Novartis International AG
Novartis Global Communications
CH-4002 Basel
Switzerland

https://www.novartis.com
https://twitter.com/novartisnews

MEDIA UPDATE

Novartis announces anti-PD-1 tislelizumab accepted by EMA for regulatory review in esophageal and lung cancers

- *European Medicines Agency validated MAAs for tislelizumab in multiple non-small cell lung cancer and esophageal squamous cell carcinoma indications*
- *Submissions based on data from Phase III RATIONALE 302, 303, 304 and 307 trials, in which tislelizumab monotherapy and in combination with chemotherapy demonstrated significant clinical benefits versus chemotherapy in multiple cancer types and lines of therapy*
- *EMA filings follow US FDA filing acceptance for tislelizumab in esophageal cancer*
- *Novartis is evaluating tislelizumab in 14 pivotal clinical trials in a broad array of solid tumors, with more than 8,800 patients enrolled to date in 35 countries*

Basel, April 6, 2022 — Novartis today announced that the European Medicines Agency (EMA) validated Marketing Authorization Applications (MAAs) for the immune checkpoint inhibitor tislelizumab for adults with:

- Locally advanced or metastatic, squamous or non-squamous non-small cell lung cancer (NSCLC) as first-line treatment in combination with chemotherapy,
- Locally advanced or metastatic NSCLC as monotherapy after prior chemotherapy, and
- Unresectable, recurrent, locally advanced or metastatic esophageal squamous cell carcinoma (ESCC) as monotherapy after prior chemotherapy.

Tislelizumab is a humanized IgG4 anti-PD-1 monoclonal antibody being developed both as a monotherapy and in combination with other therapies.[1]

"This is an important step toward expanding treatment options for cancer patients in Europe, and builds on the US FDA filing acceptance for tislelizumab in esophageal cancer," said Jeff Legos, Executive Vice President, Global Head of Oncology & Hematology Development. "We look forward to working with the EMA to make tislelizumab available to people with these aggressive cancers, while continuing to expand our development program to investigate the potential of novel, synergistic combinations."

The MAAs include data from the pivotal Phase III RATIONALE 302 trial, in which tislelizumab demonstrated a significant improvement in overall survival versus chemotherapy as treatment for people with ESCC who had received prior chemotherapy. The submissions also include data from the pivotal Phase III RATIONALE 303 trial, which showed tislelizumab significantly

improved overall survival versus chemotherapy in people with NSCLC after treatment with chemotherapy, and from RATIONALE 304 and 307, which showed tislelizumab plus chemotherapy significantly improved progression-free survival versus chemotherapy in people with untreated squamous and non-squamous NSCLC.

Lung cancer is one of the most common cancers worldwide, accounting for more than 2 million new cases diagnosed each year.[2] More people die of lung cancer every year than any other cancer.[3] ESCC is the most common type of esophageal cancer globally, with an estimated 604,000 new cases and 544,000 deaths from esophageal cancer internationally in 2020.[3]

About RATIONALE Trials

RATIONALE 302 (NCT03430843) is a multi-regional, open-label, randomized Phase III study of tislelizumab versus chemotherapy in patients with advanced unresectable/metastatic esophageal squamous cell carcinoma who had received prior systemic therapy. Approximately 513 patients were randomized 1:1 to receive tislelizumab or investigator chosen chemotherapy. The primary endpoint is overall survival (OS); the key secondary endpoint was OS in the PD-L1 positive population. Other secondary endpoints include progression-free survival (PFS), objective response rate (ORR), duration of response (DoR), health-related quality of life measures and safety.

RATIONALE 303 (NCT03358875) is a multi-regional, open-label, multicenter, randomized Phase III study of tislelizumab versus chemotherapy in patients with locally advanced or metastatic NSCLC who have progressed on a prior platinum-containing regimen. Approximately 805 patients were randomized 1:1 to receive tislelizumab or chemotherapy. The co-primary endpoints are OS in all patients and OS in PD-L1 positive patients. Secondary endpoints include PFS, ORR, DoR, health-related quality of life measures and safety.

RATIONALE 304 (NCT03663205) is an open-label, multicenter, randomized Phase III study of tislelizumab plus chemotherapy versus chemotherapy alone in patients with untreated advanced non-squamous NSCLC. Approximately 334 patients were randomized 1:1 to receive either tislelizumab plus chemotherapy or chemotherapy. The primary endpoint is PFS. Secondary endpoints include OS, ORR, DoR, health-related quality of life measures and safety.

RATIONALE 307 (NCT03594747) is an open-label, multicenter, randomized Phase III study of tislelizumab plus chemotherapy versus chemotherapy in patients with untreated advanced squamous NSCLC. Approximately 360 patients were randomized 1:1:1 to receive tislelizumab plus paclitaxel, tislelizumab plus nab-paclitaxel, or chemotherapy alone. The primary endpoint is PFS. Secondary endpoints include OS, ORR, DoR, health-related quality of life measures and safety.

About Tislelizumab

Novartis is evaluating tislelizumab, a uniquely designed anti-PD-1 monoclonal antibody, in a global clinical development program consisting of 14 pivotal clinical trials across a broad array of solid tumors, with more than 8,800 patients enrolled to date in 35 countries. Novartis four distinct therapeutic platforms (immunotherapy, radioligand therapy, cell and gene therapy, targeted therapy) offer a unique opportunity to study tislelizumab in differentiated, potentially synergistic combinations across our pipeline and portfolio of market compounds.

Novartis has the rights to develop, manufacture and commercialize tislelizumab in North America, Europe and Japan through a collaboration and license agreement with BeiGene.

Disclaimer

This media update 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,” “may,” “could,” “would,” “expect,” “anticipate,” “look forward,” “believe,” “committed,” “investigational,” “pipeline,” “launch,” or similar terms, or by express or implied discussions regarding potential marketing approvals, new indications or labeling for the investigational or approved products described in this media update, or regarding potential future revenues from such products. 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 the investigational or approved products described in this media update 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 such products will be commercially successful in the future. In particular, our expectations regarding such products 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 media update as of this date and does not undertake any obligation to update any forward-looking statements contained in this media update 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 108,000 people of more than 140 nationalities work at Novartis around the world. Find out more at https://www.novartis.com.

Novartis is on Twitter. Sign up to follow @Novartis at **https://twitter.com/novartisnews**
For Novartis multimedia content, please visit **https://www.novartis.com/news/media-library**
For questions about the site or required registration, please contact media.relations@novartis.com

References

1. Zhang T, Song X, Xu L, et al. The binding of an anti-PD-1 antibody to FcγRI has a profound impact on its biological functions. *Cancer Immunol Immunother.* 2018;67(7):1079-1090.
2. World Health Organization. Cancer. Available at: https://www.who.int/news-room/fact-sheets/detail/cancer. Accessed November 1, 2021.
3. Sung H, Ferlay J, Siegel RL, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA: a cancer journal for clinicians. 2021;71(3):209-249.

# # #

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

Anja von Treskow Dan Connelly

Novartis External Communications
+41 61 324 2279 (direct)
+41 79 392 8697 (mobile)
anja.von_treskow@novartis.com

Novartis Oncology
+1 862 210 0217 (mobile)
daniel.connelly@novartis.com

Julie Masow
Novartis US External Communications
+1 862 579 8456
Julie.masow@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
Nicole Zinsli-Somm	+41 61 324 3809	Alina Levchuk	+1 862 778 3372
Isabella Zinck	+41 61 324 7188	Parag Mahanti	+1 973-876-4912