



## **Idera Announces Presentation of Positive Data from Phase 2 Trial of TLR 7 and 9 Antagonist in Patients with Moderate-to-Severe Plaque Psoriasis**

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### *PASI Score Improvements Correlated with Downregulation of IL-17 Pathway*

CAMBRIDGE, Mass.--(BUSINESS WIRE)--May. 8, 2013-- Idera Pharmaceuticals (NASDAQ: IDRA) today announced presentation of data from its randomized, double-blind, placebo-controlled Phase 2 trial that showed improvements from baseline of up to 90% in Psoriasis Area Severity Index (PASI) scores in patients with moderate to severe plaque psoriasis following four weeks of treatment with the Toll-like Receptor (TLR) antagonist IMO-3100. Additionally, analysis of biopsy samples collected from patients during the Phase 2 trial indicated that PASI score improvements were associated with significant improvement of psoriasis disease-associated gene profile, including downregulation of activated genes in the IL-17 pathway, which is central to the pathogenesis of psoriasis. Treatment with IMO-3100 was well tolerated, with no treatment-related discontinuations. The presentation entitled "IMO-3100, an antagonist of Toll-like receptor (TLR) 7 and 9, demonstrates clinical activity in psoriasis patients with 4 weeks of treatment in a Phase 2a trial" was made by Alexa Kimball M.D., M.P.H., Vice Chair, Department of Dermatology at Massachusetts General Hospital, Boston, and an investigator in the trial, at the International Investigative Dermatology meeting in Edinburgh, Scotland May 8<sup>th</sup> through 13<sup>th</sup>, 2013.

"TLR antagonism provides a novel mechanism of action for the potential treatment of patients with moderate to severe plaque psoriasis. Clinical activity demonstrated in this four-week proof-of-concept trial encourages further development of TLR antagonists over longer treatment periods," said Dr. Kimball.

"We are very pleased that the clinical improvements observed in psoriasis patients treated with IMO-3100 for four weeks correlated with the proposed mechanism of action for TLR antagonism in autoimmune diseases," said Robert Arbeit, MD, VP of Clinical Development at Idera. "Our next step will be a 12-week Phase 2 clinical trial in patients with psoriasis, which we expect will enable us to evaluate the continued trajectory of PASI score improvement over the 12-week treatment period and maximize the clinical benefit of the treatment. We plan to conduct this 12-week Phase 2 trial with IMO-8400, an antagonist of TLRs 7, 8, and 9, and to initiate the trial during the second quarter of 2013."

### **Data from the Phase 2 Trial**

The objectives of the Phase 2 trial of IMO-3100 were to evaluate the safety and tolerability and to evaluate the clinical activity of TLR antagonism in patients with psoriasis after four weeks of treatment. Top-line data from this trial was announced in December 2012. Data presented from this trial include:

#### **Safety:**

- Treatment with IMO-3100 was well tolerated at both dose levels studied
- There were no treatment-related discontinuations or changes in laboratory parameters

#### **Clinical Activity:**

- On day 57, 48% of patients treated with either dose of IMO-3100 (12 of 25) demonstrated statistically significant improvements of 35% to 90% from baseline PASI scores compared with 0 of 12 in the placebo cohort ( $p < 0.005$ )
- Rapid improvement in PASI scores was observed in IMO-3100 treated patients compared to placebo-treated patients; Improvement in PASI was sustained through five weeks after the last dose
- The pre-specified clinical endpoint of reduction in PASI score at day 29 was achieved with statistical significance in the 0.16 mg/kg cohort ( $p < 0.02$  compared to placebo) but not in the 0.32 mg/kg cohort
- PASI 50 was achieved in 7 of 25 patients treated with IMO-3100 (3 of 12 at 0.16 mg/kg and 4 of 13 at 0.32 mg/kg), compared to 0 of 12 placebo treated patients ( $p < 0.05$ ); PASI 75 was achieved in 1 patient in each IMO-3100 cohort during the trial period
- The pre-specified clinical endpoint of improvement in induration, a measure of plaque thickness, at day 29 was achieved with statistical significance in the 0.16 mg/kg cohort ( $p < 0.02$ ) compared to placebo-treated patients

- Median change in epidermal thickness (the histologically defined primary endpoint of the trial) was -6.4% in IMO-3100 treated patients compared to +7.7% in placebo treated patients, representing a favorable, but not statistically significant, trend. A known limitation of skin biopsies after four weeks of treatment is that psoriatic plaques do not resolve in a uniform fashion, and therefore, biopsies may not provide a representative sampling of lesions (ref: Ann Rheum Dis 2005;64:65-68)
- Representative patients treated with IMO-3100 showed K16 staining (marker of keratinocyte proliferation) reverting toward normal and decreasing infiltrates of CD3+ lymphocytes and CD11c+ cells
- DNA microarray analysis of biopsies from the IMO-3100 treated patients compared to placebo treated patients (n=6 each) showed significant improvement ( $p < 10^{-6}$ ) in psoriasis disease-associated genes (Tian et al, PLoS ONE, Sep 2012) and of genes unique to the IL-17 pathway, which is central to the pathogenesis of psoriasis. Detailed data will be presented at a future scientific meeting.

#### About the Phase 2 Trial in Psoriasis

The Phase 2 trial was a randomized, double-blind, placebo-controlled trial of IMO-3100 in patients with moderate-to-severe plaque psoriasis. In the trial, 44 patients at 11 centers in the United States were randomized to receive IMO-3100 monotherapy at 0.16 or 0.32 mg/kg or placebo by subcutaneous injection once weekly for four weeks. Patients were treated on Days 1, 8, 15, and 22, and were monitored during a follow-up period through approximately Day 57. Assessments of safety were performed throughout the trial. Psoriasis Area Severity Index (PASI) scores were monitored during the treatment period on Days 1, 15, and 29, and during the follow-up period on Days 36 and 57. Skin biopsies were collected prior to treatment on Day 1 and on Day 29. The biopsies were analyzed by James Krueger, M.D., Ph.D., at The Rockefeller University, New York, for treatment-related changes in epidermal thickness, Immunology markers, and gene expression.

#### Next Step in Autoimmune Disease Program

Based on the clinical activity of IMO-3100 observed in patients with psoriasis, and the comparative profiles of IMO-3100 and IMO-8400, including the inhibition of TLR8 by IMO-8400, Idera has determined that the next step is to conduct a Phase 2 clinical trial of IMO-8400 in patients with psoriasis with a treatment period of up to 12 weeks. In this trial, 32 patients would be randomized to receive weekly doses for up to 12 weeks at one of three dose levels of IMO-8400 or placebo. This Phase 2 protocol has been approved by the Centrale Commissie Mensgebonden Onderzoek of the Netherlands. Idera anticipates initiating enrollment under this protocol during the second quarter of 2013.

#### About TLRs and Idera's Pipeline

Toll-like Receptors (TLRs) play a key role in inflammation and immunity. Idera is developing compounds targeted to TLRs 3, 7, 8, and 9, which are expressed in different cells and serve unique functions. Using its chemistry-based approach, Idera has created novel drug candidates that modulate immune responses through either activation or inhibition of specific TLRs. In autoimmune diseases, immune complexes containing self-nucleic acids activate TLRs 7, 8, and 9 and induce multiple cytokines that cause further damage to the body's own tissues and organs, thereby releasing more self-nucleic acids. Inhibition of specific TLRs may be useful in treating autoimmune diseases, such as systemic lupus erythematosus (SLE), psoriasis, and rheumatoid arthritis, by blocking the induction of multiple cytokines and signaling pathways. Idera's clinical candidates for application in autoimmune diseases are IMO-3100, an antagonist of TLR7 and TLR9, and IMO-8400, an antagonist of TLRs 7, 8, and 9.

#### About Psoriasis

Psoriasis is a systemic immune-mediated disorder, characterized by inflammatory skin and joint manifestations. The most common form, plaque psoriasis, appears as raised, red patches covered with a silvery white buildup of dead skin cells. Psoriasis can occur on any part of the body and is associated with other serious health conditions, such as diabetes, heart disease and depression.

Psoriasis is the most prevalent autoimmune disease in the U.S., according to the National Psoriasis Foundation, affecting as many as 7.5 million Americans.

#### About IID 2013

International Investigative Dermatology 2013 (IID 2013) brings together the European Society for Dermatological Research (ESDR), Japanese Society for Investigative Dermatology (JSID) and Society for Investigative Dermatology (SID) to share the latest information on cutaneous biology and skin diseases. IID 2013 takes place in Edinburgh, Scotland, from May 8th to 13th. For more information, visit [www.iid2013.org](http://www.iid2013.org).

#### About Idera Pharmaceuticals, Inc.

Idera Pharmaceuticals applies its proprietary Toll-like receptor (TLR) drug discovery platform to create immunomodulatory drug candidates and has a clinical development program in autoimmune diseases. Additionally, Idera has a collaboration with Merck & Co. for the use of TLR-targeted candidates as vaccine adjuvants for cancer, infectious diseases and Alzheimer's disease. For more information, visit <http://www.iderapharma.com>.

#### Idera Forward Looking Statements

This press release contains forward-looking statements concerning Idera Pharmaceuticals, Inc. that involve a number of risks and uncertainties. For this purpose, any statements contained herein that are not statements of historical fact may be deemed to be forward-looking statements. Without limiting the foregoing, the words "believes," "anticipates," "plans," "expects," "estimates," "intends," "should," "could," "will," "may," and similar

expressions are intended to identify forward-looking statements. There are a number of important factors that could cause Idera's actual results to differ materially from those indicated by such forward-looking statements, including whether Idera's cash resources will be sufficient to fund the Company's continuing operations and the further development of the Company's autoimmune disease program; whether results obtained in preclinical studies and early clinical trials, such as the results from the Phase 2 trial referred to in this release, will be indicative of results obtained in future clinical trials; whether products based on Idera's technology will advance into or through the clinical trial process on a timely basis or at all and receive approval from the United States Food and Drug Administration or equivalent foreign regulatory agencies; whether, if the Company's products receive approval, they will be successfully distributed and marketed; whether the Company will be able to license any of its TLR target candidates on a timely basis or at all; whether the Company's collaboration with Merck & Co, Inc., will be successful; whether the patents and patent applications owned or licensed by the Company will protect the Company's technology and prevent others from infringing it; and such other important factors as are set forth under the caption "Risk Factors" in Idera's Annual Report on Form 10-K for the year ended December 31, 2012 which important factors are incorporated herein by reference. Idera disclaims any intention or obligation to update any forward-looking statements.

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