ITM Presents Positive Topline Phase 3 COMPETE Trial Data with n.c.a. ^{177}Lu-edotreotide (ITM-11), a Targeted Radiopharmaceutical Therapy, in Patients with Grade 1 or 2 Gastroenteropancreatic Neuroendocrine Tumors at the ENETS 2025 Conference

- Trial met primary endpoint, demonstrating clinically and statistically significant improvement in progression-free survival (PFS) compared to everolimus
- Median PFS was 23.9 months on n.c.a. ^{177}Lu-edotreotide v. 14.1 months on everolimus; p value=0.022
- Company plans for U.S. New Drug Application (NDA) submission in 2025

Krakow, Poland March 6, 2025 - ITM Isotope Technologies Munich SE (ITM), a leading radiopharmaceutical biotech company, today presented positive topline data from its Phase 3 COMPETE trial in patients with Grade 1 or Grade 2 somatostatin receptor (SSTR)-positive gastroenteropancreatic neuroendocrine tumors (GEP-NETs). The trial results demonstrated that n.c.a. ^{177}Lu-edotreotide (also known as ITM-11 or ^{177}Lu-edotreotide), a proprietary, synthetic, targeted radiotherapeutic agent, met the primary endpoint and significantly prolonged progression-free survival in patients when compared to everolimus, a standard of care cancer treatment. The data were presented by study investigator Jaume Capdevila, MD, PhD, at the 22nd Annual European Neuroendocrine Tumor Society (ENETS) 2025 Conference, held in Krakow, Poland from March 5-7, 2025.

"*COMPETE is the first pivotal trial comparing a radiopharmaceutical drug candidate to a targeted molecular therapy without the routine use of accompanying somatostatin analogues in this GEP-NET patient population. These data show unequivocal support for ^{177}Lu-edotreotide's potential benefit in extending PFS,*" **said Dr. Capdevila, senior medical oncologist at Vall d'Hebron University Hospital, Barcelona**. "*Additionally, ^{177}Lu-edotreotide's convenient dosing schedule and favorable safety results reinforce its potential as a compelling new treatment option*."

COMPETE is a prospective, randomized, controlled, open-label Phase 3 trial that enrolled 309 patients with inoperable, progressive, Grade 1 or Grade 2 somatostatin receptor-positive neuroendocrine tumors of gastroenteric or pancreatic origin (Ki-67 ≤20%) in Europe, the United States, Australia and South Africa. The study objectives were to evaluate the efficacy and safety of ^{177}Lu-edotreotide compared to everolimus. ^{177}Lu-edotreotide is comprised of non-carrier-added (n.c.a.) lutetium-177, a therapeutic β-emitting radioisotope, and edotreotide, a somatostatin receptor agonist. It is the first radiopharmaceutical to be tested in the GEP-NET patient population using non-carrier-added lutetium, which has a higher isotopic purity than carrier-added lutetium.

Patients were randomized 2:1 to receive 7.5 GBq of ^{177}Lu-edotreotide with a nephroprotective amino acid solution every three months for up to four cycles, or everolimus 10 mg daily for up to 30 months, or until disease progression. There were 207 patients on the ^{177}Lu-edotreotide arm and 102 on the everolimus arm. Dosimetry was used to assess the absorbed dose in tumors compared to that in healthy tissue to enhance safety and efficacy monitoring of the study drug in patients.

Topline Clinical Results Summary

Primary endpoint	• Median progression-free survival (PFS) was significantly longer with ^{177}Lu-edotreotide v. everolimus (**23.9 vs 14.1 months);** stratified* p value = 0.022; HR 0.67, 95% CI [0.48, 0.95]
Secondary endpoint	• Interim median overall survival (OS)** was numerically higher, but not conclusive for ^{177}Lu-edotreotide v. everolimus (**63.4 vs 58.7 months)**; p value=0.206; HR 0.78, 95% CI [0.5, 1.1]
Safety	• A lower proportion of patients experienced treatment-emergent adverse events (TEAEs) related to study medication with ^{177}Lu-edotreotide v. everolimus (**82.5% vs 97.0%**); one grade 2 serious TEAE of MDS related to ^{177}Lu-edotreotide was reported • No unforeseen TEAEs
	**Stratification factors: primary tumour origin [GE-NETs vs P-NETs] and by prior medical therapy [1st line vs 2nd line]* ***OS data will continue to mature* *Statistical analysis methods: Log-rank for PFS and OS; two-sided Fisher exact test and Mantel-Haenszel test for ORR*

"*The COMPETE results represent a major step forward in the development of new treatment options for people living with progressive, inoperable GEP-NETs. By extending progression-free survival by almost ten months compared to standard of care in this trial, ^{177}Lu-edotreotide showed the potential to significantly improve the treatment paradigm for physicians and their patients*," **said Jonathan Strosberg, MD, past president, North American Neuroendocrine Tumor Society and chair, GI Research Program, Moffitt Cancer Center and Research Institute in Tampa, FL**.

The median overall survival as of January 21, 2025 was 63.4 months for the ^{177}Lu-edotreotide arm and 58.7 months for the everolimus arm. While not statistically significant, the interim analysis showed a favorable trend for ^{177}Lu-edotreotide. Patients were permitted to start an alternative therapy after disease progression, potentially confounding the overall survival data. Overall survival data will continue to be updated.

^{177}Lu-edotreotide was observed to be well-tolerated and there were no unforeseen treatment-emergent adverse events. Additional data, including objective response rate, subgroup analyses, quality of life assessments and dosimetry, are currently being evaluated and expected to be

submitted for presentations at future medical meetings. ITM is planning to submit a New Drug Application (NDA) to the FDA in 2025.

"*These successful results validate our decision to design a pivotal Phase 3 trial directly comparing a targeted radiopharmaceutical against a targeted molecular therapy in Grade 1/2 GEP-NETS, underscoring our commitment to improving the lives of people living with this challenging cancer*," **said Andrew Cavey, MD, PhD, chief executive officer, ITM**. "*With this successful readout, ^{177}Lu-edotreotide becomes the first drug candidate in ITM's broad portfolio of early- to late-stage radiopharmaceuticals to deliver positive Phase 3 results and progress towards NDA submission and commercial launch preparations. Together, with our global isotopes manufacturing business, robust supply chain, and experienced clinical and commercial team, we believe we are uniquely positioned as a standout leader in the fast-growing radiopharmaceutical industry."*

ENETS Oral Presentation Details

Title: "Efficacy and safety of [^{177}Lu]Lu-edotreotide vs. everolimus in patients with grade 1 or grade 2 gastroenteropancreatic neuroendocrine tumours: COMPETE phase 3 trial"
Date and Time: March 6, 2025; 10:05 am – 10:12 am CET
Session and Room Number: Clinical science, Session 1: Theranostics in NENs – Integrating experience for a brighter future; Auditorium Hall (S1)
Presenter: Jaume Capdevila, MD, PhD, study investigator and senior medical oncologist at Vall d'Hebron University Hospital, Barcelona

Additional n.c.a.^{177}Lu-edotreotide Clinical Trials

^{177}Lu-edotreotide is also being evaluated in a Phase 3 trial (COMPOSE) in patients with well-differentiated, aggressive Grade 2 or Grade 3, SSTR-positive GEP-NET tumors. The COMPOSE trial is a prospective, randomized, controlled, open-label trial evaluating the efficacy, safety and patient-reported outcomes of ^{177}Lu-edotreotide as first- or second-line treatment compared to physician's choice standard of care chemotherapy. Additional clinical programs with ^{177}Lu-edotreotide include a Phase 1 pediatric trial in SSTR-positive tumors (KinLET) and a Phase 3 investigator-sponsored trial in lung and thymus neuroendocrine tumors (LEVEL).

About GEP-NETS

Neuroendocrine tumors (NETs) are a rare form of cancer, with an estimated 8 new cases per 100,000 individuals diagnosed each year in the U.S. and 9 cases per 100,000 in Europe. The incidence of NETs has steadily increased over recent decades, resulting, in part, from improved diagnosis. Gastroenteropancreatic neuroendocrine tumors (GEP-NETS) originate in the neuroendocrine system and are made up of nerve cells and hormone-producing cells. They can occur anywhere in the GI tract and pancreas, including the stomach, small intestine, colon, rectum, and appendix. There is still a high unmet medical need for treatment options, as many patients are asymptomatic and diagnosed at a late stage with metastatic disease.

About n.c.a. ^{177}Lu-edotreotide

^{177}Lu-edotreotide is a radiolabeled peptide conjugate that delivers beta radiation specifically to SSTR-positive tumor cells, sparing healthy organs and tissue. The drug candidate, delivered intravenously, is comprised of non-carrier-added lutetium-177, a therapeutic β-emitting radioisotope, and edotreotide, a synthetic SSTR agonist. ^{177}Lu-edotreotide was granted orphan drug designation in the EU and the US, and fast track designation in the US for the treatment of GEP-NETs, based on positive results from a retrospective Phase 2 study with ^{177}Lu-edotreotide.

About ITM Isotope Technologies Munich SE

ITM, a leading radiopharmaceutical biotech company, is dedicated to providing a new generation of radiopharmaceutical therapeutics and diagnostics for hard-to-treat tumors. We aim to meet the needs of cancer patients, clinicians and our partners through excellence in development, production and global supply. With improved patient benefit as the driving principle for all we do, ITM advances a broad precision oncology pipeline, including multiple Phase 3 studies, combining the company's high-quality radioisotopes with a range of targeting molecules. By leveraging our two decades of pioneering radiopharma expertise, central industry position and established global network, ITM strives to provide patients with more effective targeted treatment to improve clinical outcomes and quality of life. www.itm-radiopharma.com

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References:

1. Baum RP, Kluge AW, Kulkarni H, et al. [(177)Lu-DOTA](0)-D-Phe(1)-Tyr(3)-Octreotide ((177)Lu-DOTATOC) For Peptide Receptor Radiotherapy in Patients with Advanced Neuroendocrine Tumours: A Phase-II Study. Theranostics. 2016;6(4):501-510.