

Clinical Data Published from RepliCel's Skin Rejuvenation Study

A paper entitled, “Autologous Cell Therapy for Aged Human Skin: A Randomized, Placebo-Controlled, Phase-I Study”, has been published summarizing the data from RepliCel's clinical trial of RCS-01

VANCOUVER, BC, CANADA – September 24, 2019 – RepliCel Life Sciences Inc. (OTCQB: REPCF) (TSXV: RP) (FRA:P6P2) (“RepliCel” or the “Company”), a company developing next-generation technologies in aesthetics and orthopedics, is pleased to announce the publication of clinical data from its skin rejuvenation study (RCS-01) in an article entitled, *Autologous Cell Therapy for Aged Human Skin: A Randomized, Placebo-Controlled, Phase-I Study*, published in the peer-reviewed journal **Skin Pharmacology and Physiology** (Skin Pharmacol Physiol <http://dx.doi.org/10.1159/000502240>).

The publication summarizes data from a clinical trial in which it was shown that RepliCel's RCS-01 injections are well-tolerated for up to one-year post-injection and therefore safe to use. The study also demonstrated how the injections might reverse the effects of aging skin. As summarized in the paper, the study clearly established a biological link between RCS-01 injections and changes in the expression of particular genes in the skin. These changes in gene expression are expected to be indicative of the potential for rejuvenation of the extra-cellular matrix (ECM) under the dermis that is so important to vibrant, youthful skin.

“We are very pleased that the esteemed, peer-reviewed journal, *Skin Pharmacology and Physiology* saw the merit of RepliCel's clinical work,” stated RepliCel President & CEO, R. Lee Buckler, “and the potential of our proprietary cell therapy, RCS-01, for skin rejuvenation.”

The publication presents data showing for the first time that injections of NBDS-derived autologous cells into the human skin dermis layer alters the transcriptional expression profile of genes, which are involved in ECM homeostasis. Specifically, in comparison to placebo treated skin areas, injection of NBDS-derived fibroblasts promoted the expression of the genes TGFbeta1, CTGF, COL1A1, COL1A2, COL3A1 and lumican. These genes encode for proteins which are important for ECM homeostasis, thought to be of pathogenetic relevance for skin aging. In aged skin, levels of type 1 and type 3 collagen precursors and crosslinks are reduced.

The observation that injection of NBDS-derived cells is associated with an increased transcriptional expression of these genes indicates the possibility that cell therapy treatment with RCS-01 might ameliorate the clinical and aesthetic signs of skin aging, such as wrinkles. This assumption is in line with observations that increased expression of collagen type 1 and type 3 is a prerequisite for wrinkle reduction caused by retinol.

More about the senior authors

Professor Dr. med Jean Krutmann, the paper's senior author, is Professor of Dermatology and Environmental Medicine and Director of the IUF Leibniz Research Institute for Environmental Medicine at the Heinrich-Heine-University Düsseldorf where the study was conducted. He is a coordinator of the Leibniz Research Alliance "Healthy Aging" (a strategic alliance of 23 Leibniz institutes). His research is in the field of derma-toxicology and immune-dermatology with special emphasis on environmentally-induced skin diseases and skin aging. Prof. Krutmann is author or co-author of more than 400 papers. He is the recipient of the International Arnold-Rikli-Award, the Albert Fleckenstein Award, the Paul Gerson Unna Award, the Oscar Gans Award, the C.E.R.I.E.S. Research Support Award, the Dermopharmacy Innovation Award and the Xu Guang Qi Lecturer Award.

He is a visiting and adjunct professor at the Nagoya City University, Japan, Case Western Reserve University, Cleveland, Ohio, University of Alabama, Birmingham, AL, USA, and Fudan University, Shanghai, China. He is a member of the National Academy of Science of Germany. He is a clinical consultant to RepliCel Life Sciences and is contributing to the RepliCel-YOFOTO collaboration in China as it relates to the clinical development and commercialization of RepliCel's RCS-01 skin rejuvenation product.

About Aging and UV-damaged Skin Treatment Markets

Ultra-violet (UV) light exposure from the sun is responsible for up to 80% of visible facial skin aging. According to statistics from the American Society for Plastic Surgeons, \$2.5 billion was spent on facial aesthetics in 2013 and this is predicted to grow to over \$5.4 billion by 2020. Dermal filler procedures are growing over 15% annually.

About the RCS-01 Study

The clinical trial was a randomized, double-blind, placebo-controlled, single-centre, phase I safety study of intradermal injections of RCS-01 in healthy subjects. The primary endpoint was to assess the local safety profile by recording and evaluating adverse events reported at the treatment evaluation sites. Secondary safety measures related to any reporting of systemic adverse events and assessment of histopathological abnormalities of the treatment sites. Secondary endpoints also included evaluating any changes in expression of selected gene markers (using real-time, quantitative PCR) related to intrinsic skin aging, skin wrinkling and solar degeneration of skin. After trial inclusion, all participants provided a biopsy from the scalp from which RCS-01 was prepared at a central GMP manufacturing site. Study participants were randomized to either a RCS-01 or placebo subgroup. Each participant had four treatment evaluation sites identified on their buttocks, two on each side, to allow for a within-subject comparison of single and triple injections of RCS-01 with placebo respectively. Participants in the RCS-01 Subgroup received injections of RCS-01 or placebo or a 'sham' injection (a needle penetration without injection of liquid). Participants in the Placebo Subgroup received only injections of placebo or sham injections to compare the systemic safety profile to the RCS Subgroup. Baseline evaluations of subjects' overall health and skin condition at treatment sites on their buttocks were performed before receipt of injections at Day 0. In addition to injections delivered at Day 0, the pre-selected treatment evaluation sites received intradermal injections of RCS-01, or placebo, or a sham injection four and eight weeks after Day 0 according to a randomization schedule, for a total of

three injections per treatment site. All participants returned to the clinic at regular intervals to monitor safety. Assessment of the local safety profile was performed by the investigator before each injection visit, two to four days after injection, and up to 44 weeks after the last injection. The investigator assessed local tolerance according to a comprehensive list of pre-specified adverse events. Other study assessments included recording of vital signs at each visit and routine laboratory assessments at regular intervals. At the 12-week time point, nine randomly selected participants provided biopsies from all injection sites for gene expression analysis of skin markers related to aging. At Week-26 the remaining participants provided biopsies of all injection sites for histopathological analysis. All reported pre-defined local adverse events related to injection or sham were transient and mainly mild in intensity only. No other related local or systemic adverse events were reported. No clinically relevant abnormal laboratory results or abnormal vital signs were reported. Histopathological assessments of treatment evaluation site biopsies were all judged to be normal by a blinded investigator.

About RepliCel Life Sciences

RepliCel is a regenerative medicine company focused on developing cell therapies for aesthetic and orthopedic conditions affecting what the Company believes is approximately one in three people in industrialized nations, including aging/sun-damaged skin, pattern baldness, and chronic tendon degeneration. These conditions, often associated with aging, are caused by a deficit of healthy cells required for normal tissue healing and function. The Company's product pipeline is comprised of RCT-01 for tendon repair, RCS-01 for skin rejuvenation, and RCH-01 for hair restoration. RCH-01 is currently being co-developed with, and under exclusive license by, Shiseido for certain Asian countries. All product candidates are based on RepliCel's innovative technology, utilizing cell populations isolated from a patient's healthy hair follicles. RepliCel has also developed a proprietary injection device, RCI-02, optimized for the administration of its products and licensable for use with other dermatology applications.

Please visit <http://www.replicel.com> for additional information.

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