

## Clovis Oncology Presents New Data from Phase 2 Studies of Rucaparib in Advanced Ovarian Cancer at 2017 SGO Annual Meeting on Women's Cancer

March 12, 2017 10:30 AM ET

- *New rucaparib data presented today in two oral plenary sessions*
- *Data provide additional insights from ARIEL2 Phase 2 study of rucaparib in advanced ovarian cancer*
- *FDA approved Rubraca<sup>®</sup> (rucaparib) tablets in December 2016 as monotherapy treatment for women with BRCA-mutated advanced ovarian cancer based on data from Study 10 and ARIEL2*

BOULDER, Colo.--(BUSINESS WIRE)--Mar. 12, 2017-- Clovis Oncology, Inc. (NASDAQ:CLVS) announced new data from parts 1 and 2 of the ongoing ARIEL2 Phase 2 study being presented today at the 2017 Society of Gynecologic Oncology (SGO) Annual Meeting on Women's Cancer in National Harbor, MD.

The data are being presented in two oral plenary sessions:

- **Title:** Rucaparib in patients with relapsed, primary platinum-sensitive high-grade ovarian carcinoma with germline or somatic *BRCA* mutations: Integrated summary of efficacy and safety from the phase 2 study ARIEL2  
**Time:** Sunday, March 12 at 8:22-8:37 a.m. EST  
**Presenter:** Gottfried Konecny, MD, associate professor of Medicine, Department of Medicine, David Geffen School of Medicine, UCLA, Los Angeles, CA  
**SGO selected this abstract as the recipient of the 2017 SGO Presidential Award**
- **Title:** *BRCA1* and *RAD51C* promoter hypermethylation confer sensitivity to the PARP inhibitor rucaparib in patients with relapsed, platinum sensitive ovarian carcinoma in ARIEL2 part 1  
**Time:** Sunday, March 12 at 10:30-10:40 a.m. EST  
**Presented By:** Elizabeth Swisher, MD, University of Washington Medical Center, Seattle, WA

New data from these presentations include analyses of patient subsets from the ARIEL2 trial, including an integrated summary of data in patients from ARIEL2 parts 1 and 2 with a germline or somatic *BRCA1* or *BRCA2* (*BRCA*) mutation. ARIEL2 enrolled 493 patients with relapsed ovarian cancer to identify those patients most likely to respond to treatment with rucaparib: part 1 enrolled 206 patients who received one or more prior therapies, had platinum as their last treatment, and were platinum-sensitive; part 2 enrolled 287 patients treated with three or four prior therapies who were either platinum-sensitive, -resistant or -refractory at time of enrollment.

"These results demonstrate the impressive activity of rucaparib, especially in earlier line, platinum-sensitive patients," said Dr. Konecny. "We also gain insight into important biomarker analyses that may help us predict which patients with far more advanced disease are most likely to benefit from rucaparib."

Dr. Konecny's presentation analyzed objective response rate (ORR) and progression-free survival (PFS) in the 134 ovarian cancer patients with a germline or somatic *BRCA* mutation enrolled in ARIEL2, as well as the effect of platinum sensitivity status and prior lines of therapy on these endpoints. These data demonstrate that the objective response rate (ORR), disease control rate (DCR) and median progression-free survival (PFS) in patients with a *BRCA* mutation were greatest in platinum-sensitive patients, followed in descending order by those who were platinum-resistant, and those who were platinum-refractory. All responses were assessed and confirmed according to RECIST. DCR in ARIEL2 was defined as the percentage of patients who had achieved either a complete response, partial response or stable disease that was maintained for greater than 12 weeks. Patients with disease progression occurring at least 6 months after last platinum were considered platinum-sensitive; patients with disease progression occurring less than 6 months after last platinum with best response other than progressive disease (PD) were considered platinum-resistant; and patients with best response of PD on last platinum which occurred during or up to 2 months after treatment were considered platinum-refractory. The data analysis cutoff date was January 4, 2017 and this analysis was limited to patients with

*BRCA*-mutated ovarian cancer enrolled in the ARIEL2 study.

In 57 platinum-sensitive patients whose immediate prior therapy was platinum-based, the investigator-assessed ORR was 70% (95% CI: 57-72) for the overall population, with 83% (95% CI: 59-96), 86% (95% CI: 57-98) and 52% (95% CI: 31-72) ORR observed in patients treated with one, two, or three or more prior lines, respectively. The DCR in the same population was 81% (95% CI: 68-90) for the overall population, with 94% (95% CI: 73-100), 86% (95% CI: 57-98) and 68% (95% CI: 47-85) in patients treated with one, two, or three or more prior lines, respectively. The median PFS in the overall platinum-sensitive population whose immediate prior therapy was platinum-based was 12.7 months (95% CI: 9.0-14.7; 30% censoring).

In addition, PFS and ORR were assessed by *BRCA* mutation type in platinum-sensitive patients whose immediate prior treatment was platinum. Patients with a germline or somatic *BRCA* mutation had ORRs of 75% (95% CI: 57-89) and 74% (95% CI: 49-91), and median PFS of 12.8 and 12.7 months, respectively (95% CI: 8.9-16.6; 31% censoring and 6.2-18.2; 21% censoring). Patients with a *BRCA* mutation had ORRs of 71% (95% CI: 53-85) and 70% (95% CI: 47-87), and median PFS of 12.8 and 11.2 months, respectively (95% CI: 8.1-18.2; 26% censoring and 7.3-16.6; 35% censoring).

All evaluable platinum-resistant and -refractory patients had been treated with three or more lines of therapy. In 49 platinum-resistant patients, the ORR was 25% (95% CI: 13-39), the DCR was 39% (95% CI: 25-54), and the median PFS was 7.3 months (95% CI: 5.5-7.7; 27% censoring). In 14 platinum-refractory patients, there were no responders, consistent with data previously presented at the 2016 ESMO Annual Meeting. However, the DCR was 29% (95% CI: 8-58) and the median PFS was 5.0 months (95% CI: 1.9-5.7; 21% censoring).

Dr. Konecny's presentation also discussed the potential role of secondary somatic mutations restoring *BRCA* function as a mechanism of platinum resistance in patients with platinum-resistant or -refractory disease. Published data have shown that secondary mutations in *BRCA* are more frequently observed in platinum-resistant patients than platinum-sensitive patients. Data presented show that the presence of secondary somatic *BRCA* mutations may be a better predictor of rucaparib efficacy than prior responsiveness to platinum-based chemotherapy in patients with platinum-resistant or -refractory disease. In 55 evaluable patients with platinum-resistant or -refractory disease, those without a secondary somatic *BRCA* mutation (n=47) achieved a median PFS of 7.3 months (95% CI: 5.4-9.0; 26% censoring); conversely, eight patients with a secondary somatic mutation demonstrated a median PFS of only 1.7 months (95% CI: 1.6-3.2; 0% censoring). These secondary mutations were identified by sequencing of screening tumor biopsy and/or circulating tumor DNA (ctDNA) analysis.

The most common treatment-emergent adverse events observed in ARIEL2 included nausea (78%), asthenia/fatigue (78%), and vomiting (49%). The most common treatment-emergent grade 3/4 adverse events observed in ARIEL2 included anemia/decreased hemoglobin (29%), ALT/AST increased (10%), and asthenia/fatigue (10%). Treatment-emergent adverse events led to dose reductions in 49% of patients, and treatment discontinuation in 13% of patients.

In the second presentation today, Dr. Swisher discussed an analysis of *BRCA1* and *RAD51C* hypermethylation among archival and pretreatment biopsies from part 1 of the ARIEL2 study. The analysis demonstrated that, among ovarian cancer patients, methylation of *BRCA1* and *RAD51C* is associated with high loss of heterozygosity (LOH), consistent with the HRD phenotype. Further, methylation of *BRCA1* and *RAD51C* appear to confer sensitivity to rucaparib, as do mutations of *CDK12*. These data suggest that methylation is more reliably assessed in pretreatment than archival tumor samples. Dr. Swisher concludes that routine sequencing of high-grade ovarian cancer tumor tissue biopsies would identify at least 10-15% of women with a somatic mutation and 20% of women with a germline mutation whose tumors might be sensitive to rucaparib.

"We are pleased to present these additional data from the ARIEL2 trial and are encouraged that these findings continue to reinforce rucaparib's activity and safety profile in the treatment of patients with advanced ovarian cancer," said Patrick J. Mahaffy, CEO and president of Clovis Oncology. "The data presented today demonstrate our continued commitment to investing in and conducting the rigorous scientific research that will help us and physicians better understand the patients

who can benefit most significantly from treatment with rucaparib.”

The presentations are available online at <http://clovisoncology.com/pipeline/scientific-presentations/> as of the time of Dr. Swisher’s presentation at the Meeting.

### **About Rubraca® (rucaparib) tablets**

Rubraca is a PARP inhibitor indicated as monotherapy for the treatment of patients with deleterious *BRCA* mutation (germline and/or somatic) associated advanced ovarian cancer, who have been treated with two or more chemotherapies, and selected for therapy based on an FDA-approved companion diagnostic for Rubraca. The indication for Rubraca is approved under the FDA’s accelerated approval program based on objective response rate and duration of response, and is based on results from two multicenter, single-arm, open-label clinical trials. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials. Please visit [rubraca.com](http://rubraca.com) for more information.

### **About Rucaparib**

Rucaparib is an oral, small molecule inhibitor of PARP1, PARP2 and PARP3 being developed in ovarian cancer as well as several additional solid tumor indications. The MAA submission in Europe for an ovarian cancer treatment indication was submitted and accepted during the fourth quarter of 2016. Additionally, rucaparib is being developed as maintenance therapy for ovarian cancer in the ARIEL3 trial for patients with tumors with *BRCA* mutations and other DNA repair deficiencies beyond *BRCA*, as well as biomarker negative patients. Data from ARIEL3 are expected in mid-2017, which, pending positive data, is expected to be followed by the submission of a supplemental NDA for a second line or later maintenance indication. Rucaparib is also being developed in patients with mutant *BRCA* tumors and other DNA repair deficiencies beyond *BRCA* – commonly referred to as homologous recombination deficiencies, or HRD. Studies open for enrollment or under consideration include prostate, breast, pancreatic, gastroesophageal, bladder and lung cancers. Clovis holds worldwide rights for rucaparib.

### **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](http://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 made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. Such forward-looking statements involve substantial risks and uncertainties that could cause our clinical development programs, 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 whether future study results will be consistent with study findings to-date, the clinical development programs for our drug candidates and expectations with respect to regulatory submissions and approvals. 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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