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PRESS RELEASE

Novartis Pluvicto™ demonstrates statistically significant and clinically meaningful rPFS benefit in patients with PSMA-positive metastatic hormone-sensitive prostate cancer

Ad hoc announcement pursuant to Art. 53 LR

- *At interim analysis, PSMAddition trial met its primary endpoint showing statistically significant and clinically meaningful benefit for Pluvicto™ plus hormone therapy versus hormone therapy alone, with positive trend in overall survival (OS)[1]*
- *Pluvicto is already approved for metastatic castration-resistant prostate cancer (mCRPC) and now shows potential in patients in an earlier disease setting[1,2]*
- *Novartis to present results at an upcoming medical meeting and, based on FDA feedback, will submit for regulatory review in the second half of the year*
- *Novartis is investigating a broad portfolio of RLTs in advanced cancers, including breast, colon, lung and pancreatic and is investing in multiple manufacturing facilities, with industry-leading infrastructure to accelerate delivery of RLTs to patients*

Basel, June 2, 2025 – Novartis today announced topline results from a pre-specified interim analysis of the Phase III PSMAddition trial. The trial met its primary endpoint with a statistically significant and clinically meaningful benefit in radiographic progression-free survival (rPFS) with a positive trend in overall survival (OS) in patients with prostate-specific membrane antigen (PSMA)-positive metastatic hormone-sensitive prostate cancer (mHSPC) treated with radioligand therapy (RLT), Pluvicto™ (lutetium (^{177}Lu) vipivotide tetraxetan), in combination with standard of care (SoC) versus SoC alone[1]. In PSMAddition, the SoC is a combination of androgen receptor pathway inhibitor (ARPI) therapy and androgen deprivation therapy (ADT)[3].

Almost all mHSPC patients ultimately progress to metastatic castration-resistant prostate cancer (mCRPC)[4]. There is a need for additional treatment options with novel mechanisms of action that further delay progression, prolong OS and improve disease control compared to the current SoC, while showing a favorable safety and tolerability profile.

“The progression from metastatic hormone-sensitive prostate cancer to castration-resistant disease remains a formidable challenge that can profoundly impact the survival of patients," said Shreeram Aradhye, M.D., President, Development and Chief Medical Officer at Novartis. "These results further strengthen our confidence in Pluvicto as a PSMA-targeted radioligand therapy. Following the recent FDA approval based on the PSMAfore trial in metastatic castration-resistant prostate cancer, these data suggest using it in an earlier disease setting could advance care and address a significant unmet need for hormone-sensitive prostate cancer patients."

This is the third positive read-out for Pluvicto in a Phase III trial, following the VISION and PSMAfore studies[5,6]. Results from PSMAddition in mHSPC show potential for treatment in an earlier setting with Pluvicto, which was recently granted US Food and Drug Administration (FDA) approval for earlier use in mCRPC, based on results from PSMAfore[1,2]. Novartis is harnessing the innovation of 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.

Data will be presented at an upcoming medical meeting and, based on FDA feedback, will be submitted for regulatory review in the second half of the year.

About PSMAddition study
PSMAddition (NCT04720157) is a Phase III, open-label, prospective, 1:1 randomized study comparing the efficacy and safety of Pluvicto in combination with SoC (ARPI + ADT) vs. SoC alone in adult patients with PSMA-positive mHSPC[3]. Patients randomized to the SoC alone arm are allowed to crossover to receive Pluvicto, upon confirmation of radiographic progression by blinded independent review committee (BIRC) and per the discretion of the treating physician[3]. The primary endpoint is rPFS, defined as the time to radiographic progression by PCWG3-modified RECIST V1.1 (as assessed by BIRC) or death[3]. The key secondary endpoint of OS is defined as time to death due to any cause[3].

About Pluvicto™ (INN: lutetium (^{177}Lu) vipivotide tetraxetan)
Pluvicto is an intravenous RLT that combines a targeting compound (a ligand) with a therapeutic radionuclide (a radioactive particle, in this case lutetium-177)[5,7]. After administration into the bloodstream, Pluvicto binds to PSMA-expressing target cells, including prostate cancer cells that express PSMA, a transmembrane protein[5,7]. Once bound, energy emissions from the radioisotope damage the target cells and nearby cells, disrupting their ability to replicate and/or triggering cell death[7]. Pluvicto is the only PSMA-targeted agent approved for PSMA-positive mCRPC and is the first targeted RLT to demonstrate a clinical benefit for patients with PSMA-positive mHSPC[1]. Novartis is investigating Pluvicto in earlier stages of disease, including oligometastatic prostate cancer (PSMA-DC, NCT05939414).

Novartis and radioligand therapy (RLT)
Novartis is reimagining cancer care with RLT for patients with advanced cancers. By harnessing the power of targeted radiation and applying it to advanced cancers, RLT is designed to deliver treatment directly to target cells, anywhere in the body[8,9]. Novartis is investigating a broad portfolio of RLTs, exploring new isotopes, ligands and combination therapies to look beyond gastroenteropancreatic neuroendocrine tumors (GEP-NETs) and prostate cancer and into breast, colon, lung and pancreatic cancer. Novartis has established global expertise, with specialized supply chain and manufacturing capabilities across its network of RLT production sites. To support growing demand for RLTs, we have expanded production capabilities in Millburn (NJ), Zaragoza (Spain), Ivrea (Italy) and a state-of-the-art facility in Indianapolis (IN). In Carlsbad (CA), Novartis is establishing its third US-based RLT manufacturing site to support expanded use of RLTs, create resiliency in its manufacturing network and optimize the delivery of medicines to patients on the West Coast.

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,” “will,” “may,” “could,” “trend,” “potentially,” “upcoming,” “progression,” “progress,” “investigating,” “investing,” “look beyond,” or similar terms, or by express or implied discussions regarding potential marketing approvals, new indications or labeling for Pluvicto, or regarding potential future revenues from Pluvicto. 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 Pluvicto 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 will be commercially successful in the future. In particular, our expectations regarding Pluvicto 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; 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
Novartis is an innovative medicines company. Every day, we work to reimagine medicine to improve and extend people’s lives so that patients, healthcare professionals and societies are empowered in the face of serious disease. Our medicines reach nearly 300 million people worldwide.

Reimagine medicine with us: Visit us at **https://www.novartis.com** and connect with us on **LinkedIn**, **Facebook**, **X/Twitter** and **Instagram**.

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