



NEWS RELEASE

Clovis Oncology Announces Interim Results from Rubraca® (rucaparib) Phase 2 Study in Advanced Pancreatic Cancer and Nonclinical Data in Multiple Solid Tumor Types for Rucaparib and Lucitanib Presented at AACR 2019

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- Interim data from an investigator-initiated study in first-line maintenance setting for advanced pancreatic cancer suggest that Rubraca provides disease control with no new safety signals in 19 evaluable platinum-sensitive patients with germline BRCA1, germline or somatic BRCA2, or germline PALB2 mutations
- Clovis is evaluating a potential clinical and regulatory path forward for Rubraca in pancreatic cancer
- Nonclinical studies of rucaparib and lucitanib in multiple solid tumor types and Rubraca Trials in Progress posters also presented at AACR 2019

BOULDER, Colo.--(BUSINESS WIRE)-- Clovis Oncology, Inc. (NASDAQ: CLVS) today announced multiple presentations at the 2019 American Association for Cancer Research (AACR) Annual Meeting in Atlanta, March 29 – April 3, 2019. These include today's presentation of interim results from an investigator-initiated Phase 2 trial of Rubraca® (rucaparib) in platinum-sensitive patients with advanced pancreatic cancer. Early data from the study are encouraging and suggest that first-line maintenance therapy with Rubraca following induction with platinum-based chemotherapy provides disease control with no new safety signals among patients with a pathogenic mutation in BRCA1, BRCA2 or PALB2. Between 5 to 8 percent of patients with pancreatic cancer have a pathogenic mutation in BRCA1, BRCA2 or PALB2.

"PARP inhibitors have demonstrated activity in multiple cancers that are associated with BRCA mutations," said Kim A. Reiss Binder, MD, Assistant Professor of Medicine in the Perelman School of Medicine at the University of Pennsylvania and primary investigator for the rucaparib study. "Given the seemingly intractable challenge presented by pancreatic cancer, we are very pleased that early results from this study support the mounting evidence suggesting PARP inhibitors may have a beneficial role in this disease."

The University of Pennsylvania-based study is an ongoing, single-arm phase 2 trial investigating monotherapy Rubraca (600 mg twice daily) in the first-line maintenance setting. The study will enroll a total of 42 patients with advanced pancreatic cancer and a pathogenic germline or somatic BRCA1, BRCA2 or PALB2 mutation, whose cancer has not progressed following at least four months of platinum-based chemotherapy. The primary endpoint of the trial is progression-free survival (PFS) and responses are determined using RECIST v1.1.

At the interim analysis, the median PFS in 19 evaluable patients was 278 days or 9.1 months from the start of Rubraca therapy. At a median potential follow-up of 244 days, median overall survival (OS) had not been reached. According to the authors, of the 19 patients evaluated at the last data cutoff, one patient had a complete response (CR) and six more patients had partial responses (PR), including responses in patients with germline BRCA2 mutations (n=4), germline PALB2 mutations (n=2) and somatic BRCA2 mutation (n=1).

Eight of the 19 patients were on Rubraca for >6 months and two patients remained on treatment for >1 year (13 months and 15 months). The disease control rate (defined as CR + PR + stable disease) at 8 weeks follow-up was 89.5 percent.

Overall, Rubraca treatment in this study was well tolerated without dose-limiting toxicities. The toxicities considered possibly related to treatment occurring in >1 patient included nausea (grade 1 or 2; 43.4%), dysgeusia (grade 1 or 2; 34.8%), fatigue (grade 1 or 2; 26.1%), ALT increase (grade 1 or 2; 21.7%), diarrhea (grade 1 or 2; 17.4%), vomiting (grade 1 or 2; 13%), AST increase (grade 1 or 2; 13%) and anemia (grade 1 or 2; 8.6%). There were no grade \geq 3 events reported for these treatment related toxicities.

“It is becoming clear that PARP inhibitors may offer a much-needed new treatment option for the physicians and patients who are facing the challenge of pancreatic cancer,” said Patrick J. Mahaffy, President and CEO of Clovis Oncology. “Based on the encouraging early findings from this investigator-initiated study, as well as the findings from our own RUCAPAN trial of Rubraca in pancreatic cancer, we are evaluating a potential clinical and regulatory path forward for Rubraca in the treatment of pancreatic cancer and hope to have more details later in 2019. In addition, at AACR we are presenting nonclinical data that continue to expand our understanding of both rucaparib and lucitanib to enhance our development strategies.”

A poster titled “Comprehensive genomic profiling of >1000 plasma and tumor tissue samples from metastatic castration-resistant prostate cancer (mCRPC) patients gives insight into targeted treatment strategies” was presented Sunday. This study highlighted the cancer genomics of tissue and plasma samples screened for the TRITON2 study evaluating Rubraca in mCRPC. Patients with deleterious alterations in DNA-damage repair (DDR) genes were identified using both tissue and plasma-based assays, and there was a high concordance between the alterations detected with both assay types.

A poster titled “Enhancement of anti-PD-1 antitumor efficacy in syngeneic preclinical models by the angiogenesis inhibitor lucitanib” was presented Monday and shows that lucitanib combined with an anti-PD-1 agent enhances the anti-tumor activity of either single agent in multiple syngeneic animal models. The mechanism of action is thought to be through both antiangiogenic effects and immunomodulatory effects on dendritic cells and T cells. These data provide preclinical support for a planned study of lucitanib in combination with the anti-PD-1 inhibitor nivolumab in gynecologic cancers, expected to initiate in the first half of 2019.

A poster titled “Intracranial evaluation of the in vivo pharmacokinetics, brain distribution, and efficacy of rucaparib in BRCA-mutant, triple-negative breast cancer” will be presented later today. These data describe in vitro and in vivo pharmacokinetic studies which suggest limited brain penetration of multiple PARP inhibitors in mice with an intact blood-brain barrier. However, antitumor activity was observed with Rubraca in a BRCA1-mutant intracranial triple-negative breast cancer animal model. The poster also includes a case report of a patient with breast cancer associated with a germline BRCA2 mutation and CNS involvement who had complete resolution of neurological symptoms following Rubraca treatment. The data presented in the poster provide insights into the complex pharmacokinetic and biological parameters associated with CNS activity of PARP inhibitors.

Lastly, two Trials in Progress posters describing the trial designs of the Clovis-sponsored ATHENA and ATLAS studies are also being presented today. ATHENA is a Phase 3 study of Rubraca and nivolumab following front-line platinum-based chemotherapy in ovarian cancer. ATLAS is a Phase 2 study of Rubraca in patients with locally advanced or metastatic urothelial carcinoma. Both studies are currently enrolling patients.

Each of the Clovis-sponsored posters will be available online at <http://clovisoncology.com/pipeline/scientific-presentations/> as of the time they are presented at the meeting.

About Pancreatic Cancer

Pancreatic cancer is the third leading cause of cancer death in the United States (U.S.) though it is a relatively rare cancer as the eleventh most common cancer. In 2019 in the U.S., an estimated 56,770 new cases will be diagnosed and 45,750 deaths due to the disease will occur. Approximately 9% of pancreatic cancers harbor a germline or somatic BRCA1 or BRCA2 (BRCA1/2) mutation and the majority of patients are diagnosed with unresectable, locally advanced or metastatic disease. Of the patients with resectable disease, approximately 80% will relapse following surgery. Currently, for all patients diagnosed with pancreatic cancer the 5-year survival rate is 8.5%.

About Rubraca (rucaparib)

Rucaparib is an oral, small molecule inhibitor of PARP1, PARP2 and PARP3 being developed in multiple tumor types, including ovarian, metastatic castration-resistant prostate, and bladder cancers, as monotherapy, and in

combination with other anti-cancer agents. Exploratory studies in other tumor types are also underway.

Rubraca U.S. FDA Approved Indications

Rubraca is indicated as monotherapy for the maintenance treatment of adult patients with recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in a complete or partial response to platinum-based chemotherapy.

Rubraca is indicated as monotherapy for the treatment of adult patients with deleterious BRCA mutations (germline and/or somatic) associated epithelial ovarian, fallopian tube, or primary peritoneal cancer who have been treated with two or more chemotherapies and selected for therapy based on an FDA-approved companion diagnostic for Rubraca.

Select Important Safety Information

Myelodysplastic Syndrome (MDS)/Acute Myeloid Leukemia (AML) occur uncommonly in patients treated with Rubraca and are potentially fatal adverse reactions. In approximately 1,100 treated patients, MDS/AML occurred in 12 patients (1.1%), including those in long-term follow-up. Of these, five occurred during treatment or during the 28-day safety follow-up (0.5%). The duration of Rubraca treatment prior to the diagnosis of MDS/AML ranged from 1 month to approximately 28 months. The cases were typical of secondary MDS/cancer therapy-related AML; in all cases, patients had received previous platinum-containing regimens and/or other DNA-damaging agents. Do not start Rubraca until patients have recovered from hematological toxicity caused by previous chemotherapy (\leq Grade 1).

Monitor complete blood counts for cytopenia at baseline and monthly thereafter for clinically significant changes during treatment. For prolonged hematological toxicities (> 4 weeks), interrupt Rubraca or reduce dose (see Dosage and Administration [2.2] in full Prescribing Information) and monitor blood counts weekly until recovery. If the levels have not recovered to Grade 1 or less after 4 weeks, or if MDS/AML is suspected, refer the patient to a hematologist for further investigations, including bone marrow analysis and blood sample cytogenetic analysis. If MDS/AML is confirmed, discontinue Rubraca.

Based on its mechanism of action and findings from animal studies, Rubraca can cause fetal harm when administered to a pregnant woman. Apprise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment and for 6 months following the last dose of Rubraca.

Most common adverse reactions in ARIEL3 ($\geq 20\%$; Grade 1–4) were nausea (76%), fatigue/asthenia (73%),

abdominal pain/distention (46%), rash (43%), dysgeusia (40%), anemia (39%), AST/ALT elevation (38%), constipation (37%), vomiting (37%), diarrhea (32%), thrombocytopenia (29%), nasopharyngitis/upper respiratory tract infection (29%), stomatitis (28%), decreased appetite (23%) and neutropenia (20%).

Most common laboratory abnormalities in ARIEL3 ($\geq 25\%$; Grade 1–4) were increase in creatinine (98%), decrease in hemoglobin (88%), increase in cholesterol (84%), increase in alanine aminotransferase (ALT) (73%), increase in aspartate aminotransferase (AST) (61%), decrease in platelets (44%), decrease in leukocytes (44%), decrease in neutrophils (38%), increase in alkaline phosphatase (37%) and decrease in lymphocytes (29%).

Most common adverse reactions in Study 10 and ARIEL2 ($\geq 20\%$; Grade 1–4) were nausea (77%), asthenia/fatigue (77%), vomiting (46%), anemia (44%), constipation (40%), dysgeusia (39%), decreased appetite (39%), diarrhea (34%), abdominal pain (32%), dyspnea (21%) and thrombocytopenia (21%).

Most common laboratory abnormalities in Study 10 and ARIEL2 ($\geq 35\%$; Grade 1–4) were increase in creatinine (92%), increase in alanine aminotransferase (ALT) (74%), increase in aspartate aminotransferase (AST) (73%), decrease in hemoglobin (67%), decrease in lymphocytes (45%), increase in cholesterol (40%), decrease in platelets (39%) and decrease in absolute neutrophil count (35%).

Co-administration of Rubraca can increase the systemic exposure of CYP1A2, CYP3A, CYP2C9, or CYP2C19 substrates, which may increase the risk of toxicities of these drugs. Adjust dosage of CYP1A2, CYP3A, CYP2C9, or CYP2C19 substrates, if clinically indicated. If co-administration with warfarin (a CYP2C9 substrate) cannot be avoided, consider increasing frequency of international normalized ratio (INR) monitoring. Because of the potential for serious adverse reactions in breast-fed children from Rubraca, advise lactating women not to breastfeed during treatment with Rubraca and for 2 weeks after the last dose. You may report side effects to the FDA at 1-800-FDA-1088 or www.fda.gov/medwatch. You may also report side effects to Clovis Oncology, Inc. at 1-844-258-7662.

Click here for full Prescribing Information and additional Important Safety Information.

Rubraca® ▼ (rucaparib) EU Authorized Use and Important Safety Information

Rucaparib is indicated as monotherapy for the maintenance treatment of adult patients with platinum-sensitive relapsed high-grade epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in response (complete or partial) to platinum-based chemotherapy.

Rucaparib is indicated as monotherapy treatment of adult patients with platinum sensitive, relapsed or progressive, BRCA mutated (germline and/or somatic), high-grade epithelial ovarian, fallopian tube, or primary peritoneal cancer, who have been treated with two or more prior lines of platinum-based chemotherapy, and who are unable

to tolerate further platinum-based chemotherapy.

Summary warnings and precautions: Haematological toxicity: Patients should not start Rubraca until they have recovered from haematological toxicities caused by previous chemotherapy (\leq CTCAE Grade 1). Complete blood count testing prior to starting treatment with Rubraca and monthly thereafter is advised. Rubraca should be interrupted or dose reduced and blood counts monitored weekly until recovery for the management of low blood counts. Myelodysplastic syndrome/acute myeloid leukaemia (MDS/AML): If MDS/AML is suspected, the patient should be referred to a haematologist for further investigation. If MDS/AML is confirmed, Rubraca should be discontinued. Photosensitivity: Patients should avoid spending time in direct sunlight as they may burn more easily. When outdoors, patients should wear protective clothing and sunscreen with SPF of 50 or greater. Gastrointestinal toxicities: Low grade (CTCAE Grade 1 or 2) nausea and vomiting may be managed with dose reduction or interruption. Additionally, antiemetics may be considered for treatment or prophylaxis.

Click here to access the current Summary of Product Characteristics. Healthcare professionals should report any suspected adverse reactions via their national reporting systems.

About Lucitanib

Lucitanib is an oral, potent inhibitor of the tyrosine kinase activity of vascular endothelial growth factor receptors 1 through 3 (VEGFR1-3), platelet-derived growth factor receptors alpha and beta (PDGFR α/β) and fibroblast growth factor receptors 1 through 3 (FGFR1-3).

Emerging clinical data support the combination of angiogenesis inhibitors and immunotherapy to increase effectiveness in multiple cancer indications. Angiogenic factors, such as vascular endothelial growth factor (VEGF), are frequently up-regulated in tumors and create an immunosuppressive tumor microenvironment. Use of antiangiogenic drugs reverses this immunosuppression and can augment response to immunotherapy.

Lucitanib is an unlicensed medical product.

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, with partners, diagnostic tools intended to direct a compound in development to the population that is most likely to benefit from its use. Clovis Oncology is headquartered in Boulder, Colorado; please visit www.clovisoncology.com for more information, including additional office locations in the U.S. and Europe.

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. Examples of forward-looking statements contained in this press release include, among others, statements regarding our evaluation of Rubraca and lucitanib, a candidate in development, in additional indications and tumor types and potential for clinical and regulatory paths. Such forward-looking statements involve substantial risks and uncertainties that could cause our future results, performance or achievements to differ significantly from that 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 risk that results of further trials may differ from initial or interim results, nonclinical or preclinical studies, or post-hoc analyses, as a result of many factors, including final results from a larger patient population differing from initial or interim results from a smaller patient population, and the uncertainties inherent in actions by the FDA, the EMA or other regulatory authorities regarding data required to support drug applications and whether to accept or approve drug applications that may be filed, as well as their decisions regarding drug labeling, reimbursement and pricing. 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.

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