NEWS RELEASE

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Contacts:

Michele Rozen
Pure Communications, Inc.
(617) 730-8284

Data Published in *Science Translational Medicine* Point to Role of Cellular Bioenergetics as a New Mechanistic Approach to Treat Immune Disorders

Findings Demonstrate Lycera's Compound Selectively Silences Pathogenic Cells and Arrests Graft-Versus-Host Disease

Ann Arbor, Mich. – January 26, 2011 – Lycera Corporation, a biopharmaceutical company pioneering an innovative approach to developing novel oral medicines to treat autoimmune diseases, today announced positive data from the University of Michigan demonstrating the role of bioenergetics in selectively inhibiting pathogenic lymphocytes while preserving and enhancing the normal immune system. The findings, published online today in *Science Translational Medicine*, support Lycera's promising novel therapeutic approach to treating a broad spectrum of immune diseases.

Cellular bioenergetics is a field of biology focused on studying how energy is made and utilized in living systems in both normal, healthy cells and disease-causing cells. Lycera's bioenergetics program is focused on developing orally available small molecules that exploit bioenergetic abnormalities in pathologically activated lymphocytes and result in the selective silencing of these cells, while keeping healthy immune cells intact.

The data show that bioenergetic and redox properties of alloreactive T cells differentiate them from other proliferating cells and can be exploited pharmacologically to arrest graft-versus-host disease (GVHD) in mice. In the study, treatment with Lycera's prototype compound Bz-423, a first-in-class F_1F_0-ATP synthase inhibitor, induced selective apoptosis of alloreactive donor T cells and reversed GVHD in several bone marrow transplantation models without affecting hematopoietic stem cell engraftment, immune reconstitution or normal resting lymphocytes.

"The preclinical data suggest that alloreactive T cells rely primarily on oxidative phosphorylation for their energy, challenging the current paradigm that activated T cells meet their increased demands for energy through aerobic glycolysis," said lead author Gary D. Glick, Ph.D., Lycera founder and chief scientific officer, and Werner E. Bachmann Collegiate Professor of Chemistry at the University of Michigan. "This difference, along with the phenotype of T cells, provides a mechanistic basis for the specificity of Bz-423 to eliminate disease causing cells. The specificity and the ability to preserve normal immune reconstitution differentiate Bz-423 from high dose systemic steroids, the current standard of treatment for GVHD. Efficacy has also been

demonstrated in autoimmune disease models where pathogenic cells have similar bioenergetic characteristics. The robust body of preclinical research is very compelling, and we look forward to entering the clinic with our lead compound in Lycera's bioenergetics program this year."

The researchers tested the potential of Bz-423 to halt the progress of established GVHD in two allogeneic bone marrow transplantation models. Treatment with Bz-423 significantly reduced GVHD clinical scores after one week and improved survival in mice compared to controls treated with vehicle (75% vs. 29%, $p<0.02$). Similar improvement in survival was seen when treatment was continued for 10 weeks (74% vs. 29%, $p=0.02$). In another aggressive model of GVHD using a fully allogeneic donor/recipient strain combination, Bz-423 treatment for seven weeks again significantly reduced all clinical and histological parameters of disease. Bz-423 did not impair immune reconstitution in either the thymus or spleen and all the mice treated with the drug showed complete donor bone marrow (BM) engraftment. Additionally, the compound's favorable toxicity profile is consistent with other studies and with the normal bioenergetic and redox profile of rapidly proliferating BM cells (basal rates of oxygen consumption, normal levels of anti-oxidants and stable mitochondrial membrane potential).

The *Science Translational Medicine* paper titled "Manipulating the Bioenergetics of Alloreactive T Cells Causes Their Selective Apoptosis and Arrests Graft Versus Host Disease," was published today online at www.ScienceTranslationalMedicine.org, and will appear in an upcoming print edition of the journal.

About Cellular Bioenergetics and Bz-423

Cellular bioenergetics is a field of biology focused on studying how energy is made and utilized in living systems in both normal, healthy cells and disease causing-cells. Cells generate adenosine-5'-triphosphate (ATP) by aerobic glycolysis and oxidative phosphorylation. Despite the importance of having sufficient ATP available for the energy dependent processes involved in immune activation, little is known about the metabolic adaptations that occur *in vivo* to meet the increased demand for ATP in activated and proliferating lymphocytes.

Lycera has unique expertise in the emerging area of cellular bioenergetics. The aim of Lycera's bioenergetics program, which originated from the lab of Dr. Glick at the University of Michigan, is to develop orally available small molecules that exploit bioenergetic abnormalities in pathologically activated lymphocytes and result in the selective silencing of these cells. Testing has been conducted in preclinical models of lupus, rheumatoid arthritis, psoriasis, graft-versus-host disease and other medical conditions. The mechanism has been supported by extensive published and unpublished work over the past eight years and has generated multiple potential drug candidates. Preclinical data characterizing the metabolic phenotype of pathologically activated lymphocytes were published in *Lupus* in July 2010.

Bz-423 is an important prototype for Lycera's bioenergetics program. The data with Bz-423 provide strong validation of the mechanistic approach. The company has identified other compounds that act through this same mechanism and will be the basis of further advancement in the program.

About Autoimmune Diseases
Serious autoimmune diseases are a major and growing public health problem. An autoimmune disorder is a condition that occurs when the immune system mistakenly attacks and destroys healthy body tissue. There are more than 80 different types of autoimmune disorders[1], and approximately 50 million Americans, or one in five people, suffer from autoimmune diseases[2].

Currently available biologic drugs are typically very costly and have been associated with significant risks including opportunistic infections and death. Despite these limitations, they generate more than $13 billion in annual sales. There is a clear need for oral drugs that demonstrate the efficacy of biologics, but with improved safety and administration profiles.

About Lycera
Lycera Corp. is focused on the discovery and development of selective, small-molecule immunomodulators for the treatment of patients with autoimmune diseases such as rheumatoid arthritis, psoriasis, and inflammatory bowel disease. Lycera is developing drug candidates that target two novel therapeutic pathways and have the potential for first-in-class oral efficacy without the adverse effects of current standard-of-care antiproliferative and immunosuppressive agents. Lycera is focused on the emerging area of cellular bioenergetics to selectively target and silence pathologically activated cells. The company also has a program targeting the Th17 pathway through the inhibition of ROR-gamma. Lycera's leadership team and advisors represent the core thought leaders in immunology, inflammation, organ transplantation and kinase biology and are responsible for key advances and discoveries in these fields. Founded in 2006, Lycera is headquartered in Ann Arbor, Michigan. Visit www.lycera.com for more information.

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[1] Medline Plus, http://www.nlm.nih.gov/medlineplus/ency/article/000816.htm.
[2] American Autoimmune Related Diseases Association, http://www.aarda.org/q_and_a.php.