

MEDIA & INVESTOR RELEASE

Novartis reports positive health-related quality of life data for ¹⁷⁷Lu-PSMA-617 radioligand therapy in patients with advanced prostate cancer at ESMO 2021

- *New quality of life data for ¹⁷⁷Lu-PSMA-617 plus standard of care shows delay in worsening of health-related quality of life (HRQoL) and pain in heavily pre-treated patients with PSMA-positive metastatic castration-resistant prostate cancer (mCRPC) compared to standard of care alone¹*
- *US Food and Drug Administration (FDA) granted Breakthrough Therapy designation to ¹⁷⁷Lu-PSMA-617; Submission to FDA and European Medicines Agency on track for 2H21*
- *Novartis committed to reimagining prostate cancer with targeted radioligand therapy; two Phase III studies with ¹⁷⁷Lu-PSMA-617 in earlier lines of treatment ongoing with goal to investigate earlier stages of disease*

Basel, September 17, 2021 — Novartis today announced positive health-related quality of life (HRQoL) data from its Phase III VISION study evaluating ¹⁷⁷Lu-PSMA-617, an investigational targeted radioligand therapy, plus standard of care for metastatic castration-resistant prostate cancer (mCRPC) versus standard of care alone. Many patients with mCRPC live with reduced physical functioning as well as significant pain^{2,3}. This data from a quality of life assessment of the VISION trial, referred to as HRQoL, showed delayed worsening of these difficult to bear symptoms in the ¹⁷⁷Lu-PSMA-617 plus standard of care arm compared to standard of care alone arm. No new or unexpected safety concerns, including changes in creatinine clearance, were noted¹. These results will be presented at the European Society for Medical Oncology (ESMO) Congress, 17-21 September 2021.

HRQoL ad hoc analysis showed that the ¹⁷⁷Lu-PSMA-617 plus standard of care arm resulted in an estimated 54% risk reduction in the worsening of HRQoL (measured by Functional Assessment of Cancer Therapy – Prostate (FACT-P) scale) from baseline (hazard ratio: 0.46 with 95% confidence interval (CI): (0.35, 0.61)) compared to the standard of care only arm¹. In addition, ¹⁷⁷Lu-PSMA-617 plus standard of care also resulted in an estimated 55% risk reduction of worsening of pain intensity (measured by Brief Pain Inventory – Short Form (BPI-SF) scale) from baseline (hazard ratio: 0.45 with 95% (CI): (0.33, 0.60)) compared to the standard of care only arm¹.

“Patients with mCRPC suffer from many complications associated with advanced disease that can impact their quality of life^{2,3},” said Jeff Legos, Executive Vice President, Global Head of Oncology & Hematology Development, Novartis. “These new data emphasize the potential impact on quality of life that investigational ¹⁷⁷Lu-PSMA-617 may provide as a potential new

treatment option, beyond previously reported improvements in overall survival and radiographic progression-free survival⁴.”

Two additional studies with ¹⁷⁷Lu-PSMA-617 radioligand therapy in earlier lines of treatment for metastatic prostate cancer are ongoing, investigating potential clinical utility in the mCRPC pre-taxane setting ([PSMAfore](#)) and in the metastatic hormone-sensitive setting ([PSMAddition](#)). Novartis is also evaluating opportunities to investigate ¹⁷⁷Lu-PSMA-617 radioligand therapy in earlier stages of prostate cancer.

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 testosterone⁵. In metastatic CRPC (mCRPC), the tumor spreads to other parts of the body, such as neighboring organs or bones and remains unresponsive to hormone treatment⁵. The five-year survival rate for patients with metastatic prostate cancer is approximately 30%⁶.

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 mCRPC. More than 80% of prostate cancer tumors highly express a phenotypic biomarker⁷ called Prostate Specific Membrane Antigen (PSMA)^{8-10,11,12}, making it a promising diagnostic (through positron emission tomography (PET) scan imaging) and potential therapeutic target for radioligand therapy¹³. This differs from ‘genotypic’ precision medicine which targets specific genetic alterations in cancer cells⁷.

About ¹⁷⁷Lu-PSMA-617

¹⁷⁷Lu-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)¹⁴⁻¹⁶. After administration into the bloodstream, ¹⁷⁷Lu-PSMA-617 binds to prostate cancer cells that express PSMA¹⁷, a transmembrane protein, with high tumor-to-normal tissue uptake^{14,18,19}. Once bound, emissions from the radioisotope damage tumor cells, disrupting their ability to replicate and/or triggering cell death²⁰⁻²². The radiation from the radioisotope works over very short distances to limit damage to surrounding cells^{13,14,18}.

About VISION

VISION is an international, prospective, randomized, open-label, multicenter, phase III study to assess the efficacy and safety of ¹⁷⁷Lu-PSMA-617 (7.4 GBq administered by intravenous infusion every 6 weeks for a maximum of 6 cycles) plus investigator-chosen standard of care in the investigational arm, versus standard of care in the control arm⁴. Patients with PSMA PET-scan positive mCRPC, and progression after prior taxane and androgen receptor pathway inhibitors, were randomized in a 2:1 ratio in favor of the investigational arm⁴. The study met both alternate primary endpoints of radiographic progression free survival and overall survival; secondary endpoints were also met⁴. The study enrolled 831 patients⁴.

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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 press release 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 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

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