Onconova Therapeutics Doses First Patient in Phase 1/2a Trial of Narazaciclib Combined with Letrozole in Endometrial Cancer

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Prior data provide clinical proof-of-concept for narazaciclib's mechanism of action in endometrial cancer

Preliminary data from trial's Phase 1 portion expected in 4Q 2023

NEWTOWN, Pa., May 11, 2023 (GLOBE NEWSWIRE) -- Onconova Therapeutics, Inc. (NASDAQ: ONTX), ("Onconova"), a clinical-stage biopharmaceutical company focused on discovering and developing novel products for patients with cancer, today announced that the first patient has been dosed in the Company's Phase 1/2a trial evaluating narazaciclib combined with letrozole in recurrent metastatic low-grade endometrioid endometrial cancer (LGEEC). Narazaciclib is a multi-kinase inhibitor targeting CDK 4, CDK 6, and other kinases important for cell proliferation and motility. Preliminary data from the trial's Phase 1 portion are expected in 4Q 2023.

Endometrial cancer arises in the uterine lining and is the most common cancer of the female reproductive organs. Endometrioid endometrial cancer is the most common subtype of endometrial cancer, accounting for approximately 75% of cases. Data from prior randomized and single-arm trials have demonstrated the anti-cancer activity of letrozole combined with CDK 4/6 inhibition in recurrent endometrial cancer[1-3]. Currently, there is no health authority-approved CDK 4/6 inhibitor for the treatment of endometrial cancer.

"Improved treatment options for recurrent LGEEC are urgently needed, as the CDK 4/6 inhibitors currently used off-label for this indication are marked by limitations related to safety, tolerability, and treatment resistance," said Bhavana Pothuri, M.D., Professor, Department of Obstetrics and Gynecology at NYU Grossman School of Medicine and Director, Gynecologic Oncology Research; Perlmutter Cancer Center and Principal Investigator of the trial. "Narazaciclib's kinase inhibitory profile suggests it can overcome each of these limitations thanks to reduced activity against kinases whose inhibition is associated with bone marrow toxicity and diarrhea, and increased activity against those implicated in pro-tumor immune suppression and cancer cell survival. This hypothesis is supported by data from *in vitro* and murine cancer models, and I look forward to its continued evaluation in the ongoing Phase 1/2a trial."

Steven M. Fruchtman, M.D., President and Chief Executive Officer of Onconova, commented, "Our recurrent LGEEC program provides an opportunity to establish narazaciclib as a best-in-class therapy in an indication where clinical proof-of-concept for its mechanism of action has been demonstrated. We, therefore, view the program as a key avenue for value creation and look forward to our Phase 1/2a trial's preliminary data readout expected later this year."

About the Phase 1/2a Trial

The Phase 1/2a trial is an open-label, multicenter study evaluating narazaciclib in combination with letrozole as a second or third-line treatment for patients with recurrent metastatic LGEEC. Both narazaciclib and letrozole are administered orally with a continuous daily dosing schedule. The trial begins with a Phase 1 dose escalation phase before moving to a Phase 2 expansion cohort designed to enroll approximately 30 patients. The primary objective of the Phase 1 portion of the trial is to evaluate safety, tolerability, pharmacokinetics, and pharmacodynamics in order to determine a recommended Phase 2 dose (RP2D) of the combination. The primary objective of the Phase 2 portion will be to evaluate the efficacy of the combination at the RP2D, as measured by progression-free survival at 24 weeks. The estrogen/progesterone receptor status of participants will be recorded as part of an exploratory objective. The trial will be conducted at sites including NYU Langone Health, the site of the Principal Investigator of the study, sites affiliated with MD Anderson Cancer Center, and U.S. Oncology Research sites.

References

1. Mirza MR. ESMO Virtual Congress 2020. Abstr. LBA28.

2. Konstantinopoulos PA, et al.; 2022 SGO Annual Meeting on Women's Cancer; March 18-21, 2022. Phoenix, AZ

3. Colon-Otero G, Zanfagnin V, Hou X, et al. ESMO Open. 2020 Oct;5(5):e000926. doi: 10.1136/esmoopen-2020-000926.

About Onconova Therapeutics, Inc.

Onconova Therapeutics is a clinical-stage biopharmaceutical company focused on discovering and developing novel products for patients with cancer. The Company has proprietary targeted anti-cancer agents designed to disrupt specific cellular pathways that are important for cancer cell proliferation.

Onconova's novel, proprietary multi-kinase inhibitor narazaciclib (formerly ON 123300) is being evaluated in a combination trial with estrogen blockade in advanced endometrial cancer. Based on preclinical and clinical studies of CDK 4/6 inhibitors, Onconova is also evaluating opportunities for combination studies with narazaciclib in additional indications.

Onconova's product candidate rigosertib is being studied in multiple investigator-sponsored studies, including a dose-escalation and expansion Phase 1/2a study of oral rigosertib in combination with nivolumab in patients with KRAS+ non-small cell lung cancer, and a Phase 2 program evaluating rigosertib monotherapy in advanced squamous cell carcinoma complicating recessive dystrophic epidermolysis bullosa.

For more information, please visit www.onconova.com.

Forward Looking Statements

Some of the statements in this release are forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, Section 21E of the Securities Exchange Act of 1934, as amended, and the Private Securities Litigation Reform Act of 1995, and involve risks and uncertainties. These statements relate to Onconova's expectations regarding its clinical development and trials, its product candidates, its business and financial position. Onconova has attempted to identify forward-looking statements by terminology including "believes," "estimates," "anticipates," "expects," "plans," "intends," "may," "could," "might," "will," "should," "preliminary," "encouraging," "approximately" or other words that convey uncertainty of future events or outcomes. Although Onconova believes that the expectations reflected in such forward-looking statements are reasonable as of the date made, expectations may prove to have been materially different from the results expressed or implied by such forward-looking statements. These statements are only predictions and involve known and unknown risks, uncertainties, and other factors, including the success and timing of Onconova's clinical trials, investigator-initiated trials and regulatory agency and institutional review board approvals of protocols, Onconova's collaborations, market conditions and those discussed under the heading "Risk Factors" in Onconova's most recent Annual Report on Form 10-K and quarterly reports on Form 10-Q. Any forward-looking statements contained in this release speak only as of its date. Onconova undertakes no obligation to update any forward-looking statements contained in this release to reflect events or circumstances occurring after its date or to reflect the occurrence of unanticipated events.

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