

## **MEDIA & INVESTOR RELEASE**

# **Novartis provides update on Phase III study evaluating investigational spartalizumab (PDR001) in combination with Tafinlar<sup>®</sup> + Mekinist<sup>®</sup> in advanced melanoma**

- *Phase III COMBI-i trial did not meet primary endpoint for patients with advanced BRAF V600-mutated melanoma*
- *Tafinlar + Mekinist remains an effective treatment option based on previously reported large, Phase III clinical trials<sup>1,2</sup>*
- *Spartalizumab development program continues, investigating the immunotherapy in combination with other anti-cancer agents*

**Basel, August 22, 2020** — Novartis announced today that the Phase III COMBI-i study evaluating the investigational immunotherapy spartalizumab (PDR001), in combination with the targeted therapies Tafinlar<sup>®</sup> (dabrafenib) and Mekinist<sup>®</sup> (trametinib), did not meet its primary endpoint of investigator-assessed progression-free survival. The trial was conducted among untreated patients with unresectable (Stage IIIC) or metastatic (Stage IV) BRAF V600 mutation-positive cutaneous melanoma, compared to Tafinlar + Mekinist alone<sup>3</sup>.

“While the COMBI-i trial did not reach its primary endpoint, the study’s findings give us valuable insights into the role the investigational immunotherapy spartalizumab may play in future cancer therapy combinations and underscore the previously established importance of Tafinlar + Mekinist for these patients,” said John Tsai, MD, Head of Global Drug Development and Chief Medical Officer, Novartis. “Novartis remains committed to melanoma patients through ongoing research, and we continue to deliver the approved combination therapy Tafinlar + Mekinist to patients around the world. We extend our gratitude to the patients and investigators who participated in the COMBI-i study. Their partnership has expanded our understanding of spartalizumab and its potential role in future cancer treatments.”

Novartis and the COMBI-i study investigators will continue to review the data to learn more from the results, which are expected to be submitted for presentation at a future medical meeting. Novartis remains committed to exploring new uses for immunotherapy in cancer treatment, including the ongoing development of spartalizumab, across a range of tumor types.

### **About the COMBI-i Study<sup>3</sup>**

COMBI-i was a randomized, double-blind, placebo-controlled, Phase III study comparing the combination of anti-PD1 spartalizumab with Tafinlar (dabrafenib) and Mekinist (trametinib) versus the combination of placebo with Tafinlar and Mekinist. The study was conducted among previously untreated patients with unresectable or metastatic BRAF V600 mutation-

positive melanoma. The COMBI-i study was conducted in three parts. Results reported today are from part 3 of the trial.

#### **About Spartalizumab (PDR001)**

Spartalizumab is an investigational monoclonal antibody directed against the human programmed death-1 (PD-1) receptor. Its development program continues investigating the immunotherapy across a range of tumor types.

#### **About Tafinlar + Mekinist Combination**

Tafinlar and Mekinist are prescription medicines that can be used in combination to treat people with a type of skin cancer called melanoma:

- That has spread to other parts of the body (metastatic) or cannot be removed by surgery (unresectable), and
- That has a certain type of abnormal “*BRAF*” (V600E or V600K mutation-positive) gene

Tafinlar and Mekinist are prescription medicines that can be used in combination to help prevent melanoma that has a certain type of abnormal “*BRAF*” gene from coming back after the cancer has been removed by surgery.

Tafinlar and Mekinist are prescription medications that can be used in combination to treat a type of lung cancer called non-small cell lung cancer (NSCLC) that has spread to other parts of the body (metastatic NSCLC), and that has a certain type of abnormal “*BRAF* V600E” gene.

Tafinlar and Mekinist are prescription medications that can be used in combination to treat a type of thyroid cancer called anaplastic thyroid cancer (ATC):

- That has spread to other parts of the body and you have no satisfactory treatment options, and
- That has a certain type of abnormal “*BRAF*” gene

Tafinlar, in combination with Mekinist, should not be used to treat people with wild-type *BRAF* melanoma. Mekinist should not be used to treat people who already have received a *BRAF* inhibitor for treatment of their melanoma and it did not work or is no longer working.

Your health care provider will perform a test to make sure that Tafinlar and Mekinist , in combination, are right for you.

It is not known if Tafinlar and Mekinist are safe and effective in children.

Tafinlar and Mekinist, in combination, may cause serious side effects such as the risk of new cancers, including both skin cancer and nonskin cancer. Patients should be advised to contact their health care provider immediately for any skin changes, including a new wart, skin sore, or bump that bleeds or does not heal, or a change in the size or color of a mole.

When Tafinlar is used in combination with Mekinist, it can cause serious bleeding problems, especially in the brain or stomach, that can lead to death. Patients should be advised to call their health care provider and get medical help right away if they have any signs of bleeding, including headaches, dizziness, or feel weak, cough up blood or blood clots, vomit blood or their vomit looks like “coffee grounds,” or red or black stools that look like tar.

Mekinist, alone or in combination with Tafinlar, can cause inflammation of the intestines or tears in the stomach or intestines that can lead to death. Patients should report to their health care provider immediately if they have any of the following symptoms: bleeding, diarrhea (loose stools) or more bowel movements than usual, stomach-area (abdomen) pain or tenderness, fever, or nausea.

Tafinlar, in combination with Mekinist, can cause blood clots in the arms or legs, which can travel to the lungs and can lead to death. Patients should be advised to get medical help right away if they have the following symptoms: chest pain, sudden shortness of breath or trouble breathing, pain in their legs with or without swelling, swelling in their arms or legs, or a cool or pale arm or leg.

The combination of Tafinlar and Mekinist can cause heart problems, including heart failure. A patient's heart function should be checked before and during treatment. Patients should be advised to call their health care provider right away if they have any of the following signs and symptoms of a heart problem: feeling like their heart is pounding or racing, shortness of breath, swelling of their ankles and feet, or feeling lightheaded.

Tafinlar, in combination with Mekinist, can cause severe eye problems that can lead to blindness. Patients should be advised to call their health care provider right away if they get: blurred vision, loss of vision, or other vision changes, seeing color dots, halo (seeing blurred outline around objects), eye pain, swelling, or redness.

Tafinlar, in combination with Mekinist, can cause lung or breathing problems. Patients should be advised to tell their health care provider if they have new or worsening symptoms of lung or breathing problems, including shortness of breath or cough.

Fever is common during treatment with Tafinlar in combination with Mekinist, but may also be serious. In some cases, chills or shaking chills, too much fluid loss (dehydration), low blood pressure, dizziness, or kidney problems may happen with the fever. Patients should be advised to call their health care provider right away if they get a fever.

Rash and other skin reactions are common side effects of Tafinlar in combination with Mekinist. In some cases, these rashes and other skin reactions can be severe or serious, may need to be treated in a hospital, or lead to death. Patients should be advised to call their health care provider if they get any of the following symptoms: blisters or peeling of skin, mouth sores, blisters on the lips or around the mouth or eyes, high fever or flu-like symptoms, and/or enlarged lymph nodes.

Some people may develop high blood sugar or worsening diabetes during treatment with Tafinlar in combination with Mekinist. For patients who are diabetic, their health care provider should check their blood sugar levels closely during treatment. Their diabetes medicine may need to be changed. Patients should be advised to tell their health care provider if they have increased thirst, urinate more often than normal, or produce an increased amount of urine.

Tafinlar may cause healthy red blood cells to break down too early in people with glucose-6-phosphate dehydrogenase deficiency. This may lead to a type of anemia called hemolytic anemia, where the body does not have enough healthy red blood cells. Patients should be advised to tell their health care provider if they have yellow skin (jaundice), weakness or dizziness, or shortness of breath.

Tafinlar, in combination with Mekinist, can cause new or worsening high blood pressure (hypertension). A patient's blood pressure should be checked during treatment. Patients should be advised to tell their health care provider if they develop high blood pressure, their blood pressure worsens, or if they have severe headache, lightheadedness, blurry vision, or dizziness.

Men (including those who have had a vasectomy) should use condoms during sexual intercourse during treatment with Tafinlar and Mekinist and for at least 4 months after the last dose of Tafinlar and Mekinist. For women of reproductive potential, Tafinlar and Mekinist, in combination, may harm your unborn baby. Use effective birth control (contraception) during treatment with Tafinlar and Mekinist in combination, and for 4 months after stopping treatment

with Tafinlar and Mekinist. The most common side effects for patients with metastatic melanoma are: pyrexia, nausea, rash, chills, diarrhea, headache, vomiting, hypertension, arthralgia, peripheral edema, and cough. The most common side effects for patients with stage III melanoma receiving the combination as adjuvant therapy are: pyrexia, fatigue, nausea, headache, rash, chills, diarrhea, vomiting, arthralgia, and myalgia. The most common side effects for patients with NSCLC: pyrexia, fatigue, nausea, vomiting, diarrhea, dry skin, decreased appetite, edema, rash, chills, hemorrhage, cough, and dyspnea.

**Please see full Prescribing Information for Tafinlar at <https://www.novartis.us/sites/www.novartis.us/files/tafinlar.pdf> and Mekinist at <https://www.novartis.us/sites/www.novartis.us/files/mekinist.pdf>.**

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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 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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**References**

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