Clovis Oncology Announces FDA Accelerated Approval of RUBRACA™ (rucaparib) for the Monotherapy Treatment of Advanced Ovarian Cancer in Women with Deleterious Germline or Somatic BRCA Mutations Treated with Two or More Chemotherapies

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- *First and only PARP inhibitor in the U.S. indicated to treat advanced ovarian cancer patients who have been treated with two or more chemotherapies and who have deleterious germline or somatic BRCA mutations*
- *Rubraca received approval under the FDA's accelerated approval program based on objective response rate and duration of response*
- *Most common Grade 3-4 adverse reaction was anemia; most common Grade 3-4 laboratory abnormality was decrease in hemoglobin*

BOULDER, Colo.--(BUSINESS WIRE)--Dec. 19, 2016-- Clovis Oncology, Inc. (NASDAQ:CLVS) today announced that the U.S. Food and Drug Administration (FDA) has approved Rubraca™ (rucaparib) tablets as monotherapy for the treatment of patients with deleterious BRCA mutation (germline and/or somatic) associated advanced ovarian cancer, who have been treated with two or more chemotherapies, and selected for therapy based on an FDA-approved companion diagnostic for Rubraca. Rubraca's indication is approved under the FDA's accelerated approval program, and is based on objective response rate and duration of response results from two multicenter, single-arm, open-label clinical trials, Study 10 and ARIEL2 Parts 1 and 2. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials. The ARIEL3 maintenance confirmatory study has completed enrollment and the ARIEL4 treatment confirmatory study is open for enrollment. Warning and precautions include Myelodysplastic Syndrome (MDS) and Acute Myeloid Leukemia (AML). Please see additional warnings and precautions and Select Important Safety Information below.

This Smart News Release features multimedia. View the full release here: http://www.businesswire.com/news/home/20161219006002/en/

"Recurrent ovarian cancer remains one of the most difficult cancers to treat and for so many years, medical advances in this space have been limited," said Robert L. Coleman, MD, Professor & Deputy Chairman, Vice Chair, Clinical Research, Ann Rife Cox Chair in Gynecology, Department of Gynecologic Oncology and Reproductive Medicine at University of Texas MD Anderson Cancer Center in Houston and one of the Principal Investigators in the ARIEL clinical trial program. "Today's approval of Rubraca for the treatment of advanced ovarian cancer demonstrates the value of treatment with PARP inhibitors and represents an important advance for women diagnosed with either germline or somatic *BRCA*-mutated tumors who have been treated with two or more chemotherapies."

"We believe that today's approval of Rubraca provides an important new therapy for advanced ovarian cancer patients with a germline or somatic mutation of *BRCA* after two or more chemotherapies," said Patrick J. Mahaffy, CEO and President of Clovis Oncology. "We look forward to launching Rubraca with the support of our established U.S. commercial and medical affairs organizations and bringing this much-needed precision medicine to women with advanced ovarian cancer as quickly as possible."

"NOCC commends Clovis Oncology for its commitment to bringing a new treatment option to women living with ovarian cancer, the deadliest cancer of the female reproductive system. All too often, women are diagnosed when the disease is far advanced, leaving them with few viable treatment options," said David Barley, Chief Executive Officer, National Ovarian Cancer Coalition. "The development and FDA approval of therapies for use in third-line is a promising step forward for the tens of thousands of women who will battle ovarian cancer in their lifetime."

"Ovarian cancer is one of the most difficult cancers to detect. For this reason, most women who develop ovarian cancer are diagnosed with advanced disease," said Sue Friedman, DVM, Executive Director of Facing Our Risk of Cancer Empowered. "There is a tremendous need for new ways to treat women with advanced ovarian cancer and ways to find

those women who will respond to therapies such as PARP inhibitors. PARP inhibitors, like Rubraca, represent an exciting advancement for appropriate patients."

The Rubraca NDA filing received Priority Review and was reviewed and approved under FDA's Accelerated Approval program. These programs allow for earlier approval of drugs that treat serious conditions and that fill an unmet medical need. The application was based on objective response rate and duration of response results from two multicenter, single-arm, open-label clinical trials, Study 1 (Study 10, NCT01482715) and Study 2 (ARIEL2 Parts 1 and 2, NCT01891344), in women with advanced BRCA-mutant ovarian cancer who had progressed after two or more prior chemotherapies. All 106 patients received Rubraca orally 600 mg twice daily as monotherapy until disease progression or unacceptable toxicity. Objective response rate (ORR) and duration of response (DOR) were assessed by the investigator and independent radiology review (IRR) according to Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1.

Clovis partnered with Foundation Medicine, Inc. to co-develop a companion diagnostic test, the FDA approved FoundationFocus^{TM} CDx$_{BRCA}$, to select patients for Rubraca treatment. FoundationFocus CDx$_{BRCA}$ is a tissue-based, genomic assay that detects tumor BRCA1 and BRCA2 mutations (germline and/or somatic) in ovarian cancer.

Efficacy and safety results from the U.S. Prescribing Information are summarized below:

Overall Response and Duration of Response in Patients with *BRCA*-mutant Ovarian Cancer Who Received 2 or More Chemotherapies in Study 1 and Study 2

	Investigator-assessed
	N=106
Objective Response Rate (95% CI)	54% (44, 64)
Complete Response	9%
Partial Response	45%
Median DOR in months (95% CI)	9.2 (6.6, 11.6)

Response assessment by IRR was 42% (95% CI: 32, 52), with a median DOR of 6.7 months (95% CI: 5.5, 11.1). Investigator-assessed ORR was 66% (52/79; 95% CI: 54, 76) in platinum-sensitive patients, 25% (5/20; 95% CI: 9, 49) in platinum-resistant patients, and 0% (0/7; 95% CI: 0, 41) in platinum-refractory patients. ORR was similar for patients with a *BRCA*1 gene mutation or *BRCA*2 gene mutation.

The overall safety evaluation of Rubraca 600 mg twice daily as monotherapy is based on data from 377 patients with ovarian cancer treated in two open-label, single arm trials. The most common adverse reactions (≥ 20% of patients; Grade 1-4) were nausea, asthenia/fatigue, vomiting, anemia, constipation, dysgeusia, decreased appetite, diarrhea, abdominal pain, thrombocytopenia and dyspnea. The most common laboratory abnormalities (≥ 35% of patients; Grade 1-4) were increase in creatinine, increase in ALT, increase in AST, decrease in hemoglobin, decrease in lymphocytes, increase in cholesterol, decrease in platelets and decrease in absolute neutrophil count.

About Rubraca Connections

Rubraca will be available in the United States immediately. For those who are eligible, Clovis Oncology plans to offer programs through Rubraca Connections to support patients taking Rubraca. More information about Rubraca Connections is available at RubracaConnections.com or by calling 1-844-779-7707 between 8 am and 8 pm Eastern, Monday through Friday.

About Rubraca^{TM} (rucaparib)

Rubraca is a PARP inhibitor indicated as monotherapy for the treatment of patients with deleterious *BRCA* mutation (germline and/or somatic) associated advanced ovarian cancer, who have been treated with two or more chemotherapies, and selected for therapy based on an FDA-approved companion diagnostic for Rubraca. Rubraca's indication is approved under the FDA's accelerated approval program based on objective response rate and duration of response, and is based on results from two multicenter, single-arm, open-label clinical trials. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

Select Important Safety Information

There are no contraindications with Rubraca.

Myelodysplastic Syndrome (MDS)/Acute Myeloid Leukemia (AML) was reported in 2 of 377 (0.5%) patients with ovarian cancer treated with Rubraca. The duration of Rubraca treatment prior to the diagnosis of MDS/AML was 57 days and 539 days. Both patients received prior treatment with platinum and other DNA damaging agents.

AML was reported in 2 (<1%) patients with ovarian cancer enrolled in ARIEL3, a blinded, randomized trial evaluating Rubraca versus placebo. One case of AML was fatal. The duration of treatment prior to the diagnosis of AML was 107 days and 427 days. Both patients had received prior treatment with platinum and other DNA damaging agents.

Do not start Rubraca until patients have recovered from hematological toxicity caused by previous chemotherapy (≤ Grade 1).

Monitor complete blood count testing at baseline and monthly thereafter. For prolonged hematological toxicities, interrupt Rubraca and monitor blood counts weekly until recovery. If the levels have not recovered to Grade 1 or less after 4 weeks, 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.

Rubraca can cause fetal harm when administered to pregnant women based on its mechanism of action and findings from animal studies. 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 (≥ 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 (≥ 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%).

Because of the potential for serious adverse reactions in breast-fed infants from Rubraca, advise lactating women not to breastfeed during treatment with Rubraca and for 2 weeks after the final dose.

Please see the U.S. Prescribing Information for full safety and efficacy or visit www.Rubraca.com for more information.

Conference Call Details

Clovis will hold a investor/analyst conference call to discuss the Rubraca approval this afternoon, Monday, December 19, at 4:15pm ET. Conference call details to follow.

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.

This press release contains forward-looking statements (as defined under the Private Securities Litigation Reform Act of 1995) about the potential of Rubraca™ (rucaparib) as a treatment for BRCA-mutated advanced ovarian cancer after two or more prior chemotherapies, and reflects Clovis Oncology's current beliefs. As with any pharmaceutical product, there are substantial risks and uncertainties in the process of development and commercialization that could cause actual results to differ materially from those expressed or implied by the forward-looking statements. In particular, there are no guarantees that future study results and patient experience will be consistent with the study findings to date, that Rubraca will receive regulatory approval for any future indications, or that it will prove to be commercially successful. 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. All forward-looking statements are based on information currently available to the company, and Clovis Oncology does not undertake to update or revise any forward-looking statements.

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