Garching, Germany, April 18, 2017

First Patient in Phase III Clinical Trial COMPETE with n.c.a.^{177}Lu-Edotreotide (Solucin®) in Cancer Patients with GEP-NET

Solucin® (n.c.a. ^{177}Lu-Edotreotide) to be shown as a highly precise and effective Targeted Radionuclide Therapy Agent

Promising data of Solucin® expected to be confirmed in phase III clinical trial COMPETE

Solucin® to demonstrate prolonged PFS compared to mTOR inhibitor Everolimus

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ITM Isotopen Technologien München AG (ITM), a specialized radiopharmaceutical company, today announced the enrollment of the first patient recruited in the COMPETE study, an international pivotal multi-center phase III clinical trial evaluating the efficacy and safety of n.c.a.^{177}Lu-Edotreotide (Solucin®) compared to Everolimus in patients with inoperable, progressive, somatostatin-receptor positive neuroendocrine tumors of gastroenteric or pancreatic origin (GEP-NET). The primary endpoint is progression-free survival (PFS).

With Solucin® a retrospective phase II efficacy and safety study of Targeted Radionuclide Therapy in patients with advanced neuroendocrine tumors (NET) with encouraging results has been performed. The results suggest and demonstrate a significant benefit, a substantially improved progression-free survival (PFS).[1] Therefore Solucin® received an Orphan Designation (EMA/OD/196/13). Due to these favorable data and the long-term experience with n.c.a. ^{177}Lu-Edotreotide under compassionate use, ITM is positive to verify the results in the clinical phase III trial, known as COMPETE. The study will be conducted predominantly in Europe, North America, South Africa and Australia. The first patient has been enrolled and will be treated in Australia.

Solucin® is injected into the patient´s body where it specifically accumulates at the tumor. The tumor tissue is being destroyed by the radiopharmaceutical emitting cytotoxic doses of ionizing radiation. Solucin® is composed of two molecular components. Firstly, there is the targeting molecule Edotreotide (DOTATOC), an octreotide-derived somatostatin analogue. Secondly, it consists of ITM´s EndolucinBeta® (no-carrier-added Lutetium-177), a synthetic, low-energy beta-emitting isotope of Lutetium, a recently EMA approved pharmaceutical precursor.

Steffen Schuster, Chief Executive Officer of ITM, said: *„By combining EndolucinBeta® with Edotreotide we created the highly precise and targeted radiopharmaceutical Solucin® for the treatment of GEP-NETs. GEP-NETs are considered as rare disease suggesting a high unmet medical need for effective therapies. After having achieved really promising results in clinical phase II, we are truly encouraged now to take the next step by starting our COMPETE phase III study. I am very pleased about having enrolled the first patient and we are confident to complete the recruitment within the next months. We would like to extend our thanks to the attending physicians and patients for the confidence in us."*

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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 Targeted Radionuclide Therapy 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 Targeted Radionuclide Therapy 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 progression-free survival (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 exploratively analyzed for traits predicting Targeted Radionuclide Therapy efficacy.

About Targeted Radionuclide Therapy
Targeted Radionuclide Therapy is a medical specialty using 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 Targeted Radionuclide Therapy 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 Targeted Radionuclide Therapy, 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 Targeted Radionuclide Therapies 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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