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MEDIA & INVESTOR RELEASE

Novartis Lutathera® significantly reduced risk of disease progression or death by 72% as first-line treatment for patients with advanced gastroenteropancreatic neuroendocrine tumors

- *In the Phase III NETTER-2 trial, Lutathera plus octreotide LAR significantly extended median PFS to 22.8 months vs. 8.5 months with high-dose octreotide LAR in patients with newly diagnosed grade 2 and 3 advanced gastroenteropancreatic neuroendocrine tumors (GEP-NETs)[1]*

- *NETTER-2 is the first and only positive Phase III trial for a radioligand therapy (RLT) in the first-line setting, demonstrating the potential of RLTs in earlier lines*

- *Novartis, a leader in radioligand therapy, is investigating a broad portfolio of RLTs in advanced cancers, in addition to GEP-NETs, including lung, prostate, breast, colon, glioblastoma and pancreatic cancers to continue reimagining medicine for patients*

Basel, January 19, 2024 – Novartis today presented data from the Phase III NETTER-2 trial showing that Lutathera® (INN: lutetium (177Lu) oxodotreotide / USAN: lutetium Lu 177 dotatate) plus long-acting release (LAR) octreotide reduced the risk of disease progression or death by 72% as first-line therapy in patients with somatostatin receptor-positive (SSTR+) well-differentiated grade 2/3 advanced gastroenteropancreatic neuroendocrine tumors (GEP-NETs) versus high-dose octreotide LAR alone[1]. Data were presented at the 2024 American Society of Clinical Oncology (ASCO) Gastrointestinal (GI) Cancers Symposium.

“These positive results for Lutathera are practice-changing and offer new first-line treatment data for patients who have a significant unmet need. This study confirms the clinical benefit of first-line radioligand therapy for newly diagnosed patients living with these types of advanced GEP-NETs,” said Dr. Simron Singh, Associate Professor of Medicine at the University of Toronto and cofounder of the Susan Leslie Clinic for Neuroendocrine Tumours at the Odette Cancer Centre, Sunnybrook Health Sciences Centre, Ontario, Canada. “These findings should instill confidence among physicians in using Lutathera as a first-line treatment for patients with this life-threatening type of cancer.”

Efficacy endpoint[1]	**Lutathera plus octreotide LAR vs. high-dose octreotide LAR**
Progression-free survival	HR 0.28 (95% CI: 0.18, 0.42; *p*<0.0001)

Median PFS (months)	22.8 month (95% CI: 19.4 -not estimable) vs. 8.5 months (95% CI: 7.7-13.8)
Objective response rate (ORR)*	43% (95% CI: 35.0-51.3) vs. 9.3% (95% CI: 3.8-18.3), p<0.0001

**Assessed via RECIST 1.1*

“This is the first positive Phase III trial of a radioligand therapy in the first-line setting, and the overall efficacy and safety results are amongst the most clinically relevant observed to date in this kind of advanced cancer, addressing a significant unmet need for patients with newly diagnosed advanced GEP-NETs,” said Jeff Legos, Global Head of Oncology Development at Novartis. “The positive results are a significant advancement and further reaffirm our strategy to research and develop radioligand therapies in earlier lines of treatment or stages of disease to improve outcomes for patients.”

No new or unexpected safety findings were observed in the study and data are consistent with the already well-established safety profile of Lutathera[1]. Most patients (88%) in the Lutathera arm received all four cycles of Lutathera treatment. The most common all-grade AEs (≥20%) for the Lutathera arm vs. control arm were nausea (27.2% vs 17.8%), diarrhea (25.9% vs 34.2%) and abdominal pain (17.7% vs 27.4%), and the most common grade ≥3 AE (>5%) was lymphocyte count decreased (5.4% vs 0%).

NETs are a type of cancer that originate in neuroendocrine cells throughout the body and are commonly considered slow-growing malignancies. However, some NETs are associated with rapid progression and poor prognosis and in many cases, diagnosis is delayed until patients have advanced disease[2-4]. Even though NETs are a rare (orphan) disease, their incidence has increased over the past several decades[2-5] and there is a need for continued research into treatment options for newly diagnosed patients.

The NETTER-2 trial is ongoing for further evaluation of secondary endpoints including overall survival and long-term safety.

About NETTER-2
NETTER-2 (NCT03972488) is an open-label, multi-center, randomized, comparator-controlled Phase III trial assessing whether Lutathera plus octreotide LAR when taken as a first-line treatment can prolong PFS in patients with high-proliferation rate tumors (G2 and G3), compared to treatment with high-dose (60 mg) long-acting octreotide[6]. Eligible patients were diagnosed with SSTR-positive advanced GEP-NETs within 6 months before enrollment[6].

About Lutathera®
Lutathera® (INN: lutetium (177Lu) oxodotreotide / USAN: lutetium Lu 177 dotatate) is approved in the US for the treatment of adult patients with SSTR-positive GEP-NETs, including those in the foregut, midgut and hindgut, an indication which includes the NETTER-2 population. Lutathera is also approved in Europe for unresectable or metastatic, progressive, well-differentiated (G1 and G2), SSTR-positive GEP-NETs in adults[7,8], and in Japan for SSTR-positive NETs.

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[9,10].

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.

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,” “seek,” “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.**

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