Clovis Oncology Presents Efficacy and Safety Data from New Drug Application (NDA) Population for Rucaparib in the Treatment of Advanced Mutant BRCA Ovarian Cancer at 2016 ESMO Congress

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- *Rucaparib NDA Dataset to be presented in oral presentation today at ESMO*
- *Rucaparib NDA currently under priority review with FDA*
- *Prescription Drug User Fee Act (PDUFA) date is February 23, 2017*
- *European Marketing Authorization Application (MAA) submission planned for Q4 2016*

BOULDER, Colo.--(BUSINESS WIRE)--Oct. 7, 2016-- Clovis Oncology (NASDAQ:CLVS) announced today the oral presentation of the primary efficacy and safety data from its NDA dataset for rucaparib at the 2016 ESMO Congress in Copenhagen. Rucaparib is currently under priority review with FDA for the monotherapy treatment of advanced ovarian cancer in patients with BRCA-mutated tumors inclusive of both germline and somatic BRCA mutations who have been treated with two or more chemotherapies, and the submission has a PDUFA date of February 23, 2017.

Rucaparib is the Company's oral, small molecule inhibitor of PARP1, PARP2 and PARP3 currently being developed for the treatment of ovarian cancer, specifically in patients with tumors with BRCA mutations and other DNA repair deficiencies beyond BRCA, including those with high genomic loss of heterozygosity (LOH) also known as "BRCA-like." The current NDA submission seeks approval in patients with tumor BRCA mutations, which includes both germline and somatic mutations.

"These results demonstrate that rucaparib may represent an important option for women with multiply relapsed BRCA-mutated ovarian cancer based on its encouraging efficacy and tolerability," said Rebecca S. Kristeleit, MD, PhD, The University College London, Cancer Institute, London, UK. "In my opinion, rucaparib has the hallmarks of an important new therapeutic option for ovarian cancer patients."

"We are pleased to present the primary efficacy and safety dataset that has been submitted to the FDA as the basis of our NDA for rucaparib in the treatment of advanced ovarian cancer. If approved, rucaparib would be the first PARP inhibitor in the U.S. indicated to treat ovarian cancer patients with germline or somatic BRCA mutations who have received two prior chemotherapies. Women with BRCA mutations represent about 25% of patients in the US living with ovarian cancer," said Patrick J. Mahaffy, CEO and President of Clovis Oncology. "Our NDA review is ongoing with FDA, and in addition we are actively preparing for a European submission during the fourth quarter of 2016."

Data from subgroups of two multicenter, single-arm open-label phase 2 studies, Study 10 (NCT01482715) and ARIEL2 (NCT01891344) were combined for an integrated efficacy and safety analysis which further characterized the clinical benefit of rucaparib at the recommended starting dose of 600 mg BID in women with advanced ovarian cancer. In the two studies, 377 patients met the criteria for inclusion in the safety population (diagnosis of ovarian cancer and having received one or more doses of the recommended dose of 600 mg of rucaparib), and 106 patients met the criteria for inclusion in the efficacy population (received 2 or more prior chemotherapies, including 2 or more platinum-based regimens, had a mutation of BRCA (germline or somatic), and received one or more doses of the recommended dose of 600 mg of rucaparib.

The major efficacy outcome measure for this analysis was objective response rate (ORR) and duration of response (DOR) as assessed by the investigator according to RECIST. All responses were confirmed.

For the efficacy population (n=106), the median number of prior chemotherapies was three, with 39% having received two prior therapies and 61% of patients having received three or more prior therapies. The median number of prior platinum-based therapies was two, with 57% having received two prior platinum-based therapies, and 43% having received three or more prior platinum-based therapies. Seventy-five percent of patients in the efficacy population were platinum-sensitive (as defined by recurrence after progression free interval (PFI) of ≥6 months), 19% were platinum

resistant (recurrence after PFI <6 months) and 7% were platinum refractory (progression on platinum, PFI <2 months).

Summary of Efficacy Data

The RECIST ORR (objective response rate as assessed by the investigator, which includes complete and partial responses) in the efficacy population was 57/106, or 54% (95% CI: 43.8-63.5). This includes nine (9%) complete responders (CR) and 48 (45%) partial responders (PR). Thirty-six patients (34%) had stable disease (SD) as the best response, while nine patients (9%) had progressive disease (PD) as the best response and four (4%) were not evaluable (NE). Seventy-five of 106 patients, or 71% (95% CI: 61.1-79.2) had a RECIST or CA-125 response.

For the 42 patients from Study 10 included in the efficacy population, the RECIST ORR was 25/42, or 60% (95% CI: 43.3-74.4). This included four CRs (10%) and 21 PRs (50%). In addition, 12 patients (29%) had SD, two patients (5%) had PD and three (7%) were NE. For the 64 patients from ARIEL2 included in the efficacy population, the RECIST ORR was 32/64, or 50% (95% CI: 37.2-62.8). This included five CRs (8%) and 27 PRs (42%). In addition, 24 patients (38%) had SD, seven (11%) had PD and one (2%) was NE. Study 10 was limited to platinum sensitive patients; ARIEL2 included platinum sensitive, platinum resistant and platinum refractory patients.

In addition, ORR was assessed by subgroups including BRCA mutation type, number of prior chemotherapies and prior platinum regimens, PFI and platinum status. Patients with a *BRCA1* (n=67) or *BRCA2* (n=39) mutation both showed an ORR of 54% (95% CI: 41.1-66.0, 37.2-69.9, respectively) in line with the overall population. The ORR for patients with germline BRCA mutations (n=88) and somatic BRCA mutations (n=13) was 53% (95% CI: 42.5-64.1) and 46% (95% CI: 19.2-74.9), respectively; in addition, five patients with a BRCA mutation but unknown germline or somatic status had an ORR of 80% (95% CI: 28.4-99.5). Patients who received two prior chemotherapies (n=41) achieved an ORR of 68% (95% CI: 51.9-81.9). Patients who received two prior platinum regimens (n=60) demonstrated an ORR of 65% (95% CI: 51.6-76.9). Response by length of PFI differed for patients with PFI<6 months (n=27), 6-12 months (n=56) and greater than 12 months (n=23), reporting 19% (95% CI: 6.3-38.1), 63% (95% CI: 48.6-75.1) and 74% (95% CI: 51.6-89.8), respectively. Response by platinum status was reported as 0% (95% CI: 0.0-41.0) for platinum-refractory patients (n=7), 25% (95% CI: 8.7-49.1) for platinum-resistant patients (n=20), and 66% (95% CI: 54.3-76.1) for platinum-sensitive patients (n=79).

Duration of response by investigator assessment in the efficacy population was 9.2 months (95% CI: 6.6-11.7 months), and the censoring rate among responders was 47%. As of the cutoff dates, 20 patients with a RECIST response had an ongoing response.

Additionally, analyses not contained within the NDA submission showed median progression-free survival by investigator assessment in the efficacy population to be 10.0 months. Of 106 patients, 50 patients did not have an event of disease progression or death at the data cut-off dates. Of these 50 patients, 32 patients were still on treatment, and 18 patients discontinued treatment for reasons other than disease progression or death at the data cut-off dates. Of note, 79% of patients remained progression-free at six months, and 41% remained progression-free at 12 months.

For the efficacy dataset, the cut off dates were November 30, 2015 and February 29, 2016, for Study 10 and ARIEL2, respectively.

Summary of Safety Data

Of the 377 ovarian cancer patients treated with a starting dose of rucaparib 600 mg, 377 (100%) experienced a treatment-emergent adverse event (AE) of any grade, and 229 (61%) experienced a treatment-emergent AE grade 3 or higher. A total of 360 patients (96%) experienced a treatment-related AE of any grade, and 177 (47%) experienced a treatment-related AE that was grade 3 or higher. AEs leading to dose interruption occurred in 221 patients (59%). Treatment-related AEs leading to dose reduction occurred in 167 patients (44%), and treatment discontinuation in 30 patients (8%). The primary reasons for dose reduction were anemia/decreased hemoglobin (17%), asthenia/fatigue (14%) and nausea (11%). The primary reasons for treatment discontinuation were asthenia/fatigue (2%), small intestinal obstruction (2%) and nausea (1%). Nine

patients (2%) had AEs that led to death; eight were due to disease progression, and one death was due to sepsis, which was assessed by the investigator to be unrelated to treatment.

The most common treatment-emergent AEs (all grades) reported in ≥20 percent of patients included nausea (77%), asthenia/fatigue (77%), vomiting (46%), anemia (44%), increased ALT/AST (41%) and constipation (40%). The most common Grade 3/4 treatment-emergent AEs reported in ≥10 percent of patients were anemia (25%), asthenia/fatigue (11%) and ALT/AST elevations (11%).

The increases in aspartate (AST) and alanine (ALT) aminotransferase levels that were observed were asymptomatic, reversible and were rarely associated with increases in bilirubin. The elevations normalized over time with continued rucaparib treatment.

Mild to moderate creatinine elevations were observed within the first few weeks of treatment for most patients, for whom 79 (21%) experienced an AE, of whom two (0.5%) experienced a grade 3/4 event. These elevations in creatinine likely result from inhibition of the renal transporters MATE1 and MATE2-K, which can lead to an increase in serum creatinine in the absence of renal injury.

Myelodysplastic syndrome/acute myeloid leukemia was reported in less than one percent of patients.

The cut-off dates for the safety dataset were March 31, 2016 for Study 10 and April 29, 2016 for ARIEL2.

Presentation Details

The oral presentation, titled "*Clinical activity of the poly(ADP-ribose) polymerase (PARP) inhibitor rucaparib in patients (pts) with high grade ovarian carcinoma (HGOC) and a BRCA mutation (BRCAmut): Analysis of pooled data from Study 10 (parts 1, 2a, and 3) and ARIEL2 (parts 1 and 2)"* was presented today by Rebecca S. Kristeleit, PhD, The University College London, Cancer Institute, London, United Kingdom during the Session titled "Gynecological Cancers", from 2:00pm-3:30pm CEST (Abstract 856O: 2:45pm-3:00pm CEST).

The Trials-in-Progress poster presentation, titled "*Window study of the PARP inhibitor rucaparib in patients with primary triple negative or BRCA1/2 related breast cancer (RIO)"* is being presented Monday by Christy Toms, PhD, The Institute of Cancer Research, Sutton, United Kingdom during the Poster Session titled "Breast Cancer, Early Stage" from 1:00pm-2:00pm CEST (Abstract 219TiP, Poster Board #219).

The presentations will be available online at http://clovisoncology.com/products-companion-diagnostics/scientific-presentations/ at the time of their scheduled presentation at the Congress.

About Rucaparib

Rucaparib is an oral, small molecule inhibitor of PARP-1, PARP-2 and PARP-3 being developed for advanced ovarian cancer.

Specifically, rucaparib is being developed as monotherapy treatment of advanced ovarian cancer in patients with deleterious BRCA-mutated tumors inclusive of both germline and somatic BRCA mutations (as detected by an FDA-approved test) who have been treated with two or more chemotherapies. Rucaparib was granted Breakthrough Therapy designation for this proposed indication by the U.S. FDA in April 2015; and in late June 2016, Clovis completed its New Drug Application (NDA) submission to the FDA. The filing for treatment was accepted and has an action date of February 23, 2017. Rucaparib's Marketing Authorization Application (MAA) to the European Medicines Agency for the proposed treatment indication is planned for Q4 2016.

Foundation Medicine, Clovis' companion diagnostic partner, has submitted a Premarket Approval (PMA) application for its FoundationFocus CDx$_{BRCA}$ to the FDA in June 2016. The test is designed to identify tumor BRCA mutations. The timing of the submission is expected to allow for regulatory approval of the companion diagnostic in a similar timeframe.

Additionally, rucaparib is being developed as maintenance therapy in the ARIEL3 trial (NCT01968213) for patients with tumors with BRCA mutations and other DNA repair deficiencies beyond BRCA (commonly referred to as homologous recombination deficiencies, or HRD). Data from ARIEL3 are expected in Q4 2017, which is expected to be followed by the submission of a supplemental NDA for second-line maintenance therapy.

Clovis is also exploring rucaparib in other solid tumor types with BRCA mutations or molecular evidence of the HRD signature, including prostate, breast and gastroesophageal cancers.

Clovis holds worldwide rights for rucaparib.

About Ovarian Cancer

According to the American Cancer Society, more than 22,000 women will be diagnosed with ovarian cancer in the U.S. during 2016. There are often no clearly identifiable initial symptoms, and in an estimated 80 to 85% of ovarian cancer cases, the cancer has spread to other parts of the body before a person is diagnosed and can be treated. Ovarian cancer ranks fifth in cancer deaths and causes more deaths than any other cancer of the female reproductive system. One in four women with ovarian cancer have a germline or somatic BRCA mutation, 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 diagnostic tools that direct a compound in development to the population that is most likely to benefit from its use. Clovis Oncology is headquartered in Boulder, Colorado.

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 those 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, the corresponding development pathways of our companion diagnostics, 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 regarding drug labeling, and other matters that could affect the availability or commercial potential of our drug candidates or companion diagnostics, including competitive developments. 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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