



Idera Pharmaceuticals Presents Clinical Safety and Efficacy Update from the ILLUMINATE-204 Trial of the Combination of Tilsotolimod and Ipilimumab for Unresectable or Metastatic Melanoma Following Failure of PD-1 Inhibitor Treatment

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**- 32.4% of patients evaluable for efficacy achieved partial response or better; 76.5% of patients achieved disease control -
- Tumor shrinkage observed in both injected and uninjected lesions, indicating an abscopal effect -**

EXTON, Pa., Dec. 14, 2018 (GLOBE NEWSWIRE) -- Idera Pharmaceuticals, Inc. (NASDAQ: IDRA) today is presenting data from the ongoing phase 2 expansion of the ILLUMINATE-204 trial investigating tilsotolimod, Idera's intratumorally-delivered toll-like receptor 9 (TLR9) agonist, in combination with ipilimumab (Yervoy®).

ILLUMINATE-204 Key Findings:

- 37 patients dosed with 8 mg of tilsotolimod in combination with ipilimumab were evaluated for this update:
 - 34 patients were evaluable for efficacy
 - All patients were evaluable for safety
 - Accrual is ongoing, with an additional 4 patients dosed
- Responses, including 2 Complete Responses (CR), were observed in 11 of the 34 evaluable patients (32.4%)
- Duration of response ranges from > 1 month to > 30 months, with 36% of responses ongoing
- Per RECIST v1.1, the Overall Response Rate (ORR) is 29.4%; one patient with an unconfirmed Partial Response (uPR) at the end of treatment assessment progressed due to a new lesion at the 3-month follow-up disease assessment
- Overall, 26 patients out of 34 evaluable for efficacy (76.5%) experienced disease control (CR, PR, or Stable Disease (SD))
- Analysis of spider plots show tumor shrinkage in both injected and uninjected lesions, indicating an abscopal effect
- Responding subjects include one patient with mucosal melanoma and one patient with acral melanoma, two forms of melanoma that are particularly difficult to treat
- Importantly, 2 of 5 patients with prior ipilimumab experience achieved responses, further demonstrating a signal that tilsotolimod has the potential to help overcome prior ipilimumab resistance
- The combination regimen continues to be generally well tolerated. 9/37 subjects (24.3%) had immune-related toxicities indicating that tilsotolimod + ipilimumab does not appear to add immune-related toxicity versus ipilimumab alone
- Injection-related toxicities were grade 1-2 transient fever and flu-like symptoms lasting <48 hours

Additionally:

- A RECIST v1.1 PR of > 2.5 years is ongoing in 1 patient treated with tilsotolimod 4 mg in combination with ipilimumab; and
- A RECIST v1.1 CR of > 1 year is ongoing in 1 patient treated with tilsotolimod 16 mg in combination with pembrolizumab.

"The results from this combination are among the most promising we have seen in this challenging population of metastatic melanoma patients who have not benefited from front-line immunotherapy," stated Douglas B. Johnson, M.D., Assistant Professor of Medicine, Clinical Director, Melanoma Research Program, Vanderbilt University Medical Center. "In addition to the response rate, observing over 76% of patients achieving disease control

is impressive for such a difficult-to-treat patient population.”

The ILLUMINATE-204 trial is comprised of two distinct patient populations, patients who are ipilimumab naïve (N=up to 40; Primary Efficacy Endpoint Population) and patients who have ipilimumab experience (N=up to 20; Secondary Efficacy Endpoint Population). Of the initial 34 patients evaluable for efficacy, evaluations 9 of 29 patients from the Primary Efficacy Endpoint Population and 2 of 5 patients from the Secondary Efficacy Endpoint Population achieved responses.

Indications of the specific mechanism of action for tilsotolimod were suggested in the clinical responses observed in patients whose tumor HLA-ABC RNA (MHC class I) expression was low at baseline. As recently articulated by Rodig, *et al.*¹ robust MHC class I expression is required for anti-CTLA-4 activity. These findings suggest that combining tilsotolimod with ipilimumab may overcome this resistance mechanism and, therefore, enhance the overall response rate compared to that expected with ipilimumab alone.

“The continued positive results from this trial, a response rate substantially higher than expected with ipilimumab alone, and anti-tumor activity in both injected and uninjected lesions are exciting. These reinforce our conviction that tilsotolimod may overcome an immunosuppressive tumor microenvironment and, in combination with ipilimumab, could provide a treatment option when anti PD-1 therapy fails these patients,” stated Dr. Joanna Horobin, Idera’s Chief Medical Officer. “These data, along with the translational data, bolster our confidence in both the Phase 3 trial and taking tilsotolimod beyond melanoma.”

Investor Event and Webcast

Idera will host a conference call and live webcast today, Friday, December 14, at 10:00 A.M. EST to review the data being presented along with questions and answers. To participate in the conference call, please dial (844) 882-7837 (domestic) and (574) 990-9824 (international). The webcast can be accessed live or in archived form in the “Investors” section of the company’s website at www.iderapharma.com. The company has posted a slide presentation to the Idera corporate website in the “Investors” section which will be referenced during the conference call this morning.

About Tilsotolimod (IMO-2125)

Tilsotolimod is a TLR 9 agonist that received Fast Track Designation from the US Food and Drug Administration (FDA) in 2017 for the treatment of anti-PD-1 refractory melanoma, in combination with ipilimumab as well as orphan drug designation from the FDA for the treatment of melanoma Stages IIb to IV. It signals the immune system to create and activate cancer-fighting cells (T-cells) to target solid tumors. Currently approved immunology oncology treatments, specifically check-point inhibitors, work for some but not all, as many patients’ immune response is missing or weak and thus they do not benefit from the checkpoint therapy. Intratumoral injections with tilsotolimod are designed to selectively enable the tumor-specific T-cells to recognize and attack cancers that remained elusive and unrecognized by the immune system exposed to checkpoint inhibitors alone, while limiting toxicity or impact on healthy cells in the body.

About ILLUMINATE-204

The ILLUMINATE-204 study (2125-204) is for patients who have metastatic melanoma for whom treatment with an anti-PD-1 drug like Keytruda®** (pembrolizumab) or Opdivo®* (nivolumab) has failed. ILLUMINATE-204 is a multi-center, two-arm Phase 1/2 study that tests the safety and effectiveness of tilsotolimod in combination with either ipilimumab (Yervoy®) or pembrolizumab (Keytruda®) for the treatment of patients with anti-PD-1 refractory metastatic melanoma.

For additional details about ILLUMINATE-204, please go to clinicaltrials.gov and search for study identifier NCT02644967.

About Metastatic Melanoma

Although melanoma is a rare form of skin cancer, it comprises over 75% of skin cancer deaths. The American Cancer Society estimates that there were approximately 76,000 new invasive melanoma cases and 10,000 deaths from the disease in the USA in 2016. Additionally, according to the World Health Organization, about 132,000 new cases of melanoma are diagnosed around the world every year.

About Idera Pharmaceuticals

Harnessing the approach of the earliest researchers in immunotherapy and the Company’s vast experience in developing proprietary immunology platforms, Idera’s lead development program is focused on priming the immune system to play a more powerful role in fighting cancer, ultimately increasing the number of people who can benefit from immunotherapy. Idera also continues to focus on the acquisition, development and ultimate commercialization of drug candidates for both oncology and rare disease indications characterized by small, well-defined patient populations with serious unmet needs. To learn more about Idera, visit www.iderapharma.com.

Forward Looking Statements

This press release contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. All statements, other than statements of historical fact, included or incorporated in this press release, including statements regarding the Company’s strategy, future operations, collaborations, intellectual property, cash resources, financial position, future revenues, projected costs, prospects, clinical trials, plans, and objectives of management, are forward-looking statements. The words “believes,” “anticipates,” “estimates,” “plans,” “expects,” “intends,” “may,” “could,” “should,” “potential,” “likely,” “projects,” “continue,” “will,” and “would” and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Idera cannot guarantee that it will actually achieve the plans, intentions or expectations disclosed in its forward-looking statements and you should not place undue reliance on the Company’s forward-looking statements. There are a number of important factors that could cause Idera’s actual results to differ materially from those indicated or implied by its forward-looking statements. Factors that may cause such a difference include: whether the Company’s cash resources will be sufficient to fund the Company’s continuing operations and the further development of the Company’s programs for the period anticipated; whether interim results from a clinical trial, such as the preliminary results reported in this release, will be predictive of the final results of the trial; whether results obtained in preclinical studies and clinical trials such as the results described in this release will be indicative of the results that will be generated in future clinical trials, including in clinical trials in different disease indications; whether products based on Idera’s technology will advance into or through the clinical trial process when anticipated or at all or warrant submission for regulatory approval; whether such products will receive approval from the U.S. 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’s collaborations will be successful; and such other important factors as are set forth under the caption “Risk factors” in the Company’s Annual Report filed on Form 10-K for the period ended December 31, 2017 and the Company’s Quarterly Report filed on Form 10-Q for the period ended September 30, 2018. Although Idera may elect to do so at some point in the future, the Company does not assume any obligation to update any forward-looking statements and it disclaims any intention or obligation to update or revise any forward-looking statement, whether as a result of new information, future events or otherwise.

*Yervoy (ipilimumab) and Opdivo (nivolumab) are registered trademarks of Bristol-Myers Squibb.

**Keytruda (pembrolizumab) is a registered trademark of Merck & Co., Inc.

¹ Rodig, S., *et al.*, MHC proteins confer differential sensitivity to CTLA-4 and PD-1 blockade in untreated metastatic melanoma. *Sci. Transl. Med.* 10,

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