


ENANTA Pharmaceuticals, Inc.500 Arsenal Street
Watertown, Massachusetts
02472Tel: 617.607.0800
Fax: 617.607.0530
www.enanta.comCONTACT:

Paul Kidwell

617-296-3854

paul_kidwell@hotmail.com*News Release***Enanta Pharmaceuticals presents single-step chemistry technology enabling synthesis of novel *Cyclosporin A* soft drug derivatives for treating asthma****Data presented at 224th national meeting of American Chemical Society (ACS)**

WATERTOWN, Mass., Aug. 21, 2002 -- Enanta Pharmaceuticals Inc. presented today its proprietary single-step chemistry technology that enables synthesis of novel Cyclosporin A softdrug analogs as potential asthma therapeutics. The technology is based on the olefin cross metathesis reaction of Cyclosporin A utilizing commercially available reagents. The reaction process is readily scaleable and routinely produces softdrug analogs of high yield and purity. The Cyclosporin (CsA) analogs are introduced via the airway to the lungs, where they exert a potent local anti-inflammatory effect by inhibiting T-cell activation and proliferation. These softdrug compounds are designed to be subsequently converted into an inactive metabolite by enzymes in tissues and the bloodstream.

This "softdrug" strategy drastically reduces the systematic exposure to an active Calcineurin A (CaN) inhibitor and is expected to reduce the mechanism-based nephrotoxicity observed with CsA. Enanta expects this new technology will lead to increased exposure to the inflamed tissue in the lung during local application; and, retention in the lung, combined with metabolic conversion of the active CsA analog to an inactive metabolite, resulting in lower systemic exposure to the active drug and therefore reduced nephrotoxicity.

In data presented at the American Thoracic Society and Federation of Clinical Immunologist Societies annual meetings earlier this year, the Company reported on preclinical data from a rat toxicity study of Cyclosporin and the Enanta softdrug metabolite. Both compounds were administered by daily intravenous injection for 14 days, at three dose levels in rats. Blood chemistry analyses and microscopic examination of kidneys by a pathologist were used to assess toxicity. Cyclosporin-treated animals exhibited significant changes in blood chemistry values that are consistent with kidney and liver dysfunction, and mild anemia.

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Page Two

Cyclosporin also resulted in dose-dependent adverse changes in kidney pathology, including tubular necrosis. On the other hand, the study concluded that the Enanta softdrug metabolite did not cause toxicity in contrast to Cyclosporin.

“Short-term inhalation of CsA is well tolerated in humans, but its chronic clinical administration is limited by its toxicity,” said Tsvetelina Lazarova, Ph.D., Senior Scientist who presented the study’s data. “We believe that this novel chemistry technology will lead to multiple proprietary cyclosporin analogs with improved toxicity profiles and physicochemical properties for topical and systemic uses.”

According to the Academy of Allergy, Asthma and Immunology (AAAI), between 12 and 15 million people in the United States, including close to 5 million children, have asthma. Asthma is a chronic disease in which airflow in and out of the lungs may be blocked by muscle squeezing, swelling and excess mucus.

The American Chemical Society is a self-governed individual membership organization that consists of more than 163,000 members at all degree levels and in all fields of chemistry. The organization provides a broad range of opportunities for peer interaction and career development, regardless of professional or scientific interests.

Headquartered in Watertown, Mass., Enanta Pharmaceuticals is using its breakthrough chemistry technology - *Drug Morphing*[™] and *Peptide Morphing*[®] -- to create new intellectual properties by ‘morphing’ existing drugs, natural products and biologically active peptides into novel small-molecule drugs. The Company is initially focusing on new chemical entities derived from existing drugs that address significant unmet medical needs: (a) new-generation macrolide antibiotics to overcome bacterial resistance; and (b) anti-inflammatory drugs for a variety of indications, including asthma, psoriasis and inflammatory bowel diseases.

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