Novartis International AG
Novartis Global Communications
CH-4002 Basel
Switzerland

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MEDIA & INVESTOR RELEASE

Novartis radioligand therapy Lutathera® demonstrated statistically significant and clinically meaningful progression-free survival in first line advanced gastroenteropancreatic neuroendocrine tumors (GEP-NETs)

- *Phase III NETTER-2 trial met primary endpoint of improvement in progression-free survival (PFS) and key secondary endpoint of objective response rate (ORR) in patients with Grade 2 and 3 advanced gastroenteropancreatic neuroendocrine tumors (GEP-NETs) who received first line treatment with Lutathera® in combination with long-acting octreotide, versus high-dose long-acting octreotide alone[1,2]*

- *Lutathera is the first radioligand therapy (RLT) to demonstrate clinically meaningful benefit in a first line setting[1]*

- *Findings to be presented at an upcoming medical meeting and discussed with regulatory authorities, with submissions to follow*

- *Novartis is investigating a broad portfolio of RLTs, exploring their treatment potential in a range of advanced cancers beyond prostate and GEP-NET, including lung, breast, pancreatic and colon. The company also continues to support the increasing demand for RLTs with expansions at existing manufacturing sites in the U.S. and Europe and a new state-of-the-art facility in Indianapolis, U.S., which is awaiting FDA approval*

Basel, September 25, 2023 — Today, Novartis announced the Phase III NETTER-2 trial with Lutathera® (INN: lutetium (^{177}Lu) oxodotreotide / USAN: lutetium Lu 177 dotatate) met its primary endpoint. First line treatment with Lutathera in combination with long-acting octreotide demonstrated a significant improvement in progression-free survival (PFS) in patients with newly diagnosed somatostatin receptor (SSTR)-positive, Grade 2 and 3, advanced gastroenteropancreatic neuroendocrine tumors (GEP-NETs) versus high-dose long-acting octreotide alone[1,2]. No new or unexpected safety findings were observed in the study and data are consistent with the already well-established safety profile of Lutathera[1-4].

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[5-7]. Even though NETs are a rare (orphan) disease, their incidence has grown over 500% in the last three decades[5-8] and there is an urgent need for additional treatment options for patients newly diagnosed with inoperable or advanced disease.

With these results, NETTER-2 is Lutathera's second Phase III trial showing clinically meaningful results for patients[2,4]. The approval of Lutathera was originally based on the pivotal NETTER-1 trial, which demonstrated highly significant and clinically meaningful PFS prolongation for patients treated with Lutathera in combination with long-acting octreotide versus high-dose (60 mg) long-acting octreotide for SSTR-positive, inoperable midgut neuroendocrine tumors (NETs) who were progressing despite standard treatment[3-4,9].

"These positive results for Lutathera are quite remarkable and they represent the potential for radioligand therapy to make a meaningful impact for newly diagnosed patients living with advanced GEP-NETs," said Jeff Legos, Executive Vice President, Global Head of Oncology Development at Novartis. "Exploring the use of radioligand therapies in earlier lines of treatment for patients with cancer is part of our larger, collaborative effort to precisely deliver novel treatment modalities directly to the cancer cells to improve patient outcomes."

The findings from NETTER-2 will be presented at an upcoming medical meeting and discussed with regulatory authorities.

About NETTER-2
NETTER-2 (NCT03972488) is an open-label, multi-center, randomized, comparator-controlled Phase III trial assessing whether Lutathera plus long-acting octreotide 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[2]. Eligible patients were diagnosed with SSTR-positive advanced GEP-NETs within 6 months before enrollment[2].

About Lutathera®
Lutathera® (INN: lutetium (^{177}Lu) oxodotreotide / USAN: lutetium Lu 177 dotatate) is an Advanced Accelerator Applications RLT approved in the United States for the treatment of SSTR-positive GEP-NETs, including foregut, midgut and hindgut neuroendocrine tumors in adults and in Europe for unresectable or metastatic, progressive, well-differentiated (G1 and G2), SSTR-positive GEP-NETs in adults[10-11].

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[12-13]. Novartis has established global expertise, specialized supply chain and manufacturing capabilities across its network of RLT production sites. In order to support growing demand for our RLT platform, we have expanded our RLT production capabilities in Millburn, New Jersey (U.S.), Zaragoza (Spain) and Ivrea (Italy), and are building a new radioligand manufacturing facility in Indianapolis, Indiana (U.S.), which is planned to be operational later in 2023. We are continually evaluating additional opportunities to expand capacity.

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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 such as COVID-19; 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 reimagining medicine to improve and extend people's lives. We deliver high-value medicines that alleviate society's greatest disease burdens through technology leadership in R&D and novel access approaches. In our quest to find new medicines, we consistently rank among the world's top companies investing in research and development. About 103,000 people of more than 140 nationalities work together to bring Novartis products to nearly 800 million people around the world. Find out more at https://www.novartis.com

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Novartis Media Relations
E-mail: media.relations@novartis.com

Central		North America	
Richard Jarvis	+41 79 584 2326	Julie Masow	+1 862 579 8456
Anja von Treskow	+41 79 392 9697	Michael Meo	+1 862 274 5414
Anna Schäfers	+41 79 801 7267	Marlena Abdinoor	+1 617 335 9525

Switzerland	
Satoshi Sugimoto	+41 79 619 2035

Novartis Investor Relations
Central investor relations line: +41 61 324 7944
E-mail: investor.relations@novartis.com

Central		North America	
Samir Shah	+41 61 324 7944	Sloan Simpson	+1 862 345 4440
Nicole Zinsli-Somm	+41 61 324 3809	Parag Mahanti	+1 973 876 4912
Isabella Zinck	+41 61 324 7188		