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**CORNERSTONE PHARMACEUTICALS ANNOUNCES THE JOURNAL OF MOLECULAR  
MEDICINE'S PUBLICATION OF RESEARCH SHOWING SELECTIVE INHIBITION OF CANCER  
CELL ENERGY METABOLISM WITH ITS NOVEL LIPOATE DERIVATIVE COMPOUNDS**

*Study Provides Insight Into How Cornerstone Agents Profoundly Disrupt Cancer Cell Energy  
Metabolism*

**CRANBURY, NJ, July 25, 2011**– Cornerstone Pharmaceuticals, Inc., ([www.cornerstonepharma.com](http://www.cornerstonepharma.com)), a leader in the growing field of cancer metabolism-based therapeutics, today announced the publication of a paper in *The Journal of Molecular Medicine* (<http://tinyurl.com/3ugohzd>) describing the selective inhibition of cancer cell energy metabolism by its novel lipoate derivative compounds. Specifically, the publication illuminates the mechanism by which CPI-613, a lipoic acid analog, selectively attacks the regulatory aspects of tumor cell mitochondrial metabolism, activating both apoptotic (programmed cell death) and non-apoptotic (necrosis-like) cell death pathways. This research was conducted in collaboration between scientists at Stony Brook University and Cornerstone Pharmaceuticals. The paper “Non-redox-active lipoate derivatives disrupt cancer cell mitochondrial metabolism and are potent anti-cancer agents in vivo” is available today in the advanced online publication of *The Journal of Molecular Medicine*. The full author’s version of the paper is available here: <http://tinyurl.com/3gvx5oa>

“The highly reconfigured metabolism of cancer cells has recently gained wide attention as a possible source of novel drug targets,” said Dr. Zuzana Zachar, Ph.D., the lead author of the paper who is Director of Research at Cornerstone and a Research Assistant Professor at Stony Brook University School of Medicine.

"CPI-613 attacks cancer cell metabolism in a powerful new way, yielding very strong anti-cancer effects in pre-clinical human tumor models," added Dr. Paul Bingham, Ph.D., co-author, and Vice President of Research at Cornerstone and Associate Professor at Stony Brook University School of Medicine.

CPI-613 is the lead drug candidate from Cornerstone's Altered Energy Metabolism Directed (AEMD) platform. Dr. Zachar's paper states that CPI-613 induces cancer-specific regulatory hyper-phosphorylation of the E1 subunits of the centrally important TCA enzyme complex, pyruvate dehydrogenase (PDH), resulting in the inhibition of PDH function. These and related cancer-specific effects of the drug lead to catastrophic disruption of tumor mitochondrial metabolism. Tumor cells are thereby starved of energy and biosynthetic intermediates, culminating in cell death.

The paper also reports that CPI-613 is a potent inhibitor of human tumor growth in pre-clinical animal models, producing apparent tumor clearance in some animals. CPI-613 strongly inhibits tumor growth in a non-small cell human lung cancer and a human pancreatic cancer pre-clinical mouse tumor model. In the pancreatic model, treated animals were further examined for long term survival after completion of a brief treatment regimen and a substantial fraction showed no tumor regrowth.

Robert Shorr, CEO, added "This research demonstrates that our active analogs of lipoic acid can act as potent anti-cancer agents that are highly selective in animal models by disrupting the activity of at least one key bioenergetic enzyme. In view of the novel mechanism of action of these drugs and their potency in pre-clinical models, it is of great interest to assess their efficacy in human clinical trials and to be able to predict which patients will be most likely to benefit."

"Alterations in cancer cell metabolism are distinctive hallmarks of cancer and represent a new frontier in the development of novel and selective classes of chemotherapeutic interventions for use in the treatment of cancer. Candidates for application of this new approach are so far, very few and lipoate analogs such as CPI-613 represent a promising new addition," said Dr. Bob



Weinberg, a member of Cornerstone’s scientific advisory board and a founder and member of the Whitehead Institute at MIT.

Cornerstone’s proprietary Altered Energy Metabolism Directed (AEMD) drug platform disrupts biochemical alterations in the conversion of glucose to energy that occur in many types of cancer cells. These essential “bioenergetic” differences are linked to pathways that control, among other things, cancer cell growth and development, as well as various forms of cell death, including apoptosis and necrosis. The platform is designed to produce drugs, such as the company’s lead drug CPI-613, that disrupt energy-production pathways whose organization or regulation are altered specifically in cancer cells. CPI- 613 is currently being evaluated in several ongoing Phase I/II trials.

### **About Cornerstone Pharmaceuticals**

Cornerstone Pharmaceuticals, Inc. is a privately held company that is committed to changing the way cancer is treated through the discovery and development of innovative therapies capitalizing on the unique metabolic processes of cancer cells. The company’s founding members, management and scientific advisory team include pre-eminent scientists focused on cancer cell metabolism, cancer research and drug development. The company’s unique approach to targeting cancer metabolism has led to the discovery of first-in-class drugs with the potential to transform the way cancer is treated. [www.CornerstonePharma.com](http://www.CornerstonePharma.com)

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