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MEDIA & INVESTOR RELEASE

Novartis announces positive result of phase III study with radioligand therapy ^{177}Lu-PSMA-617 in patients with advanced prostate cancer

- *Phase III VISION study with ^{177}Lu-PSMA-617 met both primary endpoints, significantly improving overall survival (OS) and radiographic progression-free survival (rPFS) in patients with PSMA-positive metastatic castration-resistant prostate cancer[1]*
- *VISION trial findings to be presented at upcoming medical meeting, with regulatory submissions in the US and EU anticipated in 2021*
- *Novartis is committed to reimagining prostate cancer through targeted radioligand therapy with ^{177}Lu-PSMA-617*
- *More than 15 dedicated early to late development and research programs underway to identify the next wave of radioligand therapies for cancer*

Basel, March, 23, 2021 — Novartis today reported the first interpretable results of the Phase III VISION study evaluating the efficacy and safety of ^{177}Lu-PSMA-617, a targeted radioligand therapy in patients with progressive PSMA-positive metastatic castration-resistant prostate cancer (mCRPC) compared to best standard of care alone. The trial met both primary endpoints of overall survival and radiographic progression-free survival[1], helping to move closer the ambition of becoming the targeted treatment for >80% of patients with advanced prostate cancer. The safety profile was consistent with data reported in previous clinical studies[1]. Results from the VISION trial will be presented at an upcoming medical meeting and included in US and EU regulatory submissions.

“Patients with metastatic castration-resistant prostate cancer have a less than 1 in 6 chance of surviving 5 years[2] and need new treatment options. These groundbreaking data confirm our belief in the potential of ^{177}Lu-PSMA-617 to reimagine outcomes for these patients through phenotypic precision medicine. We intend to submit these data to regulatory authorities as soon as possible,” said John Tsai, Head of Global Drug Development and Chief Medical Officer for Novartis. “We would like to thank the patients who volunteered to participate in this study as well as the clinical teams at each of the trial sites. We would not be able to realize our commitment to reimagining medicine without the partnership of patients and their families.”

Radioligand therapy combines a targeting compound that binds to markers expressed by tumors and a radioactive isotope, causing DNA damage that inhibits tumor growth and replication. This therapeutic approach enables targeted delivery of radiation to the tumor, while limiting damage to the surrounding normal tissue. Novartis has established global

expertise and specialized supply chain and manufacturing capabilities across its network of four radioligand therapy production sites, and is further increasing capacity to ensure delivery of radioligand therapies like ^{177}Lu-PSMA-617 to patients in need.

Novartis is the only pharmaceutical company which is pursuing four different cancer treatment platforms. These include radioligand therapy, cell and gene therapy, and targeted therapy and immunotherapy, with an opportunity to combine these platforms for the best outcomes for each cancer patient.

About Advanced Prostate Cancer
Prostate cancer is a form of cancer that develops in the prostate gland, a small walnut shaped gland in the pelvis of men. In castration resistant prostate cancer (CRPC), the tumor shows signs of growth, such as rising Prostate Specific Antigen (PSA) levels, despite the use of hormone treatments that lower testosterone[3]. In metastatic CRPC (mCRPC), the tumor spreads to other parts of the body, such as neighboring organs or bones and remains unresponsive to hormone treatment[4]. The five-year survival rate for patients with mCRPC is approximately 15%[2].

About Phenotypic Precision Medicine in Advanced Prostate Cancer
Despite advances in prostate cancer care, there is a high unmet need for new targeted treatment options to improve outcomes for patients with metastatic castration resistant prostate cancer. More than 80% of prostate cancer tumors highly express a phenotypic biomarker[5] called Prostate Specific Membrane Antigen (PSMA)[4,6-9], making it a promising diagnostic (through positron emission tomography (PET) scan imaging) and therapeutic target for radioligand therapy[6].

About ^{177}Lu-PSMA-617
^{177}Lu-PSMA-617 is an investigational PSMA-targeted radioligand therapy for metastatic castration-resistant prostate cancer. It is a type of precision cancer treatment combining a targeting compound (ligand) with a therapeutic radioisotope (a radioactive particle)[10-12]. After administration into the bloodstream, ^{177}Lu-PSMA-617 binds to prostate cancer cells that express PSMA[13], a transmembrane protein, with high tumor-to-normal tissue uptake[10,14,15]. Once bound, emissions from the radioisotope damage tumor cells, disrupting their ability to replicate and/or triggering cell death. The radiation from the radioisotope works over very short distances to limit damage to surrounding cells[14,16].

About VISION
VISION is an international, prospective, randomized, open-label, multicenter, phase III study to assess the efficacy and safety of ^{177}Lu-PSMA-617 (7.4 GBq administered by i.v. infusion every 6 weeks for a maximum of 6 cycles) plus investigator-chosen best standard of care in the investigational arm, versus best standard of care in the control arm[17]. Patients with PSMA PET-scan positive mCRPC, and progression after prior taxane and androgen receptor-directed therapy (ARDT), were randomized in a 2:1 ratio in favor of the investigational arm. The alternate primary endpoints were rPFS and OS. The study enrolled 831 patients[1].

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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 ^{177}Lu-PSMA-617 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 ^{177}Lu-PSMA-617 will be commercially successful in the future. In particular, our expectations regarding ^{177}Lu-PSMA-617 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 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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