FDA Accepts Clovis Oncology's New Drug Application for Rucaparib for Priority Review for the Treatment of Advanced Mutant BRCA Ovarian Cancer

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- *Seeking approval for mutant BRCA patients treated with two or more prior therapies*
- *FDA Grants Priority Review Status*
- *Assigns PDUFA Date of February 23, 2017*

BOULDER, Colo.--(BUSINESS WIRE)--Aug. 23, 2016-- Clovis Oncology, Inc. (NASDAQ: CLVS) announced today that the U.S. Food and Drug Administration (FDA) has accepted Clovis' New Drug Application (NDA) for accelerated approval of rucaparib and granted priority review status to the application with a Prescription Drug User Fee Act (PDUFA) date of February 23, 2017. In late June 2016, Clovis completed its NDA submission of rucaparib to the FDA for the 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), and who have been treated with two or more chemotherapies. Rucaparib was granted Breakthrough Therapy Designation for the proposed indication by the FDA in April 2015.

"The acceptance of the rucaparib NDA submission represents an important milestone for rucaparib, and for Clovis," said Patrick J. Mahaffy, President and CEO of Clovis Oncology. "There is tremendous need for additional therapeutic options for patients with advanced mutant BRCA ovarian cancer and we look forward to cooperating with FDA on the rucaparib NDA review."

"Recurrent ovarian cancer remains a very difficult disease to treat, even among women who carry, or whose tumors have a mutation in the *BRCA* genes. Despite the available treatment options, few effective therapies are at our disposal. Thus, the opportunity to treat women with germline or somatic *BRCA* mutations with rucaparib after two prior lines of platinum-based therapy, represents a meaningful step forward for our patients," 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.

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, including germline and somatic BRCA mutations. The timing of the submission is expected to allow for regulatory approval of the companion diagnostic in a similar timeframe.

About the Submission: Efficacy

The efficacy of rucaparib was assessed in 106 patients from two multicenter, single-arm, open-label clinical trials, Study 1 (Study 10, NCT01482715) and Study 2 (ARIEL2 Parts 1 and 2, NCT01891344), in patients with advanced BRCA-mutant ovarian cancer who had progressed after two or more prior chemotherapies. Median age was 59 years and median number of prior chemotherapy regimens was three.

Study 1 was limited to platinum sensitive patients; Study 2 included platinum sensitive, platinum resistant and platinum refractory patients.

All 106 patients received the starting dose of rucaparib 600 mg twice daily. The major efficacy outcome measure of both trials was objective response rate (ORR) and duration of response (DOR) as assessed by the investigator according to Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1. All responses were confirmed.

Efficacy results from Study 1 and Study 2 in all patients treated are summarized in the table 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

	Study 1	**Study 2**	**Overall[1]**
Activity by RECIST 1.1 per Investigator Assessment			
	N=42	**N=64**	**N=106**
Objective Response Rate (95% CI)	60% (43, 74)	50% (37, 63)	54% (44, 64)
Complete Response	10%	8%	9%
Partial Response	50%	42%	45%
Median Duration of Response in months (95% CI)	7.8 (5.6, 10.5)	11.6 (5.5, 18.2)	9.2 (6.6, 11.6)

[1] Pooled analysis of Study 1 and Study 2
Confidence Interval (CI)

Nine (9%) of the 106 patients overall had progressive disease as best response. The ORR was similar for patients with germline BRCA-mutant ovarian cancer or somatic *BRCA*-mutant ovarian cancer and for patients with a BRCA1 gene mutation or BRCA2 gene mutation.

About the Submission: Safety

The safety population is comprised of the 377 ovarian cancer patients treated with starting dose of rucaparib 600 mg twice daily in Study 1 and Study 2.

The Grade 3/4 treatment emergent adverse events (AEs) reported in ≥10% of patients were anemia/decreased or low hemoglobin (25%), fatigue/asthenia (11%) and increased ALT/AST (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.

The discontinuation rate for ovarian cancer patients due to rucaparib-related AEs was 8%.

Myelodysplastic syndrome (MDS) was reported in 1 of 377 (0.3%) patients with ovarian cancer.

In addition, in the ongoing ARIEL3 maintenance trial, a blinded, randomized trial evaluating rucaparib versus placebo, acute myeloid leukemia (AML) was reported in 2 (<0.5%) patients with ovarian cancer. One case of AML was fatal. Both of these patients had received prior treatment with platinum and other DNA damaging agents.

About Rucaparib

Rucaparib is an oral, small molecule inhibitor of PARP1, PARP2 and PARP3 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.

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 and HRD populations, including prostate, breast and gastroesophageal cancers.

Clovis holds worldwide rights for rucaparib.

About Rucaparib Clinical Development in Ovarian Cancer

The ARIEL (Assessment of Rucaparib in Ovarian Cancer Trial) program is a novel, integrated translational-clinical program designed to accurately and prospectively identify ovarian cancer patients with tumor genotypes associated with benefit from rucaparib therapy.

- ARIEL2 is a two-part single-arm open label study designed to identify pre-specified tumor characteristics that predict sensitivity to rucaparib using DNA sequencing to evaluate each patient's tumor. Part 1 enrolled 204 platinum-sensitive patients and updated results were presented in June 2016. Part 2 enrolled 286 patients with advanced ovarian cancer who have received at least three prior chemotherapy regimens and includes platinum-sensitive, -resistant and -refractory patients. ARIEL2 is evaluating clinical response in patients classified into molecularly-defined subgroups, including germline BRCA-mutant, somatic BRCA-mutant and HRD by a prospectively defined genomic signature.
- The phase 2 portion of Study 10, the initial dose finding study, enrolled patients with relapsed, high-grade ovarian cancer associated with a deleterious germline BRCA mutation who received 2-4 prior lines of chemotherapy.
- The ARIEL3 pivotal study is a randomized, double-blind study comparing the effects of rucaparib against placebo to evaluate whether rucaparib given as a maintenance therapy to platinum-sensitive patients can extend the period of time for which the disease is controlled after a positive outcome with platinum-based chemotherapy. Patients are randomized to receive either placebo or rucaparib and the primary endpoint of the study is PFS. The primary efficacy analysis will evaluate, in a step-down process, BRCA-mutant patients, all patients with a HRD signature (including BRCA and non-BRCA), followed by all patients. Target enrollment in ARIEL3 was completed during the second quarter of 2016.
- The ARIEL4 confirmatory study (NCT 02855944), expected to begin during the second half of 2016, is a Phase 3 multicenter, randomized study of rucaparib versus chemotherapy in relapsed ovarian cancer patients with BRCA mutations who have failed two prior lines of therapy. The primary endpoint of the study is PFS.
- For more information, please visit www.arielstudy.com.

In addition to the ARIEL program in ovarian cancer, the Company is exploring rucaparib in other solid tumor types with BRCA and HRD populations, including two monotherapy prostate cancer studies as well as multiple combination studies, including with inhibitors of PD-L1, are planned to initiate in late 2016 and early 2017.

An abstract based on the ovarian NDA dataset has been accepted for an oral presentation at the ESMO 2016 Congress in October 2016.

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 aimed 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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