



NEWS RELEASE

## Clovis Oncology Presents Patient-Centered Outcomes Data from Phase 3 ARIEL3 Study for Rubraca®▼ in Advanced Ovarian Cancer

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Quality-adjusted progression free survival (QA-PFS) and quality-adjusted time without cancer related symptoms or toxicity (Q-TWiST) demonstrate the benefit of Rubraca maintenance treatment over placebo from a patient perspective

Data presented at the International Society for Pharmacoeconomics and Outcomes (ISPOR) 2019 Annual Meeting

BOULDER, Colo.--(BUSINESS WIRE)-- Clovis Oncology, Inc. (NASDAQ: CLVS) today announced data demonstrating that patients with recurrent ovarian cancer who received Rubraca in the Phase 3 ARIEL3 study had longer periods of quality-adjusted time without clinically relevant symptoms as compared to patients who received placebo, and that Rubraca maintenance treatment continued to provide significant benefit in progression-free survival when weighted with patients' perceptions of their wellbeing. The presentation today at the International Society for Pharmacoeconomics and Outcomes (ISPOR) Annual Meeting in New Orleans highlights post-hoc evaluations of quality-adjusted time without symptoms or toxicity (Q-TWiST) and quality-adjusted PFS (QA-PFS) from the randomized, placebo-controlled study of Rubraca®▼ (rucaparib) for the maintenance treatment of patients with recurrent ovarian cancer. To the company's knowledge, this is the first time that Q-TWiST data will be presented in the maintenance therapy setting in recurrent ovarian cancer.

"The goal of maintenance therapy for recurrent ovarian cancer is to delay disease progression without compromising a patient's quality of life," said Robert L. Coleman, MD, professor of Department of Gynecologic Oncology and Reproductive Medicine, The University of Texas MD Anderson Cancer Center. "The findings from QA-PFS and Q-TWiST analyses of ARIEL3 data demonstrate that the clinical benefits of rucaparib as maintenance therapy were retained across all trial populations. These results further support the positive benefit-risk profile of rucaparib in ARIEL3, including the absence of a detrimental effect on patient-centered outcomes across all treatment cohorts in the study."

During the study, patients were asked to complete EuroQol's five-dimension, three-level (EQ-5D-3L) questionnaire at screening, on day 1 of each treatment cycle, at the treatment discontinuation visit, and at the 28-day follow-up visit. QA-PFS and Q-TWiST analyses were calculated using EQ-5D-3L data as described in the poster. Patient-centered outcomes were examined in the intent-to-treat (ITT) population (all randomized patients), in patients with a BRCA mutation, and in subgroups of patients with BRCA wild-type carcinomas based on loss of heterozygosity (LOH) status (BRCA wild type/LOH high; BRCA wild type/LOH low; and BRCA wild type/LOH indeterminate).

Results from the study include:

- Mean QA-PFS was significantly longer in the Rubraca arm than placebo arm (12.02 vs 5.74 months) for the ITT population and for patients with a BRCA mutation (15.28 vs. 5.92 months)
- In patients with a BRCA wild-type carcinoma, mean QA-PFS was longer in the Rubraca arm than the placebo arm regardless of LOH status
- Mean Q-TWiST analysis using all grade  $\geq 3$  treatment-emergent adverse events (TEAEs) was significantly longer in the rucaparib arm than placebo for the ITT population (13.32 vs 6.44 months) and for patients with a BRCA mutation (16.42 vs 6.70 months)
- In the analyses using TEAEs of interest (grade  $\geq 2$  TEAEs of nausea, vomiting, fatigue, and asthenia), Q-TWiST was also longer in the rucaparib arm than placebo for the ITT population (13.16 vs 6.40 months) and for patients with BRCA mutation (16.24 vs 6.68 months)
- In patients with BRCA wild-type carcinoma, longer Q-TWiST was also observed in the Rubraca treated arm, regardless of LOH status

"It is very important to evaluate patients' perceptions of their well-being during any type of treatment, particularly in the maintenance therapy setting in which patients may be on therapy for an extended period of time," said Professor Jonathan Ledermann, M.D., Professor of Medical Oncology, UCL Cancer Institute and UCL Hospitals, London. "These QA-PFS and Q-TWiST data from ARIEL3 integrate the patient perspective over the course of follow-up until progression to reflect their overall experience over time and suggests that the toxicity which may occur with rucaparib doesn't outweigh its clinical benefit as maintenance treatment for women with recurrent ovarian cancer."

The Rubraca ISPOR poster will be available online at <http://clovisoncology.com/pipeline/scientific-presentations/> as of the time it is presented at the meeting.

About Quality-Adjusted PFS (QA-PFS) and Quality-Adjusted Time Without Symptoms or Toxicity (Q-TWiST)

- QA-PFS represents the duration of survival without disease progression, adjusted for the value the patient placed on their health status – i.e. it is a survival measure that adjusts for patient perceptions of treatment toxicity and any associated detrimental effects.
- Q-TWiST results were derived by subtracting from the survival endpoint all time in which patients experienced treatment toxicity or disease symptoms, and then multiplying this area under the curve by a patient-derived utility value. Q-TWiST therefore adds additional value not available in a traditional TWiST analysis because it reflects patients' perceptions of the impact of toxicity on the survival endpoint.

## About the ARIEL3 Clinical Trial

The ARIEL3 pivotal study of rucaparib is a confirmatory randomized, double-blind study comparing the effects of rucaparib against placebo to evaluate whether rucaparib given as a maintenance treatment to platinum-sensitive ovarian cancer patients can extend the period of time for which the disease is controlled after a complete or partial response to platinum-based chemotherapy. The study enrolled 564 patients with high-grade epithelial ovarian, fallopian tube or primary peritoneal cancer. To be eligible for the study, participants had to have received at least two prior platinum-based treatment regimens, been sensitive to the penultimate platinum regimen, and achieved a complete or partial response to their most recent platinum-based regimen. There were no genomic selection criteria for this study. Trial participants were randomized 2:1 to receive 600 milligrams of rucaparib twice daily (BID) or placebo. The study achieved its primary endpoint of improved PFS by investigator review in each of three populations. PFS was also improved in the rucaparib group compared with placebo by independent review, a key secondary endpoint, in all three populations. In addition, rucaparib improved objective response rate vs placebo among evaluable trial participants in all three study populations.

## About Rubraca (rucaparib)

Rucaparib is an oral, small molecule inhibitor of PARP1, PARP2 and PARP3 being developed in multiple tumor types, including ovarian and metastatic castration-resistant prostate cancers, as monotherapy, and in combination with other anti-cancer agents. Exploratory studies in other tumor types are also underway.

## Rubraca U.S. FDA Approved Indications

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 mutations (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 1100 treated patients, MDS/AML occurred in 12 patients (1.1%), including those in long-term follow-up. Of these, five 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 cytogenetic analysis. 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](http://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.

## Rubraca® ▼ (rucaparib) EU Authorized Use and Important Safety Information

Rucaparib is indicated as monotherapy for the maintenance treatment of adult patients with platinum-sensitive relapsed high-grade epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in response (complete or partial) to platinum-based chemotherapy.

Rucaparib is indicated as monotherapy treatment of 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.

**Summary warnings and precautions:** Haematological toxicity: Patients should not start Rubraca until they have recovered from haematological toxicities caused by previous chemotherapy ( $\leq$  CTCAE Grade 1). Complete blood count testing prior to starting treatment with Rubraca and monthly thereafter is advised. Rubraca should be interrupted or dose reduced and blood counts monitored weekly until recovery for the management of low blood counts. Myelodysplastic syndrome/acute myeloid leukaemia (MDS/AML): If MDS/AML is suspected, the patient should be referred to a haematologist for further investigation. If MDS/AML is confirmed, Rubraca should be discontinued. Photosensitivity: Patients should avoid spending time in direct sunlight as they may burn more easily.

When outdoors, patients should wear protective clothing and sunscreen with SPF of 50 or greater. Gastrointestinal toxicities: Low grade (CTCAE Grade 1 or 2) nausea and vomiting may be managed with dose reduction or interruption. Additionally, antiemetics may be considered for treatment or prophylaxis.

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

## 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, for those indications that require them, 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, with additional office locations in the U.S. and Europe. Please visit [www.clovisoncology.com](http://www.clovisoncology.com) for more information.

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. 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, whether future study results will be consistent with study findings to date and whether future study results will support continued development or regulatory approval. 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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