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MEDIA & INVESTOR RELEASE

Novartis provides update on Phase III study evaluating canakinumab (ACZ885) as second or third-line treatment in combination with chemotherapy in non-small cell lung cancer

- *Phase III CANOPY-2 trial did not meet primary endpoint of overall survival in patients with advanced or metastatic non-small cell lung cancer whose cancer progressed while on or after previous treatments*[1]

- *Canakinumab development program continues; two Phase III non-small cell lung cancer clinical trials are ongoing in first-line and adjuvant settings*[2,3]

- *The CANOPY clinical trial program is designed to help answer critical questions about the role of interleukin-1 beta (IL-1β) in pro-tumor inflammation in lung cancer, with multiple clinical trials investigating canakinumab in different stages of disease using distinct treatment combinations*[2-5]

Basel, March 9, 2021 — Novartis announced today the Phase III CANOPY-2 study evaluating canakinumab (ACZ885), an inhibitor of interleukin-1beta (IL-1β), in combination with the chemotherapy agent docetaxel, did not meet its primary endpoint of overall survival (OS)[1]. The trial was conducted among 237 adults with locally advanced or metastatic non-small cell lung cancer (NSCLC) whose disease progressed while on or after previous platinum-based chemotherapy and PD-(L)1 inhibitor immunotherapy[4]. Two Phase III CANOPY trials continue, evaluating canakinumab in first-line and adjuvant settings[2,3]. Novartis and CANOPY-2 investigators will analyze the study data and are expected to submit its findings for presentation at an upcoming medical meeting.

“While results from the CANOPY-2 trial are not what we hoped for in patients with advanced or metastatic non-small cell lung cancer who have been treated with other lines of therapy, these data give us valuable insights into IL-1β inhibition,” said John Tsai, MD, Head of Global Drug Development and Chief Medical Officer at Novartis. “Ongoing Phase III studies in non-small cell lung cancer continue, evaluating canakinumab in earlier treatment settings. We sincerely thank the patients and clinical investigators involved in the CANOPY-2 study for their partnership.”

CANOPY-1, a Phase III study evaluating canakinumab in combination with immunotherapy and chemotherapy, is expected to report final results before the end of the year[2]. CANOPY-A, another Phase III study, is investigating canakinumab as an adjuvant therapy and has enrolled more than 950 patients to date and is expected to enroll a total of 1,500 patients[3].

About canakinumab (ACZ885)
Canakinumab is a human monoclonal antibody that binds with high affinity and selectivity to human interleukin-1beta (IL-1β)[6,7] and neutralizes IL-1β activity by blocking its interaction with its receptors[8]. By neutralizing IL-1β, preliminary evidence suggests that canakinumab

inhibits pro-tumor inflammation (PTI) to 1) enhance anti-tumor immune response; 2) reduce tumor cell proliferation, survival and invasiveness; and 3) impair angiogenesis[8]. Pro-tumor inflammation enables tumor development by driving cancer-causing processes and by suppressing anti-tumor immune responses[9,10]. Canakinumab is a first-in-class interleukin-1beta (IL-1β) inhibitor of PTI in non-small cell lung cancer[10].

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 (CRP≥2 mg/L)[8,9]. Patients in the CANTOS trial were also at high risk for inflammatory cancers, like lung cancer, due to advanced age, smoking history and other clinical risk factors[8,9]. 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-1 (NCT03631199)** is a Phase III trial evaluating canakinumab as a first-line treatment for locally advanced or metastatic NSCLC in combination with pembrolizumab and platinum-based doublet chemotherapy[2]
- **CANOPY-2 (NCT03626545**) is a 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 NSCLC. Part 1 of the CANOPY-2 trial – a safety run-in study to determine the appropriate dosage, was previously presented at ASCO 2019. Part 2 of the trial, reported today, evaluated overall survival (OS)[4]
- **CANOPY-A (NCT03447769)** is a Phase III trial studying canakinumab in the adjuvant setting, following surgical resection and cisplatin-based chemotherapy. The adjuvant study is designed to determine if treatment with canakinumab can prevent cancer relapse[3]
- **CANOPY-N (NCT03968419)** is a non-registrational Phase II neoadjuvant trial evaluating canakinumab in combination with pembrolizumab among patients with resectable NSCLC prior to their planned surgery[5]

Novartis and Lung Cancer

Lung cancer is the most common cancer worldwide, accounting for more than 2 million new cases diagnosed each year[11]. There are two main types of lung cancer – small cell lung cancer (SCLC) and non-small cell lung cancer (NSCLC)[12]. NSCLC accounts for approximately 85% of lung cancer diagnoses, resulting in nearly 1.7 million new cases each year[11,13]. Currently, the five-year survival rate for lung cancer is less than 20%[14], decreasing further when the disease is diagnosed at later stages[15]. The majority of people with NSCLC are diagnosed with advanced or Stage III or IV disease[16], and treatment options are limited for people with lung cancer who experience cancer growth or progression while on standard of care treatments[17-19]. More people die of lung cancer every year than any other cancer type[11]. Novartis is committed to developing best-in-class treatments for lung cancer patients around the world. With a focus on both targeted, personalized medicine and the role of newer, immuno-oncology therapies, the lung cancer drug development program at Novartis is among the most robust in the industry. With research activities informed by long-term relationships with leading lung cancer thought leaders and patient advocates, Novartis is focused on reimagining the treatment of lung cancer.

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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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References

1. Novartis Data on File
2. ClinicalTrials.gov. Study of Efficacy and Safety of Pembrolizumab Plus Platinum-based Doublet Chemotherapy With or Without Canakinumab in Previously Untreated Locally Advanced or Metastatic Non-squamous and Squamous NSCLC Subjects (CANOPY-1). Available at: https://clinicaltrials.gov/ct2/show/NCT03631199. Accessed on February 9, 2021.
3. ClinicalTrials.gov. Brief Title: Study of Efficacy and Safety of Canakinumab as Adjuvant Therapy in Adult Subjects With Stages AJCC/UICC v. 8 II-IIIA and IIIB (T>5cm N2) Completely Resected Non-

small Cell Lung Cancer Acronym: CANOPY-A (Canopy-A). Available at: https://www.clinicaltrials.gov/ct2/show/NCT03447769. Accessed on February 9, 2021.
4. ClinicalTrials.gov. Phase III Study Evaluating Efficacy and Safety of Canakinumab in Combination With Docetaxel in Adult Subjects With Non-small Cell Lung Cancers as a Second or Third Line Therapy (CANOPY-2). Available at: https://clinicaltrials.gov/ct2/show/NCT03626545. Accessed on February 9, 2021.
5. ClinicalTrials.gov. A Randomized, Open-label, Phase II Study of Canakinumab or Pembrolizumab as Monotherapy or in Combination as Neoadjuvant Therapy in Subjects With Resectable Non-small Cell Lung Cancer (CANOPY-N). Available at: https://clinicaltrials.gov/ct2/show/NCT03968419. Accessed on February 9, 2021.
6. Dhimolea E, mAbs 2010;2:3–13; 3. Ilaris [Prescribing Information T2016-102].
7. Rondeau JM, Ramage P, Zurini M, Gram H. The molecular mode of action and species specificity of canakinumab, a human monoclonal antibody neutralizing IL-1β. MAbs. 2015;7(6):1151-1160.
8. Novartis data on file: Clinical Trial Protocol CACZ885M2301.
9. Ridker PM, Thuren T, Zalewski A, et al. Interleukin-1β inhibition and the prevention of recurrent cardiovascular events: rationale and design of the Canakinumab Anti-inflammatory Thrombosis Outcomes Study (CANTOS). *Am Heart J*. 2011;162:597–605.
10. Lu H, Ouyang W, Huang C. Inflammation, a key event in cancer development. *Mol Cancer Res*. 2006;4(4):221-233.
11. World Health Organization. Cancer. Available at: https://www.who.int/news-room/fact-sheets/detail/cancer. Accessed on February 9, 2021.
12. Lemjabbar-Alaoui H, Hassan O, Yang UW, et al. Lung cancer: biology and treatment options. *Biochim Biophys Acta*. 2015. 1856(2):189-210.
13. American Cancer Society. About Lung Cancer. Available at https://www.cancer.org/cancer/non-small-cell-lung-cancer/about/what-is-non-small-cell-lung-cancer.html. Accessed February 9, 2021.
14. Siegel R, Miller K, Jemal A. Cancer statistics, 2020. *CA Cancer J Clin*. 2020;70(1):7-30.
15. Rami-Porta R, Asamura H, Traves W, et al. Lung cancer – major changes in the American Joint Committee on Cancer eight edition cancer staging manual. *CA Cancer J Clin*. 2017;67:138.
16. Mascaux C, Tomasini P, Greillier L, et al. Personalised medicine for non-small cell lung cancer. *Eur Respir Rev*. 2017;26:170066.
17. National Comprehensive Cancer Network Guidelines. Non-small cell lung cancer. Version 3. 2020.
18. Sandler A, Gray R, Perry M, et al. Paclitaxel-carboplatin alone or with bevacizumab for non-small cell lung cancer. *New Engl J Med*. 2006; 355: 2452-2550.
19. Gadgeel S, Rodriguez-Abreu D, Speranza G, et al. Updated analysis from KEYNOTE-189: pembrolizumab or placebo plus pemetrexed and platinum for previously untreated metastatic nonsquamous non-small cell lung cancer. *J Clin Oncol*. 2020; 38:1505-1517.

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