



NEWS RELEASE

Clovis Oncology Presents Initial Results from the Ongoing Rubraca® (rucaparib) TRITON Program in Metastatic Castration Resistant Prostate Cancer (mCRPC) at ESMO 2018 Congress

10/19/2018

- 44% confirmed objective response rate (ORR) reported in 25 RECIST-evaluable patients with a BRCA1/2 alteration in initial data from ongoing TRITON2 Phase 2 study; median duration of response has not yet been reached
- 51% confirmed PSA response rate shown in 45 PSA-evaluable patients with a BRCA1/2 alteration
- Reductions in target lesion diameters and PSA measurements have been observed in patients with an ATM alteration
- Preliminary safety data for Rubraca in men with mCRPC are consistent with those observed in patients with ovarian cancer and other solid tumors
- TRITON screening poster discussion provides initial genomic profiling data from TRITON clinical program
- Plasma samples identified alterations in BRCA1 or BRCA2 in approximately 12% of mCRPC patients screened for the TRITON2 study
- Data demonstrate plasma cell-free circulating tumor DNA (cfDNA) samples highly consistent with tumor tissue in identifying BRCA1 or BRCA2 alterations
- Breakthrough Therapy designation (BTD) granted by FDA to Rubraca for treatment of patients with BRCA1/2 alterations in mCRPC based on initial data from ongoing TRITON2 Phase 2 study

BOULDER, Colo.--(BUSINESS WIRE)-- Clovis Oncology, Inc. (NASDAQ: CLVS) today announced initial data from its ongoing **Phase 2 TRITON2** clinical trial of Rubraca at the ESMO 2018 Congress (European Society for Medical Oncology). The data show a 44% confirmed objective response rate (ORR) by investigator assessment in 25 RECIST*/PCWG3** response-evaluable patients with a BRCA1/2 alteration. The median duration of response in these

patients has not yet been reached. In addition, a 51% confirmed prostate specific antigen (PSA) response rate was observed in 45 PSA response-evaluable patients with a BRCA1/2 alteration.

The TRITON2 results were the basis for Breakthrough Therapy designation for Rubraca as a monotherapy treatment of adult patients with BRCA1/2 mutated mCRPC who have received at least one prior androgen receptor (AR)-directed therapy and taxane-based chemotherapy, which was granted on October 2, 2018 by the U.S. Food and Drug Administration (FDA). These data will be highlighted in a poster authored by Dr. Wassim Abida, Medical Oncologist, Memorial Sloan Kettering Cancer Center, and principal investigator for the TRITON2 study. The data have been selected for a poster discussion session that will be led by invited discussant Dr. Joaquin Mateo, of the **Prostate Cancer Translational Research Group**, Vall d'Hebron Institute of Oncology (VHIO) on 21 October at 09:15-9:40 CEST.

"Rubraca has previously demonstrated antitumor activity in its approved indications for women with advanced ovarian cancer," said Dr. Abida. "These new data show that Rubraca may also offer a new approach for the treatment of mCRPC associated with BRCA1 and BRCA2 alterations, with the potential to achieve a clinical response in patients with few remaining therapy options."

Patients enrolled in the TRITON2 study had received prior treatment with at least one androgen receptor (AR)-directed therapy and taxane-based chemotherapy and were screened for a deleterious germline or somatic alteration in BRCA1, BRCA2 or one of 13 other pre-specified homologous recombination (HR) genes. Study participants were allocated into three cohorts based on the type of gene alteration and disease status, which was determined by genomic sequencing and RECIST criteria, respectively. Each cohort received 600mg Rubraca twice daily and were grouped based on the following criteria: A) alteration in either BRCA1, BRCA2 or ATM genes, with tumors that can be measured with visceral and/or nodal disease; B) alteration in either BRCA1, BRCA2 or ATM genes, with tumors that cannot be measured with visceral and/or nodal disease, or C) alteration in another HR gene associated with sensitivity to PARP inhibition, with or without measurable disease. The primary study endpoints include confirmed ORR per RECIST/PCWG3 in patients with measurable disease at baseline and PSA response in patients with no measurable disease at baseline. Secondary endpoints include overall survival (OS), clinical benefit rate, and safety and tolerability.¹

As of the visit cut-off date of June 29, 2018, 85 patients were treated with Rubraca; the overall median treatment duration was 3.7 (range, 0.5–12.9) months and median follow up was 5.7 (range, 2.6–16.4) months. The median treatment duration in patients with a BRCA1/2 alteration was 4.4 months (range, 0.5–12.0 months). Forty-six patients (54.1%) were evaluable for RECIST/PCWG3 response, including 25 patients with a BRCA1/2 alteration. By investigator-assessed RECIST/PCWG3, the confirmed ORR in patients with a BRCA1/2 alteration treated with Rubraca was 44.0% (11/25). Among the 45 evaluable patients with a BRCA1/2 alteration, 51.1% (23/45) had a

confirmed PSA response (95% CI, 35.8–66.3).

Overall, the most common treatment-emergent adverse events (TEAEs) of any grade (CTCAE Grade 1-4) in all patients regardless of causality included asthenia/fatigue (44.7%, or 38/85), nausea (42.4%, or 36/85), anemia/decreased hemoglobin (22.4%, or 19/85) and constipation (28.2%, or 24/85). Five patients (5.9%) discontinued therapy due to a non-progression TEAE. One patient died due to disease progression.¹

“We are very encouraged by these initial findings from the TRITON2 study, which demonstrate the potential of Rubraca to treat men with advanced prostate cancer whose disease has progressed after receiving multiple prior lines of therapy,” said Patrick J. Mahaffy, President and CEO of Clovis Oncology. “PARP inhibitors are now a validated therapeutic class in oncology in multiple tumor types, and these new data underscore the benefit that Rubraca may provide for men with advanced, BRCA-mutant castration-resistant prostate cancer. Having recently received Breakthrough Therapy designation based on these data, we are committed to the rapid development of Rubraca for men with this very difficult-to-treat disease.”

The poster discussion session also will include the first presentation of genomic profiling data based on tumor tissue and plasma cfDNA samples from the TRITON clinical program. The poster, authored by Dr. Simon Chowdhury, Consultant Medical Oncologist, Guy’s Hospital & Sarah Cannon Research Institute and co-principal investigator for the TRITON clinical studies, will be included in the same poster discussion session as the TRITON2 data, led by invited discussant Dr. Joaquin Mateo, of the **Prostate Cancer Translational Research Group**, Vall d’Hebron Institute of Oncology (VHIO). The poster discussion session takes place on 21 October at 09:15-9:40 CEST.

The data suggest cfDNA detected from plasma can be used to identify deleterious HR gene alterations in a manner that is less invasive than tumor tissue testing. Additionally, due to the invasiveness of tumor tissue sample collection, archival primary prostate samples are often used, and data suggest these samples are not representative of the somatic alterations which emerge in mCRPC.

In the study evaluation, patients’ HR gene alteration status was determined by screening a total of 1,311 tumor and 638 plasma specimens, collected from a total of 1,516 patients to determine eligibility for TRITON2 and TRITON3. There was high concordance (74%) in identifying patients with deleterious BRCA1/2 mutations by both tissue and plasma sample. The results demonstrate that detecting genetic alterations within HR genes using cfDNA sequencing could prove to be a convenient method to identify patients who might be suitable candidates for treatment with Rubraca.² Approximately 12% of men screened for the TRITON2 study were identified as having a BRCA1/2 alteration by plasma screening.

“Tumor tissue testing relies heavily on archival samples taken when a patient is newly diagnosed but may not capture all the alterations that emerge in patients with metastatic disease,” said Dr. Chowdhury. “The screening

data demonstrate that there is a high concordance between alterations detected in the tissue and plasma assays. Due to the less invasive nature of obtaining cfDNA through plasma testing, this method may be more suitable for both physicians and patients and may also identify more patients eligible for clinical trials of Rubraca.”

Clovis' Rubraca poster presentations will be available online at clovisoncology.com at 07:30 CEST on Saturday, October 20, 2018.

About the TRITON2 Clinical Study

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 homologous recombination (HR) repair genes, including ATM. The study is currently enrolling across sites worldwide. For more information, please visit www.tritontrials.com.

About Prostate Cancer

The American Cancer Society estimates that more than 164,000 men in the United States will be diagnosed with prostate cancer in 2018,³ and the GLOBOCAN Cancer Fact Sheets estimate that approximately 345,000 men in Europe were diagnosed with prostate cancer in 2012.⁴ Castration-resistant prostate cancer has a high likelihood of developing metastases. Metastatic castration-resistant prostate cancer, or mCRPC, is an incurable disease, usually associated with poor prognosis. According to the American Cancer Society, the five-year survival rate for mCRPC is approximately 29%.⁵ Approximately 12% of mCRPC patients have a deleterious mutation in BRCA1 or BRCA2, according to an article published in the Journal of Clinical Oncology Precision Oncology in 2017.⁶ These molecular markers may be used to select patients for treatment with a PARP inhibitor.

About Rubraca

Rubracais an oral, small molecule inhibitor of PARP1, PARP2 and PARP3 being developed in multiple tumor types, including ovarian, metastatic castration-resistant prostate, and bladder 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 Europe.

Rubraca EU Authorized Use

Rubraca is licensed for 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.

Click here to access the current Summary of Product Characteristics. Healthcare professionals should report any suspected adverse reactions via their national reporting systems.

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 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 (\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. 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.

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 and Oakland, California and Cambridge, UK. Please visit clovisoncology.com for more information.

Clovis Oncology Forward-looking Statement

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 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 diagnostic tests. 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, 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.

References

1. Abida W, Bryce AH, Vogelzang NJ et al. Preliminary results from TRITON2: a phase 2 study of rucaparib in patients with metastatic castration-resistant prostate cancer (mCRPC) associated with homologous recombination repair (HRR) gene alterations. Presented at the European Society of Medical Oncology (ESMO), 19–23 October 2018. Abstract 793PD.
2. Chowdhury S, McDermott R, Piulats JM et al. Genomic profiling of circulating tumour DNA (ctDNA) and tumour tissue for the evaluation of rucaparib in metastatic castration-resistant prostate cancer (mCRPC). Presented at the European Society of Medical Oncology (ESMO), 19–23 October 2018. Abstract 795PD.
3. Key Statistics for Prostate Cancer | Prostate Cancer Facts Available at: <https://www.cancer.org/cancer/prostate-cancer/about/key-statistics.html> (accessed October 8, 2018).

4. Fact Sheets by Cancer. Available at http://globocan.iarc.fr/Pages/fact_sheets_cancer.aspx

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6. Abida W, Armenia J, Gopalan A et al. Prospective genomic profiling of prostate cancer across disease states reveals germline and somatic alterations that may affect clinical decision making. *Journal of Clinical Oncology Precision Oncology*. 2017;1;1-16. Available at: <http://ascopubs.org/doi/full/10.1200/PO.17.00029> (accessed October 8, 2018)

* Response Evaluation Criteria in Solid Tumors (RECIST) is a standardized methodology for determining therapeutic response to anticancer therapy 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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