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**New Study Indicates Multiple Mechanisms Involved In The Inhibition
Of The Growth Of LNCaP Prostate Cancer Cells By Plant Lignans**

Secaucus, NJ – May 2, 2006 – Linnea has announced that new research performed by the Department of Clinical Medicine at the University of Insubria in Italy has shed further light into the multiple mechanisms involved in the inhibition of the growth of LNCaP prostate cancer cells by plant lignans.

Several lines of evidence suggest that plant-derived dietary lignans may play a role in chemoprevention and prostate health promotion, through complex pharmacological activities that may include pro or anti-estrogenic, pro-apoptotic, antioxidant, and anti-angiogenic mechanisms. In particular, in-vivo research had shown the novel lignan, hydroxymatairesinol (HMRLignan), and its human lignan metabolite enterolactone, to inhibit tumor growth rate and tumor take rates in animal models (Bylund et al, *Exp Biol Med*, March 2005).

In this new study, designed to investigate the mechanisms involved in the modulation of cell viability of the human androgen-dependent prostate cancer, LNCaP cells lines were incubated with either enterolactone (70-100 microMols) or hydroxymatairesinol (70-100 microMols) for 48 hours, with estradiol (100 microMols) and the cytotoxic agent cycloheximide (10 microMols) used as the experimental controls. Results showed a concentration-dependent increase in the proportion of apoptotic cells for both substances -- enterolactone was about two-fold as effective as hydroxymatairesinol in this experiment but less than half that of cycloheximide and estradiol. In these experiments the estrogen receptor antagonist tamoxifene significantly reduced the effects of both enterolactone and hydroxymatairesinol, as well as that of estradiol.

Subsequent RT-PCR assays showed that treatment of LNCaP cells with either enterolactone or hydroxymatairesinol (0,01-1 microMols) also increased mRNA levels for the proapoptotic protein Bax and decreased mRNA levels for the antiapoptotic protein Bcl-2, thus resulting in an overall decrease of the ratio Bcl-2/Bax, which can be taken as an index of cell viability. In agreement with this observation, both substances in the same concentration range also increased the expression of the mRNA for caspase-3, which is the common final effector of the intracellular pro-apoptotic cascade.

Commenting on the results, research pharmacologist, Dr. Marco Cosentino, stated, “these results indicate that, in-vitro, the viability of human prostate cancer cells is impaired by the lignans enterolactone and, to a lesser extent, hydroxymatairesinol. The effect is, however, milder than that of an established cytotoxic agent such as cycloheximide, and is likely to be exerted at least in part via estrogen-like mechanisms. This is the first study showing the ability of enterolactone and hydroxymatairesinol to modify the intracellular balance between pro- and anti-apoptotic proteins, an action which likely contributes to the overall pro-apoptotic effect of both lignans. Such an action is, however, exerted at concentrations that are several tenfold lower than those affecting cell viability, suggesting that additional mechanisms are involved in the final pro-apoptotic effect. On the other side, one could also speculate that the ability of enterolactone and hydroxymatairesinol to affect the intracellular mechanisms regulating cell death and survival may also result in ‘sensitization’ of the cells to the effects of other antiproliferative agents.”

Cosentino added, “Our data support the notion that hydroxymatairesinol, and to a greater extent its human metabolite enterolactone, may suppress the growth of prostate cancer cells. Also in view of its well-established tolerability and bioavailability, hydroxymatairesinol represents a viable dietary supplement providing a suitable source for endogenous enterolactone that, in turn, may play a role in the promotion of prostate health.”

About HMRLignan™

Derived from Norway spruce, hydroxymatairesinol (HMRLignan™) is a direct enterolactone precursor dietary supplement standardized to contain 80,000 mg/100 g of lignans. It is a proprietary and patent protected product developed in Finland by Hormos

Medical Corporation, and manufactured and marketed worldwide under license by Linnea, Switzerland. For more information about HMRlignan™, visit our Web site at www.hmrlignan.com or call 1-888-253-0044.