



Esperite (ESP) leads international consortium for clinical translation of extracellular vesicles use in various therapies

Extracellular vesicles (EVs) disruptive technology targets unmet needs in neuroinflammatory diseases at lower costs than allogenic stem cell therapies.

Esperite's business unit The Cell Factory develops EVs-based therapeutics in treatment of drug-resistant epilepsy in children jointly with Bambino Gesù Children's Hospital, Mario Negri Institute for Pharmacological Research and the Women's and Children's Health Department of the University of Padua.

Zutphen, The Netherlands – 30 September 2016

Esperite N.V. (Euronext: ESP, "Esperite") sponsors an international consortium of the leading teams in paediatric regenerative medicine to bring extracellular vesicles (EVs) technology to the clinic with niche applications in treatment of severe neuro-inflammatory diseases. Its first project focuses on EVs application in untreatable-yet acute and chronic drug-resistant epilepsy in children. The consortium will also investigate EVs and exosomes characteristics, potency, and a mode of action and will further improve the EVs production processes.

Led by Professor Federico Vigevano at Bambino Gesù Children's Hospital with Dr Alessandra Fierabracci providing her expertise in Immunology and Dr. Annamaria Vezzani at Mario Negri Institute, pre-clinical tests of mesenchymal stem cells (MSC)-derived EVs are underway to confirm the safety and efficacy already demonstrated in multiple in vitro and in vivo models. This project will enable the first-in-man use of MSC-derived EVs and exosomes

in treatment of drug-resistant epilepsy in children. The project follows a long-term collaboration between the Children's Hospital and the Esperite group initiated and liaised by Professor Stefano Grossi, Esperite's Scientific Director in Italy.

In parallel, Esperite's regenerative medicine division, The Cell Factory, in partnership with Professor Maurizio Muraca's team at University of Padua, are better characterising EVs to establish clinical grade standards for production, purification, quantification, bio-distribution and molecular characterisation of new EV-based therapeutics.

Professor Muraca has also agreed to join the Scientific Board of The Cell Factory to support EVs products development and clinical translation. Professor Muraca has extensive and long-term experience in immunology, EVs and MSCs research, and the expertise in regulations of advanced therapies use in clinic.

The Cell Factory produces ultra-pure EVs and exosomes according to GLP/GMP guidelines, using proprietary technology for expansion of MSC in fully defined media with no use of animal-derived components at any stage. Stem cells expansion is performed in the most efficient and scalable 3D culture systems using microcarrier beads. The Cell Factory's proprietary closed cell culture system produces high purity EVs and exosomes using pharmaceutical-quality sequential filtration system for EVs extraction and purification. The system can be easily scaled up improving significantly EVs production costs, footprint and process scalability. EVs products can be manufactured with this technology at least 10x more efficiently and cheaper when comparing to MSC equivalent.

The consortium will investigate the anti-inflammatory and anti-epileptic effect of the "off-the-shelf" EVs derived from non-HLA-matched MSC lines. The advantages of using EVs in treatment of acute and chronic epilepsy are product stability and low production costs providing the "off-the-shelf" drug for immediate and repeated non-invasive application. In a broader perspective, the positive results of using immunosuppressive EVs in a central nervous system would open up a possibility of immediate intervention in acute diseases in neurology such as stroke, traumatic brain, spinal cord injury, newborn hypoxic ischemia and many others.

Diseases of central nervous system are among most devastating for patients and their relatives. Neurological disorders are generating a significant additional cost related to hospitalisation, rehabilitation, often eliminate the patients and their relatives from a job market. CDC estimated that annual costs related to epilepsy exceeds 15 billion USD in the United States alone with 50 million patients worldwide (WHO). Cost related to brain stroke in the United States is estimated to 34 billion USD per year (CDC), with 15 million new patients worldwide each year (WHO). Cumulative cost related to traumatic brain injury (TBI) and spinal cost injury in the United States is over 80 billion USD per year (CDC and AANS), with up to 0.5 million new incidents of spinal cord injury and 10 million of TBI per year (WHO). Most of these diseases have no effective therapy yet. It is expected that EVs products will be effective in the niche indications of above-mentioned conditions preventing neuroinflammatory-related damage of central nervous system. Moreover, EVs will be able to target an acute diseases i.e. TBI, brain stroke, spinal cord injury, more effectively when comparing to allogenic MSCs, due to the EV's stability and easier administration at shorter

time what is critical for successful therapy. The latter would additionally expand a potential market of EVs products beyond the competitive allogenic MSCs products.

Epilepsy is one of the most common brain diseases affecting about 1 in 100 children under 17-year old according to CDC. Epilepsy carries significant detrimental effects on the quality of life and can lead to a secondary brain damage. The disease can have different aetiology, including stroke, brain trauma, and neuro-inflammation. Severity of the seizures is variable and the antiepileptic drugs are effective only in about 2/3 of the patients.

About the consortium partners:

Ospedale Pediatrico Bambino Gesù OPBG (Rome, Italy) is the largest paediatric Hospital and research center in Europe, providing over 1.550.000 healthcare services each year to children and adolescents from all over the world. OPBG pursues excellency in health care through advanced research and clinical activities, while improving processes to exploit the progress of biomedical science. The Hospital's clinical activities run side by side with its scientific research, aiming at constantly improving and innovating diagnostic and therapeutic procedures. OPBG's Research Laboratories are located in a 5,000 sqm research facility, fully equipped with high-tech systems, supporting genomics, metagenomics, metabolomics, proteomics, microarray technology, cytogenetic and FISH applications, cytofluorimetry and cell sorting, cell and molecular biology. Within the Research Laboratories the team led by the Immunologist Dr Alessandra Fierabracci has established potency assays for evaluating the immunomodulatory activity of MSC-derived exosomes in vitro.

The IRCCS-Istituto di Ricerche Farmacologiche "Mario Negri" (www.marionegri.it) in Milan, Italy is a non-profit biomedical research institute. The Institute's constant research areas include cardiovascular, psychiatric and neurological diseases, and tumours. Over the years, in line with technical advances, research has spread into the fields of environment and health, kidney diseases, organ transplantation, and rare diseases,

The Institute works regularly with various associations, hospital groups with different specialties, general practitioners, and nurses, setting up nation-wide cooperation networks. Underlying all this is basic research in pharmacokinetics, pharmacology, immunology, cell biology, genomics, proteomics, and metabolomics; it organizes controlled randomized clinical trials, studies on cohorts of elderly people, systemic reviews and meta-analyses.

Dr Annamaria Vezzani is Head of the Laboratory Experimental Neurology, Dept of Neuroscience, and she will be contributing to the project by sharing her long standing expertise with animal models of epilepsy and neuroinflammation to test the therapeutic anticonvulsive potential of extracellular vesicles and provide proof-of-concept evidence for clinical applications.

The department of Woman's and Child's Health of the University of Padua is a 269-bed tertiary paediatric academic care centre, serving the entire North East region of Italy, devoted to provide excellence in patient's care, teaching and research, also including a ten-store research building. It is one of the eleven fully recognised Italian Children's Hospitals.

The University of Padova was founded in 1222. It includes 32 Departments, 1 University Hospital, 1 Veterinary Hospital, 1 Experimental Farm, 1 School of Excellence. It counts 61,000 Students and 12,000 Graduates per year.

ESPERITE Group, listed at Euronext Amsterdam and Paris, is a leading international company in regenerative and predictive medicine established in 2000.

The Cell Factory is a biotech platform-based business unit of ESPERITE Group. The Cell Factory led by Dr. Marcin Jurga develops highest quality therapeutic tools for affordable regenerative medicine.

To learn more about ESPERITE Group, or to book an interview with CEO Frederic Amar: +31 575 548 998 - ir@esperite.com or visit the websites at www.esperite.com and www.genoma.com.