Ovarian cancer is presently the second deadliest form of cancer amongst women and has poor prognosis, despite significant research efforts in that domain. The most current cure combines chemotherapy and surgery. Often the pathology is diagnosed at an advanced stage of the disease. This type of cancer is then difficult to treat with external radiotherapy, because of possible presence of metastasis and because this organ is difficult to irradiate without collateral damages. New treatments are therefore highly needed.

New treatments using theranostics isotope pairs to detect metastasis and have selective systemic radiotherapy have this potential. The field of molecular oncology and nuclear medicine is rapidly evolving. Indeed this personalised medicine approach combines diagnosis by PET imaging and subsequent treatment with a similar radiopharmaceutical for which the imaging isotope is replaced by a treatment isotope.

In the recent years, PET/CT functional imaging using 18F-based FDG radiopharmaceutical (a glucose analog with an isotope which gives contrast in PET imaging) has had a significant impact on how the patients were managed during their treatment. Alongside the recent marketing of new drugs exploiting new radioisotopes and radioactivity such as Xofigo® and Luthatera® have shown important results to cure other forms of advanced cancers. This field is expected to further expand rapidly and provide new types of treatments - known as theranostics pairs - combining imaging and personalized treatment with the same radiopharmaceutical and different types of isotopes, emitting positron or gamma light for imaging on one side, and Auger electron, beta and alpha radiation for treatment on the other side.

In addition, positron emitting isotopes such as 11Carbon can personalize hadron therapy treatments by imaging the dose distribution of the implanted ions in European radiotherapy facilities using Carbon treatment such as the CNAO, Centro Nazionale de e Oncologia and Medaustron near Milano and Maedaustron near Vienna.

MEDICIS-PROMED proposes to significantly advance the use of radioisotopes for personalized medicine in Europe. This will be done in three interconnected scientific intersectorial Work-Packages, with 11 Early Stage Researchers hired by the beneficiaries and 4 recruited in Swiss partner organizations.

A new marker of ovarian cancer has recently been identified and can now be used as a possible target for diagnosis and treatment. It is the TEM1/endosialin protein. An antibody was shown to specifically target this marker in preclinical imaging
studies in animal models; this now opens the route for investigations of personalized treatments combining functional imaging and either alpha-emitting or beta-emitting isotopes.

This domain can now rapidly progress on a European level thanks to the present training network proposal where leading academic, medical institutes and high-tech companies will contribute to a multidisciplinary coordinated program. This will build on the new CERN-MEDICIS medical radioisotope beams facility that can produce unique batches of innovative isotopes, such as 149Terbium.

The program will develop along three R&D work packages integrating multidisciplinary intersectorial training teams:

• Development of new radioisotopes and techniques using isotope mass separation for medicine and based on CERN-MEDICIS
• Development and test of 11Carbon PET-aided hadron therapy
• Synthesis & tests of radiopharmaceuticals to diagnose & treat ovarian cancer

**Progress beyond the state of the art and expected potential impact (including the socio-economic impact and the wider societal implications of the project so far)**

MEDICIS-PROMED is training a new generation of fifteen scientists, bringing together a network of world renown scientists in isotope mass-separation and lasers, accelerators, material science, oncology, robotics and imaging, to bring new solutions to the 2nd deadliest cancer for women, around a newly build facility CERN-MEDICIS. This is done by the design and engineering of subsystems along the supply chain and tests of radiopharmaceuticals, and PET-aided hadron therapy. This is expected to become an expanding field for such newly trained scientists. The new isotope supply chain resulting from MEDICIS-PROMED is going beyond the present common practices, thanks to the expected results of the ambitious R&D program, and to the new generation of young scientists trained in the relevant fields.

In Work Package 1,
ESR 4 has demonstrated the successful synthesis of graphene monoatomic coating onto isotope production tantalum targets. If these results can be produced on other types of targets, for instance those for the production of 99Mo, this has the potential to provide a new method of production for 99mTechnetium generators. 99mTechnecium is the most used radioisotopes for diagnostics protocols worldwide.

in Work Package 2
Carbon hadron therapy is available in centers such as HIT, CNAO and soon MEDAUSTRON. While some proof of feasibility has been demonstrated at NIRS in Japan, some accelerator components are still missing to make PET Carbon hadron therapy. ESR 3 at CERN has demonstrated that EBIS ion sources can be used in the injector chain to deliver appropriate rates of 11Carbon ions. Upon validation of these preliminary results, the proper accelerator chain can be defined and proposed to European centers, making the possibility of carbon ion treatment and subsequent treatment verification by PET scanners a new method to improve the patient treatments.

Work-Package 3
Activities in MEDICIS-Promed are expected to significantly impact and speed-up the research in theranostics in Europe, that is combining diagnostic and therapeutic isotopes. 149Tb is an alpha-emitting therapeutic isotopes which can be combined with its diagnostics counterparts 152Tb and 155Tb. While some proof-of-principle results have already been obtained at CHUV by ESR 13, the investigations in targeted alpha therapy will only become possible when 149Tb will be produced from CERN-MEDICIS, the only worldwide medical mass separation dedicated facility. ESR 6 at AAA has shown that the industrial production of 149Tb at large cyclotrons can be investigated. The MEDICIS-Promed network has thus the possibility to bring a sustainable source of theranostic Terbium isotopes for pre-clinical, and eventually later on, for clinical trials, putting the European research laboratories in a leading position in this field.