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MEDIA & INVESTOR RELEASE

Novartis Pluvicto™ approved by FDA as first targeted radioligand therapy for treatment of progressive, PSMA-positive metastatic castration-resistant prostate cancer

Ad hoc announcement pursuant to Art. 53 LR

- *FDA also approved complementary diagnostic imaging agent, Locametz®, after radiolabeling with gallium-68 for the identification of PSMA-positive lesions[2]*
- *Metastatic prostate cancer has a 5-year survival rate of less than 30%[3]; mCRPC patients who progress on multiple lines of therapy have limited treatment options*
- *FDA approval was based on pivotal Phase III VISION trial, where patients with pre-treated PSMA-positive mCRPC who received Pluvicto plus standard of care had a statistically significant reduction in risk of death[1]; both alternate primary endpoints of overall survival and radiographic progression free survival were met[1]*
- *Novartis is committed to reimagining medicine in prostate cancer with targeted radioligand therapy - a type of precision cancer treatment combining a targeting compound (ligand) with a therapeutic radioisotope (a radioactive particle)*
- *Two pivotal Phase III studies evaluating Pluvicto in earlier lines of treatment for metastatic prostate cancer are underway, with a goal to move into earlier stages of disease*

Basel, March 23, 2022 — Novartis announced today that the US Food and Drug Administration (FDA) approved Pluvicto™ (lutetium Lu 177 vipivotide tetraxetan) (formerly referred to as ^{177}Lu-PSMA-617) for the treatment of adult patients with a certain type of advanced cancer called prostate-specific membrane antigen–positive metastatic castration-resistant prostate cancer (PSMA-positive mCRPC) that has spread to other parts of the body (metastatic)[1]. These patients have already been treated with other anticancer treatments (androgen receptor pathway inhibition and taxane-based chemotherapy)[1].

“The approval of Pluvicto is an important clinical advancement for people with progressing mCRPC, as it can significantly improve survival rates for those who have limited treatment options,” said Oliver Sartor, MD, Medical Director at Tulane Cancer Center. “Pluvicto is a step forward in the evolution of precision medicine for prostate cancer.”

Pluvicto is the first FDA-approved targeted radioligand therapy (RLT) for eligible patients with mCRPC that combines a targeting compound (ligand) with a therapeutic radioisotope (a

radioactive particle)[1]. Pluvicto is expected to be available to physicians and patients within weeks.

The FDA has also approved Locametz® (kit for the preparation of gallium Ga 68 gozetotide injection)[2]. After radiolabeling, this imaging agent may be used to identify PSMA-positive lesions in adult patients with mCRPC through a positron emission tomography (PET) scan[2]. Gallium-68 labeled Locametz can identify tumor lesions expressing the PSMA biomarker and locate where in the body tumors may have spread (eg, in soft tissue, lymph nodes, or bone), identifying patients eligible for targeted treatment with Pluvicto[1,2]. PSMA is highly expressed in more than 80 percent of patients with prostate cancer, making it an important phenotypic biomarker for assessing the progression of metastatic prostate cancer[4-10]. Locametz is expected to be available to physicians and patients within weeks.

“With our unique strategy to tackle cancer by leveraging four therapeutic platforms, I am thrilled that with Pluvicto, we are bringing the targeted RLT platform to bear for treating eligible patients with mCRPC,” said Susanne Schaffert, PhD, President, Novartis Oncology. “Today’s approval builds upon our history in prostate cancer, a devastating disease where we believe our innovation can make a meaningful difference to patients.”

FDA approval of Pluvicto is based on the results of the Phase III VISION trial which demonstrated that PSMA-positive mCRPC patients previously treated with androgen receptor (AR) pathway inhibition and taxane-based chemotherapy who received Pluvicto plus standard of care (SOC) had improved overall survival compared to SOC alone[1]. Participants treated with Pluvicto plus SOC had a 38% reduction in risk of death and a statistically significant reduction in the risk of radiographic disease progression or death (rPFS) compared to SOC alone[1]. Interpretation of the magnitude of the rPFS effect was limited due to a high degree of censoring from early drop out in the control arm[1].

In addition, about a third (30%) of patients with evaluable disease at baseline demonstrated an overall response (per RECIST 1.1) with Pluvicto plus SOC, compared to 2% in the SOC alone arm[1]. The most common adverse events (all grades) in the Pluvicto arm of the study were fatigue (43%), dry mouth (39%), nausea (35%), anemia (low red blood cell counts) (32%), decreased appetite (21%), and constipation (20%)[1].

“Prostate cancer is the second leading cause of cancer-related death in Americans with a prostate gland[13]. Although the treatment landscape for mCRPC continues to evolve, there is a high unmet need for additional precision medicine treatment options to improve outcomes for these patients,” said Jamie Bearse, CEO and President at ZERO – The End of Prostate Cancer. “The approval of Pluvicto offers new hope to the mCRPC community.”

Pluvicto and Locametz are registered products of Advanced Accelerator Applications, the radioligand business of Novartis, approved in the United States for physicians to prescribe to appropriate patients. Additional safety details for Pluvicto and Locametz, and full Prescribing Information can be found on the Novartis website.

About Pluvicto

Pluvicto™ (lutetium Lu 177 vipivotide tetraxetan) is indicated for the treatment of adult patients with prostate-specific membrane antigen (PSMA)-positive metastatic castration-resistant prostate cancer (mCRPC) who have already been treated with other anticancer treatments (androgen receptor pathway inhibition (ARPI) and taxane-based chemotherapy)[1]. It is a type of precision cancer treatment combining a targeting compound (ligand) with a therapeutic radioisotope (a radioactive particle)[1]. After administration into the bloodstream, Pluvicto binds to target cells, including prostate cancer cells that express PSMA, a transmembrane protein[1]. Once bound, energy emissions from the radioisotope damage the target cells and nearby cells disrupting their ability to replicate and/or triggering cell death[1].

Novartis has submitted marketing authorization for Pluvicto to the European Medicines Agency and other health authorities.

About Locametz
Locametz® (gallium Ga 68 gozetotide), diagnostic kit for radiopharmaceutical injectable preparation is indicated for positron emission tomography (PET) of PSMA-positive lesions in adult patients with prostate cancer with suspected metastasis who are candidates for initial definitive therapy; with suspected recurrence based on elevated serum prostate-specific antigen (PSA) level; and for selection of patients with metastatic prostate cancer, for whom lutetium Lu 177 vipivotide tetraxetan PSMA-directed therapy is indicated[2].

Novartis has submitted marketing authorization for Locametz to the European Medicines Agency and other health authorities.

About VISION
VISION is an international, prospective, randomized, open-label, multicenter, phase III study that assessed the efficacy and safety of Pluvicto (lutetium Lu 177 vipivotide tetraxetan) (7.4 GBq administered by IV infusion every 6 weeks for a maximum of 6 cycles) plus investigator-chosen standard of care (SOC) in the investigational arm, versus SOC in the control arm[1]. Patients with PSMA PET-scan positive mCRPC who have received androgen receptor (AR) pathway inhibition and taxane-based chemotherapy, were randomized in a 2:1 ratio in favor of the investigational arm[1]. The alternate primary endpoints were rPFS and OS[1]. The study enrolled 831 patients[1].

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 patients with prostate cancer highly express a phenotypic biomarker[9] called prostate specific membrane antigen (PSMA)[4-6,8,9], making it a promising diagnostic (through positron emission tomography (PET) scan imaging) and therapeutic target for radioligand therapy[10]. This differs from 'genotypic' precision medicine which targets specific genetic alterations in cancer cells[7].

Novartis and Prostate Cancer
With more 1.4 million new cases and 375,000 deaths in 2020 alone, prostate cancer is the most frequently diagnosed cancer in 112 countries—more than half the world[12].

At Novartis, we are harnessing the innovation of our world-class scientists, strategic partnerships, and one of the industry's most competitive pipelines to explore the potential of new, targeted therapies and precision medicine platforms to address the greatest unmet needs in prostate cancer.

Through the bold science of targeted therapies, our goal is to reduce the global disease burden, extend the lives of patients with prostate cancer, and elevate current standards of care.

Patient Access and Support
Novartis is committed to helping ensure that our medicines are accessible to as many patients as possible. With the approval of Pluvicto in the United States, we offer support and services to address a range of needs through AAA PatientCONNECT™. AAA PatientCONNECT™ is a support center staffed by dedicated case managers who can help eligible patients throughout their treatment journey to start and stay on treatment. Patients or providers can call 1-844-638-7222 or visit AAApatientconnect.com to enroll and learn more about AAA PatientCONNECT™.

Disclaimer
This press release 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,” “may,” “expected,” “believe,” “committed,” “investigational,” “pipeline,” "goal," "expected," "evolution," "to evolve," "continues," "hope," or similar terms, or by express or implied discussions regarding potential marketing approvals, new indications or labeling for Pluvicto or Locametz, 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 Pluvicto or Locametz 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 Pluvicto or Locametz will be successfully launched in the markets where it is approved, or at any particular time. Neither can there be any guarantee that Pluvicto or Locametz will be commercially successful in the future. In particular, our expectations regarding Pluvicto or Locametz 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 Advanced Accelerator Applications
Advanced Accelerator Applications (AAA), a Novartis company, specializes in targeted radioligand therapies and precision imaging radioligands for oncology indications. We are committed to transforming patients’ lives by leading innovation in nuclear medicine. AAA has a legacy as a leader in radiopharmaceutical drugs for Positron Emission tomography (PET) and Single-Photon Emission Computed Tomography (SPECT) diagnostic imaging. For more information, please visit: https://www.adacap.com.

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.

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