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Novartis announces JCO publication of Lutathera® NETTER-1 data showing significantly longer time to deterioration of key quality of life measures in patients with progressive midgut NETs

- *Patients reported prolonged maintenance of global health status[1](overall health)*
- *Longer time to deterioration (TTD) seen across multiple clinically relevant symptom categories including diarrhea, fatigue and pain[1]*
- *Functional health-related quality of life (HRQoL) categories, including those pertaining to basic and advanced activities of daily living, were sustained for a longer time[1]*

Basel, June 7, 2018 – Novartis today announced that the *Journal of Clinical Oncology* has published results of an analysis of the impact of Lutathera® (lutetium Lu 177 dotatate*) treatment on time to deterioration in HRQoL in the pivotal phase III NETTER-1 trial. The data demonstrate that treatment with Lutathera provides significantly longer time to deterioration of quality of life for patients with progressive midgut Neuroendocrine tumors (NETs) compared to octreotide LAR alone[1]. Lutathera is the first Peptide Receptor Radionuclide Therapy (PRRT) to receive regulatory registration, with approval by the European Commission in September 2017 and by the US Food and Drug Administration (FDA) in January 2018. Lutathera is an Advanced Accelerator Applications product.

“Neuroendocrine tumor progression is often associated with deterioration in quality of life due to tumor growth and production of hormones[2,3],” said Jonathan Strosberg, MD, Associate Professor, Section Head, Neuroendocrine Tumor Program at Moffitt Cancer Center, and lead author of the publication. “In patients with advanced NETs, maintenance of an acceptable HRQoL is particularly important given the relatively long durations of treatment and overall survival compared to other advanced malignancies. These data provide hope for these patients and their families.”

TTD was significantly longer in the Lutathera arm versus the comparator arm for the following domains: global health status (self-assessment of overall health and quality of life), physical functioning, role functioning, fatigue, pain, diarrhea, disease related worries and body image[1]. Differences in median TTD were clinically significant in several domains: 28.8 months vs. 6.1 months for global health status, and 25.2 months vs. 11.5 months for physical functioning[1]. Domains where Lutathera treatment did not show a significant benefit in TTD include nausea and vomiting, dyspnea, insomnia, appetite loss, constipation, financial difficulties, endocrine scale (flushing, sweats), GI scale (bloating, flatulence), treatment scale, social functioning scale, muscle/bone pain, sexual function, and information/communication function. There were no domains in which TTD analysis showed significant benefit for the comparator arm[1].

“The results demonstrated by Lutathera in the NETTER-1 study continue to be encouraging in a patient population with limited therapeutic options for control of progressive disease[1],” said

Samit Hirawat, MD, Head of Novartis Oncology Global Drug Development. “We are focused on developing medicines that offer meaningful outcomes for patients, like Lutathera.”

The NETTER-1 trial is an international phase III study in patients with progressive, somatostatin receptor-positive midgut neuroendocrine tumors. Patients were randomized to treatment with Lutathera and best supportive care (30 mg octreotide LAR), or 60 mg octreotide LAR alone[4]. European Organisation for Research and Treatment of Cancer (EORTC) quality of life questionnaires, a commonly used metric for analysis of HRQoL in cancer patients, were assessed during the trial to determine the impact of treatment on HRQoL[5]. Patients completed the questionnaires at baseline and every 12 weeks until tumor progression. TTD was defined as the time from randomization to the first QoL deterioration ≥10 points (on a 100-point scale) compared to baseline score for the same domain. Patients with no deterioration were censored at the last QoL assessment date. Patients with no baseline and/or no follow-up were censored at randomization. Analysis cut-off date was June 30, 2016. In total, 231 patients were randomized in the HRQoL study (117 in the Lutathera arm and 114 in the 60 mg octreotide LAR arm).

About Lutathera®
Lutathera is a lutetium Lu 177-labeled somatostatin analog peptide. Lutathera belongs to a class of treatments called Peptide Receptor Radionuclide Therapy (PRRT). Lutathera is comprised of a targeting molecule which carries a radioactive component. Lutathera has received orphan drug designation from the FDA and the European Medicines Agency (EMA). In the US, Lutathera is indicated for the treatment of somatostatin receptor positive gastroenteropancreatic neuroendocrine tumors (GEP-NETs), including foregut, midgut, and hindgut neuroendocrine tumors in adults[6]. In Europe, Lutathera is indicated for the treatment of unresectable or metastatic, progressive, well differentiated (G1 and G2), somatostatin receptor positive gastroenteropancreatic neuroendocrine tumors (GEP-NETs) in adults[7]. Lutathera can cause serious side effects that may include bone marrow problems, kidney problems, liver problems, hormonal gland problems, fertility problems and problems arising from radiation exposure. Please see Important Safety Information and Full Prescribing Information at: www.lutathera.com.

* USAN: lutetium Lu 177 dotatate / INN: lutetium (177Lu) oxodotreotide

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preferences of physicians and patients; general political and economic conditions; safety, quality 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 Advanced Accelerator Applications
Advanced Accelerator Applications, a Novartis company, is an innovative radiopharmaceutical company developing, producing and commercializing nuclear medicine theragnostics. AAA is also an established leader in radiopharmaceuticals for Positron Emission tomography (PET) and Single-Photon Emission Computed Tomography (SPECT) diagnostic imaging, mainly used in clinical oncology, cardiology and neurology. For more information, please visit: https://www.adacap.com/.

About Novartis
Novartis provides innovative healthcare solutions that address the evolving needs of patients and societies. Headquartered in Basel, Switzerland, Novartis offers a diversified portfolio to best meet these needs: innovative medicines, cost-saving generic and biosimilar pharmaceuticals and eye care. Novartis has leading positions globally in each of these areas. In 2017, the Group achieved net sales of USD 49.1 billion, while R&D throughout the Group amounted to approximately USD 9.0 billion. Novartis Group companies employ approximately 124,000 full-time-equivalent associates. Novartis products are sold in approximately 155 countries around the world. For more information, please visit http://www.novartis.com.

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6. LUTATHERA Prescribing Information
7. LUTATHERA Summary of Product Characteristics

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