



Clovis Oncology Announces First Patient Enrolled in the Phase 3 ATHENA Trial

August 8, 2018

Trial to Evaluate the Combination of Rubraca® (rucaparib) and OPDIVO® (nivolumab) in Patients with Advanced Ovarian Cancer

BOULDER, Colo.--(BUSINESS WIRE)--Aug. 8, 2018-- Clovis Oncology, Inc. (NASDAQ: CLVS) announced today the randomization of the first patient in the Phase 3 ATHENA trial evaluating the combination of Clovis' Rubraca® (rucaparib), a poly (ADP ribose) polymerase inhibitor (PARP), and Bristol-Myers Squibb's PD-1 inhibitor, OPDIVO® (nivolumab), for the treatment of advanced ovarian cancer. ATHENA, sponsored by Clovis, is part of a clinical collaboration with Bristol-Myers Squibb and is being conducted in association with the Gynecologic Oncology Group (GOG) and the European Network for Gynecological Oncological Trials (ENGOT). GOG and ENGOT are the two largest cooperative groups in the U.S. and Europe dedicated to the treatment of gynecological cancers.

"I am pleased the GOG and ENGOT are conducting the first trial designed to investigate whether the combination of a PARP inhibitor and PD-1 blocking antibody can demonstrate not only an improvement in progression-free survival in the first-line maintenance setting for women with advanced ovarian cancer, but also whether the combination can change the natural course of the disease by delaying or reducing recurrence following front-line therapy," said Brad Monk, M.D., FACS, FACOG, Arizona Oncology (US Oncology Network), Professor, Gynecologic Oncology at University of Arizona and Creighton University, Medical Director of US Oncology Research Gynecology program in Phoenix, Arizona and Lead Investigator of the ATHENA trial.

"Rubraca combination trials such as ATHENA are encouraging to see, because the possible implications are particularly meaningful for women with advanced ovarian cancer, who need a wide range of treatment options," said Dr. Rebecca Kristeleit, Clinical Senior Lecturer and Consultant Medical Oncologist, University College London, U.K. and ATHENA ENGOT/Non-U.S. Lead Investigator. "The participation by the GOG and the ENGOT in the evaluation of a PARP inhibitor in combination with a PD-1 agent reflects the interest around this approach."

ATHENA is a Phase 3, randomized, multinational, double-blind, placebo-controlled, four-arm trial evaluating Rubraca and *Opdivo* as maintenance treatment following response to front-line treatment in newly-diagnosed ovarian cancer patients. Response to treatment will be analyzed based on homologous recombination (HR) status of tumor samples. The primary endpoint is investigator assessed progression-free survival (PFS); secondary endpoints include overall survival (OS), objective response rate (ORR), duration of response (DOR), and safety.

"The initiation of the Phase 3 ATHENA trial is an important milestone for Clovis and a critical step towards helping women with advanced ovarian cancer, who are in need of new treatment options. We are particularly excited about the potential clinical utility of Rubraca in combination with *Opdivo* in this setting," said Patrick J. Mahaffy, President and Chief Executive Officer of Clovis Oncology. "The importance of this trial is also underscored by the participation of ENGOT and GOG, which we anticipate may facilitate enrollment."

The trial will enroll approximately 1,000 ovarian cancer patients at clinical trial centers in the United States and internationally. More information about the trial is available at www.clinicaltrials.gov, identifier NCT03522246.

About Rubraca® (rucaparib)

Rubraca is an oral, small molecule inhibitor of PARP1, PARP2 and PARP3 being developed in multiple tumor types, including ovarian, metastatic castration-resistant prostate, and bladder cancers, as monotherapy, and in combination with other anti-cancer agents. Exploratory studies in other tumor types are also underway. Clovis holds worldwide rights for Rubraca. Rubraca is an unlicensed medical product outside of the U.S. and Europe.

Rubraca EU Authorized Use

Rubraca is licensed for adult patients with platinum sensitive, relapsed or progressive, BRCA mutated (germline and/or somatic), high-grade epithelial ovarian, fallopian tube, or primary peritoneal cancer, who have been treated with two or more prior lines of platinum based chemotherapy, and who are unable to tolerate further platinum based chemotherapy.

[Click here](#) to access the current Summary of Product Characteristics. Healthcare professionals should report any suspected adverse reactions via their national reporting systems.

Rubraca U.S. FDA Approved Indications and Important Safety Information

Rubraca is indicated as monotherapy for the maintenance treatment of adult patients with recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in a complete or partial response to platinum-based chemotherapy.

Rubraca is indicated as monotherapy for the treatment of adult patients with deleterious BRCA mutation (germline and/or somatic) associated epithelial ovarian, fallopian tube, or primary peritoneal cancer who have been treated with two or more chemotherapies and selected for therapy based on an FDA-approved companion diagnostic for Rubraca.

Select Important Safety Information

Myelodysplastic Syndrome (MDS)/Acute Myeloid Leukemia (AML) occur uncommonly in patients treated with Rubraca, and are potentially fatal adverse reactions. In approximately 1,100 treated patients, MDS/AML occurred in 12 patients (1.1%), including those in long term follow-up. Of these, 5 occurred during treatment or during the 28-day safety follow-up (0.5%). The duration of Rubraca treatment prior to the diagnosis of MDS/AML ranged from 1 month to approximately 28 months. The cases were typical of secondary MDS/cancer therapy-related AML; in all cases, patients had received previous platinum-containing regimens and/or other DNA damaging agents. Do not start Rubraca until patients have recovered from hematological toxicity caused by previous chemotherapy (\leq Grade 1).

Monitor complete blood counts for cytopenia at baseline and monthly thereafter for clinically significant changes during treatment. For prolonged hematological toxicities (> 4 weeks), interrupt Rubraca or reduce dose (see Dosage and Administration (2.2) in full Prescribing Information) and monitor blood counts weekly until recovery. If the levels have not recovered to Grade 1 or less after 4 weeks or if MDS/AML is suspected, refer the patient to a hematologist for further investigations, including bone marrow analysis and blood sample for cytogenetics. If MDS/AML is confirmed, discontinue Rubraca.

Based on its mechanism of action and findings from animal studies, Rubraca can cause fetal harm when administered to a pregnant woman. Apprise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment and for 6 months following the last dose of Rubraca.

Most common adverse reactions in ARIEL3 ($\geq 20\%$; Grade 1-4) were nausea (76%), fatigue/asthenia (73%), abdominal pain/distention (46%), rash (43%), dysgeusia (40%), anemia (39%), AST/ALT elevation (38%), constipation (37%), vomiting (37%), diarrhea (32%), thrombocytopenia (29%), nasopharyngitis/upper respiratory tract infection (29%), stomatitis (28%), decreased appetite (23%), and neutropenia (20%).

Most common laboratory abnormalities in ARIEL3 ($\geq 25\%$; Grade 1-4) were increase in creatinine (98%), decrease in hemoglobin (88%), increase in cholesterol (84%), increase in alanine aminotransferase (ALT) (73%), increase in aspartate aminotransferase (AST) (61%), decrease in platelets (44%), decrease in leukocytes (44%), decrease in neutrophils (38%), increase in alkaline phosphatase (37%), and decrease in lymphocytes (29%).

Most common adverse reactions in Study 10 and ARIEL2 ($\geq 20\%$; Grade 1-4) were nausea (77%), asthenia/fatigue (77%), vomiting (46%), anemia (44%), constipation (40%), dysgeusia (39%), decreased appetite (39%), diarrhea (34%), abdominal pain (32%), dyspnea (21%), and thrombocytopenia (21%).

Most common laboratory abnormalities in Study 10 and ARIEL2 ($\geq 35\%$; Grade 1-4) were increase in creatinine (92%), increase in alanine aminotransferase (ALT) (74%), increase in aspartate aminotransferase (AST) (73%), decrease in hemoglobin (67%), decrease in lymphocytes (45%), increase in cholesterol (40%), decrease in platelets (39%), and decrease in absolute neutrophil count (35%).

Co-administration of Rubraca can increase the systemic exposure of CYP1A2, CYP3A, CYP2C9, or CYP2C19 substrates, which may increase the risk of toxicities of these drugs. Adjust dosage of CYP1A2, CYP3A, CYP2C9, or CYP2C19 substrates, if clinically indicated. If co-administration with warfarin (a CYP2C9 substrate) cannot be avoided, consider increasing frequency of international normalized ratio (INR) monitoring. Because of the potential for serious adverse reactions in breast-fed children from Rubraca, advise lactating women not to breastfeed during treatment with Rubraca and for 2 weeks after the last dose. You may report side effects to the FDA at 1-800-FDA-1088 or www.fda.gov/medwatch. You may also report side effects to Clovis Oncology, Inc. at 1-844-258-7662.

[Click here](#) for full Prescribing Information and additional Important Safety Information.

About Clovis Oncology

Clovis Oncology, Inc. is a biopharmaceutical company focused on acquiring, developing and commercializing innovative anti-cancer agents in the U.S., Europe and additional international markets. Clovis Oncology targets development programs at specific subsets of cancer populations, and simultaneously develops, with partners, diagnostic tools intended to direct a compound in development to the population that is most likely to benefit from its use. Clovis Oncology is headquartered in Boulder, Colorado, and has additional offices in San Francisco, California and Cambridge, UK. Please visit clovisoncology.com for more information.

Clovis Oncology Forward-Looking Statement

To the extent that statements contained in this press release are not descriptions of historical facts regarding Clovis Oncology, they are forward-looking statements reflecting the current beliefs and expectations of management made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. Examples of forward-looking statements contained in this press release include, among others, statements regarding the timing and pace of commencement of and enrollment in our clinical trials, including those being planned or conducted in collaboration with partners, and the potential results of such clinical trials. Such forward-looking statements involve substantial risks and uncertainties that could cause our future results, performance or achievements to differ significantly from that expressed or implied by the forward-looking statements. Such risks and uncertainties include, among others, the uncertainties inherent in our clinical development programs for our drug candidates and those of our partners, and the initiation, enrollment, timing and results of our planned clinical trials. Clovis Oncology does not undertake to update or revise any forward-looking statements. A further description of risks and uncertainties can be found in Clovis Oncology's filings with the Securities and Exchange Commission, including its Annual Report on Form 10-K and its reports on Form 10-Q and Form 8-K.

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