Novartis expands production of Pluvicto® with addition of its largest and most advanced radioligand therapy manufacturing facility in Indianapolis

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- *FDA approval of the company's second US Radioligand Therapy (RLT) manufacturing facility increases RLT production capacity to 250,000 doses in 2024 and beyond*
- *New 70,000-square foot RLT facility is the company's largest and most advanced in the world to date and centrally located in the US to maximize access for patients and treatment centers*
- *With four active RLT manufacturing sites and unconstrained supply, Novartis can sufficiently meet current and future demand as ongoing clinical trials may present the potential to bring Pluvicto and Lutathera® to more patients in earlier lines of treatment*
- *Novartis is investigating a broad portfolio of RLTs in advanced cancers including breast, colon, neuroendocrine, lung, pancreatic and prostate to continue meeting global patient needs*

East Hanover, January 5, 2024— Novartis announced today that it has received approval from the US Food and Drug Administration (FDA) for commercial manufacturing of Pluvicto® (lutetium Lu 177 vipivotide tetraxetan) at its new large-scale, state-of-the-art radioligand therapy (RLT) manufacturing facility in Indianapolis, Indiana, United States. The 70,000-square foot site, the company's second US location, is designed specifically for RLT manufacturing and is now the largest and most advanced Novartis facility of its kind in the world. The Indianapolis site represents the next phase of RLT manufacturing growth as this new addition brings substantial supply increases for the foreseeable future.

"The intricate process of providing RLTs to patients within hours of production requires precision manufacturing expertise to bring these medicines to individuals who critically need them," said Steffen Lang, President, Operations, Novartis. "Adding a second US RLT facility, our largest and most advanced yet, into our manufacturing network underscores our commitment to ensure a consistent and reliable experience for patients and their healthcare teams for years to come. We also recently announced plans to build our manufacturing capabilities in Sasayama, Japan and Haiyan, Zhejiang, China, as we continue to look for opportunities to further expand our worldwide reach."

The Indianapolis facility, centrally located within the US, is purpose-built from the ground up to manufacture RLTs now and into the future and includes space for continued line expansion including plans for fully automated lines, a first for the radiopharmaceutical industry. The new site will supply the growing demand for patients in the US and eventually in Canada, upon approval, together with the company's Millburn, New Jersey location. The site in Ivrea, Italy will continue to supply patients in and outside the US while the facility in Zaragoza, Spain will solely provide RLTs for patients outside the US.

Novartis recently announced that supply of Pluvicto is unconstrained. Having doubled weekly production, Novartis currently has more than sufficient supply to treat patients within two weeks of diagnosis, which is important for these patients with advanced disease who may need treatment quickly.

Novartis is committed to improving access to its RLTs, Pluvicto and Lutathera® (lutetium Lu 177 dotatate) by adding more treatment sites in closer proximity to patients over the coming months.

With four active manufacturing facilities, and a RLT production capacity of 250,000 doses in 2024 and beyond, Novartis continues to expand its worldwide RLT manufacturing network as ongoing clinical trials may present the potential to bring Pluvicto and Lutathera to more patients in earlier lines of treatment.

Novartis and Radioligand Therapy (RLT)
Novartis is committed to expanding the radioligand therapy platform to shape the future of RLT as a treatment class. By harnessing the power of radioactive atoms and applying it to advanced cancers, RLT is theoretically able to deliver radiation to target cells anywhere in the body[1,2].

We are 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 recently presented data at the 2023 European Society for Medical Oncology (ESMO) Congress studying Pluvicto in the pre-taxane setting for patients with prostate-specific membrane antigen (PSMA)-positive metastatic castration-resistance prostate cancer (mCRPC).

With established global expertise, and specialized supply chain and manufacturing capabilities across its network, we are supporting growing demand for our RLT medicines. Our production capabilities continue to expand and now include sites in Millburn, US, Zaragoza, Spain, Ivrea, Italy and our new state-of-the-art facility in Indianapolis, US. We recently announced plans to expand our manufacturing capabilities and build additional points of supply in Sasayama, Japan and Haiyan, Zhejiang, China to produce RLTs for patients in Japan and China. We are continually evaluating additional opportunities to increase capacity around the world.

What is Pluvicto?
PLUVICTO is a radiopharmaceutical used to treat adults with an 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), and
- has already been treated with other anticancer treatments

Pluvicto Important Safety Information
Use of PLUVICTO involves exposure to radioactivity. Long-term, accruing radiation exposure is associated with increased risk for cancer. To minimize radiation exposure to others following administration of PLUVICTO, patients are advised to limit close contact (less than 3 feet) with household contacts for 2 days or with children and pregnant women for 7 days, to refrain from sexual activity for 7 days, and to sleep in a separate bedroom from household contacts for 3 days, from children for 7 days, or from pregnant women for 15 days.

PLUVICTO may cause low level of blood cell counts. Patients should tell their doctor right away if they develop any new or worsening symptoms, including tiredness or weakness, pale skin, shortness of breath, bleeding or bruising more easily than normal or difficulty to stop bleeding, or frequent infections with signs such as fever, chills, sore throat, or mouth ulcers. PLUVICTO may also cause problems with kidneys. Patients should tell their doctor right away if they develop any new or worsening symptoms, including passing urine less often or passing much smaller amounts of urine than usual.

Before receiving PLUVICTO, patients should tell their doctor if they have low level of blood cell counts (hemoglobin, white blood cell count, absolute neutrophil count, platelet count); if they have or have had tiredness, weakness, pale skin, shortness of breath, bleeding or bruising more easily than normal or difficulty

stopping bleeding, or frequent infections with signs such as fever, chills, sore throat, or mouth ulcers (possible signs of myelosuppression); if they have or have had kidney problems; if they have or have had any other type of cancer or treatment for cancer, as PLUVICTO contributes to long-term cumulative radiation exposure; and if they are sexually active, as all radiopharmaceuticals, including PLUVICTO, have the potential to cause harm to an unborn baby. Patients should use effective contraception for intercourse during treatment with PLUVICTO and for 14 weeks after the last dose. PLUVICTO may cause temporary or permanent infertility.

Before administration of PLUVICTO patients should drink plenty of water in order to urinate as often as possible during the first hours after administration.

The most common side effects of PLUVICTO include tiredness, dry mouth, nausea, low red blood cell count, loss of appetite, changes in bowel movements (constipation or diarrhea), vomiting, low blood platelet count, urinary tract infection, weight loss, and abdominal pain.

Please see full Prescribing Information for PLUVICTO
at https://www.novartis.us/sites/www.novartis.us/files/pluvicto.pdf.

What is Lutathera?
LUTATHERA is a prescription medicine used to treat adults with a type of cancer known as gastroenteropancreatic neuroendocrine tumors (GEP-NETs) that are positive for the hormone receptor somatostatin, including GEP-NETs in the foregut, midgut, and hindgut.

Lutathera Important Safety Information
What are some important things to know about the safety of LUTATHERA?
LUTATHERA is associated with some serious safety considerations and, in some cases, these may require your health care provider to adjust or stop your treatment. You should always follow your health care provider's instructions. Safety considerations include:

- **Radiation exposure:** Treatment with LUTATHERA will expose you to radiation, which can contribute to your long-term radiation exposure. Overall radiation exposure is associated with an increased risk for cancer. The radiation will be detectable in your urine for up to 30 days following administration of the drug. It is important to minimize radiation exposure to household contacts consistent with good radiation safety practices as advised by your health care provider.
- **Bone marrow problems:** Treatment with LUTATHERA increases the risk of myelosuppression, a condition in which bone marrow activity is decreased, resulting in a drop in blood cell counts. You may experience blood-related side effects such as low red blood cells (anemia), low numbers of cells that are responsible for blood clotting (thrombocytopenia), and low numbers of white blood cells (neutropenia). Speak with your health care provider if you experience any signs or symptoms of infection, fever, chills, dizziness, shortness of breath, or increased bleeding or bruising. Your health care provider may need to adjust or stop your treatment accordingly.
- **Secondary bone marrow and blood cancers:** Other serious conditions that you may develop as a direct result of treatment with LUTATHERA include blood and bone marrow disorders known as secondary myelodysplastic syndrome and cancer known as acute leukemia. Your health care provider will routinely check your blood cell counts and tell you if they are too low or too high.
- **Kidney problems:** Treatment with LUTATHERA will expose your kidneys to radiation and may impair their ability to work as normal. You may be at an increased risk for kidney problems after LUTATHERA treatment if you already have kidney impairment before treatment. In some cases, patients have experienced kidney failure after treatment with LUTATHERA. Your health care provider will provide you with an amino acid solution before, during, and after LUTATHERA to help protect your kidneys. You should stay well hydrated before, on the day of, and on the day after your treatment. You should urinate

frequently before, on the day of, and on the day after administration of LUTATHERA. Your doctor will monitor your kidney function and may withhold, reduce, or stop your LUTATHERA treatment accordingly.

- **Liver problems:** In clinical studies of LUTATHERA, less than 1% of patients were reported to have tumor bleeding (hemorrhage), swelling (edema), or tissue damage (necrosis) to the liver. If you have tumors in your liver, you may be more likely to experience these side effects. Tell your health care provider right away if you have any of these signs and symptoms of liver problems: yellowing of the skin or the whites of the eyes (jaundice), unusual darkening of the urine, unusual tiredness, right upper stomach area (abdomen) pain, confusion, and/or swelling of the stomach area (abdomen). Your health care provider will monitor your liver using blood tests and may need to withhold, reduce, or stop your LUTATHERA treatment accordingly.
- **Allergic reactions:** Allergic reactions have occurred in people who were treated with LUTATHERA. Notify your health care provider if you develop symptoms of an allergic reaction. Seek emergency help right away for any serious allergic reactions. Symptoms may include trouble breathing or swallowing; raised bumps (hives); rash or itching; and swelling of the face, lips, tongue, throat, or arms.
- **Hormonal gland problems (carcinoid crisis):** During your treatment you may experience certain symptoms that are related to hormones released from your cancer. These symptoms may include flushing, diarrhea, difficulty breathing (bronchospasm), and low blood pressure (hypotension), and may occur during or within the 24 hours after your first LUTATHERA treatment. Your health care provider will monitor you closely. Speak with your health care provider if you experience any of these signs or symptoms.
- **Pregnancy warning:** Tell your health care provider if you are pregnant. LUTATHERA can harm your unborn baby. Females should use an effective method of birth control during treatment and for 7 months after the last dose of LUTATHERA. Males with female partners should use an effective method of birth control during treatment with LUTATHERA and for 4 months after the last dose.
- **Breastfeeding warning:** You should not breastfeed during treatment with LUTATHERA and for 2.5 months after your last dose of LUTATHERA.
- **Fertility problems:** Treatment with LUTATHERA may cause infertility. This is because radiation absorbed by your testes or ovaries over the treatment period falls within the range of exposure in which temporary or permanent infertility may occur.

What are the most common side effects of LUTATHERA?
The most common and most serious side effects of LUTATHERA include decreased blood cell counts, increased liver enzymes, vomiting, nausea, increased blood glucose, and decreased blood potassium levels.

Talk to your doctor if you experience any of these side effects. There are other possible side effects of LUTATHERA. For more information and to learn more about LUTATHERA, talk to your doctor or health care provider.

What other medicines may interact with LUTATHERA?
Tell your health care provider if you are taking any other medications. Somatostatin analogs and glucocorticoids may affect how your LUTATHERA treatment works. You should stop taking your long-acting somatostatin analog at least 4 weeks before LUTATHERA treatment. You may continue taking short-acting somatostatin analogs up to 24 hours before your LUTATHERA treatment. Avoid repeated high doses of glucocorticoids during treatment with LUTATHERA.

You are encouraged to report negative side effects of prescription drugs to the FDA.
Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.

Please see full Prescribing Information for LUTATHERA at https://www.novartis.com/us-en/sites/novartis_us/files/lutathera.pdf**.**

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,” “plan,” “may,” “could,” “would,” “expect,” “anticipate,” “look forward,” “believe,” “committed,” “investigational,” “pipeline,” “launch,” or similar terms, or by express or implied discussions regarding potential marketing approvals, new indications or labeling for the investigational or approved products described in this press release, 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 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; 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 more than 250 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.**

References

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Novartis Media Relations

E-mail: media.relations@novartis.com

North America

Julie Masow +1 862 579 8456

Michael Meo +1 862 274 5414

Marlena Abdinoor +1 617 335 9525

Novartis Investor Relations

E-mail: investor.relations@novartis.com

North America

Sloan Simpson +1 862 345 4440

Jonathan Graham +1 201 602 9921

Parag Mahanti +1 973 876 4912

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11. mailto:investor.relations@novartis.com