Clovis Oncology’s Phase 2 Studies of Rucaparib in Ovarian Cancer Demonstrate Highly Compelling Clinical Activity, in Both BRCA-mutant and BRCA-like Patients, Together Comprising Approximately 60 Percent of Patients

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- Data from ARIEL2 in platinum-sensitive BRCA-mutant patients demonstrated an overall response rate (ORR) of 82%, a disease control rate (DCR) of 94% and a median progression-free survival (PFS) of 9.4 months
  - Complete responses (CRs) observed in 10% of patients
- Data from ARIEL2 in patients with BRCA-like signature demonstrated ORR of 45% and DCR of 73% in and a median PFS of 7.1 months
- In ARIEL2, approximately 60% of patients treated to date exhibit BRCA-mutant status or BRCA-like DNA signature
- Data from Study 10, a Phase 2 study of heavily pretreated germline BRCA-mutant ovarian cancer patients, demonstrated an ORR of 74%
  - 77% ORR observed in patients treated with at least three prior lines of chemotherapy; median duration of response in these patients is currently greater than 11 months
- 74% ORR, median duration of response greater than 11 months observed in 23 BRCA-mutant patients treated with at least three prior lines of chemotherapy from ARIEL2 and Study 10 combined
  - CRs observed in 13% of patients in this group
- Enrollment in ARIEL2 Part 2 single-arm study in heavily pre-treated patients (≥3 prior lines of chemotherapy) continues with planned NDA submission in 2016
- Data presented at ASCO demonstrate that rucaparib is well-tolerated with a manageable safety profile. The most common grade 3/4 treatment-related adverse events (AEs) were anemia/decreased hemoglobin, fatigue, nausea and transient ALT/AST elevations
- Only PARP inhibitor to be granted Breakthrough Therapy designation by the FDA

CHICAGO--(BUSINESS WIRE)--May 30, 2015-- Clovis Oncology (NASDAQ:CLVS) today announced updated Phase 2 results from two ongoing clinical studies with rucaparib: ARIEL2 and Study 10. Rucaparib is the Company’s investigational oral, potent, small molecule inhibitor of PARP1 and PARP2 being developed for the treatment of advanced ovarian cancer, specifically in patients with BRCA mutations and other DNA repair deficiencies beyond BRCA, commonly referred to as “BRCA-like.” Updated data from the ARIEL2 study in 204 patients with advanced ovarian cancer are being presented Monday in an oral presentation by Professor Iain McNeish at the 2015 American Society of Clinical Oncology (ASCO) annual meeting in Chicago. Additional data from Study 10, a Phase 2 study of 40 platinum sensitive ovarian cancer patients with germline BRCA mutations were also presented in a poster session today.

“To see the encouraging progression-free survival rates mirror the impressive response rates in both the BRCA-mutant and BRCA-like populations represents a very exciting step forward in the treatment of advanced ovarian cancer,” 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 two principal investigators of the ARIEL3 study. “The opportunity to provide a very compelling targeted therapy in an ovarian cancer population in addition to those who carry germline or somatic BRCA mutation represents a potentially practice changing advance in the treatment of this terrible disease.”

“With these data presented at ASCO, we believe rucaparib has clearly emerged as a unique and best-in-class PARP inhibitor,” said Patrick J. Mahaffy, President and CEO of Clovis Oncology. “In addition, with our now clinically proven BRCA-like clinical assay, we have validated our commitment to develop rucaparib not only for the 25 percent of women with germline and somatic BRCA mutations, but for the additional approximately 35 percent of women with the prospectively identified BRCA-like signature. With the ARIEL2 extension enrolling rapidly, we look forward to submitting our NDA for rucaparib for the treatment of advanced ovarian cancer next year.”
Study objectives of the ARIEL2 trial include determining rucaparib activity in prospectively defined molecular subgroups through the assessment of PFS in patients with tumors that have germline and somatic BRCA mutations, those with a BRCA-like signature (patients whose tumors have DNA repair deficiencies that behave like BRCA mutations, but with normal BRCA genes), and patients whose tumors are biomarker negative. ORR, safety and pharmacokinetics are also analyzed. At the time of analysis, patients in the study had 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).

Updated Results of ARIEL2

Data from the ARIEL2 study of 204 patients show compelling clinical activity, including the first presentation of PFS for each subgroup followed in the study. A median PFS of 9.4 months in BRCA-mutant patients and a median of 7.1 months in patients with a BRCA-like signature were observed, compared to biomarker negative patients, in which median PFS was 3.7 months.

The most robust clinical responses were observed in patients with tumor BRCA mutations: 82 percent (32/39) of BRCA-mutant patients achieved a RECIST and/or CA-125 response and 69 percent (27/39) achieved a RECIST response. Responses were observed in both germline and somatic BRCA-mutant tumors. Four CRs were observed in the somatic BRCA-mutant group. A 94 percent DCR (CR, PR or SD > 24 weeks) was also observed. Responses were durable with 18 of 27 responders still ongoing at time of analysis. These patients had received a median of two prior therapies with a range of one to five prior therapies.

Importantly, results from ARIEL2 demonstrate that tumor HRD analysis can identify a broader range of patients who may benefit from rucaparib therapy. Forty-five percent (33/74) of patients with the pre-specified BRCA-like signature achieved a RECIST and/or CA-125 response, and 30 percent (22/74) achieved a RECIST response. Responses were durable with 17 of 22 responders still ongoing at time of analysis. A 73 percent DCR was also observed.

As expected, activity was limited in biomarker negative patients, 21 percent (13/62) of patients achieved a RECIST and/or CA-125 response and 13 percent (8/62) achieved a RECIST response. A 39 percent DCR was also observed.

Data presented demonstrate that rucaparib is well tolerated with a manageable safety profile. The most common treatment-related AEs reported in ≥15 percent of all patients included nausea, asthenia/fatigue and transient ALT/AST elevations. These events were mostly Grade 1/2. The most common Grade 3/4 treatment-related AEs were anemia/decreased hemoglobin (16%) and transient ALT/AST elevations (11%).

Study 10 Data in Platinum-Sensitive Germline BRCA-mutant Patients

Data from a second Phase 2 study of rucaparib in ovarian cancer were presented today in a poster presentation and poster discussion session.

The Phase 2 portion of Study 10, the initial dose finding study of rucaparib, was expanded to enroll 41 patients with relapsed, high-grade platinum-sensitive ovarian cancer associated with a deleterious germline BRCA mutation. These patients had all received 2-4 prior treatment regimens, and had a progression-free interval of six months or greater after their most recent platinum regimen. Patients were treated with the recommended Phase 2 dose of 600mg BID.

Consistent with the ARIEL2 data in BRCA-mutant patients, a robust ORR was observed in this patient population. In 35 patients evaluable for activity, 74 percent (26/35) of patients achieved a RECIST and/or CA-125 response, and 66 percent (23/35) achieved a RECIST response; a 77 percent disease control rate (DCR) was observed. Robust activity was observed regardless of type of BRCA mutation, length of progression-free interval between platinum therapies and number of prior treatments: response rates (RECIST and CA-125) ranged from 72 to 80 percent in those categories, or 61 to 78 percent for RECIST alone. Responses to rucaparib were durable: 15 of 23 responses were still ongoing at time of analysis with a median duration of response of over 11 months. Importantly, 77 percent of patients treated with at least 3
lines of chemotherapy achieved a RECIST and/or CA-125 response, and 69 percent achieved a RECIST response. This is the subject population of the ongoing ARIEL2 Extension registration study.

Rucaparib was well tolerated with a manageable safety profile; the most common AEs were fatigue/asthenia, nausea and anemia. Any Grade 3/4 AEs were successfully managed with dose modification. No patients discontinued due to treatment-related adverse events.

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, initiated in Q4 2013, has completed enrollment of approximately 200 ovarian cancer patients with relapsed, platinum-sensitive disease. 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 provisional results are described above. Part 2, referred to as the ARIEL2 Extension, is enrolling advanced ovarian cancer patients who have received at least three prior chemotherapy regimens and will evaluate clinical response in patients classified into molecularly-defined subgroups, including germline BRCA-mutant, somatic BRCA mutant and the BRCA-like signature, by a prospectively defined genomic signature.
- The Phase 2 portion of Study 10, the initial dose finding study, has been expanded to enroll an additional 40 patients with relapsed, high-grade ovarian cancer associated with a deleterious BRCA mutation (germline or somatic) and who received ≥3 prior chemotherapy regimens.
- 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.

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.

Following on the recent Breakthrough Therapy designation status of rucaparib by the FDA, data from the ARIEL2 study, if positive, are expected to form the basis of a planned new drug application (NDA) filing for treatment of advanced ovarian cancer in 2016.

Presentation Details

The oral presentation, titled, “Results of ARIEL2: A Phase 2 trial to prospectively identify ovarian cancer patients likely to respond to rucaparib using tumor genetic analysis” is being presented on Monday, June 1, during the Oral Abstract Session titled, “Gynecologic Cancers”, from 8:00 to 11:00am CDT. (Abstract 5508)

The poster presentation, titled “A Phase 2 open-label, multicenter study of single-agent rucaparib in the treatment of patients with relapsed ovarian cancer and a deleterious BRCA mutation” is being presented today during the Poster Session titled, “Gynecologic Cancers”, from 1:15 to 4:45pm CDT and in the subsequent poster discussion session from 4:45 to 6:00pm CDT. (Abstract 5513; poster board 71)

The presentations will be made available online at that time at www.clovisoncology.com.

Event Webcast Details
Clovis will host an investor/analyst event during ASCO on Sunday, May 31\textsuperscript{st} at 6:00pm CDT. The event will be simultaneously webcast on the Company’s web site at www.clovisoncology.com, and archived for future review.

**About Rucaparib**

Rucaparib is an oral, potent inhibitor of PARP1 and PARP2 being developed for the treatment of advanced ovarian cancer in patients with BRCA mutations (genes that are linked to breast and ovarian cancers) and other DNA repair deficiencies.

**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. For more information, please visit our website at www.clovisoncology.com.

*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, Inc.

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