Esperite's (ESP) The Cell Factory received European funding to develop the 2nd generation EVs drug for treatment of Stroke

Esperite's biotech company The Cell Factory, Belgium has received funding from the European Union's Horizon 2020 research and innovation Programme for development and characterization of the extracellular vesicles (EVs) drug CF-MEV-126 for treatment of stroke. The project is focused on the development of the 2nd generation EVs drug, with enhanced anti-inflammatory and neuroprotective activities.

Amsterdam, The Netherlands –3rd May 2018

The Cell Factory is investigating therapeutic properties of the EVs biologic drugs in the treatment of neurological diseases. Currently, the Company is developing two drug candidates for the treatment of neuroinflammatory diseases, CF-MEV-117 for drug-resistant epilepsy in children and CF-MEV-126 for treatment of stroke.

The EU funding will support the development of the new generation EVs drug CF-MEV-126 containing an additional genetic cargo (miRNAs) to enhance their anti-inflammatory and neuroprotective properties. In addition, the funding will allow a better understanding of the EVs mode of action in the treatment of stroke and other neurological diseases.

Stroke is the second leading cause of disability in Europe, and 10-35% of these patients die within 28-30 days. Current stroke therapy is very limited and mainly focused on general care and rehabilitation. In the EU 28 countries, the annual cost of stroke is estimated to €27 billion (WHO). The number of stroke events in Europe is projected to rise from 1.1 million in 2000 to 1.5 million per year by 2025 due to the aging population.

Most of the stroke injuries are caused by the brain ischemia (87%), and the rest by haemorrhage. Inflammation plays a crucial role in the brain's response to stroke incident. The pathologic processes proceeding the stroke event can be divided into 3 phases: acute (minutes to hours), subacute (hours to days) and chronic (days to months). EVs drug products could target all the phases. However, the most important property of the EVs, when comparing to the cell therapy, is their potential use during the acute phase. The EVs products can be cryopreserved without cryoprotectants, and therefore they can be used immediately after thawing

with no need of washing, centrifugation and viability tests. EVs are also safer when comparing to the MSCs due to their small size and lack of HLA markers (both class I and II). All these properties would make possible to use EVs drugs outside the hospital immediately after the stroke incident. Another advantage of the EVs, when comparing to MSCs and other cell therapies, is their penetration through the blood-brain barrier what is crucial for any effective treatment targeting the central nervous system.

An increasing number of studies are focusing on the involvement of microRNAs in the regulation of immune responses. Experimental data suggest that specific microRNAs in MSC-EVs could modulate the expression of inflammation-related genes. In addition, the EVs' miRNA cargo can be modified at the stage of the MSCs culture (before the EVs secretion) or after the EVs release by MSCs. The Cell Factory will use the new generation sequencing (NGS) technology for the analysis of miRNA in the newly established Esperite's genetic laboratory in Niel.

Dr. Marcin Jurga, R&D Director at The Cell Factory and the project coordinator, said: "The funding granted to The Cell Factory by the prestigious and competitive the European Union's Horizon 2020 programme confirms the importance of the EVs drugs in the regenerative medicine field. This project will let us progress with the development of the EVs drug for one of the most devastating and incurable diseases. Also, we hope that this project will encourage the pharma industry, investors, and other funding bodies to support the EVs field development."

The 2nd generation EVs drugs will be developed using the existing technology of The Cell Factory. The Company is leading the EVs field manufacturing the ultra-pure vesicles according to the GMP guidelines. The Cell Factory has developed a proprietary production process of MSCs and MSC-derived EVs using only fully defined raw materials (ancillary products) during the entire production process. MSCs and EVs are manufactured without animal-derived components, and human-derived undefined components, i.e., serum, undefined serum replacements, plasma, platelet lysates, gelatine, etc. The Cell Factory technology eliminates the risk of product contamination with pathogens, unknown active substances, and external EVs. The Cell Factory production process significantly improves the EVs purity, quality, and batch-to-batch reproducibility. Our company controls the entire production process starting from procurement of the source material (via bio-bank), donor selection, international transport of the biological products (controlled cold-chain), tissue processing, storage (cryopreservation in liquid nitrogen), cell extraction and expansion, EV bioproduction and purification, final product preparation and release. The production process is designed and validated according to GLP/GMP standards and follows the international guidelines dedicated to production and clinical use of biological medicinal products. Stem cells expansion is performed in the most efficient culture systems using 3D microcarrier beads and scalable stirring bioreactor systems. In addition, the closed system can be fully automated and the entire production process (including downstream concentration and filling) can be performed in a lower sterility grade lab environment. The Cell Factory's proprietary closed cell culture system and multi-harvest EVs batch production provide new standards in biologic drugs production and resulting in significant cost reductions without compromising product quality. Ultimately, EVs can be produced at least 10-times more efficiently and cheaper when comparing to allogenic MSCs equivalent.

In addition to the EVs production system, The Cell Factory has developed the new method for EVs quantification available for the scientific and biotech community. Current quantification methods do not allow precise enumeration of EVs and EVs quantification is currently one of the most significant challenges in the EVs field. Lack of standardized analytical instruments and methods for the EVs quantification have a considerable impact on the quality and reproducibility of scientific data and clinical translation of the EVs drug candidates. The Cell Factory has developed and validated a new method for EVs quantification using a combination of 3 techniques: nanoparticle tracking (NTA), multiparametric immunophenotyping (FACS) and immunomagnetic cell sorting adopted to EVs particles (MACS). Using our method different EVs can be precisely quantified based on different markers combination, e.g., tetraspanin proteins (CD9, CD63, CD81). This method is not limited however to the tetraspanins, and other markers can be used for detection and quantification of EVs. The method will be presented during the congresses in 2018 and will be published in the peer-review journal soon. We hope that using our quantification method the EVs field will develop faster and bring more quality EVs drug products into the clinic.

The Cell Factory is currently developing the EVs biologic drugs for:

- CF-MEV-107 for Crohn's disease (drug-resistant perianal fistulae)

The Cell Factory is leading a translational project on EVs first in man use in the treatment of Crohn's disease perianal fistulas. Inflammatory bowel disease (IBD) encompasses a spectrum of conditions affecting the gastrointestinal tract. The most common are Crohn's disease and ulcerative colitis. IBD is a chronic and often recurring inflammation of the intestines with unknown cause and limited treatment options. In the most severe cases of Crohn's disease, the patients suffer from perianal fistulas that significantly affect normal activity and may lead to complications such an increased risk of cancer and life-threating systemic inflammation.

Epidemiology and market estimation: IBD affects approximately 0.5% of the western countries population, and this number is rapidly increasing. There are over 0.5 million people in the US and over 1 million in Europe with Crohn's disease, with over 10 new cases per 100.000 people every year. The annual cost of therapy exceeds 5 billion USD in the US only (CDC). Up to 50% of Crohn's disease patients are affected significantly to treat perianal fistulas, and 75% require surgery (according to CDC) what estimates the potential market size of the CF-MEV-107. The Crohn's disease market was valued at $9.2 billion in 2016 and is set to reach $13.4 billion by 2026, a CAGR of 3.8%.

- CF-MEV-117 for Epilepsy (acute and chronic drug-resistant epilepsy)

The Cell Factory is developing the MSC-EVs drug candidate for the treatment of untreatable-yet acute and chronic drug-resistant epilepsy. Epilepsy carries significant detrimental effects on the quality of life and can lead to secondary brain damage. The disease can have different etiology, including stroke, brain trauma, and neuro-inflammation.

Epidemiology and market estimation: Epilepsy is one of the most common brain diseases affecting about 1 in 100 children under 17-year old according to CDC. The severity of the seizures is variable, and the antiepileptic drugs are effective only in about 2/3 of the patients. CDC estimated annual costs related to epilepsy exceeds 15 billion USD in the United States alone. It is estimated that sales of anti-epileptic drugs (AEDs) were approximately $6.1Bn.

- CF-MEV-126 for stroke (brain stroke and acute injuries of the central nervous system)

Brain stroke is the most devastating neurological disease with no effective therapy available yet. The brain damage could be significantly reduced if anti-inflammatory and neuroprotective treatment is applied immediately after stroke or injury. Esperite is looking for partners to support the development of extracellular vesicle therapeutics.

Epidemiology and market estimation: According to WHO, 1 in 6 people will have a stroke during lifetime and 6 million people die because of a stroke every year. Those who survive, very often suffer from severe physical and cognitive impairments due to brain damage following a stroke. CDC estimates the brain stroke-related costs around 34 billion USD every year only in the United States.

About the Company:

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

The Cell Factory is a company of ESPERITE Group, focused on innovative drug products development, clinical translation and commercialization using autologous mesenchymal stromal cells (MSCs) and allogenic MSC-derived extracellular vesicles (MSC-EVs). TCF-Biotech goal is a development of the highest quality therapeutic tools for affordable treatment of unmet medical needs.

The Cell Factory will hire the geneticist Dr. Gabrielis Kundrotas who will be working on this project.

This project focused on development of the EVs drug CF-MEV-126 for treatment of stroke has received funding from the European Union's Horizon 2020 research and innovation programme under the Marie Sklodowska-Curie grant agreement No 797424.

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 website at www.esperite.com.

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This press release contains inside information as referred to in article 7 paragraph 1 of Regulation (EU) 596/2014 (Market Abuse Regulation).