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22nd April, 2015
FOR IMMEDIATE RELEASE

CellOxess to unveil *in-vivo* efficacy data for Fertilix®, a novel antioxidant formulation designed to prevent Sperm Oxidative Stress at ESHRE 2015

Princeton, NJ 08540 USA

Current estimates from the World Health Organization suggest that more than 1 in 5 couples worldwide seek medical assistance for their fertility. In 40-50% of couples, male factors contribute to the lowering of fertility potential. These factors include, among other things, reduced sperm motility, count, morphology, and poor DNA integrity. In fact, a recent report from the WHO indicated that average sperm concentrations in the male population have been falling 2% each year.

Scientists have now discovered that the body's own uncontrolled metabolic species, commonly known as Reactive Oxygen Species (ROS), can affect the male reproductive tract resulting in a phenomenon called "Sperm Oxidative Stress" or SOS. Sperm health depends on a low oxidative state of the male reproductive tract to allow for normal growth and development in the testes. Accumulation of ROS in the male reproductive tract can overwhelm the body's natural antioxidant defense mechanisms, consequently damaging the molecular components of sperm cells including membrane lipids, proteins and mitochondrial and nuclear DNA. This cellular damage can cause reduced sperm count and motility, poor morphology, and decreased DNA integrity which in turn may result in reduced male fertility, higher chance of miscarriage and the incorrect transmission of paternal DNA code.

Scientists at CellOxess Biotechnology believe they have found an effective solution to ameliorate SOS. After a decade of research and development by Dr. Parviz Gharagozloo and several teams of academic and industrial collaborators, the company formulated the first range of male preconceptual antioxidants, trademarked Fertilix®, to combat SOS. This June, at the prestigious European Society of Human Reproduction and Embryology's annual meeting, CellOxess scientist Aron Moazamian will present the first *in-vivo* data demonstrating the efficacy of Fertilix® in mouse models of SOS.

Two independent labs, led by Professor Joël Drevet at Clermont University in France, and Professor Alfonso Gutiérrez-Adán at the INIA University of Madrid, verified that treatment of mice with Fertilix® prevented DNA damage, restored pregnancy rates to near normal levels and protected testicular tissue from the damaging effects of heat and ROS accumulation in established models of sperm oxidative stress. The official conference abstract is on the next page.

These groundbreaking results will be presented in detail at the ESHRE Annual Conference in Lisbon, Portugal, at 15:45 on June 16th in Room Braga of the International Lisbon Fair; http://www.eshre2015.eu/.

It is fitting that CellOxess will also be showcasing Fertilix® for the first time in Europe at the world's most prestigious reproductive conference. Several representatives, including Dr. Gharagozloo himself, will be present to discuss interest in the dietary supplement and opportunities for collaboration.

For more information, visit www.celloxess.com and www.fertilix.com, or visit booth #F10 from June 14th-17th on the conference floor.

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Fertilix, a novel antioxidant formulation designed to treat male infertility emanating from sperm oxidative DNA damage: Promising preclinical evidence from mouse models.

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Study question:
Does Fertilix, a novel antioxidant formulation designed for the male reproductive tract, reduce Sperm DNA Damage (SDD) and increase pregnancy rates in mouse models of sperm oxidative stress (SOS)?

Summary answer:
Oral administration of Fertilix for a period of 2 weeks significantly reduces SDD in Glutathione Peroxidase 5 (GPX-5) knockout mice and restores pregnancy rates almost back to normal levels in mice subjected to Scrotal Heat Shock (SHS).

What is known already:
Animal and human studies document the adverse effect of SDD on fertilization rate, embryo quality, miscarriage rates and the transfer of *de novo* sporadic mutations to the offspring. Semen samples of infertile men are known to be deficient in several key antioxidants relative to fertile counterparts. Antioxidants alone, or in combination, have consistently demonstrated a measure of efficacy against sperm oxidative stress or DNA damage in numerous human clinical trials.

Study design, size, duration:
Fertilix efficacy was evaluated in two, well-established mouse models of SOS, SHS and GPX-5 knockout mice, each with n=12, by independent laboratories. Mice were provided Fertilix in their drinking water for 2-4 weeks and compared with control groups for SDD and pregnancy rates.

Participants/materials, setting, methods:
In SHS model, each male's fertility was tested by partnering with 3 females for 5 days. The percentage of pregnant females, number of vaginal plugs, resorptions per litter, and litter size were recorded. Sperm DNA oxidative damage was evaluated by immunocytochemical detection of 8-OHdG residues in GPX-5 KO mice.

Main results and the role of chance:
8-Hydroxy-deoxy Guanosine (8-OHdG) is a biomarker of DNA oxidation. The average background levels of 8-OHdG in WT mice is around 30%. This level doubles up to about 60% in transgenic mice deficient in the antioxidant enzyme GPX-5. Our results indicate that a 2 week pretreatment of GPX-5 KO mice with Fertilix provides complete protection of sperm DNA against oxidation. In mouse models of SHS, only 35% (19/54) female mice got pregnant resulting in 169 fetuses. This is in contrast to the Fertilix pretreated group where 74% (42/57) female mice got pregnant resulting in 427 fetuses. The role of chance in obtaining supporting results for the efficacy of Fertilix in both models is minimal.

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Limitations, reason for caution:
It was not possible to ensure that every mouse took 100% of the product for the treatment period.

Wider implications of the findings:
The present situation is gravely concerning as clinical studies confirm moderate to severe SDD in about 60% of all men visiting IVF centers and about 80% of men diagnosed with idiopathic male infertility. These results, if confirmed in humans, will impact clinical fertility practice. Antioxidant supplementation will be an adjuvant therapy prior to undertaking ART procedures to improve fertilization rates, maintain a healthy pregnancy, and reduce *de novo* sporadic mutations being passed onto children.

Study funding/competing interest(s):
The study was funded by the University of Clermont-Ferrand and the University of Madrid. The corresponding author, A.M., is an employee of CellOxess LLC, which has a commercial interest in the detection and resolution of oxidative stress. The author, P.G., is the Managing Director of CellOxess LLC, which has a commercial interest in the detection and resolution of oxidative stress.