Novartis radioligand therapy Lutathera® FDA approved as first medicine specifically for pediatric patients with gastroenteropancreatic neuroendocrine tumors

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- Approval based on NETTER-P trial in which Lutathera demonstrated a consistent safety profile and comparable drug exposure between pediatric (ages 12-17) and adult patients
- Gastroenteropancreatic neuroendocrine tumors (GEP-NETs) are a rare cancer that is often unresectable and commonly diagnosed in the late stages of disease
- Novartis, a leader in radioligand therapy (RLT), is investigating a portfolio of RLTs to treat a broad range of cancers, including GEP-NETs, lung, prostate, breast, colon, brain and pancreatic cancers

EAST HANOVER, N.J., April 23, 2024 -- Novartis today announced that the U.S. Food and Drug Administration (FDA) approved Lutathera® (lutetium Lu 177 dotatate) for the treatment of pediatric patients 12 years and older with somatostatin receptor-positive (SSTR+) gastroenteropancreatic neuroendocrine tumors (GEP-NETs), including foregut, midgut, and hindgut NETs. This approval makes Lutathera the first therapy specifically reviewed and approved for use in pediatric patients with GEP-NETs.

"Lutathera is now the very first therapy approved specifically for children with GEP-NETs, offering new hope to young patients living with this rare cancer," said Tina Deignan, Therapeutic Area Head, Oncology US. "Radioligand therapies have extraordinary potential to shape the future of cancer care. With this approval, we have taken another vital step toward fulfilling that vision, strengthening our commitment to researching and developing the RLT platform across multiple cancer types and treatment settings."

NETs are a type of cancer that originates in neuroendocrine cells throughout the body and are commonly considered slow-growing malignancies[1]. The diagnosis of NETs is often delayed due to the inactive nature of the disease, and approximately 10% to 20% of pediatric patients are diagnosed with metastatic disease[2,3]. Even though NETs are an orphan disease, their incidence has increased over the past several decades[1,4-6].

"While GEP-NETs in children and adolescents are rare, the impact can be devastating. Today's approval addresses a critical need for new treatment options for these vulnerable patients," said Dr. Theodore Laetsch, trial investigator and Director, Developmental Therapeutics Program, Children's Hospital of Philadelphia (CHOP), a NETTER-P clinical trial site. "The introduction of radioligand therapy significantly advanced how we treat GEP-NETs, and I'm encouraged that younger patients now have the potential to benefit from this innovation."

The approval was based on the NETTER-P trial, which evaluated Lutathera in patients aged 12 to <18 years old with SSTR+ GEP-NETs[7]. The study reported a safety profile consistent with the adult population studied in NETTER-1, the pivotal trial for approval of Lutathera in adults. In addition, the estimated radiation absorbed dose in pediatric patients was within established organ thresholds for external beam radiation and comparable to that in adults for the approved dose.

About Lutathera®

Lutathera® (lutetium Lu 177 dotatate) is approved in the US for the treatment of adults and children 12 years and older with SSTR-positive GEP-NETs, including those in the foregut, midgut and hindgut, an indication which includes the populations studied in the randomized, controlled Phase III trials NETTER-1 and NETTER-2. Lutathera is also approved in Europe for unresectable or metastatic, progressive, well-differentiated (G1 and G2), SSTR-positive GEP-NETs in adults, and in Japan for SSTR-positive NETs[8,9].

Novartis and Radioligand Therapy (RLT)

Novartis is reimagining cancer care with RLT for patients with advanced cancers. 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[10,11].

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.

With established global expertise, and specialized supply chain and manufacturing capabilities across the Novartis 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 Lutathera?

LUTATHERA is a prescription medicine used to treat adult and pediatric patients 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.

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.

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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Novartis Media Relations

E-mail: media.relations@novartis.com

North America

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
