Novartis begins construction of two new radioligand therapy facilities in the US, expanding its world-class RLT manufacturing and supply network

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- Indianapolis site expansion will establish in-house production of isotopes critical for production of radioligand therapies (RLTs) for cancer treatment
- New facility in California will be third US-based RLT production facility
- Novartis is exploring a diverse portfolio of new isotopes, ligands and combination therapies to expand the use of RLTs in additional cancer types beyond prostate and neuroendocrine tumors

EAST HANOVER, N.J., Sept. 4, 2024 -- Novartis today announced the construction of two new radioligand therapy (RLT) manufacturing facilities in the US that will extend its world-class manufacturing and supply chain capabilities. The new facilities represent Novartis' continued investment in developing a robust infrastructure to support the expanding use of RLTs to treat cancer.

Novartis broke ground on a new facility at its Indianapolis site that will produce radioisotopes critical for the manufacturing of RLTs. In Carlsbad, Calif., Novartis is establishing its third RLT manufacturing site in the US to support expanded use of RLTs, create resiliency in its manufacturing network and optimize the delivery of medicines to patients on the West Coast.

RLTs are a form of precision medicine that combine a tumor-targeting molecule (ligand) with a therapeutic radioisotope, enabling the delivery of radiation to the tumor while limiting damage to the surrounding cells. Novartis is actively investigating the application of RLTs across cancer types and settings, with one of the deepest and most advanced pipelines in the industry. Both facilities will be built with room for further expansion to enable the potential production of different isotopes, ligands and RLTs. Once completed and approved, these new facilities will further strengthen the Novartis RLT manufacturing and supply network.

"Novartis pioneered the adoption at scale of radioligand therapies across different indications as a targeted approach to treat cancers," said Victor Bultó, President, US, Novartis. "Building on this experience and knowledge, we are confident in the potential of RLTs to meaningfully benefit many more patients affected by different types of cancer in the future. We are investing in our supply chain capabilities today to ensure that we are prepared to consistently deliver these complex treatments to the growing number of eligible patients in the long-term."

Novartis was the first to scale the availability of RLTs in the market across different cancer types with Pluvicto® (lutetium Lu 177 vipivotide tetraxetan) and Lutathera® (lutetium Lu 177 dotatate). The company's early- and late-stage pipeline has several programs in or entering the clinic, as well as other preclinical and discovery programs to identify the next wave of RLTs. Following regulatory approvals, isotopes produced in Indianapolis will be used to manufacture Pluvicto, Lutathera, and investigational RLTs in Novartis' pipeline.

Important Safety Information for 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 been treated with androgen receptor (AR) pathway inhibition and taxane-based chemotherapy.

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.

Important Safety Information for Lutathera

Lutathera® (lutetium Lu 177 dotatate) is a prescription medicine used to treat adults and children aged 12 years and older 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.

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.

Adverse reactions observed in pediatric patients were similar to those observed in adults treated with LUTATHERA.

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.

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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 https://www.novartis.us and connect with us on LinkedIn, LinkedIn US, Facebook, X/Twitter, X/Twitter US and Instagram.

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