NEWS RELEASE

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Kronos Longevity Research Institute (KLRI) Announces 5-Year Study on Risks and Benefits of Early Menopausal Hormone Therapy

Kronos Early Estrogen Prevention Study (KEEPS) Will Be a Randomized, Controlled Trial of 900 Women that Examines the Effects o Estrogen on the Progression of Atherosclerosis

Kronos Longevity Research Institute (KLRI) today announced plans for the **Kronos Early Estrogen Prevention Study** (KEEPS), a five-year study of female hormone replacement therapy aimed at providing prospective data on the risks and benefits of early menopausal hormonal intervention, particularly as it relates to the progression of atherosclerosis. Atherosclerosis is a medical condition in which fatty material is deposited along the walls of arteries. This fatty material thickens, hardens and may eventually block arteries and cause heart disease.

The study also will compare conjugated oral with transdermal estrogen treatment to further elucidate the potential role of their differential actions in mediating adverse effects of menopausal hormone therapy (MHT).

"Despite more than 40 years of research, menopausal hormone replacement therapy with estrogen or estrogen/progestin remains one of the most debatable areas in medicine," said Dr. S. Mitchell Harman, director of KLRI. "The controversial Women's Health Initiative (WHI) study has left many questions unanswered. We have concluded that additional trials of MHT in a target population much younger than the mean age of 62.7 that was studied in the WHI will be required to shed light on the risk-benefit ratio of early MHT."

Prior to the WHI study, most data suggested that hormone replacement therapy was associated with a high degree of protection (40-60 percent reductions) against coronary heart disease, all-cause mortality and osteoporotic fractures, in addition to a small increase in breast cancer risk.

KEEPS Design

The Kronos Early Estrogen Prevention Study will be a randomized, placebo-controlled, double-blinded examination of healthy peri-menopausal women ages 40 to 55. Researchers will recruit 900 study participants at 8 yet-to-be-determined clinical trial sites. KLRI will serve as the coordinating center, but will not recruit study participants.

The study participants will be divided equally into three groups. The first group will receive an oral tablet containing conjugated estrogens and a placebo skin patch. The second group will receive an oral placebo tablet and a skin patch delivering estradiol. The third group (control) will receive a placebo tablet and a placebo skin patch.

All participants will be evaluated at 10 formal sessions for data collection procedures and additional visits for study monitoring, including a compliance check, a review for adverse effects and a brief physical exam.

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Subjects will be monitored at three-month intervals by questionnaire for any potential adverse effects. The subjects also will undergo lab monitoring at various points during the study. All major adverse effects will be reported immediately to the local center's institutional review board and to KLRI, which will relay reports to the data safety monitoring board (DSMB). All adverse effects, major and minor, will be reported quarterly to KLRI for consideration by the DSMB.

ABOUT DR. S. MITCHELL HARMAN, DIRECTOR OF KLRI

Dr. Harman, a graduate of Emory University, received his medical and doctoral degrees from the State University of New York Health Sciences Center at Brooklyn and trained in internal medicine at Yale and in endocrinology at the National Institutes of Health (NIH).

He was an NIH investigator with the Intramural Program of the National Institutes on Aging (NIA) for more than 25 years. He served as both the acting clinical director of the NIA and the chief of endocrinology for the NIA's Laboratory of Clinical Physiology. Dr. Harman founded the NIA laboratory for the study of aging of the male and female reproductive hormone systems. He is a captain (retired) in the U.S. Public Health Service and is a former 25-year faculty member of Johns Hopkins University School of Medicine.

Dr. Harman holds a dual certification from the boards of internal medicine and endocrinology. He has authored one book and 19 book chapters, many in major textbooks of medicine, geriatric medicine and endocrinology. He is an internationally recognized expert on hormones and aging, and also has published more than 70 original research papers. *(Please see Dr. Harman's biography for additional information.)*

ABOUT KLRI

Phoenix-based KLRI is a not-for-profit 501(c)(3) organization that conducts state-of-the-art clinical translational research on the prevention of age-related diseases and the extension of healthier human life. Translational research is the critical link between promising findings from the basic research laboratory and corresponding improvements in clinical care.

Some of KLRI's current studies include: Validation of Oxidative Stress Assessments; Omega-3 Fatty Acids and Endocrine/Immune Dysfunction in Humans; and Testosterone Replacement and Cardiovascular Disease. KLRI soon will launch studies focusing on the Effects of Coenzyme Q10 and Statin Drugs on Heart and Muscle Function.

For more information, visit KLRI's Web site at www.kronosinstitute.org.

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