



Fertility treatment for men and women based on telomerase activation

Prof. Esther Priel, Department of Microbiology, Immunology and Genetics, School of Pharmacy, Faculty of Health Sciences, Ben-Gurion University of the Negev, Beer-Sheva, Israel

Technology

The global fertility services market is expected to witness a substantial growth in the future owing to rising incidence of infertility cases, emerging trend of delayed pregnancies among women, technological advancements in fertility procedures, and increased occurrences of gamete donations.

Telomerase is the re-elongation of telomeres. Telomerase male and female KO mice are sterile but upon telomerase re-induction and expression full fertility is regained. Long-term adverse effects of low telomerase activity and increased ROS exposure are likely associated with telomere shortening in oocytes from reproductive aged female mice. Human and mouse granulosa cells contain telomerase activity which is associated with their proliferation and differentiation and which is regulated by steroid hormones. Telomere shortening in mice reduces synapsis and chiasmata, increases embryo fragmentation, cell cycle arrest, apoptosis, spindle dysmorphologies and chromosome abnormalities. Telomere are shorter in the oocytes from women undergoing in vitro fertilization, who then produce fragmented, aneuploid embryos that fail to implant.

Current invention provides a single-dose fertility treatment based on novel class of tri-phenyl molecules with telomeraseactivating properties. The ability of our compounds to transiently increase TERT expression and telomerase activity, in a dose and time-dependent manner, in various *in vitro* and *in vivo* models was demonstrated. The treatment enhanced the expression of steroidogenic genes in human granulosa cells derived from women under IVF procedure and *in vivo* in mouse ovary. The compunds were found safe in animal studies and also demonstrated a protective effect on ovaries and testes of mice undergoing radiation suggesting it might be able to protect and improve fertility in individuals undergoing radiation therapy. The technology was developed in discussion with the In-Vitro Fertilization laboratory at the Soroka University Medical Center, Israel.

Advantages

- Our telomerase based-approach is unisex, supported by a novel MOA and can revolutionize the market of infertility.
- A proof of concept that the biological effects of the AGS NCE are mediated by telomerase was already published.
- AGS compounds (already undergo some preclinical validation for PK, safety etc), are at nM concentrations. transiently activate the cellular telomerase gene expression and activity in various human & mouse cells in-vitro and in different animal models invivo (3-6 mg/Kg s.c. inj.) in a dose and time dependent manner.

Applications

• Single-dose <u>unisex</u> fertility treatment based on telomerase activation.

Patent: Package: The technology and products including the use in infertility are covered by multiple issued patent families. US2019/0350878; US9670138