Garching, Germany, December 6, 2017

First gastroenteropancreatic-neuroendocrine tumor (GEP-NET) patient in Europe for the COMPETE phase III clinical trial with n.c.a.^{177}Lu-Edotreotide (Solucin®)

First Patient enrolled in Europe for the clinical study COMPETE at the University Hospital Marburg, Germany

COMPETE to investigate a broad indication with non-functional GE-NET /functional or nonfunctional P-NET

Targeted Radionuclide Therapy (TRT) with n.c.a. ^{177}Lu-Edotreotide (Solucin®) to demonstrate prolonged PFS compared to standard of care mTOR inhibitor Everolimus

ITM Isotopen Technologien München AG (ITM), a specialized radiopharmaceutical company, today announced the enrollment of the first patient recruited in Europe for the COMPETE phase III clinical trial at the University Hospital Marburg, Germany.

COMPETE is led as an international pivotal multi-center phase III clinical trial evaluating the efficacy and safety of (no-carrier-added) n.c.a.^{177}Lu-Edotreotide (Solucin®) compared to Everolimus. The enrollment requires patients with inoperable, progressive, somatostatin-receptor positive neuroendocrine tumors of gastroenteric or pancreatic origin (GEP-NET). The primary endpoint is progression-free survival (PFS). The study will be conducted predominantly in Europe, North America, South Africa and Australia. The first patient to be enrolled and treated was in Australia.

The compound under investigation, Solucin®, is known as a Targeted Radionuclide Therapy (TRT) agent, which consists of the targeting molecule Edotreotide, an octreotide-derived somatostatin analogue and ITM´s EndolucinBeta® (no-carrier-added Lutetium-177). EndolucinBeta® is a synthetic, low-energy beta-emitting isotope of Lutetium, a recently EMA approved pharmaceutical precursor. The radiopharmaceutical Solucin® is administered as an intravenous infusion, specifically targeting and destroying the tumor cells with ionizing radiation.

Solucin® received an Orphan Designation (EMA/OD/196/13) for the treatment of GEP-NET, based on early clinical experience[1], which has demonstrated a substantial clinical benefit with increased PFS and quality of life.

Steffen Schuster, Chief Executive Officer of ITM, said: *„GEP-NETs are rare diseases with complex clinical features and reduced life expectancy. COMPETE sets a milestone, as there are only few suitable and well tolerated treatment options, where prospective clinical trials with radiopharmaceuticals are limited. We are happy to having enrolled the first patient in Europe for the COMPETE study at the University Hospital Marburg, Germany. This marks the starting point of COMPETE in Europe, whereby we expect a rapid increase in the number of recruits."*

Dr Anja Rinke, coordinator of the NET center at the University Hospital Marburg, added: *"COMPETE offers us the opportunity to answer critical questions regarding the treatment of GEP-NETs with Targeted Radionuclide Therapy. In particular, we expect to learn at which point of the treatment algorithm Targeted Radionuclide Therapy should be used most sensibly. Moreover we would like to know whether Targeted Radionuclide Therapy with ^{177}Lu-Edotreotide provides better results than the treatment with a licensed substance, Everolimus."*

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Study Design
The phase III clinical trial COMPETE is led as an international, prospective, randomized, controlled, open-label, multicenter phase III study to evaluate efficacy and safety of TRT with n.c.a. ^{177}Lu-Edotreotide (Solucin®) compared to targeted molecular therapy with Everolimus in patients with inoperable, progressive, somatostatin receptor-positive (SSTR^{+}) neuroendocrine tumors of gastroenteric or pancreatic origin (GEP-NET). The trial, which is carried out in collaboration with the Clinical Research Organization ABX-CRO advanced pharmaceutical services Forschungsgesellschaft mbH, will be conducted worldwide in 11 countries and 35 sites.

In total, 300 GEP-NET patients will be randomized 2:1 to receive either TRT with Solucin® consisting of a maximum of four cycles (7.5 GBq ^{177}Lu-Edotreotide each), administered as i.v. infusion at 3-monthly intervals for 9 months, or until diagnosis of progression (200 patients), or 10 mg Everolimus daily, administered orally as a tablet until diagnosis of progression (100 patients). Study duration per patient will be 24 months.

Primary endpoint is PFS. Diagnosis of progression and liver tumor burden will be established based on radiological information from morphological imaging (MRI and/or CT) according to RECIST 1. Secondary endpoints include overall survival (OS), parameters of morphological and functional tumor response, safety and health-related quality of life (HRQL). Furthermore, patient and tumor characteristics, as well as the uptake of n.c.a. ^{177}Lu-Edotreotide will be analyzed for criteria predicting the efficacy and safety of TRT.

About Targeted Radionuclide Therapy
Targeted Radionuclide Therapy uses very small amounts of radioactive compounds, called radiopharmaceuticals, to diagnose and treat various diseases, like cancer. Targeted radiopharmaceuticals contain a targeting molecule (e.g. peptide or antibody) and a medical radioactive isotope. The technique works by injecting the radio-conjugate into the patient's body where it accumulates in the affected organs or lesions. The targeting molecule binds to a tumor-specific receptor or antigen, according to a lock and key principle and is absorbed by the tumor cells. In most cases the targeting molecule can be used for both diagnosis and therapy – only the radioisotope has to be changed. This opens up the way for the application of Theranostics.

For diagnostic applications radioisotopes with short half-lives are used. With highly sensitive molecular imaging technologies like PET (Positron Emission Tomography) or SPECT (Single Photon Emission Tomography), images of organs and lesions can be created and diseases can therefore be diagnosed in their early stages. Medical radioisotopes with longer half-lives are applied for treatment. The tumor tissue is being destroyed by the radiopharmaceutical emitting cytotoxic doses of ionizing radiation. A highly precise localization of the radioactivity ensures that healthy tissue in the surroundings of the targeted tumor is minimally affected.

About Solucin®
Solucin® (n.c.a. ^{177}Lu-Edotreotide / n.c.a. ^{177}Lu-DOTATOC) is known as an innovative TRT agent with favorable safety profile and promising efficacy. Solucin® consists of two molecular components – firstly of Edotreotide (DOTATOC), an octreotide-derived somatostatin analogue, and secondly, of EndolucinBeta® (no-carrier-added Lutetium-177) a synthetic, low-energy beta-emitting isotope of Lutetium.

The targeting molecule Edotreotide (DOTATOC) contains DOTA which functions as a chelator for radioisotopes and TOC, a synthetic somatostatin receptor ligand. It binds with high affinity somatostatin receptors (subtype 2 and 5) and retains both its receptor binding properties and its physiological function when labeled with ^{177}Lu. Somatostatin receptors type 2 (SSTR2) are predominantly overexpressed by neuroendocrine tumors. Solucin®, upon binding to SSTR2 receptors *in vivo*, is internalized and retained by tumor cells. Upon decay, the isotope emits cytotoxic medium-energy beta particles of ≤1.7 mm path length in soft tissue.

The radioactive isotope EndolucinBeta® respectively n.c.a. ^{177}Lu chloride is used in TRT, e.g. in the field of Precision Oncology. It is a radiopharmaceutical precursor, used for radiolabeling of disease-specific carrier molecules. EndolucinBeta® has a half-life of 6.647 days and provides the highest specific activity of more than 3,000 GBq/mg at Activity Reference Time (ART), whereas the day of ART can be flexibly selected by the customer. EndolucinBeta® exhibits an extraordinary level of radionuclidic purity. It does not contain metastable ^{177m}Lu, thus, there is no need of logistics and storage of contaminated radioactive waste. EndolucinBeta® is GMP certified and recently received marketing authorization in the EU.

About ITM

ITM Isotopen Technologien München AG is a privately held group of companies dedicated to the development, production and global supply of innovative diagnostic and therapeutic radionuclides and radiopharmaceuticals. Since its foundation in 2004, ITM and its subsidiaries have established the GMP manufacturing and a robust global supply network of a novel, first-in-class medical radionuclides and -generator platform for a new generation of targeted cancer diagnostics and therapies. Furthermore, ITM is developing a proprietary portfolio and growing pipeline of targeted treatments in various stages of clinical development addressing a range of cancers such as neuroendocrine cancers or bone metastases. ITM's main objectives, together with its scientific, medical and industrial collaboration partners worldwide, are to significantly improve outcomes and quality of life for cancer patients while at the same time reducing side-effects and improving health economics through a new generation of TRT in Precision Oncology.
For more information about ITM, please visit: www.itm.ag

References

1) Baum RP, Kluge A, Kulkarni H, Schorr-Neufing U, Niepsch K, Bitterlich N, and Van Echteld C, (2016). [177Lu-DOTA]0-D-Phe1-Tyr3-octreotide (177Lu-DOTATOC) for Peptide Receptor Radiotherapy in patients with advanced Neuroendocrine Tumors: A retrospective Phase II study of efficacy and safety. Theranostics). 6(4):501-510

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