NEWS RELEASE

# Clovis Oncology Highlights Rubraca® (rucaparib) Updated Data from the Ongoing TRITON2 Clinical Trial in Patients with mCRPC and Exploratory and Integrated Analyses in Recurrent Ovarian Cancer at the ESMO Congress 2019

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- 43.9% confirmed objective response rate (ORR) in 57 RECIST * -evaluable patients with metastatic castration-resistant prostate cancer (mCRPC) and a BRCA1/2 mutation
- 52.0% confirmed prostate-specific antigen (PSA) response in 98 PSA-evaluable patients with mCRPC and a BRCA1/2 mutation
- The safety profile of Rubraca was consistent with prior reports from TRITON2 and for those patients with ovarian cancer and other solid tumors
- Supplemental new drug application (NDA) for Rubraca in BRCA1/2-mutant advanced prostate cancer on track for Q4 2019
- Clovis Oncology also highlights efficacy and safety of Rubraca in recurrent ovarian cancer

BOULDER, Colo.--(BUSINESS WIRE)-- Clovis Oncology, Inc. (NASDAQ: CLVS) today announced updated data from the Phase 2 TRITON2 trial at the European Society for Medical Oncology (ESMO) Congress 2019, reinforcing the potential of Rubraca® (rucaparib) for the treatment of patients with metastatic castration-resistant prostate cancer (mCRPC) with a BRCA1/2 mutation. The data show a 43.9% confirmed objective response rate (ORR) by investigator assessment in 57 RECIST*/PCWG3** response-evaluable patients with a BRCA1/2 mutation. When assessed by independent radiological review, the response rate was similar (40.4%). In addition, a 52.0% confirmed prostate-specific antigen (PSA) response rate was observed in 98 response-evaluable patients with a BRCA1/2 mutation. Confirmed radiographic responses were durable, with 60 percent lasting 24 weeks or longer (15/25).

The TRITON2 data will be used to support the filing of Clovis Oncology's planned supplemental NDA to the Food and Drug Administration (FDA) for Rubraca in BRCA1/2-mutant advanced prostate cancer.

“The updated data from the TRITON2 trial confirm the potential role of rucaparib in treating metastatic castration-resistant prostate cancer,” said Wassim Abida, M.D., Medical Oncologist, Memorial Sloan Kettering Cancer Center, and principal investigator for the TRITON2 study. “These data specifically demonstrate the efficacy of rucaparib in eligible mCRPC patients with a BRCA1/2 mutation and reinforce the known safety profile in this treatment setting, showing it has the potential to offer clinical benefit to eligible patients.”

Confirmed investigator-assessed RECIST* and PSA responses were also observed in patients with alterations in other DDR genes, including ATM, CDK12, CHEK2, PALB2, BRIP1, FANCA, and RAD51B.

The median duration of follow-up (as of July 2, 2019) for patients in TRITON2 was 13.1 months (range 4.1–28.5 months) with the safety profile consistent with prior reports. The most common any-grade treatment-emergent adverse events (TEAE) >20% in the TRITON2 trial were asthenia/fatigue (55.3%), nausea (49.5%), anemia/decreased hemoglobin (37.9%), decreased appetite (27.9%), transient increased aspartate transaminase/alanine aminotransferase (ALT/AST) (24.7%), constipation (24.7%), vomiting (22.1%) and diarrhea (21.1%).

Clovis Oncology is further evaluating the potential of Rubraca to treat advanced prostate cancer in the TRITON3 clinical trial - a multicenter, randomized, open-label Phase 3 study of Rubraca versus physician’s choice of therapy - for patients with mCRPC. TRITON3 is currently enrolling patients with BRCA1/2-mutant and ATM-mutant (both inclusive of germline and somatic) tumors with a primary objective of assessing radiographic progression-free survival (PFS) in these patients.

## Rubraca in Recurrent Ovarian Cancer

An exploratory data analysis from the pivotal Phase 3 ARIEL3 trial evaluating Rubraca for the maintenance treatment of recurrent ovarian cancer assessed PFS in the subgroups who had achieved a partial response (PR) or complete response (CR) on the most recent platinum regimen. The data show that PFS was longer in patients receiving Rubraca than placebo regardless of whether patients achieved a CR or PR on their last platinum-based regimen. Patients in the intent-to-treat population who received rucaparib treatment had a significantly greater reduction in risk for progression or death versus placebo whether they had achieved a CR (hazard ratio of 0.33 [95% CI, 0.23-0.49]; rucaparib, n=126; placebo, n=64) or a PR (hazard ratio of 0.38 [95% CI, 0.30-0.49]; rucaparib, n=249; placebo, n=125) to their last platinum-based therapy. Improvements in investigator-assessed PFS were also demonstrated in patients from the BRCA mutant and BRCA mutant or BRCA wild type/high loss of heterozygosity populations who were treated with Rubraca compared with placebo. The safety profile in Rubraca-treated patients who had either a CR or PR to their last platinum-based chemotherapy was consistent with that of the ITT population reported. Among patients with residual disease at baseline, confirmed RECIST responses were seen in a number of patients treated with rucaparib, including 23/104 (22.1%) patients with non-measurable but assessable disease at baseline.

An integrated analysis of safety data from Study 10, ARIEL2 and ARIEL3 are consistent with the known safety profile of Rubraca in patients with platinum-sensitive, recurrent ovarian cancer, in both the treatment and maintenance settings. The analysis included 937 patients treated with Rubraca in the treatment (Study 10 and ARIEL2, n=565) and maintenance (ARIEL3, n=372) settings. Overall, 102/937 (10.9%) patients discontinued due to any grade treatment-related TEAE (treatment setting: 53/565 [9.4%]); (maintenance setting: 49/372 [13.2%]). The most frequent any grade adverse events leading to discontinuation were asthenia/fatigue (23/937 [2.5%]), anemia/ hemoglobin decreased (20/937 [2.1%]) and thrombocytopenia/platelets decreased (19/937 [2.0%]). The most frequent grade ≥3 treatment-related TEAE leading to discontinuation was anemia/hemoglobin decreased (15/937 [1.6%]) and asthenia/fatigue (7/937 [0.7%]).

“The ARIEL3 data presented at ESMO this year demonstrate that rucaparib contributes to a significant increase in progression-free survival over placebo, irrespective of whether a patient had CR or PR to previous platinum-based therapy and provides strong evidence for efficacy in women with recurrent ovarian cancer in the second-line maintenance setting,” said Professor Jonathan Ledermann, M.D., Professor of Medical Oncology, UCL Cancer Institute and UCL Hospitals, London, Global Principal Investigator for non-U.S. sites in the ARIEL3 study. “The current data provide physicians with a compelling argument to make maintenance therapy essential for all eligible patients, including women who have had a complete response.”

Data from the Study 10, ARIEL2 and ARIEL3 trials supported the approvals of Rubraca for the treatment and maintenance treatment of recurrent ovarian cancer in the U.S. and EU. The European Commission authorization of Rubraca, resulted in Rubraca being the first poly (ADP ribose) polymerase (PARP) inhibitor to be approved for both treatment and maintenance treatment among eligible women with ovarian cancer in the EU.

“Rubraca continues to demonstrate meaningful clinical benefit in the recurrent ovarian cancer treatment and maintenance settings, and our updated prostate data are highly consistent with the data presented at ESMO last year,” said Patrick J. Mahaffy, President and CEO of Clovis Oncology. “We are moving forward with plans to file an sNDA in advanced mCRPC by the end of 2019, and we believe that, similar to its ovarian cancer profile, Rubraca may offer an important treatment option for patients with advanced prostate cancer, for whom new options are needed. We are committed to further exploring the potential of Rubraca and look forward to starting the tumor-agnostic study before year-end and furthering our combination studies that are now enrolling patients.”

Clovis Oncology’s ESMO Rubraca poster presentations are available online at **clovisoncology.com**.

## Clovis Analyst/Investor Event at ESMO Webcast Details

In addition, the Company will present greater detail about its planned sNDA filing and regulatory strategy in mCRPC

at its Investor/Analyst event today at 6:30pm CEST, which will be webcast live and available via replay from the following link: **https://ir.clovisoncology.com/investors-and-news/events-and-presentations/event-details/2019/Investor-Analyst-Presentation-at-ESMO-2019/default.aspx**.

## About Rubraca® (rucaparib)

Rubraca is an oral, small molecule inhibitor of PARP1, PARP2 and PARP3 that is being developed in multiple tumor types, including ovarian and mCRPC, 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 CR or PR 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 ≥2 chemotherapies and selected for therapy based on an FDA-approved companion diagnostic for Rubraca.

## Select important safety information

MDS/AML occurs 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 (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 (≥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 (≥25%, grade 1–4) were increase in creatinine (98%), decrease in hemoglobin (88%), increase in cholesterol (84%), increase in ALT (73%), increase in 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 (≥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 (≥35%; grade 1–4) were increase in creatinine (92%), increase in ALT (74%), increase in 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 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**. 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) European Union (EU) authorized use and Important Safety Information

Rubraca 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.

Rubraca 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 ≥2prior lines of platinum-based chemotherapy, and who are unable to tolerate further platinum-based chemotherapy.

Efficacy of Rubraca as treatment for relapsed or progressive EOC, FTC, or PPC has not been investigated in patients who have received prior treatment with a PARP inhibitor. Therefore, use in this patient population is not recommended.

## Summary warnings and precautions:

Hematological toxicity

During treatment with Rubraca, events of myelosuppression (anemia, neutropenia, thrombocytopenia) may be observed and are typically first observed after 8–10 weeks of treatment with Rubraca. These reactions are manageable with routine medical treatment and/or dose adjustment for more severe cases. Complete blood count testing prior to starting treatment with Rubraca, and monthly thereafter, is advised. Patients should not start Rubraca treatment until they have recovered from hematological toxicities caused by previous chemotherapy (CTCAE grade ≥1).

Supportive care and institutional guidelines should be implemented for the management of low blood counts for the treatment of anemia and neutropenia. Rubraca should be interrupted or dose reduced according to Table 1 (see Posology and Method of Administration [4.2] of the Summary of Product Characteristics [SPC]) and blood counts monitored weekly until recovery. If the levels have not recovered to CTCAE grade 1 or better after 4 weeks, the patient should be referred to a hematologist for further investigations.

MDS/AML

MDS/AML, including cases with fatal outcome, have been reported in patients who received Rubraca. The duration of therapy with Rubraca in patients who developed MDS/AML varied from less than 1 month to approximately 28 months.

If MDS/AML is suspected, the patient should be referred to a hematologist for further investigations, including bone marrow analysis and blood sampling for cytogenetics. If, following investigation for prolonged hematological toxicity, MDS/AML is confirmed, Rubraca should be discontinued.

Photosensitivity

Photosensitivity has been observed in patients treated with Rubraca. Patients should avoid spending time in direct sunlight because they may burn more easily during Rubraca treatment; when outdoors, patients should wear a hat and protective clothing, and use sunscreen and lip balm with sun protection factor of 50 or greater.

Gastrointestinal toxicities

Gastrointestinal toxicities (nausea and vomiting) are frequently reported with Rubraca, and are generally low grade (CTCAE grade 1 or 2), and may be managed with dose reduction (refer to Posology and Method of Administration [4.2], Table 1 of the SPC) or interruption. Antiemetics, such as 5-HT3 antagonists, dexamethasone, aprepitant and fosaprepitant, can be used as treatment for nausea/vomiting and may also be considered for prophylactic (i.e. preventative) use prior to starting Rubraca. It is important to proactively manage these events to avoid prolonged or more severe events of nausea/vomiting which have the potential to lead to complications such as dehydration or hospitalization.

Embryofetal toxicity

Rubraca can cause fetal harm when administered to a pregnant woman based on its mechanism of action and findings from animal studies. In an animal reproduction study, administration of Rubraca to pregnant rats during the period of organogenesis resulted in embryo-fetal toxicity at exposures below those in patients receiving the recommended human dose of 600 mg twice daily (see Preclinical Safety Data [5.3] of the SPC).

Pregnancy/contraception

Pregnant women should be informed of the potential risk to a fetus. Women of reproductive potential should be advised to use effective contraception during treatment and for 6 months following the last dose of Rubraca (see section 4.6 of the SPC). A pregnancy test before initiating treatment is recommended in women of reproductive potential.

**Click here** to access the current SPC. 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** 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, the timing and pace of commencement of and enrollment in our clinical trials, including those being planned or conducted in collaboration with partners, the potential results of such clinical trials, our expectations regarding the suitability of Rubraca for, and our plans to develop Rubraca in, additional indications and tumor types. 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, the timing of availability of data from our clinical trials and the initiation, enrollment, timing and results of our planned clinical trials and the corresponding development pathways, effectiveness and suitability of diagnostic tests, the risk that final results of ongoing trials may differ from initial or interim results as a result of factors such as final results from a larger patient population may be different from initial or interim results from a smaller patient population, the risk that additional pre-clinical or clinical studies may not support further development in certain additional indications or tumor types, and actions by the FDA, the EMA or other regulatory authorities regarding data required to support drug applications and whether to approve drug applications. 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.

* Response Evaluation Criteria in Solid Tumors (RECIST) is a standardized methodology for determining therapeutic response to anticancer using changes in lesion appearance on imaging studies
** Prostate Cancer Working Group (PCWG3) is an international expert committee of prostate cancer clinical investigators who have recommended modifications to RECIST for use in the conduct of trials in metastatic castration-resistant prostate cancer (mCRPC), which were adopted in the TRITON2 protocol.

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