

Clovis Oncology Presents Data from Phase 2 Studies of Rucaparib in Advanced Ovarian Cancer and Pancreatic Cancer at 2016 ASCO Annual Meeting

June 6, 2016 8:30 AM ET

BOULDER, Colo.--(BUSINESS WIRE)--Jun. 6, 2016-- Clovis Oncology (NASDAQ:CLVS) announced updated phase 2 results from Part 1 of the ongoing ARIEL2 study in patients with advanced ovarian cancer as well as the final results of the RUCAPANC study of rucaparib in pancreatic cancer at the 2016 American Society of Clinical Oncology (ASCO) Annual Meeting in Chicago. Rucaparib is the Company's oral, potent, small molecule inhibitor of PARP1, PARP2 and PARP3 currently being developed for the treatment of ovarian cancer, specifically in patients with tumors with BRCA mutations and other DNA repair deficiencies beyond BRCA, including those with high genomic loss of heterozygosity (LOH) also known as "BRCA-like."

"We are pleased to present our mature dataset from Part 1 of the ARIEL2 study for rucaparib in ovarian cancer at ASCO, which demonstrates its encouraging clinical activity in selected patients and its potential in the treatment of advanced ovarian cancer," said Patrick J. Mahaffy, CEO and President of Clovis Oncology. "We are also encouraged by the results of the RUCAPANC study of rucaparib in advanced pancreatic cancer patients with mutations of BRCA, and look forward to exploring rucaparib in additional tumor types in which mutations in BRCA and other DNA repair deficiencies play a significant role."

Study objectives of the global, two-part single-arm open-label ARIEL2 trial in patients with advanced ovarian cancer include determining rucaparib activity in prospectively defined molecular subgroups through the assessment of progression-free survival (PFS) in patients with tumors that have germline and somatic BRCA mutations, those with a BRCA-like signature (patients whose tumors have other DNA repair deficiencies, including those with high genomic LOH but with normal BRCA genes ($BRCA^{wt}/LOH^{high}$)), and patients whose tumors are biomarker negative (those with low genomic LOH, or $BRCA^{wt}/LOH^{low}$). Objective response rate (ORR), safety and pharmacokinetics were also analyzed. Patients in ARIEL2 were treated with the recommended phase 2 dose (RP2D) of 600mg twice daily (BID). ARIEL2 Part 1 was initiated in October 2013 and completed enrollment in 2014. At the data cutoff date of January 18, 2016, 28 of the 204 patients enrolled in ARIEL2 Part 1 remained on study. These patients were required to be platinum-sensitive for enrollment and received a median of one prior treatment regimen and a median of one prior platinum-based chemotherapy regimen. Enrollment continues for ARIEL2 Part 2, which expanded the ARIEL2 study in early 2015 into up to 300 additional patients with recurrent disease after at least three prior lines of chemotherapy. Enrollment into ARIEL2 Part 2 is not limited to platinum-sensitive disease, but also includes patients with platinum-resistant or platinum-refractory disease. Presentation of ARIEL2 Part 2 data will follow at a future medical meeting.

A NGS-based assay developed with Foundation Medicine, Inc. was used to determine the percentage of genomic LOH, mutations in BRCA, and other homologous recombination genes in archival tumor tissue and pretreatment biopsies for patients enrolled in ARIEL2. A prespecified cutoff of $\geq 14\%$ for LOH^{high} was determined through analysis of microarray and survival data for patients in The Cancer Genome Atlas who had ovarian carcinoma and had received platinum-based chemotherapy. A planned post hoc analysis using outcome data from ARIEL2 Part 1 was performed to refine the genomic cutoff. The data for both the prespecified and refined cutoff percentages are presented in today's poster presentation.

Updated Results of ARIEL2 Part 1

Data presented from the ARIEL2 Part 1 study demonstrated clinical activity in patients with tumors with germline and somatic BRCA mutations as well as those with tumors classified as $BRCA^{wt}/LOH^{high}$.

Using the prespecified $\geq 14\%$ cutoff, patients in the $BRCA^{mut}$ subgroup demonstrated a 73 percent reduction in the risk of progression, and patients in the $BRCA^{wt}/LOH^{high}$ subgroup demonstrated a 38 percent reduction in the risk of progression, both compared to the $BRCA^{wt}/LOH^{low}$ subgroup (hazard ratio: 0.27 [95% CI: 0.16, 0.44; $p < 0.001$] and hazard ratio: 0.62 [95% CI: 0.42, 0.90; $p = 0.01$], respectively). Median PFS for the $BRCA^{mut}$, $BRCA^{wt}/LOH^{high}$, and

BRCA^{wt}/LOH^{low} subgroups was 12.8 months, 5.7 months and 5.2 months, respectively.

An analysis of platinum-sensitive patients from ARIEL2 Part 1 identified a refined LOH cutoff of $\geq 16\%$ that provided further discrimination of PFS, objective response rate and duration of response in patients with LOH^{high} and LOH^{low} tumors who received a median of one prior treatment regimen. Using the refined LOH cutoff of $\geq 16\%$, patients in the BRCA^{mut} subgroup demonstrated a 75 percent reduction in the risk of progression, and patients in the BRCA^{wt}/LOH^{high} subgroup demonstrated a 49 percent reduction in the risk of progression, both compared to the BRCA^{wt}/LOH^{low} subgroup (hazard ratio: 0.25 [95% CI: 0.15, 0.42; $p < 0.001$] and hazard ratio: 0.51 [95% CI: 0.34, 0.74; $p < 0.001$], respectively). Median PFS for the BRCA^{mut}, BRCA^{wt}/LOH^{high}, and BRCA^{wt}/LOH^{low} subgroups was 12.8 months, 7.2 months and 5.0 months, respectively.

The confirmed investigator-assessed ORR based on RECIST criteria was significantly higher in the BRCA^{mut} subgroup than in the BRCA^{wt}/LOH^{low} with the prespecified LOH cutoff. As expected, the most robust clinical responses were observed in patients with tumor (germline and somatic) BRCA mutations: 80 percent (32/40) of BRCA^{mut} patients achieved a response. Responses were observed in both germline and somatic BRCA^{mut} tumors, including 85 percent (17/20) of patients with a gBRCA mutation and 74 percent (14/19) of patients with a sBRCA mutation. One patient with a BRCA mutation was indeterminate for mutation type. In the BRCA^{wt}/LOH^{high} subgroup, the ORR was 29 percent (24/82) and 33 percent (23/69) based on the prespecified and refined cutoff, respectively. In the BRCA^{wt}/LOH^{low} subgroup, the ORR was 10 percent for both the prespecified and refined cutoffs, representing responses in 7 of 70 and 8 of 83 patients, respectively. Median duration of response for the prespecified and refined LOH cutoffs for the BRCA^{mut} and BRCA^{wt}/LOH^{high} subgroups were the same at 9.2 months and 10.8 months, respectively, and highly similar for the BRCA^{wt}/LOH^{low} subgroup at 5.6 months and 5.5 months, respectively.

The most common treatment-emergent AEs reported in ≥ 20 percent of all patients included nausea (80%), asthenia/fatigue (78%), constipation (46%), vomiting (44%) and dysgeusia (43%). These events were mostly Grade 1/2. The most common Grade 3/4 treatment-emergent AEs were anemia/decreased hemoglobin (21%) and ALT/AST elevations (12%). No treatment-related deaths were reported. Nineteen patients (9%) discontinued treatment because of an adverse event.

These results support the predictive utility of an HRD signature to identify patients with platinum-sensitive ovarian cancer who may benefit from rucaparib treatment. The NGS-based HRD assay will be prospectively applied to assess the utility of a rucaparib treatment-based LOH^{high} cutoff in predicting response to rucaparib in the phase 3 ARIEL3 study investigating rucaparib in the maintenance setting in platinum-sensitive ovarian cancer.

Feasibility of Monitoring Response to Rucaparib with ctDNA

A study at the University of Cambridge was conducted to assess *TP53* mutant allele fraction (MAF) in circulating tumor DNA (ctDNA) from a subset of 18 patients in ARIEL2 Part 1 and will be presented in a poster session this afternoon. Plasma samples were collected from 18 patients in the ARIEL2 Part 1 study during screening, on day 1 of each cycle, and at the end of rucaparib treatment. The objective was to assess monitoring responses to rucaparib with targeted amplicon deep sequencing (TADS) of ctDNA. Seven of 9 patients with a $>50\%$ reduction of *TP53* MAF in ctDNA at cycle 2 achieved a RECIST PR; this included 5/6 patients with either a germline or somatic BRCA mutation. No patients with a $<50\%$ reduction at cycle 2 ($n=5$) achieved a RECIST response. TADS detected different types of *TP53* mutation in plasma including substitutions ($n=12$) and indels ($n=6$) across a wide spectrum of allele fractions (0.01–42.3%) with 100% concordance for *TP53* mutation status in matched tumor-plasma samples. ctDNA is a potential biomarker for monitoring responses to the PARP inhibitor rucaparib.

Final Results of RUCAPANC

The open-label phase 2 RUCAPANC study investigated the safety and efficacy of rucaparib in patients with advanced pancreatic cancer and a known deleterious germline or somatic BRCA mutation and final results were presented in a poster session on June 4. A total of 19 patients were enrolled and received one or more doses of rucaparib, with a median of three

cycles (range 1-18) of treatment started. The confirmed investigator-assessed ORR based on RECIST criteria was 16%, in which two partial responses (PR) and one complete response (CR) were observed. The disease control rate was 32% for all patients (6/19) and 50% for patients with one prior chemotherapy (3/6). All three patients with a confirmed response received only one prior line of therapy. Common treatment-emergent AEs included nausea (63%) and anemia (47%). These findings are expected to inform future rucaparib study designs in patients with advanced BRCA^{mut} pancreatic cancer.

About Rucaparib Clinical Development

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. Part 1 is in platinum-sensitive patients designed to identify pre-specified tumor characteristics that predict sensitivity to rucaparib using DNA sequencing to evaluate each patient's tumor and updated results are described above. Part 2, also referred to as the ARIEL2 Extension, is enrolling up to 300 patients with advanced ovarian cancer who have received at least three prior chemotherapy regimens and includes platinum-sensitive, -resistant and -refractory patients. It will evaluate clinical response in patients classified into molecularly-defined subgroups, including gBRCA-mutant, sBRCA-mutant and the BRCA-like signature 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 have 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 BRCA-like signature (including BRCA and non-BRCA), and then all patients.
- The ARIEL4 confirmatory study is expected to begin during the second half of 2016, and will compare treatment with rucaparib vs chemotherapy in relapsed ovarian cancer patients with BRCA mutations. The primary endpoint of the study is PFS.
- In addition to the ARIEL program in ovarian cancer, the Company is exploring rucaparib in other solid tumor types with significant BRCA and BRCA-like populations, including a pivotal prostate cancer study expected to initiate during the second half of 2016.
- Multiple combination studies are planned to initiate in the second half of 2016, including with inhibitors of PD-L1.
- For more information, please visit www.arielstudy.com.

Subgroup analysis of later-line BRCA-mutant patients from ARIEL2 Parts 1 and 2 and Study 10 will form the basis of rucaparib's rolling New Drug Application (NDA) to the U.S. FDA. The NDA submission will include platinum-sensitive, -resistant and -refractory patients from ARIEL2 Part 2, in addition to the platinum-sensitive patients from ARIEL2 Part 1 and Study 10.

The NDA submission is expected to complete by the end of Q2 2016, and a European Marketing Authorization Application (MAA) to the European Medicines Agency is planned for Q4 2016. Rucaparib was granted Breakthrough Therapy designation from the U.S. Food and Drug Administration in April 2015.

Presentation Details

The poster presentation, titled "*RUCAPANC: An open-label, phase 2 trial of the PARP inhibitor rucaparib in patients (pts) with pancreatic cancer (PC) and a known deleterious germline or somatic BRCA mutation*" was presented Saturday by Robert Vonderheide, MD, D. Phil., University of Pennsylvania, Philadelphia, PA during the Poster Session titled "Gastrointestinal (Noncolorectal) Cancer", from 8:00am-11:30am CDT (Abstract 4110; Poster Board #102).

The poster presentation, titled “*Refinement of prespecified cutoff for genomic loss of heterozygosity (LOH) in ARIEL2 part 1: A phase II study of rucaparib in patients (pts) with high grade ovarian carcinoma (HGOC)*” is being presented today by Robert L. Coleman, MD, The University of Texas MD Anderson Cancer Center, Houston, TX during the Poster Session titled “Gynecologic Cancers” from 1:00pm-4:30pm CDT (Abstract 5540 Poster Board #363).

The poster presentation, titled “*Feasibility of monitoring response to the PARP inhibitor rucaparib with targeted deep sequencing of circulating tumor DNA (ctDNA) in women with high grade serous carcinoma on the ARIEL2 trial*” is being presented today by Mitch Raponi, D. Phil, Biochemistry and Molecular Genetics, Clovis Oncology on behalf of the author, Anna Piskorz, PhD, Cancer Research UK Cambridge Institute, University of Cambridge during the Poster Session titled “Gynecologic Cancers” from 1:00pm-4:30pm CDT (Abstract 5549 Poster Board #372).

The poster presentations will be available online at <http://clovisoncology.com/products-companion-diagnostics/scientific-presentations/> as of the time of their scheduled presentation at the meeting.

About Rucaparib

Rucaparib is an oral, potent small molecule inhibitor of PARP1, PARP2 and PARP3 being developed for the treatment of ovarian cancer, specifically in patients with tumors with BRCA mutations and other DNA repair deficiencies beyond BRCA, including those with high genomic loss of heterozygosity (LOH) commonly referred to as “BRCA-like.” Clovis is also exploring rucaparib in other solid tumor types with significant BRCA and BRCA-like populations, including prostate, breast and gastroesophageal cancers. Rucaparib was granted Breakthrough Therapy designation by the U.S. FDA in April 2015. Clovis holds worldwide rights for rucaparib.

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.

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.

View source version on businesswire.com: <http://www.businesswire.com/news/home/20160606005594/en/>

Source: Clovis Oncology, Inc.

Clovis Oncology, Inc.

Anna Sussman, 303.625.5022

asussman@clovisoncology.com

and

Breanna Burkart, 303.625.5023
bburkart@clovisoncology.com