

MEDIA & INVESTOR RELEASE

Novartis top-line results for CANOPY-1 Phase III study support further evaluation of canakinumab in lung cancer

Ad hoc announcement pursuant to Art. 53 LR

- *CANOPY-1 Phase III study did not meet its primary endpoints of overall survival (OS) and progression-free survival (PFS) in patients with previously untreated locally advanced or metastatic non-small cell lung cancer (NSCLC)¹*
- *Potentially clinically meaningful improvements in both PFS and OS were observed among pre-specified subgroups of patients with inflammatory biomarkers; additional analyses are ongoing¹*
- *Results support continued study of canakinumab in earlier stages of lung cancer, as potential adjuvant and neoadjuvant therapies, and further evaluation of Pro-Tumor Inflammation in all lung cancer settings¹*
- *Patients in the CANOPY-A study more closely reflect the earlier CANTOS study population than those in the CANOPY-1 trial^{2,3,4}; CANTOS was the first study to suggest that the inhibition of interleukin-1beta (IL-1 β) may play a role in lung cancer³*
- *Canakinumab showed no unexpected safety signals when combined with pembrolizumab plus platinum-based chemotherapy*

Basel, October 25, 2021 — Novartis announced today that the CANOPY-1 Phase III study did not demonstrate the statistically significant primary endpoints of overall survival (OS) and progression-free survival (PFS) in patients treated with canakinumab (ACZ885) combined with pembrolizumab plus platinum-based doublet chemotherapy, compared to patients receiving placebo in combination with pembrolizumab plus platinum-based doublet chemotherapy¹. The trial data, however, showed potentially clinically meaningful improvements in both PFS and OS in pre-specified subgroups of patients based on the baseline inflammatory biomarker, hs-CRP, as well as other biomarker-defined subgroups. These data support further evaluation of canakinumab in lung cancer.

“CANOPY-1 provides critical insights into the treatment of this devastating disease, and we will continue to analyze the data and conclusions, as well as their potential clinical implications,” said John Tsai, MD, Head of Global Drug Development and Chief Medical Officer, Novartis. “While this trial did not confirm the benefit for all patients we hoped for, we

are energized by the overall CANOPY-1 findings as they support our commitment to continue studying canakinumab in lung cancer. We share our gratitude and thanks to the CANOPY-1 study patients and clinical investigators for their partnership.”

Novartis and investigators are collaborating on further data analysis and will present the full dataset at an upcoming medical meeting. The company is continuing with the evaluation of canakinumab in lung cancer, and is applying findings to the overall lung cancer development plan.

The comprehensive CANOPY clinical trial program continues with CANOPY-A, a Phase III study investigating canakinumab as an adjuvant therapy (after surgery)², and CANOPY-N, a Phase II study in the neoadjuvant setting (before surgery)⁵. Enrollment for both trials is ongoing^{2,5}. Patients in the CANOPY-A trial more closely reflect the earlier CANTOS study population than those in the CANOPY-1 trial^{2,3,4}. CANTOS was the first study to show that blocking the IL-1 β inflammatory signal may potentially reduce lung cancer’s incidence and mortality³.

Canakinumab is a potential first-in-class interleukin-1beta (IL-1 β) inhibitor of the Pro-Tumor Inflammation (PTI) pathway in NSCLC⁶. PTI, which enables tumor development by driving cancer-causing processes and suppressing anti-tumor immune responses, is one of the potential hallmarks of cancer and targets in NSCLC^{3,6}. Novartis is developing other potential PTI pathway inhibitors, which are at various stages of development, including gevokizumab^{7,8}.

About canakinumab (ACZ885)

Canakinumab is a human monoclonal antibody that binds with high affinity and selectivity to human interleukin-1beta (IL-1 β) and neutralizes IL-1 β activity by blocking its interaction with its receptors^{9,10}. By neutralizing IL-1 β , preliminary evidence suggests that canakinumab may inhibit Pro-Tumor Inflammation (PTI) to 1) enhance anti-tumor immune response; 2) reduce tumor cell proliferation, survival, and invasiveness; and 3) impair angiogenesis¹¹. PTI enables tumor development by driving cancer-causing processes and suppressing anti-tumor immune responses^{3,6}. Canakinumab is a potential first-in-class IL-1 β inhibitor of the PTI pathway in NSCLC⁶.

About the CANOPY program

Novartis launched the CANOPY study program after observing significantly lower than expected rates of lung cancer mortality among patients in the Phase III cardiovascular CANTOS trial. The CANTOS trial evaluated canakinumab as a secondary prevention measure for cardiovascular events in patients following a heart attack^{3,11}. Patients in the CANTOS trial also were at high risk for inflammatory cancers, like lung cancer, due to advanced age, smoking history, and other clinical risk factors^{3,11}. Based on these findings, Novartis launched three large-scale, randomized, Phase III clinical trials and a Phase II clinical trial to investigate canakinumab as a potential treatment option in non-small cell lung cancer (NSCLC).

- **CANOPY-A (NCT03447769)** is a double-blind, placebo-controlled Phase III trial studying canakinumab in the adjuvant setting following surgical resection and cisplatin-based chemotherapy, if required². The adjuvant study is designed to determine if treatment with canakinumab can prevent cancer relapse².
- **CANOPY-N (NCT03968419)** is a Phase II neoadjuvant trial evaluating canakinumab either as monotherapy or in combination with pembrolizumab among patients with resectable NSCLC prior to their planned surgery⁵.
- **CANOPY-1 (NCT03631199)** was a double-blind, placebo-controlled Phase III trial evaluating canakinumab as a first-line treatment for locally advanced or metastatic NSCLC in combination with pembrolizumab and platinum-based doublet chemotherapy⁴. As reported today, the trial did not meet its primary endpoints of overall survival (OS) and progression-free survival (PFS)¹.
- **CANOPY-2 (NCT03626545)** was a double-blind, placebo-controlled Phase III trial investigating the role of canakinumab in combination with the chemotherapy agent docetaxel in second- or third-line therapy versus docetaxel alone in NSCLC¹². In March 2021, Novartis announced that the trial did not meet its primary endpoint,

and data were presented at the European Society of Medical Oncology (ESMO) 2021 Congress¹³.

Novartis and lung cancer

Lung cancer is one of the most common cancers worldwide, accounting for more than 2 million new cases diagnosed each year¹⁴. More people die of lung cancer every year than any other cancer¹⁴. There are two main types of lung cancer—small cell lung cancer (SCLC) and non-small cell lung cancer (NSCLC)¹⁵. NSCLC accounts for approximately 85% of lung cancer diagnoses^{14,16}.

Novartis is committed to working with the scientific and medical communities to reimagine the treatment of lung cancer and pursue advances in medicine that could extend the survival of people living with lung cancer. With one of the most diverse lung cancer development programs in the industry, Novartis is: developing experimental therapies that block cancer growth; learning more about ways to activate the body's immune system; increasing understanding of the relationship between chronic inflammation and tumor growth and progression; and exploring the potential for advanced nuclear medicine to fight the disease. As part of this continuing and broad commitment to targeting lung cancer, data from CANOPY-1 will be evaluated and used to inform canakinumab's future development program, including potential combination studies with tislelizumab.

Disclaimer

This press release contains forward-looking statements within the meaning of the United States Private Securities Litigation Reform Act of 1995. Forward-looking statements can generally be identified by words such as "potential," "can," "will," "plan," "could," "expect," "committed," "investigational," "continues," "ongoing," "exploring," "to develop," "potentially," "hope," "investigating," "enables," "to determine," "evaluating," "committed," "developing," "learning," "continuing," "commitment," "further evaluation," "collaborating," or similar terms, or by express or implied discussions regarding potential marketing approvals, new indications or labeling for canakinumab alone or in combination with other treatments, or regarding potential future revenues from canakinumab alone or in combination with other treatments. You should not place undue reliance on these statements. Such forward-looking statements are based on our current beliefs and expectations regarding future events, and are subject to significant known and unknown risks and uncertainties. Should one or more of these risks or uncertainties materialize, or should underlying assumptions prove incorrect, actual results may vary materially from those set forth in the forward-looking statements. There can be no guarantee that canakinumab, alone or in combination with other treatments, will be submitted or approved for sale or for any additional indications or labeling in any market, or at any particular time. Nor can there be any guarantee that canakinumab, alone or in combination with other treatments, will be commercially successful in the future. In particular, our expectations regarding canakinumab, alone or in combination with other treatments, could be affected by, among other things, the uncertainties inherent in research and development, including clinical trial results and additional analysis of existing clinical data; regulatory actions or delays or government regulation generally; global trends toward health care cost containment, including government, payor and general public pricing and reimbursement pressures and requirements for increased pricing transparency; our ability to obtain or maintain proprietary intellectual property protection; the particular prescribing preferences of physicians and patients; general political, economic and business conditions, including the effects of and efforts to mitigate pandemic diseases such as COVID-19; safety, quality, data integrity or manufacturing issues; potential or actual data security and data privacy breaches, or disruptions of our information technology systems, and other risks and factors referred to in Novartis AG's current Form 20-F on file with the US Securities and Exchange Commission. Novartis is providing the information in this press release as of this date and does not undertake any obligation to update any forward-looking statements contained in this press release as a result of new information, future events or otherwise.

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 109,000 people of more than 140 nationalities work at Novartis around the world. Find out more at <https://www.novartis.com>.

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