Idera Pharmaceuticals Announces Positive Top-line Results from Phase 2 Trial of IMO-3100 in Patients with Moderate-to-Severe Plaque Psoriasis

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TLR antagonist achieves statistically significant improvement in PASI scores after four weeks of treatment

Reduction in PASI score sustained for up to four weeks post-treatment

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Dec. 19, 2012-- Idera Pharmaceuticals (NASDAQ: IDRA) today announced that 48% of patients with moderate-to-severe plaque psoriasis (12 of 25) treated with IMO-3100, a selective antagonist of Toll-like Receptors (TLRs) 7 and 9, demonstrated improvements in Psoriasis Area Severity Index (PASI) scores of 35% to 90% from baseline at the completion of a randomized, double-blind, placebo-controlled Phase 2a clinical trial of two dose levels of IMO-3100 administered for four weeks, with a four-week follow-up period. None of the 12 placebo-treated patients had improvement in this range; this difference was statistically significant ($p<0.005$). The Company believes the results of this trial provide clinical proof-of-concept for the mechanism of action of selective TLR inhibition in patients with psoriasis and potentially other autoimmune and inflammatory disorders.

“The clinical activity of IMO-3100 demonstrated in patients with moderate-to-severe plaque psoriasis is encouraging, especially given the short duration of treatment in this study that was designed for initial explorations of safety and efficacy,” commented Alexa Kimball, M.D., M.P.H., Vice Chair, Department of Dermatology at Massachusetts General Hospital, Boston, and an investigator in the trial.

“The achievement of statistically significant PASI reductions with only four weeks of treatment in a placebo-controlled double-blind trial directly supports the rationale that the modulation of specific TLRs plays a key role in the treatment of psoriasis and, potentially, other autoimmune and inflammatory disorders,” commented James Krueger, M.D., Ph.D., of The Rockefeller University, New York. “We are excited to see these data, which demonstrate the translation of targeting a novel mechanism of action into clinical activity and support further studies of TLR antagonists for the treatment of psoriasis. Our laboratory is continuing to evaluate the immunological pathways by which TLR antagonists suppress the signaling cascades that underlie psoriasis and have the potential to open up a new approach to disease treatment.”

About the IMO-3100 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 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 with four weeks of follow-up. Assessments of safety were performed throughout the treatment and follow-up periods. Multiple parameters were monitored to assess the clinical activity of IMO-3100, including Psoriasis Area Severity Index (PASI), mean focal psoriasis severity and Physician Global Assessment (PGA) scores. In addition to the clinical assessments, biopsies of psoriasis plaques were evaluated for treatment-related changes in epidermal thickness and immune cell infiltrates consistent with the intended mechanism of action. Patients were enrolled at eleven sites in the United States.

Top-line clinical results from this trial include:

- Of the 44 enrolled patients, 40 were clinically evaluable at the end of the four-week treatment period and 37 were evaluable following the four-week follow up period
- Treatment at both IMO-3100 dose levels was well tolerated, with no treatment-related discontinuations
- Among evaluable patients, the median PASI scores at treatment initiation were 14.9, 16.1, and 12.5 in the 0.16 mg/kg, 0.32 mg/kg, and placebo cohorts, respectively
- A treatment effect was demonstrated in measures of clinical efficacy in patients in both IMO-3100 dose cohorts; PASI reductions at both dose levels were sustained throughout the four-week follow-up period
- At the end of the four-week follow-up period, 48% of patients treated with either dose of IMO-3100 (12 of 25) demonstrated improvements of 35% to 90% from baseline PASI scores compared with 0 of 12 in the placebo cohort; this difference was statistically significant ($p<0.005$)
- The trial achieved the pre-specified clinical endpoint of reduction in PASI scores at the end of treatment in the 0.16 mg/kg dose cohort with statistical significance ($p<0.02$) compared to the placebo cohort, but not in the 0.32 mg/kg dose cohort

- The 0.16 mg/kg cohort also achieved, with statistical significance ($p<0.02$), the pre-specified clinical endpoint of improvement in induration, a measure of plaque thickness, at the end of treatment and during the follow-up period
- At the end of the four-week follow-up period, 25% (3 of 12) of patients treated with 0.16 mg/kg dose and 31% (4 of 13) with 0.32 mg/kg dose achieved PASI 50 or greater, compared to 0 of 12 placebo patients

Skin biopsies were collected at baseline and after completion of treatment to investigate changes in epidermal thickness and immune cell infiltrates. Change in epidermal thickness was the primary endpoint for the trial. Placebo treated patients had a median change in epidermal thickness of +7.7% compared to a median change of -6.4% among IMO-3100 treated patients; this difference was not statistically significant. 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).

The Company plans to present complete clinical data from this trial at an upcoming medical meeting.

“We believe this trial in patients with moderate-to-severe plaque psoriasis provides clinical proof-of-concept for this first-in-class TLR antagonist, which represents a novel approach to the treatment of autoimmune diseases. We are very pleased to have observed clinical responses after only four weeks of treatment,” stated Sudhir Agrawal, D. Phil., Chief Executive Officer of Idera. “The insights gained from this trial support expansion of our TLR antagonist program for the treatment of autoimmune diseases. In 2013, we plan to advance the clinical development of a selective TLR antagonist for the treatment of moderate-to-severe plaque psoriasis and also for the treatment of lupus.”

About TLRs and Idera's Pipeline

Toll-like Receptors (TLRs) play a key role in inflammation and immunity. Of the 10 human TLRs identified to date, 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. Inhibition of specific TLRs may be useful in treating autoimmune disorders, 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.

A characteristic of autoimmune diseases such as SLE and psoriasis is the production of immune complexes with self-nucleic acids. These abnormal immune complexes 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. Thus, a pathologic amplification cycle is established, promoting disease maintenance and progression. In preclinical models of several autoimmune diseases, IMO-3100 and IMO-8400 inhibited TLR-mediated immune responses, interrupted the cycle of disease maintenance and progression through decreases in Th1, Th17 and inflammasome pathways, and led to improvements in multiple measures of disease.

About IMO-3100

IMO-3100, an antagonist of TLR7 and TLR9, is a lead drug candidate in development to treat autoimmune diseases, including psoriasis. In preclinical mouse models of psoriasis, IMO-3100 exerted therapeutic activity by inhibiting disease-associated gene expression and cytokines, such as IL-6, IL-22, IL-17, IL-23, NLRP3 and IL-1β, and proteins in the skin such as S100A7, DEFB4 and LL37. In addition, histological evaluation showed that the psoriatic lesions in IMO-3100-treated animals had reduced epidermal thickness and decreased lymphocyte infiltration compared to control mice.

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 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. The Company is also exploring its gene-silencing oligonucleotide (GSO) technology for the purpose of inhibiting the expression of disease-promoting genes. 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 and the preclinical studies 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 Quarterly Report on Form 10-Q for the quarter ended September 30, 2012 which important factors are incorporated herein by reference. Idera disclaims any intention or obligation to update any forward-looking statements.

Source: Idera Pharmaceuticals

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