tolerated at all doses (75mg, 225mg and 600mg) – with 75mg the planned dose for further development*

- *Ensovibep continues to maintain potent in vitro pan-variant activity against all variants of concern identified so far, including Omicron*

- *Ensovibep is a multi-specific DARPin (Designed Ankyrin Repeat Protein), specifically designed to block the receptor binding domains of SARS-CoV-2 spike protein through highly potent and cooperative binding, making it challenging for escape mutants*

- *Novartis confirms it will exercise its option, paying CHF150 million to in-license ensovibep from Molecular Partners, accelerate manufacturing scale-up, and plans to seek expedited regulatory authorizations globally – first via the U.S. Food and Drug Administration's (FDA) Emergency Use Authorization (EUA)*

Basel, January 10, 2022 — Novartis and Molecular Partners today announced that Part A of the EMPATHY clinical trial[1] that compared single intravenous doses of ensovibep, a DARPin antiviral therapeutic candidate vs. placebo to treat COVID-19, met the primary endpoint of viral load reduction over eight days. The two secondary endpoints also showed clinically meaningful benefit over placebo – (1) composite endpoint of hospitalization and/or Emergency Room (ER) visits or death, and (2) time to sustained clinical recovery. Novartis confirms it will now exercise its option to in-license ensovibep from Molecular Partners and, following exercise of the option, will seek expedited access globally, first via the FDA's EUA process.

The global EMPATHY clinical trial, which is being conducted by Novartis, with Molecular Partners as sponsor, is a randomized, double-blind, placebo controlled study in ambulatory (non-hospitalized) adult patients with COVID-19. EMPATHY Part A enrolled 407 patients to identify a dose of ensovibep with optimal safety and efficacy and recruited patients in the USA, South Africa, India, the Netherlands and Hungary to explore three doses: 75mg, 225mg and 600mg.

Results from the study showed that the primary endpoint was met with a statistically significant reduction in viral load over eight days, compared to placebo, for all three dosing arms. The secondary endpoint of hospitalization and/or ER visits related to COVID-19, or death showed an overall 78% reduction in risk of events across ensovibep arms compared to placebo. Treatment arms were generally balanced in terms of demographic, baseline and disease characteristics. The placebo arm with 99 patients had a total of six events (event rate of 6.0%); five patients were hospitalized, two of whom died due to worsening of COVID-19 and one patient had an ER visit only. In the 301 patients treated with ensovibep, there were four events, hospitalizations occurred in two patients and two needed to visit ER (event rate of 1.3%). No deaths occurred in any of the patients treated with ensovibep. All doses were well-tolerated and no unexpected safety issues were identified for any of the doses[2] . The lowest dose of 75mg is the planned dose for further development. The data will now undergo further review so that Novartis and Molecular Partners can determine the appropriate next steps for the program.

“We are pleased that the results from the EMPATHY trial demonstrate the positive therapeutic effect of ensovibep, with the potential to be an important new treatment option to combat the rapidly evolving SARS-CoV-2 pandemic,” said Vas Narasimhan, CEO of Novartis. “As COVID-19 continues to burden healthcare systems across the globe, a range of treatments will be needed, and Novartis is proud to continue our collaboration with Molecular Partners on this unique treatment for COVID-19 and contribute ensovibep to this suite of options.”

With the decision made to exercise the option, Novartis will become responsible for development, manufacturing, distribution and commercialization activities of ensovibep. Novartis has already initiated scale-up activities in its large-scale biologics production facilities.

As the SARS-CoV-2 virus evolves, a multi-solution strategy is needed to combat the pandemic and there will be a need for antiviral treatments to complement the global vaccination efforts. Despite availability of vaccinations, there continues to be disease transmission, either through pockets of unvaccinated populations, in patients with compromised immune systems and co-morbidities or through emerging variants, and breakthrough infections are likely to continue. A recent in vitro analysis[3] also showed that ensovibep maintains full neutralization of the pseudoviruses containing the mutations identical to the Omicron variant of concern.

“These encouraging results come at a time when the need for therapies with pan-variant activity, such as ensovibep, has never been greater. We are incredibly excited about the opportunity to provide a potential therapeutic option for patients around the world who require access to effective COVID-19 treatments,” said Patrick Amstutz, Ph.D., CEO of Molecular Partners. “Today’s data are a culmination of a persistent team effort, between ourselves and Novartis, to deliver a tailored antiviral with demonstrated safety and efficacy in global clinical trials. As pioneers of DARPin therapeutics, our team has the unique ability to rapidly generate and develop multi-specific DARPin therapeutics. We look forward to continue to demonstrate our capabilities and the potential of our pipeline in oncology, virology and for patients in need.”

Given the pressing public health emergency and the rapid spread of the Omicron variant across the world, Novartis and Molecular Partners are in close liaison with regulatory bodies to seek expedited review and approval of ensovibep as soon as possible. If approved, ensovibep will be the first multi-specific antiviral molecule for the treatment of COVID-19.

About ensovibep

Ensovibep is a DARPin therapeutic candidate, designed specifically to inactivate SARS-CoV-2, the virus that causes COVID-19. DARPins (Designed Ankyrin Repeat Proteins) are mono or multi-specific protein-based therapies, designed to specifically engage their targets for various effects. Ensovibep was designed to include three individual DARPin domains, each highly neutralizing to SARS-CoV-2. With these domains constructed into a single molecule, ensovibep can block the receptor-binding domain (RBD) of the SARS-CoV-2 spike protein through highly potent and cooperative binding. This design ensures strong neutralization, even in the presence of mutations of the spike protein and limits the development of escape mutants. Several characteristics of DARPin therapeutics make them suitable for COVID-19 treatment, including multi-specific binding, the rapid onset of action, and scalable bacterial production.

In vitro testing has shown high neutralization activity of ensovibep against all known SARS-CoV-2 variants, including the variants of concern: Alpha, Beta, Gamma, Delta and Omicron.[3]

About the EMPATHY clinical trial program[2]

Following promising Phase 1 clinical data for ensovibep the global EMPATHY clinical trial was initiated by Novartis, with Molecular Partners as sponsor, in May 2021. EMPATHY is a Phase 2 and 3 study looking at the safety and efficacy of ensovibep in symptomatic COVID-19 patients in the ambulatory (non-hospitalized) setting. Ensovibep is administered via a single dose IV infusion.

The EMPATHY clinical trial plans to enroll 2,100 patients. 407 patients were randomized into four arms of Part A of the study to identify a dose with optimal safety and efficacy. The clinical efficacy and safety of this dose vs. placebo will be further evaluated in Part B, the Phase 3 component of the EMPATHY study which will enroll an additional 1,700 patients globally.

The EMPATHY clinical trial enrolled both vaccinated and unvaccinated adult patients who have experienced at least two mild/ moderate symptoms of COVID-19 within seven days of onset and had a positive rapid antigen test on the day of dosing, confirmed by a PCR test at baseline. The COVID-19 symptoms include fever, cough, sore throat, low energy, tiredness, headache, muscle or body aches, chills and/ or shortness of breath.

The collaboration with Molecular Partners

Novartis is proud to collaborate with Molecular Partners on the development of ensovibep, a DARPin therapeutic candidate designed for potential use against COVID-19. With the decision made to exercise the option, Novartis will be responsible for further development, manufacturing, distribution and commercialization activities of ensovibep. Under the terms of the agreement, Molecular Partners had received an upfront payment of CHF 60 million, including equity. Molecular Partners will receive a further payment of CHF 150 million, upon Novartis electing to take up the option on the therapeutic candidate, and significant royalties on sales. Molecular Partners has agreed to forgo royalties in lower income countries, and is aligned with Novartis' plans to ensure affordability based on countries' needs and capabilities.

Novartis response to the COVID-19 pandemic

Novartis is making a number of contributions to the global fight against the COVID-19 pandemic and supporting the stability of global health systems. The company announced an initial agreement with BioNtech to provide manufacturing capacity for a COVID-19 vaccine at its site in Stein, Switzerland. Novartis has also donated US $40 million to help communities affected by the pandemic around the world.

At Novartis Institutes of Biomedical Research, we have started a collaborative, longer-term drug discovery effort to develop the first oral medicines for COVID-19 and other coronaviruses. More information about the Novartis response to COVID-19 is available at www.novartis.com/COVID-19.

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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 108,000 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

Michael Meo
Novartis External Communications
+1 862 274 5414
michael.meo@novartis.com

Satoshi Jean Sugimoto
Novartis Switzerland Communications
+41 79 619 20 35
satoshi_jean.sugimoto@novartis.com

Julie Masow
Novartis US External Communications
+1 862 579 8456
julie.masow@novartis.com

Arzum Ustun
Novartis Global Health Communications
+41 79 108 5314
arzum.ustun@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	+1 862 345 4440
Isabella Zinck	+41 61 324 7188	Alina Levchuk	+1 862 778 3372
		Parag Mahanti	+1 973-876-4912