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FDA Acceptance of IND to advance Phase III Clinical Trial COMPETE with Solucin® for Treatment of GEP-NET in the U.S.

Recruitment in the U.S. for the COMPETE trial to begin shortly

Solucin® studied as a first-line therapy

Exclusively-produced nephroprotective amino acid solution administered

ITM Isotopen Technologien München AG (ITM), a specialized radiopharmaceutical company, announced today that the U.S. Food and Drug Administration (FDA) has accepted the company's Investigational New Drug Application (IND) to advance its innovative radiopharmaceutical Solucin® (n.c.a. ^{177}Lu-Edotreotide), into a phase III clinical trial in the U.S..

The COMPETE trial is led as an international, pivotal, multi-center, phase III clinical trial, evaluating the efficacy and safety of Targeted Radionuclide Therapy with Solucin® compared to Everolimus[1] in patients with inoperable, progressive, somatostatin-receptor positive neuroendocrine tumors of gastroenteric or pancreatic origin (GEP-NET). The primary objective of the trial is to prolong progression-free survival (PFS) compared to Everolimus. COMPETE will be conducted predominantly in Europe, North America, South Africa and Australia. The company plans to start recruitment immediately at five designated sites in the U.S.: Excel Diagnostics & Nuclear Oncology Center, Mayo Clinic, Moffitt Cancer Center & Research Institute, University of Michigan Comprehensive Cancer Center, and Virginia Mason Medical Center.

The study protocol of COMPETE was designed together with renowned neuroendocrine experts, including members of the European Neuroendocrine Tumor Society (ENETS). Accordingly, a broad indication was chosen with non-functional GE-NET / functional or nonfunctional P-NET. Everolimus, the current standard of care therapy, was chosen as the comparator for Targeted Radionuclide Therapy with Solucin®. The COMPETE clinical trial will also be the first to test Targeted Radionuclide Therapy as a first-line therapy against NET. The results of the trial could therefore influence the future treatment algorithm of NETs.

In order to both maximize the therapeutic properties of Targeted Radionuclide Therapy and ensure that patients in the COMPETE study are exposed to as few side effects as possible, an amino acid solution consisting of arginine and lysine will be administered shortly before treatment. This amino acid solution has nephroprotective properties but is not yet commercially available. The Mayo Clinic, the Society of Nuclear Medicine and Molecular Imaging (SNMMI), the Washington University School of Medicine in St. Louis, and the Memorial Sloan Kettering Cancer Center have jointly filed comments with the FDA recommending that regulatory changes be made to make arginine and lysine more easily available as bulk drug for patients who undergo Targeted Radionuclide Therapy.[2]

"We are pleased to have received FDA acceptance for our clinical trial protocol and look forward to beginning recruitment for COMPETE in the U.S.", said Steffen Schuster, Chief Executive Officer of ITM. *"The commencement of this clinical trial in the U.S. marks a significant milestone for us. We are delighted to be able to collaborate with distinguished American experts in the fields of Targeted Radionuclide Therapy, Oncology, and Endocrinology to provide the best possible treatment for NET patients."*

– Ends –

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 GmbH, will be conducted worldwide in min. 12 countries and approx. 43 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 objective is to demonstrate the efficacy of Targeted Radionuclide Therapy with ^{177}Lu-Edotreotide to prolong progression-free survival (PFS) in patients with inoperable, progressive, $SSTR^+$ GEP-NET, compared to Everolimus. Key secondary objectives are to show an increase in objective response rates (ORR), defined as the proportion of patients achieving partial response (PR) or complete response (CR) as best outcome, with ^{177}Lu-Edotreotide compared to Everolimus and to assess overall survival (OS) defined as the time from date of randomization until death.

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 Targeted Radionuclide Therapy agent with favorable safety profile and promising efficacy. Solucin® consists of two molecular components –Edotreotide (DOTATOC), an octreotide-derived somatostatin analogue, and 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), and 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 received marketing authorization in the EU in 2016.

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 GMP manufacturing and a robust global supply network of 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, which address 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) Afinitor [prescribing information]. East Hanover, NJ: Novartis Pharmaceuticals Corp; 2018.
2) http://www.snmmi.org/NewsPublications/NewsDetail.aspx?ItemNumber=29116

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