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MEDIA & INVESTOR RELEASE

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

- *New quality of life data for ^{177}Lu-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 alone[1]*

- *US Food and Drug Administration (FDA) granted Breakthrough Therapy designation to ^{177}Lu-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 ^{177}Lu-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 ^{177}Lu-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 ^{177}Lu-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 noted[1]. 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 ^{177}Lu-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 arm[1]. In addition, ^{177}Lu-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 arm[1].

“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 ^{177}Lu-PSMA-617 may provide as a potential new

treatment option, beyond previously reported improvements in overall survival and radiographic progression-free survival[4]."

Two additional studies with ^{177}Lu-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 ^{177}Lu-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 testosterone[5]. 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[5]. 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 biomarker[7] 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 therapy[13]. This differs from 'genotypic' precision medicine which targets specific genetic alterations in cancer cells[7].

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)[14-16]. After administration into the bloodstream, ^{177}Lu-PSMA-617 binds to prostate cancer cells that express PSMA[17], 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 death[20-22]. 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 ^{177}Lu-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 arm[4]. 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 arm[4]. The study met both alternate primary endpoints of radiographic progression free survival and overall survival; secondary endpoints were also met[4]. The study enrolled 831 patients[4].

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