Idera Pharmaceuticals Presents Data from the ILLUMINATE-204 Trial of the Combination of Tilsotolimod and Ipilimumab for Unresectable or Metastatic Melanoma Following Failure of PD-1 Inhibitor Treatment at the 2018 European Society for Medical Oncology (ES

October 19, 2018 10:00 AM EDT

- Key findings presented in poster discussion demonstrate clear abscopal effect of intratumoral tilsotolimod -

- Data demonstrate contribution of tilsotolimod to overcome resistance to ipilimumab in patients with low HLA-ABC expression -

- Company plans to provide additional clinical safety and efficacy data for up to 35 patients during the 4th quarter -

EXTON, Pa., Oct. 19, 2018 (GLOBE NEWSWIRE) -- Idera Pharmaceuticals, Inc. (NASDAQ: IDRA), a clinical-stage biopharmaceutical company focused on the 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, today presented data from the ongoing ILLUMINATE-204 trial investigating tilsotolimod, Idera's intratumorally-delivered toll-like receptor 9 (TLR9) agonist, in combination with ipilimumab (Yervoy®*) at the 2018 European Society for Medical Oncology (ESMO) Congress.

The poster, which was selected for a poster discussion session, highlighted additional analyses of data for 21 patients for whom efficacy and safety analysis were originally presented at the 2018 American Society of Clinical Oncology Annual Meeting this past June (data cut-off May 9th).

The new analyses address the potential of intramural tilsotolimod to induce an antitumor response in combination with ipilimumab in injected tumors as well as uninjected tumors via an abscopal effect. As previously reported the overall response rate (ORR, by RECIST 1.1) for these 21 patients was 39%. Notably, in 7 of the 8 responders tumor shrinkage was observed in both the injected and uninjected tumors. Tumor shrinkage at uninjected lesions was observed in an additional four patients who had not met the criteria for RECIST v.1.1 response status as of this analysis.

Clinical responses were seen in patients whose HLA-ABC RNA (MHC class I) expression is low at baseline. Rodig and colleagues[1] have recently shown that robust MHC class I expression is required for anti-CTLA-4 activity. Our findings suggest that combining tilsotolimod with ipilimumab may overcome this resistance mechanism, and therefore, enhance clinical activity and increase the overall response rate compared to that expected with ipilimumab monotherapy.

The ILLUMINATE-204 trial is enrolling two distinct patient populations, both patients who are naïve to ipilimumab therapy (N=40; Primary Efficacy Endpoint Population) and patients who have prior ipilimumab experience (N=Up to 20; Secondary Efficacy Endpoint Population). Of the initial 21 patients available for efficacy evaluations 6 of 17 patients from the Primary Efficacy Endpoint Population and 2 of 4 patients from the Secondary Efficacy Endpoint Population achieved RECIST v.1.1 responses, further demonstrating a signal that tilsotolimod has the potential to help overcome prior ipilimumab resistance.

"The data presented at ESMO demonstrate that in patients with melanoma progressing on or after PD-1 inhibitor therapy, injecting a single tumor lesion with tilsotolimod, in combination with ipilimumab, produced tumor shrinkage in distant uninjected lesions in nearly all patients with reported responses by RECIST v1.1 criteria," stated Adi Diab, M.D., Lead Trial Investigator, Assistant Professor, Department of Melanoma Medical Oncology, Division of Cancer Medicine, The University of Texas, MD Anderson Cancer Center. "Moreover, clinical responses were seen in tumors where MHC class I expression was low at baseline. In a recent clinical study in melanoma, it was shown that robust MHC class I expression is required for anti-CTLA-4 activity. Our findings suggest that combining tilsotolimod with ipilimumab may overcome this mechanism of resistance to anti-CTLA-4 monotherapy."

"The clear demonstration of tumor shrinkage in uninjected tumors following the injection of a single tumor lesion with tilsotolimod, provides clinical confirmation of our translational data and addresses an important frequently asked question," stated Joanna Horobin, Idera's Chief Medical Officer. "Additionally, the new observation that tilsotolimod may overcome the requirement for MHC class 1 expression for effective anti-tumor therapy with ipilimumab in patients otherwise unlikely to respond, is a very exciting finding and addresses another important question regarding the contribution of tilsotolimod when given in combination with ipilimumab."

The poster discussion is scheduled for Saturday, October 20, 2018 at 2:45 PM CEST (8:45 AM EST) in Room ICM-14b at the Messe Munchen Congress Center in Munich, Germany.

In addition to the poster discussion, the company also presented a Trials in Progress (TiPS) poster on the trial design for the ongoing ILLUMINATE-301 Phase 3 clinical trial of the combination of tilsotolimod and ipilimumab for unresectable or metastatic melanoma following failure of PD-1 inhibitor treatment. This poster will be on display on Sunday, October 21, 2018 from 12:45 – 1:45 PM CEST (6:45 – 8:45 AM EST) in Hall A3 at the Messe Munchen Congress Center in Munich, Germany.

Copies of these poster presentations are currently available on Idera's corporate website at http://www.iderapharma.com/our-approach/key-publications/.

4th Quarter Clinical Efficacy and Safety Update
Based on the timing of disease assessment visits, the company plans an additional data cut later this quarter for the ILLUMINATE-204 trial to provide an update on clinical efficacy and safety data for up to 35 patients, including overall response rate (ORR) for all patients as well as for the Primary and Secondary Efficacy Patient Populations.

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 immuno-

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 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. Melanoma is the most dangerous type of skin cancer. When it is metastatic, it means that the melanoma has spread to different parts of the body. 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 ILLUMINATE-301
The ILLUMINATE-301 study (2125-MEL-301) 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-301 is a global, multi-center, randomized Phase 3 study that compares the effectiveness and safety between two treatment groups: IMO-2125 combined with ipilimumab (Yervoy®) versus ipilimumab given alone.

For additional details about ILLUMINATE-301, please go to clinicaltrials.gov and search for study identifier NCT03445533.

About Metastatic Melanoma
Melanoma is a type of skin cancer that begins in a type of skin cell called melanocytes. As is the case in many forms of cancer, melanoma becomes more difficult to treat once the disease has spread beyond the skin to other parts of the body such as the lymphatic system, liver or other visceral organs (metastatic disease). Because melanoma occurs in younger individuals, the years of life lost to melanoma are also disproportionately high when compared with other cancers. 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 March 31, 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 (nivolimumab) are registered trademarks of Bristol-Myers Squibb.

**Keytruda (pembrolizimab) 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, eaar3342 (2018).

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