



NEWS RELEASE

## Expanded Rubraca® (Rucaparib) Data from Clovis Oncology's ARIEL3 and TRITON2 Trials in Ovarian and Prostate Cancers to be Presented at 2019 ASCO Annual Meeting

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- In exploratory analysis of ARIEL3 data, Rubraca significantly improved clinically meaningful endpoints including chemotherapy free interval and PFS on next therapy line for women with advanced ovarian cancer in maintenance treatment setting
- Updated Rubraca safety profile was consistent with the safety profile previously observed in ARIEL3
- TRITON2 findings show that tumor tissue and plasma assays successfully identified patients with a DNA damage repair gene mutation
- Responses to Rubraca were observed in TRITON2 patients with germline or somatic BRCA1/2 mutations
- Two investigator-initiated studies highlighting the potential of Rubraca in multiple cancer types also presented

BOULDER, Colo.--(BUSINESS WIRE)-- Clovis Oncology, Inc. (NASDAQ: CLVS) today announced multiple datasets being presented at the 2019 American Society of Clinical Oncology (ASCO) Annual Meeting in Chicago, May 31 – June 4, 2019. These include presentations of exploratory endpoint evaluations and updated safety data from the pivotal Phase 3 ARIEL3 trial evaluating Rubraca® (rucaparib) for the maintenance treatment of advanced ovarian cancer, as well as genomic characteristics of BRCA1/2 mutations among metastatic castration-resistant prostate cancer (mCRPC) patients in the Phase 2 TRITON2 trial evaluating Rubraca in mCRPC.

“The breadth and depth of data from both company and investigator-sponsored Rubraca trials presented at this year’s ASCO meeting demonstrate the growing strength of the data and clinical development programs behind Rubraca,” said Patrick J. Mahaffy, President and CEO of Clovis Oncology. “Accordingly, we look forward to presenting updated clinical data from the TRITON2 study at an upcoming medical conference in the second half of 2019 and submitting our planned supplemental NDA filing for BRCA-mutant advanced prostate cancer in Q4 2019.”

## ARIEL3 Exploratory Endpoints and Updated Safety Data

During an afternoon session on Saturday, June 1, Robert L. Coleman, MD, professor of Gynecologic Oncology and Reproductive Medicine, The University of Texas MD Anderson Cancer Center in Houston and co-coordinating investigator in the ARIEL3 clinical trial program, will present the poster “Exploratory analysis of the effect of maintenance rucaparib on post-progression outcomes in patients with platinum-sensitive recurrent ovarian carcinoma and updated safety data from the phase 3 study ARIEL3” (Abstract #5522/Poster Board #345).

Data from this analysis of the ARIEL3 trial, which enrolled patients with platinum-sensitive recurrent ovarian carcinoma, demonstrated that Rubraca significantly improved the clinically meaningful exploratory endpoints of chemotherapy-free interval (CFI), time to start of first subsequent therapy (TFST), time to investigator-assessed progression on the subsequent line of treatment or death (PFS2), and time to second subsequent therapy (TSST) vs. placebo.

The updated safety profile generated in this analysis is consistent with the previously-reported primary efficacy data analysis based on a data cutoff date of April 15, 2017. As of December 31, 2017, the most common treatment-emergent adverse events (TEAEs) of any grade (rucaparib vs. placebo) were nausea (75.8% vs. 36.5%), asthenia/fatigue (70.7% vs. 44.4%), dysgeusia (39.8% vs. 6.9%), and anemia/decreased hemoglobin (39.0% vs. 5.3%). The most common grade  $\geq 3$  TEAEs were anemia/decreased hemoglobin (21.5% vs. 0.5%) and alanine/aspartate aminotransferase increase (10.2% vs. 0.0%).

“These data positively reinforce our current clinical utilization and understanding of rucaparib as maintenance treatment for women with advanced ovarian cancer,” said Dr. Coleman. “They provide further confirmation that rucaparib may help women and their physicians sustain a response to platinum-based chemotherapy.”

## Genomic Characteristics of BRCA1/2 Alterations in Patients with mCRPC Enrolled in TRITON2

Also on Saturday, June 1, Wassim Abida, MD, Medical Oncologist, Memorial Sloan Kettering Cancer Center, and coordinating investigator for the TRITON2 study, will present the poster “Genomic characteristics of deleterious BRCA1 and BRCA2 alterations and associations with baseline clinical factors in patients with metastatic castration-resistant prostate cancer (mCRPC) enrolled in TRITON2” (Abstract #5031/Poster Board #143).

The ongoing phase 2 TRITON2 (NCT02952534) study is evaluating the poly(ADP-ribose) polymerase inhibitor rucaparib in mCRPC patients harboring a deleterious germline or somatic mutation in BRCA1, BRCA2, ATM, or other DNA damage repair (DDR) genes as determined by central screening of tumor tissue or plasma, or from local testing. Next-generation sequencing (NGS) assays evaluating tumor tissue and circulating cell-free tumor DNA (ctDNA) in plasma were both used to successfully identify patients with eligible alterations in BRCA1/2. The plasma

assay is minimally invasive and reliably detects alterations in patients with disease that is difficult to biopsy.

In this analysis, associations between baseline genomic and clinical characteristics were assessed. Several findings support the hypothesis that germline BRCA1/2 alterations are a prognostic factor in prostate cancer associated with more rapid progression to advanced disease. Patients with germline BRCA1/2 alterations were younger at time of enrollment into TRITON2, had more advanced disease at time of diagnosis and had a shorter time between diagnosis and enrollment into TRITON2 as compared to patients with somatic BRCA1/2 alterations. However, responses to rucaparib were observed in patients with germline or somatic BRCA1/2 alterations, highlighting the potential of rucaparib to benefit both groups of patients.

Today's poster includes the confirmed objective response rate (ORR) data based on the same June 29, 2018 visit cut-off date presented at ESMO 2018 and presents those data by germline or somatic BRCA1/2 mutation status. By investigator-assessed RECIST/PCWG3, the confirmed ORR in patients with a germline or somatic BRCA1/2 mutation treated with Rubraca was 50% (5/10) or 40% (6/15), respectively. By PSA response, the confirmed ORR in patients with a germline or somatic BRCA1/2 mutation treated with Rubraca was 66.7% (10/15) or 43.3% (13/30), respectively.

"These data reinforce the importance of genomic testing to inform clinical decision making, including consideration of plasma testing in patients with mCRPC," said Dr. Abida. "Clinicians are increasingly reliant on a patient's unique genomic profile to determine therapeutic options, especially as targeted agents such as PARP inhibitors advance toward additional approved indications."

The Clovis-sponsored ASCO posters will be available online at <http://clovisoncology.com/pipeline/scientific-presentations/> as of the time they are presented at the meeting.

### Additional Rubraca Poster Presentations: Investigator-Initiated Trials

Two trials in progress posters describe investigator-initiated studies that were selected for poster presentations at the 2019 ASCO Annual Meeting. These include a multi-center Phase 2 trial of rucaparib in combination with nivolumab as maintenance therapy for patients with advanced biliary tract cancer (Abstract #TPS4153/Poster Board #252a) to be presented on Monday, June 3 from 8:00-11:00am CDT in Hall A; and a Phase 1b/2a study of rucaparib combined with nivolumab in mCRPC and advanced/recurrent endometrial cancer (Abstract #TPS2663/Poster Board #297b) presented today from 8:00-11:00am CDT in Hall A.

### 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 the TRITON2 Clinical Trial

TRITON2 is an international, multicenter, open-label Phase 2 study of Rubraca in men with metastatic castration-resistant prostate cancer with BRCA gene alterations (inclusive of germline or somatic), which is also enrolling patients with deleterious alterations of other DNA damage repair (DDR) genes, including ATM. The study is currently enrolling across sites worldwide. For more information, please visit [www.tritontrials.com](http://www.tritontrials.com).

### 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.

Clovis holds worldwide rights for Rubraca. Rubraca is an unlicensed medical product outside of the U.S. and the EU.

### 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 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 1,100 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. Examples of forward-looking statements contained in this press release include, among others, statements regarding our expectations for submission of regulatory filings, our plans for presentation of data from ongoing trials, our expectations regarding ongoing or planned trials and the timing and pace of commencement of and enrollment in our clinical trials, including those being considered, planned or conducted in collaboration with partners. 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, whether future study results will be consistent with study findings to date and whether future study results will support continued development or regulatory approval, the corresponding development pathways of our companion diagnostics, the timing of availability of data from our clinical trials and the results, 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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