Clovis’ “BRCAness” DNA signature predicts which patients respond to rucaparib therapy

- Overall response rate (ORR) of 70% in BRCA-mutant patients; responses observed in patients with both germline and somatic mutations
- ORR of 40% in patients with BRCAness signature (all BRCA wild-type)
- ORR of only 8% in patients without BRCAness signature (all BRCA wild-type)
- Approximately 67% of patients treated to date exhibit BRCAness DNA signature or BRCA-mutant status
- Rucaparib is well-tolerated; no drug discontinuations due to treatment-related adverse events
- Molecular tumor analysis may identify a broad selection of ovarian cancer patients who could benefit from rucaparib therapy – including both BRCA-mutant and BRCAness patients

BARCELONA, Spain--(BUSINESS WIRE)--Nov. 19, 2014-- Clovis Oncology (NASDAQ:CLVS) today announced initial Phase 2 results from the ARIEL2 (Assessment of Rucaparib In Ovarian Cancer Trial) study. 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, specifically in patients with tumors with BRCA mutations and other DNA repair deficiencies beyond BRCA, commonly referred to as “BRCA-like” or “BRCAness.” These data are being presented today in an oral presentation (Abstract No. 215) by Dr. Elizabeth Swisher from the University of Washington School of Medicine at the 26th EORTC-NCI-AACR (ENA) Symposium on Molecular Targets and Cancer Therapeutics in Barcelona, Spain.

“These preliminary data from the ARIEL2 study of rucaparib in ovarian cancer demonstrate compelling clinical activity and tolerability in patients with tumor 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 exciting, given the novelty of the observation, are the preliminary data from ARIEL2, which suggest that identification of a tumor BRCA-like signature can identify a broader range of patients who may benefit from rucaparib therapy. Such molecular analysis may provide 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 for women with relapsed ovarian cancer, not only those with germline BRCA mutations but also the much larger numbers of patients, with somatic BRCA mutations or BRCA-like signatures for whom few options exist today, and for whom new treatments are very much needed.”

“These data confirm our commitment to select patients beyond BRCA-mutant who also have the potential to benefit from rucaparib therapy based on their BRCAness signature,” said Patrick J. Mahaffy, President and CEO of Clovis Oncology. “The clinical community has spoken about BRCAness for a long time, but we are the only company who have prospectively developed and applied a BRCAness signature in a clinical setting. These data also demonstrate that platinum sensitivity alone does not predict which patients will benefit from rucaparib or any PARP inhibitor. These data suggest that clinicians and their patients will benefit from applying a molecular analysis to determine the best treatment options in women with ovarian cancer and validates our decision to prospectively apply this analysis in our ARIEL3 trial.”

Data from 121 patients with platinum-sensitive ovarian cancer who are currently enrolled in the ARIEL2 study are being presented today. Study objectives include determining rucaparib sensitivity in prospectively-defined molecular subgroups, through the assessment of progression-free survival (PFS) in patients with tumors that have BRCA mutations, BRCA-like mutations (DNA repair deficiencies but normal BRCA genes), and biomarker negative; as well as ORR, safety and pharmacokinetics. Patients in the study to date received a median of one prior treatment regimen and one prior platinum-based therapy regimen. Patients were treated with the recommended Phase 2 dose (RP2D) of 600mg twice daily (BID). Few progression events have occurred to date, and so objective response rate data are reported for this interim
Preliminary Results of ARIEL2

These are the first clinical outcome data to be presented from the ARIEL2 program.

Target lesion reduction was observed in 77 percent of patients with screening biopsy results (n=61) and a first staging scan; the most robust clinical activity was observed in patients with tumor BRCA mutations. Seventy percent (16/23) of BRCA-mutant patients achieved a RECIST and/or CA-125 response, and 61% (14/23) achieved a RECIST response. Responses were observed in both germline and somatic BRCA-mutant tumors.

In addition, in those patients with normal BRCA genes, rucaparib activity was different between those with the prospectively-defined BRCA-like signature versus biomarker negative patients. Forty percent (10/25) of patients with normal BRCA and the BRCA-like signature achieved a RECIST and/or CA-125 response, and 32% (8/25) achieved a RECIST response. In biomarker negative patients, few responses were observed: Eight percent (1/13) of patients achieved a RECIST and/or CA-125 response.

Data presented at ENA demonstrate that rucaparib is well-tolerated with a manageable safety profile. At the RP2D of 600mg BID, the most common treatment-related adverse events (AEs) reported in ≥15 percent of all patients included nausea, fatigue, transient ALT/AST elevations, dysgeusia, decreased appetite, anemia/low hemoglobin, constipation, and vomiting. These events were mostly Grade 1/2; no patient has discontinued rucaparib due to a treatment-related AE.

ARIEL Pivotal Study Program

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

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 prospectively test molecular features that predict sensitivity to rucaparib using DNA sequencing to evaluate each patient’s tumor. In this study, rucaparib efficacy is assessed and correlated with the genotype of each patient’s tumor, and these data will inform the final definition of BRCA-ness 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 the BRCA-ness signature, with or without BRCA mutations, and finally in all randomized patients.

Presentation Details

The presentation, titled “Updated clinical and preliminary correlative results of ARIEL2, a Phase 2 study to identify ovarian cancer patients likely to respond to rucaparib” is being presented on Thursday, November 20, during Plenary Session 6, from 13:30 to 15:30 CET. The presentation will be made available online at that time at www.clovisoncology.com.

Event Webcast Details

Clovis will host an investor/analyst webcast conference call following the rociletinib data presentation at ENA today from 14:00 to 15:00 CET. Dial-in information for the event: U.S. 877.280.4960, International 857.244.7317, passcode 78436017. The event will be simultaneously webcast on the Company’s web site at www.clovisoncology.com, and
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

Clovis Oncology
Anna Sussman, 303-907-5358
asussman@clovisoncology.com
or
Breanna Burkart, 303-907-5162
bburkart@clovisoncology.com