NEWS RELEASE

# Clovis Oncology's Rubraca® (rucaparib) Significantly Improves Progression-Free Survival versus Chemotherapy in Patients with Later-line Ovarian Cancer Associated with a BRCA Mutation

3/19/2021

- Data from the randomized, Phase 3 ARIEL4 study to be presented today at the Society of Gynecologic Oncology Virtual Annual Meeting on Women's Cancer
- The ARIEL4 study met its primary endpoint, showing a statistically significant improvement in investigator-assessed progression-free survival (PFS) for Rubraca versus chemotherapy
- The safety of Rubraca observed in the ARIEL4 study was highly consistent with both the U.S. and EU product labels

BOULDER, Colo.--(BUSINESS WIRE)-- Clovis Oncology, Inc. (NASDAQ: CLVS) announced that the first presentation of data from the randomized, Phase 3 ARIEL4 study of Rubraca® (rucaparib) will take place today in an oral presentation at the Society of Gynecologic Oncology Virtual Annual Meeting on Women's Cancer (SGO). The data demonstrate that Rubraca significantly improves PFS compared to standard-of-care chemotherapy, including platinum-based chemotherapy, among patients with advanced, relapsed ovarian cancer and a deleterious BRCA mutation who have received two or more prior lines of chemotherapy.

"Data from the ARIEL4 study meaningfully enhance our understanding about the role of Rubraca among women with BRCA mutation-positive relapsed ovarian cancer, as well as the clinical relevance of BRCA reversion mutations," said Dr. Rebecca Kristeleit, Co-Coordinating Investigator of ARIEL4 and Consultant Medical Oncologist, Guy's and St Thomas' NHS Foundation Trust, London, UK. "This is important because women with more advanced disease have fewer treatment options, and it is increasingly important to understand how specific mutations affect treatment outcomes."

Dr. Kristeleit will present "Rucaparib versus chemotherapy in patients with advanced, relapsed ovarian cancer and a

deleterious BRCA mutation: efficacy and safety from ARIEL4, a randomized phase 3 study" today during the SGO Scientific Plenary I: Innovation and Progress in Gynecologic Oncology session from 2:35 pm - 3:45 pm CT. The presentation can also be viewed at **https://www.clovisoncology.com/pipeline/scientific-presentations/** starting today at 2:35 pm CT.

The ARIEL4 study (NCT02855944) is a Phase 3 multicenter, randomized study evaluating Rubraca versus chemotherapy in fully platinum-sensitive, partially platinum-sensitive and platinum-resistant patients with relapsed ovarian cancer and a BRCA mutation (inclusive of germline and/or somatic) who have received two or more prior lines of chemotherapy. The primary endpoint of the study is investigator-assessed PFS, with a step-down analysis from the primary efficacy population (if significant) to the intent-to-treat (ITT) population.

The study enrolled 349 women in Europe, Israel and North and South America. The primary efficacy population (n=325) comprised the group of patients with a deleterious tumor BRCA mutation and excluded those with a BRCA reversion mutation as determined by a blood test. The rucaparib arm in this population (n=220) achieved statistical significance over the chemotherapy arm (n=105) for the primary endpoint of PFS with a hazard ratio of 0.64 (p=0.001). The median PFS for the patients in the efficacy population treated with rucaparib was 7.4 months versus 5.7 months among those who received chemotherapy.

Additionally, in the ITT population (n=349), the rucaparib arm (n=233) achieved statistical significance over the chemotherapy arm (n=116) for the primary endpoint of PFS with a hazard ratio of 0.67 (p=0.002). The median PFS for the patients in the ITT population treated with rucaparib was 7.4 months versus 5.7 months among those who received chemotherapy.

Adverse events were consistent with the known safety profiles of Rubraca and chemotherapy. The most common (>5%) treatment-emergent ≥grade 3 adverse events (TEAEs) among all patients treated with rucaparib (n=232) in the ARIEL4 study were anemia/decreased hemoglobin (22%), neutropenia/decreased absolute neutrophil count (10%), asthenia/fatigue (8%), thrombocytopenia/decreased platelets (8%), and increased ALT/AST (8%).

"The ARIEL4 data add to the growing scientific understanding about the clinical utilization of Rubraca compared to chemotherapy, including platinum-based chemotherapy, for women diagnosed with BRCA mutation-positive advanced ovarian cancer," said Patrick J. Mahaffy, President and CEO of Clovis Oncology. "We remain committed to expanding treatment options for patients living with cancer and are pleased to share these data with physicians and their patients to help improve outcomes for women with ovarian cancer."

According to the American Cancer Society, an estimated more than 21,000 women will be diagnosed with ovarian cancer in the United States and there will be an estimated nearly 14,000 deaths from ovarian cancer in 2021, and according to GLOBOCAN in 2020, an estimated 66,000 women in Europe are diagnosed each year with ovarian

cancer, and ovarian cancer is among those cancers with the highest rate of deaths. According to the American Cancer Society, more than 75% of women are diagnosed with ovarian cancer at an advanced stage, and patients who are diagnosed with advanced ovarian cancer have a 70-95% chance of recurrence according to the Ovarian Cancer Research Alliance.

## About Rubraca (rucaparib)

Rucaparib is an oral, small molecule inhibitor of PARP1, PARP2 and PARP3 being developed in multiple tumor types, including ovarian and metastatic castration-resistant prostate cancers, as monotherapy, and in combination with other anti-cancer agents. Exploratory studies in other tumor types are also underway.

## Rubraca Ovarian Cancer U.S. FDA Approved Indications

Rubraca is indicated for the maintenance treatment of adult women 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 for the treatment of adult women with a deleterious BRCA mutation (germline and/or somatic)-associated epithelial ovarian, fallopian tube, or primary peritoneal cancer who have been treated with two or more chemotherapies. Select patients for therapy based on an FDA-approved companion diagnostic for Rubraca.

## Select Important Safety Information

Myelodysplastic Syndrome (MDS)/Acute Myeloid Leukemia (AML) have occurred in patients treated with Rubraca, and are potentially fatal adverse reactions. In 1146 treated patients, MDS/AML occurred in 20 patients (1.7%), including those in long term follow-up. Of these, 8 occurred during treatment or during the 28 day safety follow-up (0.7%). The duration of Rubraca treatment prior to the diagnosis of MDS/AML ranged from 1 month to approximately 53 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 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 for cytogenetics. 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 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%).

Co-administration of rucaparib 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.

**Click here** or 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 ≥2 prior lines of platinum-based chemotherapy, and who are unable to tolerate further platinum-based chemotherapy.

Efficacy of Rubraca as treatment for relapsed or progressive epithelial ovarian cancer (EOC), fallopian tube cancer (FTC), or primary peritoneal cancer (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 the potential results of such clinical trials, our expectations regarding the suitability of Rubraca for certain patient populations or indications, and our plans to develop Rubraca in additional indications and tumor types, and

our expectations regarding the outcomes of early studies or trials supporting further development, both non-clinical and clinical. 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.

View source version on **businesswire.com**: **https://www.businesswire.com/news/home/20210319005072/en/**


## Clovis Investor Contacts:

Anna Sussman, 303.625.5022 **asussman@clovisoncology.com**

or

Breanna Burkart, 303.625.5023 **bburkart@clovisoncology.com**

## Clovis Media Contacts:

### U.S.

Lisa Guiterman, 301.217.9353 **clovismedia@sambrown.com**

### Europe

Jake Davis, +44 (0) 20.3946.3538

**Jake.Davis@publicisresolute.com**


Source: Clovis Oncology, Inc.