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Phoenix-based Kronos Longevity Research Institute Expands Role in Kronos Early Estrogen Prevention Study (KEEPS), Becomes Recruitment Center

PHOENIX (August 10, 2006) – The Phoenix-based Kronos Longevity Research Institute (KLRI) is now recruiting women for the **Kronos Early Estrogen Prevention Study (KEEPS)** along with eight other national study centers. KEEPS, which focuses on the effects of hormone therapy (HT) as it relates to the progression of heart disease in recently menopausal women, is also being coordinated by KLRI. The eight other participating research centers include:

- ? Albert Einstein College of Medicine/Montefiore Medical Center (New York City)
- ? Columbia University College of Physicians and Surgeons (New York City)
- ? Harvard Medical School/Brigham and Women's Hospital (Boston)
- ? Mayo Clinic College of Medicine (Rochester, MN)
- ? University of California, San Francisco/Center for Reproductive Health
- ? University of Utah School of Medicine (Salt Lake City)
- ? University of Washington School of Medicine (Seattle)
- ? Yale University School of Medicine (New Haven, CT)

"Women who participate in KEEPS will be providing useful new data to help shape future research on hormone therapy," said Director of KLRI S. Mitchell Harman, M.D., Ph.D. "There are still many questions left unanswered regarding whether estrogen protects younger women from cardiovascular disease, as earlier observational studies have indicated."

About KEEPS

KEEPS is a randomized, controlled, double-blind trial of 720 women, designed to provide prospective data on the risks and benefits of HT in recently menopausal women. The results of the Women's Health Initiative (WHI) estrogen plus progestin trial, which was halted by the National Institutes of Health in July 2002, prompted a consortium of health researchers to study the risks and benefits of HT on a younger subset of women who recently entered menopause. Prior to the WHI, most data suggested HT was associated with a high degree of protection (30 to 50 percent reductions) against coronary heart disease, all-cause mortality and osteoporotic fractures, in addition to a small increase in breast cancer risk. Recent studies in the *Journal of Women's Health* and the *Archives of Internal Medicine* indicate that HT may indeed provide coronary heart protection if given to recently menopausal women.

KEEPS is designed to explore issues raised by the WHI, specifically:

Age of Participants – The study will explore whether beginning HT in recently menopausal women (six months to three years since last menses) protects against atherosclerosis, the major cause of heart attacks. WHI

participants were postmenopausal, with a mean age of 62.7, yet most women begin hormone treatment much younger, at the onset of menopausal symptoms.

Transdermal Application – KEEPS also will study whether the natural human estrogen, estradiol, delivered through the skin via a patch is equally effective as and potentially safer than oral estrogen. Researchers have speculated this method may be safer since transdermal estrogen does not go to the liver in high concentrations and has been shown to have little or no effect on clotting. On the other hand, transdermal estradiol may be less effective since it does less to increase HDL-cholesterol levels.

Imaging of Key Arteries – KEEPS will image the carotid and coronary arteries in order to measure the effects of HT on heart disease. Carotid intimal medial thickness (IMT) will be measured by ultrasound and the progression of coronary calcium will be tracked by X-ray tomography. In addition, KEEPS investigators will measure both protective and risk factors for heart disease, which are believed to be affected by hormones. This detailed analysis is particularly important in view of findings from earlier research indicating that estrogen may be beneficial for preventing early lesions of atherosclerosis, but ineffective, or even harmful, once disease is established.

About Recruitment

KLRI will be recruiting at least 65 women in the Phoenix area, ages 42-58, for the four-year, \$19 million KEEPS. The participants will be divided into three groups. The first group will receive an oral tablet containing low dose conjugated equine estrogens (Premarin[®], 0.45 mg daily) and a placebo (inactive) skin patch. The second group will receive an oral placebo tablet and a skin patch delivering low dose estradiol (Climara[®], 0.50 mcg/day). The third group (control) is receiving a placebo tablet and a placebo skin patch. Women receiving active estrogen also will take progesterone capsules (Prometrium[®], 200 mg daily for first 12 days of each month) to protect the uterine lining from overgrowth. Subjects not receiving active estrogens will take placebo capsules. The study will last four years.

All participants will be evaluated at 10 formal sessions for data and sample collection procedures and at additional visits for study monitoring, including a compliance check, a review for adverse effects and a brief physical exam. The subjects also will undergo lab monitoring at various points during the study.

About KLRI

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 findings from the basic research laboratory and corresponding improvements in clinical care. In addition to KEEPS, KLRI currently is studying Testosterone's Effects on Atherosclerosis in Aging Men (TEAAM Study). For more information on KEEPS, visit www.keepstudy.org or call 1(866) 878-1221.

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