



## PIONEERS IN AUTOIMMUNE TREATMENT

Lycera Corp. is an emerging biopharmaceutical company pioneering innovative approaches to the discovery and development of first-in-class oral medicines for treating autoimmune diseases. The company is targeting novel pathways to develop new classes of selective, oral immunomodulators for the treatment of patients with diseases such as rheumatoid arthritis, multiple sclerosis, psoriasis and inflammatory bowel disease.

Lycera's goal is to develop drug candidates with efficacy and safety profiles that change the treatment paradigm for patients with autoimmune diseases. Based on preclinical studies, the company's emerging drug candidates have the potential for previously unseen oral efficacy and improved safety compared to the current standard-of-care treatments. The company believes it has two of the most promising programs for treating autoimmune diseases: a bioenergetics program, focused on modulating energy producing and transducing pathways to selectively target and silence pathologically activated cells, and a program targeting the Th17 pathway through the inhibition of ROR $\gamma$ t. In 2011, Lycera announced a significant research collaboration with Merck for its ROR $\gamma$ t program.

Together, Lycera's management and scientific teams are worldwide thought leaders and scientists in immunology, inflammation, organ transplantation and kinase biology. Located in Ann Arbor, Mich., Lycera was founded in 2006 and is backed by top-tier investors: ARCH Venture Partners, Clarus Ventures, EDF Ventures and InterWest Partners. The company raised \$36 million in Series A financing in 2009.

### Autoimmune Diseases: A Major Public Health Concern

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<sup>1</sup>, and approximately 50 million Americans, or one in five people, suffer from autoimmune diseases<sup>2</sup>.

#### Major autoimmune diseases include:

- Psoriasis and psoriatic arthritis
- Multiple sclerosis
- Rheumatoid arthritis
- Inflammatory bowel disease
- Lupus

Currently available biologic drugs are typically very costly and have been associated with significant risks including opportunistic infections and death. There is a clear need for oral drugs that demonstrate the efficacy of biologics, but with improved safety and administration profiles.

Drugs that emerge from Lycera's pipeline will offer patients first-in-class oral efficacy, avoiding the burdensome injections of today's biologic therapies.

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](http://www.aarda.org/q_and_a.php).

3 E. Gatzka, D. R. Wahl, A. W. Pipari, T. B. Sundberg, P. Reddy, C. Liu, G. D. Glick, J. L. M. Ferrara, Manipulating the Bioenergetics of Alloreactive T Cells Causes Their Selective Apoptosis and Arrests Graft-Versus-Host Disease. *Sci. Transl. Med.* 3, 67ra8 (2011).

### Positive Data Published in *Science Translational Medicine* Support Lycera's Novel Therapeutic Approach to Treating Immune Diseases

In January 2011, Lycera 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 in *Science Translational Medicine*<sup>3</sup>, support Lycera's promising novel therapeutic approach to treating a broad spectrum of immune diseases. 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<sub>1</sub>F<sub>0</sub>-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. Lycera is exploiting these findings with new oral compounds for a range of autoimmune conditions.

#### Contact Information

**Lycera Corp.**  
2800 Plymouth Rd., NCRC, Building 26  
Ann Arbor, MI 48109  
734.233.3060  
[info@lycera.com](mailto:info@lycera.com)

**Julia Owens, Ph.D.**  
Senior Vice President, Corporate  
Development and Strategy  
734.233.3144

**Michele Rozen**  
Pure Communications, Inc.  
617.730.8284

## A Promising Pipeline Targeting Novel Autoimmune Pathways

Lycera is developing a robust pipeline of selective, oral immunomodulators targeting novel autoimmune pathways. Based on preclinical studies, the company's bioenergetics and ROR $\gamma$ t programs have the potential for previously unseen oral efficacy and improved safety compared to the current standard-of-care agents.

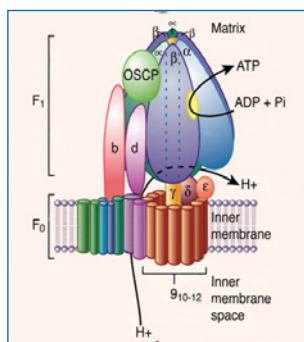
### Bioenergetics Program

Lycera has unique expertise in the exciting area of cellular bioenergetics, a field studying how energy is made and utilized in both normal, healthy cells and disease-causing cells. Lycera's bioenergetics program is focused on developing orally bioavailable small molecules that exploit bioenergetics abnormalities in pathologically activated lymphocytes selectively silencing these cells, while keeping healthy immune cells intact.

This program originated from the lab of the company's founder and chief scientific officer Gary D. Glick, Ph.D., at the University of Michigan. Testing has been conducted in many preclinical models including lupus, rheumatoid arthritis, psoriasis and graft-versus-host disease. These compounds differ from current therapies as they are not broadly toxic and are highly selective for pathogenic, disease-causing lymphocytes over normal immune cells that fight infection.

These agents modulate the mitochondrial F<sub>1</sub>F<sub>0</sub>-ATPase, an enzyme that is central to energy production within cells. Differences in the way disease-causing immune cells make ATP compared to normal lymphocytes sensitizes them to this mechanism. Drugs developed from this program are expected to have significant advantages over existing products, including better efficacy, fewer side effects (particularly unwanted immunosuppression) and greater ease of administration. The mechanism has been supported by extensive published and unpublished work and has generated multiple drug candidates.

Lycera is on track to enter human clinical trials with its lead compound in bioenergetics in 2012.



Mitochondrial F<sub>1</sub>F<sub>0</sub> - ATPase

### ROR $\gamma$ t Program

Lycera has developed a proprietary program that targets T-helper 17 (Th17) cells, a unique subset of CD4<sup>+</sup> T cells. Th17 cells are characterized by the production of interleukin-17 (IL-17), a highly inflammatory cytokine that plays an important role in the pathogenesis of immune-mediated diseases, including psoriasis, rheumatoid arthritis, multiple sclerosis, inflammatory bowel disease and asthma. ROR $\gamma$ t is the key transcription factor that orchestrates the differentiation of Th17 cells, inducing transcription of the genes encoding IL-17. Mice with ROR $\gamma$ t deficient T cells have attenuated disease and lack tissue-infiltrating Th17 cells. Thus, ROR $\gamma$ t is a key regulator of immune homeostasis and a potential therapeutic target for immune diseases. Lycera has identified novel, potent and specific inhibitors of ROR $\gamma$ t that reduce IL-17 production in primary cells and *in vivo*.

In March 2011, the company announced an exclusive joint research collaboration with Merck to discover, develop and commercialize small molecules that target Th17 cells. Within the collaboration, Merck is responsible for clinical development and will have worldwide marketing and commercialization rights, subject to a U.S. profit share option retained by Lycera to all resulting products. In addition to the \$12 million upfront payment, Lycera will receive significant research funding and is eligible to receive up to \$295 million in research, development and regulatory milestone payments, along with up to low double digit tiered royalty payments and sales milestones on global sales. In December 2011, Lycera achieved its first milestone in its research collaboration with Merck.



### Management Team

**Kathleen M. Metters, Ph.D.**  
President and Chief Executive Officer

**Gary D. Glick, Ph.D.**  
Founder and Chief Scientific Officer

**Julia C. Owens, Ph.D.**  
Senior Vice President, Corporate Development and Strategy

**JoAnn Scatina, Ph.D.**  
Senior Vice President, Preclinical Development

**Peter L. Toogood, Ph.D.**  
Senior Vice President, Chemistry and Chemical Biology

### Board of Directors

**Steven Gillis, Ph.D., Chairman**  
Managing Director, ARCH Venture Partners

**Kristina Burow**  
Partner, ARCH Venture Partners

**Gary D. Glick, Ph.D.**  
Founder and Chief Scientific Officer, Lycera

**Robert Kamen, Ph.D.**  
Former President, Abbott Bioresearch Center

**Nina Kjellson**  
General Partner, InterWest Partners

**Timothy M. Mayleben**  
President and CEO, Aastron Biosciences

**Kathleen M. Metters, Ph.D.**  
President and Chief Executive Officer, Lycera

**Michael Steinmetz, Ph.D.**  
Managing Director, Clarus Ventures

**Mary Campbell, Observer**  
Founder and Managing Director, EDF Ventures

