Clovis Oncology Presents Comprehensive Dataset from Successful Phase 3 ARIEL3 Maintenance Treatment Trial of Rucaparib in Advanced Ovarian Cancer at ESMO 2017

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- **ARIEL3 study successfully achieved its primary endpoint of improved progression-free survival (PFS) by investigator review in each of the three populations studied (tumor BRCA-mutant, HRD and overall intent-to-treat)**
- **ARIEL3 study also successfully achieved the key secondary endpoint of improved PFS by blinded, independent central review (BICR) in all three study populations**
- **Rucaparib improved objective response rate vs. placebo among evaluable trial participants in all three study populations**
- **Safety data from ARIEL3 demonstrate consistency with prior rucaparib studies**
- **ARIEL3 data to be presented by Professor Jonathan A. Ledermann, MD, during Proffered Paper session on Gynecological Cancers on Friday, September 8**
- **Data also will be highlighted in ESMO press program on Friday, September 8**

BOULDER, Colo.--(BUSINESS WIRE)--Sep. 7, 2017-- Clovis Oncology, Inc. (NASDAQ: CLVS) announced the first presentation of a comprehensive dataset from its Phase 3 ARIEL3 study of rucaparib at the 2017 European Society for Medical Oncology (ESMO) Congress taking place in Madrid. The ARIEL3 study successfully achieved its primary endpoint and key secondary endpoint, demonstrating improved progression-free survival (PFS) by both investigator review and blinded independent central review (BICR) in each of the three populations studied. The data will be presented by Professor Jonathan A. Ledermann, MD, European and ROW Principal Investigator for the ARIEL3 study, during the Proffered Paper session on Gynecological Cancers the afternoon of Friday, September 8.

“The comprehensive ARIEL3 results presented for the first time today demonstrate the potential of rucaparib to extend the time during which the disease is controlled for women with platinum-sensitive, advanced ovarian cancer,” said Patrick J. Mahaffy, President and CEO of Clovis Oncology. “Very importantly, this benefit was demonstrated across all three ARIEL3 populations by both investigator review and blinded independent central assessment, including among women whose cancer does not exhibit a BRCA mutation or homologous recombination deficiency. In particular, ARIEL3 shows 13.7 months – well over a year – of median PFS in the all-comers population in the trial as determined by blinded independent review, which we believe could be extremely important for women battling this difficult disease. We are grateful to the patients, caregivers and investigators who participated in this study, and are working closely with European regulatory authorities to make rucaparib available to women living with ovarian cancer.”

“These results reinforce rucaparib’s potential to provide an enduring and significant clinical benefit in women with advanced ovarian cancer, regardless of their tumor genetics,” said Professor Jonathan Ledermann, MD, Professor of Medical Oncology, Director, Cancer Research UK and UCL Cancer Trials Centre, UCL Cancer Institute, and European and ROW Principal Investigator for the ARIEL3 study. “It is both impressive and encouraging that rucaparib demonstrated improvements in key primary, secondary and exploratory endpoints in all three ARIEL3 patient populations. It is also clinically significant that rucaparib not only sustained patients’ most recent response to platinum, but in some trial participants also enhanced that response, including the radiological elimination of residual tumor.”

In December 2016, Rubraca® became the first PARP inhibitor approved by the U.S. Food and Drug Administration (FDA) as monotherapy for treatment of patients with deleterious BRCA mutation (germline and/or somatic) associated advanced ovarian cancer who have been treated with two or more prior chemotherapies. During the fourth quarter of 2016, a Marketing Authorization Application (MAA) was submitted and accepted in Europe for Rubraca in the same ovarian cancer-treatment indication. Based on the ARIEL3 findings, Clovis Oncology plans to submit a supplemental New Drug Application (sNDA) to the U.S. FDA for a second line or later maintenance treatment indication in ovarian cancer by the end of October 2017, and in early 2018, plans to file an MAA in Europe for the maintenance treatment indication upon

receipt of a potential approval for the treatment indication.

ARIEL3 is a double-blind, placebo-controlled, phase 3 trial of rucaparib that enrolled 564 women with platinum-sensitive, high-grade ovarian, fallopian tube, or primary peritoneal cancer. The primary efficacy analysis evaluated three prospectively defined molecular sub-groups in a step-down manner: 1) tumor BRCA mutant (tBRCAmut) patients, inclusive of germline and somatic mutations of BRCA (n=196); 2) HRD patients, including BRCA-mutant patients and BRCA wild-type with high loss of heterozygosity, or LOH-high patients (n=354), and, finally, 3) the intent-to-treat population, or all patients treated in ARIEL3 (n=564).

Following is a table and summary of the primary efficacy analyses and selected exploratory PFS endpoints per Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1 by each of investigator review, which was the primary analysis of ARIEL3, and BICR, a key secondary endpoint of the study. Each of these analyses, and their related Kaplan-Meier curves, will be included in today's presentation by Professor Ledermann.

ARIEL3 Analysis Population	**PFS by Investigator Review** ***(Primary Endpoint)***		**PFS by Blinded Independent Central Review** ***(Key Secondary Endpoint)***	
Primary Analyses	**Hazard Ratio**	**Median PFS (months) Rucaparib vs. Placebo**	**Hazard Ratio**	**Median PFS (months) Rucaparib vs. Placebo**
tBRCAmut (n=196)	0.23; p<0.0001	16.6 vs. 5.4	0.20; p<0.0001	26.8 vs. 5.4
HRD (n=354)	0.32; p<0.0001	13.6 vs. 5.4	0.34; p<0.0001	22.9 vs. 5.5
Intent-to-Treat (n=564)	0.36; p<0.0001	10.8 vs. 5.4	0.35; p<0.0001	13.7 vs. 5.4
Exploratory Analyses				
$BRCA^{wt}$ / LOH high (n=158)	0.44; p<0.0001	9.7 vs. 5.4	0.55; p=0.0135	11.1 vs. 5.6
$BRCA^{wt}$ / LOH low (n=161)	0.58; p=0.0049	6.7 vs. 5.4	0.47; p=0.0003	8.2 vs. 5.3

PFS: progression-free survival; tBRCAmut: tumor BRCA mutant; HRD: homologous recombination deficiency; BRCAwt: BRCA wild type; LOH: loss of heterozygosity

Significant Improvement in PFS in the tBRCAmut Patient Population

The most robust clinical outcomes were observed among ARIEL3 patients with a germline or somatic BRCA mutation (n=196). By investigator review, the rucaparib arm successfully achieved statistical significance over the placebo arm for the primary endpoint of PFS with a hazard ratio of 0.23 (95% CI, 0.16-0.34; p<0.0001). The median PFS for the tBRCAmut patients treated with rucaparib was 16.6 months (95% CI, 13.4-22.9) vs. 5.4 months (95% CI, 3.4-6.7) among those who received placebo.

By BICR, the rucaparib arm improved PFS over the placebo arm with a hazard ratio of 0.20 (95% CI, 0.13-0.32; p<0.0001). The median PFS for the tBRCAmut patients treated with rucaparib was 26.8 months (95% CI, 19.2-NR) vs. 5.4 months (95% CI, 4.9-8.1) among those who received placebo.

Results were consistent for the germline BRCA (n=130) and somatic BRCA (n=56) populations.

Significant Improvement in PFS in the HRD Patient Population

This population included patients with a germline or somatic mutation of BRCA, as well as those whose tumors were BRCA wild type (BRCAwt) but determined to be HRD as defined by a Foundation Medicine assay (n=354). By investigator review, the rucaparib arm successfully achieved statistical significance over the placebo arm for the primary endpoint of PFS with a hazard ratio of 0.32 (95% CI, 0.24-0.42; p<0.0001). The median PFS for the HRD patients treated with rucaparib was 13.6 months (95% CI, 10.9-16.2) vs. 5.4 months (95% CI, 5.1-5.6) among those who received placebo.

By BICR, the rucaparib arm improved PFS over the placebo arm with a hazard ratio of 0.34 (95% CI, 0.24-0.47; p<0.0001). The median PFS for the HRD patients treated with rucaparib was 22.9 months (95% CI, 16.2-NR) vs. 5.5 months (95% CI, 5.1-7.4) among those who received placebo.

Significant Improvement in PFS in All Patients Studied

Rucaparib also showed statistical significance in all 564 patients enrolled in the study. By investigator review, the rucaparib arm successfully achieved statistical significance over the placebo arm for the primary endpoint of PFS with a hazard ratio of 0.36 (95% CI, 0.30-0.45; p<0.0001). The median PFS for all patients treated with rucaparib was 10.8 months (95% CI, 8.3-11.4) vs. 5.4 months (95% CI, 5.3-5.5) for those who received placebo.

By BICR, the rucaparib arm improved PFS over the placebo arm with a hazard ratio of 0.35 (95% CI, 0.28-0.45; p<0.0001). The median PFS for all patients enrolled in ARIEL3 and treated with rucaparib was 13.7 months (95% CI, 11.0-19.1) vs. 5.4 months (95% CI, 5.1-5.5) for those who received placebo.

Exploratory PFS Endpoint Achieved in BRCAwt/LOH High Subgroup

The exploratory PFS endpoint was achieved in the 158 patients identified as BRCAwt LOH high. By investigator review, the rucaparib arm successfully achieved its endpoint over the placebo arm for the primary endpoint of PFS with a hazard ratio of 0.44 (95% CI, 0.29-0.66; p<0.0001). The median PFS for these patients treated with rucaparib was 9.7 months (95% CI, 7.9-13.1) vs. 5.4 months (95% CI, 4.1-5.7) for those who received placebo.

By BICR, the rucaparib arm improved PFS over the placebo arm with a hazard ratio of 0.55 (95% CI, 0.35-0.89; p=0.0135). The median PFS for these patients treated with rucaparib was 11.1 months (95% CI, 8.2-NR) vs. 5.6 months (95% CI, 2.9-8.2) for those who received placebo.

Exploratory PFS Endpoint Achieved in BRCAwt/LOH Low Subgroup

The exploratory PFS endpoint was achieved in the 161 patients identified as BRCAwt and LOH low. By investigator review, the rucaparib arm successfully achieved its endpoint over the placebo arm for the primary endpoint of PFS with a hazard ratio of 0.58 (95% CI, 0.40-0.85; p=0.0049). The median PFS for these patients treated with rucaparib was 6.7 months (95% CI, 5.4-9.1) vs. 5.4 months (95% CI, 5.3-7.4) for those who received placebo.

By BICR, the rucaparib arm improved PFS over the placebo arm with a hazard ratio of 0.47 (95% CI, 0.31-0.71; p=0.0003). The median PFS for these patients treated with rucaparib was 8.2 months (95% CI, 5.6-10.1) vs. 5.3 months (95% CI, 2.8-5.5) for those who received placebo.

Exploratory Endpoint of Response Rate

Enrollment in ARIEL3 included one-third of patients who had achieved a complete response to their prior platinum-based therapy, and two-thirds of patients who had achieved a partial response to their prior platinum-based therapy. Of those with a partial response, 37% had measurable disease at the time of enrollment and were therefore evaluable for response.

By investigator-assessed RECISTv1.1, the confirmed objective response rate (ORR) in the tBRCAmut group treated with rucaparib was 38% (15/40), of these, 18% (7/40) were complete responses. This compared with 9% (2/23) ORR in the placebo group (p=0.0055) and 0% complete responses. The confirmed ORR in the HRD group treated with rucaparib was 27% (23/85), of these, 12% (10/85) were complete responses. This compared with 7% (3/41) ORR in the placebo group (p=0.05) and 0% complete responses. Finally, among the intent-to-treat population, the confirmed ORR in patients treated with rucaparib was 18% (26/141), of these 7% (10/141) were complete responses. This compared with 8% (5/66) ORR in the placebo group (p=0.05) and 2% (1/66) complete responses.

RECIST responses were not assessed by independent blinded review.

Summary of ARIEL3 Safety

The most common treatment-emergent adverse events (TEAEs) of grade ≥3 reported in patients treated with rucaparib in the ARIEL3 study were anemia/decreased hemoglobin (19%), increase in ALT/AST (10%), neutropenia (7%), asthenia/fatigue (7%), thrombocytopenia (5%), vomiting (4%) and nausea (4%). The discontinuation rate for TEAEs (excluding disease progression) was 13.4% for rucaparib-treated patients and 1.6% for the placebo arm. The rate of treatment-emergent myelodysplastic syndrome (MDS)/acute myeloid leukemia (AML) in the rucaparib arm was <1% (3/372), and no patients on the placebo arm experienced treatment-emergent MDS/AML.

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.

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. In December 2016, rucaparib became the first PARP inhibitor approved by the U.S. Food and Drug Administration (FDA) as monotherapy for treatment of patients with deleterious BRCA mutation (germline and/or somatic) associated advanced ovarian cancer who have been treated with two or more prior chemotherapies. During the fourth quarter of 2016, the Marketing Authorization Application (MAA) submission in Europe for rucaparib in the same ovarian cancer treatment indication was submitted and accepted for review. By the end of October 2017, Clovis Oncology plans to submit a supplemental New Drug Application (sNDA) in the U.S. for a second line or later maintenance treatment indication in ovarian cancer based on the ARIEL3 data, and in early 2018, plans to file an MAA in Europe for the maintenance treatment indication upon receipt of a potential approval for the treatment indication. Studies open for enrollment or under consideration include ovarian, prostate, breast, pancreatic, gastroesophageal, bladder, lung and urothelial cancers. Clovis is also developing rucaparib in patients with mutant BRCA tumors and other DNA repair deficiencies beyond BRCA – commonly referred to as homologous recombination deficiencies, or HRD. Clovis holds worldwide rights for rucaparib.

About Ovarian Cancer

Ovarian cancer is the sixth deadliest cancer amongst women in Europe,[i] where more than 65,000 women are diagnosed annually.[ii] Ovarian cancer is challenging to treat, and most women will relapse after surgery and chemotherapy. The 80 to 85 percent of women diagnosed in the later stages of the disease (III and IV) have particularly poor outcomes.[iii]

Approximately one in four women with ovarian cancer have a germline or somatic BRCA mutation,[iv] and new treatment options are needed to treat unique patient populations.

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.

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 our expectation of timing for submission of the sNDA for rucaparib, European approval of rucaparib for the treatment indication and the filing of an MAA for a second line or later maintenance indication for rucaparib. 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 the clinical development programs for our drug candidates, including the result of clinical trials, whether future study results will be consistent with study findings to-date, the corresponding development pathways of our companion diagnostics, the timing of availability of data from our clinical trials and the results of our clinical trials, the initiation, enrollment and timing of our planned clinical trials, actions by the FDA, the EMA or other regulatory authorities regarding whether to approve drug applications that may be filed, as well as their decisions that may affect drug labeling, pricing and reimbursement, and other matters that could affect the availability or commercial potential of our drug candidates or companion diagnostics. 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.

[i] World Health Organization. Globocan 2012: estimated cancer incidence, mortality and prevalence worldwide in 2012. http://globocan.iarc.fr/Pages/fact_sheets_population.aspx

[ii] Ferlay J, *et al*. *Eur J Cancer* 2013;49:1374–1403

[iii] American Cancer Society. Survival rates for ovarian cancer, by stage. https://www.cancer.org/cancer/ovarian-cancer/detection-diagnosis-staging/survival-rates.html

[iv] Pennington KP, Walsh T, Harrell MI, et al. Germline and somatic mutations in homologous recombination genes predict platinum response and survival in ovarian, fallopian tube, and peritoneal carcinomas. Clin Cancer Res. 2014;20(3):764-775.

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Clovis Investor Contacts:
Anna Sussman, 303.625.5022
asussman@clovisoncology.com
or
Breanna Burkart, 303.625.5023
bburkart@clovisoncology.com
or

Clovis Media Contacts:
US
Lisa Guiterman, 301.217.9353
clovismedia@sambrown.com
or
Christy Curran, 615.414.8668
clovismedia@sambrown.com
or
EU
Ann Hughes, +44 (0) 7944 168 187
Ann.Hughes@publicisresolute.com