Data from Ongoing Phase 2 Studies of Rucaparib in Ovarian Cancer Demonstrate Safety and Clinical Activity, Validate Differentiated Strategy

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- Encouraging disease control rate of 93 percent, RECIST response rate of 71 percent observed in Phase 2 study of ovarian cancer patients with BRCA mutations; no drug discontinuations due to treatment-related adverse events
- 56 percent of non-mutant BRCA patients in the ARIEL2 study to date exhibit HRD and may benefit from rucaparib treatment
- Initial ARIEL2 clinical efficacy data to be presented in oral plenary session at 26th EORTC-NCI-AACR (ENA) Symposium on Molecular Targets and Cancer Therapeutics meeting in November

BOULDER, Colo.--(BUSINESS WIRE)--Sep. 28, 2014-- Clovis Oncology (NASDAQ:CLVS) today announced preliminary Phase 2 results from the ARIEL2 (Assessment of Rucaparib In Ovarian Cancer Trial) study and updated results from the ongoing Phase 1/2 monotherapy study of rucaparib. Rucaparib is the Company’s investigational oral, potent, small molecule inhibitor of PARP1 and PARP2 being developed for the treatment of platinum-sensitive ovarian cancer in patients with homologous recombination deficient (HRD) tumors, defined as those with BRCA mutations and other DNA repair deficiencies. These data are being presented today at the European Society of Medical Oncology (ESMO) 2014 Congress in Madrid.

"New treatments are desperately needed for women with ovarian cancer. The data presented for rucaparib in ovarian cancer demonstrate compelling clinical activity and tolerability in patients with BRCA mutations," said Professor Iain McNeish, Professor of Gynaecological Oncology, Institute of Cancer Sciences, University of Glasgow and one of the two principal investigators of the ARIEL2 study. "Even more encouraging are the preliminary data from ARIEL2, which show that tumor HRD analysis can identify a broader range of patients who may benefit from rucaparib therapy. HRD analysis may be a more robust and precise method to select patients for PARP inhibitor therapy than platinum sensitivity alone. I am delighted to be involved in this study, which may ultimately lead to an additional treatment option, not only for germline BRCA mutation carriers but also for large numbers of ovarian cancer patients, for whom few options exist today."

"We are enthusiastic about the possibility of identifying ovarian cancer patients beyond those with germline BRCA mutations who may benefit from rucaparib therapy with the ARIEL2 study," said Patrick J. Mahaffy, President and CEO of Clovis Oncology. "And we look forward to sharing the first clinical outcome data at the ENA Symposium in November, which were accepted for an oral plenary session. We believe we are the only company seeking to prospectively demonstrate a PARP inhibitor’s activity in a molecularly-selected ovarian cancer population beyond germline BRCA mutations, and this may have the potential to meaningfully differentiate rucaparib.

Both posters are being presented today at ESMO in the Gynaecological Cancers poster session from 13:00-14:00 in the Salamanca meeting room:

- Phase 1/2 Study of Oral Rucaparib: Updated Phase 1 and Preliminary Phase 2 Results (882PD)
- Preliminary Results of ARIEL2, A Phase 2 Open-label Study to Identify Ovarian Cancer Patients Likely to Respond to Rucaparib (883PD)

Phase 1/2 Study of Oral Rucaparib

Data are being presented on 20 patients currently enrolled in the Phase 2 portion of the Phase 1/2 rucaparib monotherapy study at the recommended Phase 2 dose of 600mg twice daily (BID). Study objectives for the Phase 2 portion of the study include assessing overall response rate, safety and tolerability, and duration of response in women with germline BRCA-associated ovarian cancer. Patients in the Phase 2 study to date received a median of two prior platinum-based
Phase 2 results to be presented at the ESMO Congress indicate early, robust and durable responses observed in platinum-sensitive, relapsed ovarian cancer patients with a germline BRCA mutation. Objective responses include both RECIST and CA-125 responses. Disease control rate (DCR) is defined as complete response, partial response or stable disease greater than 12 weeks.

The DCR for the evaluable patients treated with rucaparib was 93 percent (14/15). Eighty-two percent of patients (14/17) achieved a RECIST and/or CA-125 response, of whom 71 percent (12/17) achieved a RECIST Partial Response (PR). Target lesion regressions were observed in 16 of 17 patients, and CA-125 decreases were observed in 12 of 14 patients with elevated CA-125 levels at baseline.

All patients who have achieved a PR are ongoing, with the longest duration of therapy currently measured at 198 days. Rapid responses were observed; eight of the 12 patients who achieved a PR did so by Week 6 of therapy.

Data presented at ESMO demonstrate that rucaparib is well-tolerated with a manageable safety profile. At the recommended Phase 2 dose of 600mg BID, the most common treatment-related adverse events (AEs) reported in ≥15 percent of all patients included: nausea (45 percent), asthenia (35 percent), vomiting (35 percent), increased ALT/AST (35 percent), anemia (30 percent), dysgeusia (25 percent), fatigue (25 percent), diarrhea (20 percent), abdominal pain (20 percent), and headache (15 percent). These events were mostly Grade 1/2, and none of the Phase 2 patients has discontinued rucaparib due to a treatment-related AE.

**Preliminary Results of ARIEL2**

These data are the first to be presented from the ARIEL2 program. The ESMO poster session describes the application of the HRD algorithm to the tumor genetic data from the patients enrolled in the study. The assay being used in ARIEL2 detects tumor BRCA1/2 mutations (either germline or somatic) and genomic loss of heterozygosity (LOH), and has identified patients belonging to each of the three potentially rucaparib-sensitive populations: BRCA mutant with high genomic LOH; BRCA mutant with low genomic LOH; and BRCA wild-type with high genomic LOH. Data suggest that a test that incorporates tumor BRCA1/2 mutation status with genomic LOH analysis may better predict ovarian cancer patients likely to respond to rucaparib therapy. The HRD algorithm may be optimized using data from this study and will then be prospectively applied to patients in the primary efficacy analysis of the pivotal ARIEL3 study.

Initial clinical outcome data from the ARIEL2 study will be presented in an oral plenary session at the 26th EORTC-NCI-AACR (ENA) Symposium on Molecular Targets and Cancer Therapeutics in Barcelona in November.

**ARIEL Pivotal Study Program**

The ARIEL (Assessment of Rucaparib in Ovarian Cancer Trial) program is a novel, integrated translational-clinical program designed to refine the definition of patients with homologous recombination deficiency (HRD), which includes those with BRCA mutations (genes that are linked to breast and ovarian cancers) and other DNA repair deficiencies, who may benefit from rucaparib. Approximately 50 percent of ovarian cancers are deficient in homologous recombination as a result of BRCA and other mutations.

The global ARIEL2 study is currently enrolling 180 ovarian cancer patients with relapsed, platinum-sensitive disease. The single-arm, open-label Phase 2 study is designed to identify molecular features that predict sensitivity to rucaparib using DNA sequencing to evaluate each patientâ€™s tumor. In this study, rucaparib efficacy is assessed and correlated with the genotype and phenotype of each patientâ€™s tumor, and these data will inform the final definition of HRD for the ARIEL3 pivotal study.

The global ARIEL3 pivotal study is currently enrolling a total of 540 patients, in a randomized, double-blind Phase 3 study that compares the effects of rucaparib versus placebo. The study will evaluate whether maintenance rucaparib...
treatment in platinum-sensitive, high-grade ovarian cancer patients can extend the period of time for which a response to a prior chemotherapy is maintained. Efficacy is assessed in a pre-specified step-down manner, first in tumor BRCA-mutant patients, then in a larger group of patients with evidence of HRD, with or without BRCA mutations, and finally in all randomized patients.

About Rucaparib

Rucaparib is an oral, potent inhibitor of PARP1 and PARP2 being developed for the treatment of platinum-sensitive ovarian cancer in patients with BRCA mutations (genes that are linked to breast and ovarian cancers) and other DNA repair deficiencies. Rucaparib is also being explored in patients with BRCA-mutant pancreatic cancer in the RUCAPANC study.

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.

Source: Clovis Oncology

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