Ongoing Phase I Monotherapy Study of Rucaparib in Patients with Solid Tumors Demonstrates Clinical Activity, Establishes Dose and Schedule

September 29, 2013 3:30 AM ET

- Objective responses seen in BRCA-mutant ovarian, breast and pancreatic cancer patients
- Disease control rate in BRCA-mutant ovarian cancer patients across all doses of 100% and 63% at 12 weeks and 24 weeks, respectively
- Rucaparib well-tolerated at recommended Phase II dose of 600 mg BID
- Consistent therapeutic drug exposures observed with BID dosing

BOULDER, Colo.--(BUSINESS WIRE)--Sep. 29, 2013-- Clovis Oncology (NASDAQ:CLVS) today announced updated results from an ongoing Phase I/II monotherapy study of rucaparib, the Company’s oral, potent, small molecule poly (ADP-ribose) polymerase (PARP) inhibitor being developed for the treatment of ovarian cancer. Data from the Phase I dose-escalation portion of this Phase I/II study are being presented today at a poster session during the European Cancer Congress 2013 in Amsterdam.

“We’ve seen significant clinical activity with one complete response in breast cancer and six partial responses in ovarian, breast and pancreatic cancers to date, and a disease control rate in patients with germline BRCA mutant ovarian (platinum-sensitive and platinum-resistant) cancer of 100% and 63% at 12 and 24 weeks, respectively. I am pleased to be participating in the Phase II and pivotal Phase III trials (ARIEL2 and ARIEL3) which aim to build on the clear activity of rucaparib in BRCA-mutant ovarian cancer and prospectively identify and test other genetic mutations associated with sensitivity to PARP inhibition in ovarian cancer. This approach has the potential to broaden applicability of PARP inhibitor treatment for ovarian cancer as well as other solid tumors and hopefully benefit many patients,” said Dr. Rebecca Kristeleit, Clinical Senior Lecturer and Consultant Medical Oncologist UCLH and UCL Cancer Institute in London.

“These data demonstrate that rucaparib is both well-tolerated and predictably absorbed, and provides meaningful clinical benefit to certain ovarian cancer patients,” said Patrick J. Mahaffy, President and CEO of Clovis Oncology. “Now that we have identified the recommended Phase II dose, we plan to commence our late-stage development program in platinum-sensitive ovarian cancer. This includes a now-open biomarker study known as ARIEL2 (the Assessment of Rucaparib in Ovarian Cancer Phase 2 Trial) which will refine the definition of patients beyond those with BRCA mutations who may benefit from rucaparib. By the end of 2013 we expect to initiate a Phase III pivotal trial known as ARIEL3 in a broad set of ovarian cancer patients with a stratified efficacy analysis in genetically-defined groups, including somatic and germline BRCA mutations as well as a population with mutations beyond BRCA, utilizing insights from the ARIEL2 study.”

Today’s poster presentation includes data from the Phase I dose escalation portion of the study, which is open to patients with any solid tumor. Study objectives were typical for a Phase I trial, including determining safety and tolerability, evaluating the pharmacokinetic profile, identifying the maximum tolerated dose (MTD) and recommended Phase II dose (RP2D) as well as the preliminary efficacy signals in various solid tumors.

Fifty-three patients have been treated with rucaparib monotherapy in this study as of September 2013, in once-daily (QD) and twice-daily (BID) dosing cohorts, up to 500 mg QD and 840 mg BID. A dose of 600 mg BID has been selected as the recommended Phase 2 dose based on maximum exposure, manageable toxicity and activity. Rucaparib is well tolerated up to 600 mg BID with minimal Grade 3 and no Grade 4 adverse events. No patients have discontinued rucaparib due to a treatment-related adverse event.

Patients have received a median of four previous anticancer regimens and 40 percent have received five or more previous therapies. Twenty-six patients (50%) have breast tumors, 19 patients (37%) have ovarian/peritoneal tumors and seven patients (13%) have other solid tumors.

Key data from the study presented at the conference include the following:

Evidence of Activity

To date, seven RECIST responses have been observed during the dose escalation phase of the study (note: measurable disease and/or elevated CA-125 was not required for study entry). In ovarian cancer patients with a germline BRCA (gBRCA) mutation, two RECIST partial responses (PRs) and one GCIC CA-125 response have been observed to date. Responses have been
observed in both platinum-sensitive and platinum-resistant disease. In breast cancer patients with a germline BRCA mutation, one RECIST complete response (CR) and three RECIST PRs have been observed. In addition, a pancreatic cancer patient with a gBRCA2 mutation who progressed rapidly on FOLFIRINOX therapy achieved a RECIST PR which is ongoing at 25 weeks.

Overall, 100% (11/11) of ovarian cancer patients with gBRCA mutations achieved disease control as defined by CR, PR, or stable disease (SD) >12 weeks and 63% (5/8) have achieved disease control as defined by CR, PR, or SD >24 weeks – the three patients who progressed by week 24 were all treated in dose cohorts of 300 mg QD or lower.

Safety and Tolerability

Safety data to date shows rucaparib to be well-tolerated, which is important for a drug intended to be used in a maintenance setting. Adverse events (AEs) were almost all low-grade and manageable. There have been no grade 4 AEs reported to date, and no discontinuations due to treatment-related adverse events. The most common adverse events attributed to rucaparib therapy include nausea (29%), vomiting (21%) and fatigue (23%). There was one dose-limiting toxicity (DLT) in a patient in the 360 mg BID cohort who reported grade 3 nausea. Six patients (11%) had a dose reduction and/or re-treatment delay, due to grade 3 thrombocytopenia (n=1), grade 3 anemia (n=1), grade 3 nausea (n=1), grade 2 neutropenia (n=2), and grade 2 abdominal pain (n=1). Myelosuppression is dose-related.

Pharmacokinetics

Oral rucaparib demonstrates attractive pharmacokinetic (PK) properties as a potential oral cancer therapeutic, including plasma drug concentrations maintained over a 24-hour period after BID dosing, which is likely important for optimal activity. Intra- and inter-patient variability was also low, which is advantageous for uniform flat dosing strategies. This tight correlation between administered dose and plasma exposure suggests that rucaparib dosing will lead to predictable results across the ovarian cancer population. Predictable PK following oral dosing may lead to low rates of over- and under-dosing, potentially minimizing adverse events associated with high unpredictable exposures, an important attribute for maintenance therapy. Greater than 85 percent of ovarian cancer patients treated with rucaparib doses of 300 mg QD or higher remain on study, with duration of benefit up to 60 weeks to date.

The poster, titled “A Phase I Dose Escalation and Pharmacokinetic Study of Continuous Oral Rucaparib in Patients with Advanced Solid Tumors”, is being presented on Sunday, September 29, 2013, 9:30am – 12:00pm CEST, in Hall 4, Poster Board: P076 at Amsterdam RAI in Amsterdam. The poster will also be available at http://www.clovisoncology.com/products-companion-diagnostics/scientific-presentations/.

About Rucaparib

Rucaparib is an oral, potent inhibitor of PARP1 and PARP2 in development for the treatment of ovarian cancer. Rucaparib is currently in two Company-sponsored Phase I clinical studies; one to determine the MTD of oral rucaparib administered on a daily basis as monotherapy; and a second trial to determine the MTD of oral rucaparib that can be combined with intravenous platinum chemotherapy for the treatment of solid tumors. Now that the optimal dose and schedule of 600 mg BID have been established in the Phase I portion of the monotherapy study, the Company intends to initiate a Phase II expansion cohort to assess efficacy in gBRCA ovarian cancer patients. In addition, the Company has initiated the ARIEL2 biomarker study in platinum-sensitive ovarian cancer patients, and expects to initiate the ARIEL3 pivotal Phase III study in platinum-sensitive ovarian cancer patients by the end of 2013.

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, and has additional offices in San Francisco, California and Cambridge, UK.

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 the initiation of future clinical trials, availability of data from ongoing clinical trials, expectations for regulatory approvals, and other matters that could affect the availability or commercial potential of our drug candidates. Clovis Oncology undertakes no obligation to update or revise any forward-looking statements. For a further description of the risks and uncertainties that could cause actual results to differ from those expressed in these forward-looking statements, as well as risks relating to the business of the company in general, see Clovis Oncology’s Annual Report on Form 10-K for the year ended December 31, 2012 and its other reports filed with the Securities and Exchange Commission.

Source: Clovis Oncology, Inc.

Clovis Oncology, Inc.
Anna Sussman, 303-625-5022
asussman@clovisoncology.com
or
Breanna Burkart, 303-625-5023
bburkart@clovisoncology.com