Clovis Oncology Announces First Patient Enrolled in TIGER-1 Study

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Study to compare rociletinib (CO-1686) to standard-of-care erlotinib as treatment for patients with newly-diagnosed EGFR-mutant advanced non-small cell lung cancer (NSCLC)

BOULDER, Colo.--(BUSINESS WIRE)--Nov. 12, 2014-- Clovis Oncology, Inc. (NASDAQ: CLVS) announced today that the Phase 2 portion of the seamless Phase 2/3 TIGER-1 (Third-Generation Inhibitor of Mutant EGFR in Lung Cancer) study has commenced with the dosing of the first patient at a U.S. study site. Rociletinib is the Company’s novel, oral, targeted covalent (irreversible) mutant-selective inhibitor of the epidermal growth factor receptor (EGFR) for the treatment of non-small cell lung cancer (NSCLC) in patients with initial activating EGFR mutations as well as the primary resistance mutation T790M.

“I am pleased to lead the US trial of first-line rociletinib in patients with EGFR-mutant NSCLC,” said Ross Camidge, MD, PhD, Associate Professor, Division of Medical Oncology, University of Colorado School of Medicine and the lead investigator for the TIGER-1 study in the United States. “The rociletinib clinical data observed to date in the second-line EGFR-mutant population after failure of drugs like erlotinib have been highly encouraging and consistent, really making the case to try this drug in these patients from the outset. The absence of side effects associated with wild-type EGFR inhibition from this drug is also likely to be welcomed by patients.”

“It is exciting that less than five years after the initial TKI was confirmed as standard first-line treatment for EGFR-mutant NSCLC, we are ready to begin the first randomized study proving the role of a third-generation EGFR inhibitor in this population,” said Tony Mok, Professor of Clinical Oncology, the Chinese University of Hong Kong, and the lead investigator for the TIGER-1 study in Asia. “Rociletinib is a very promising compound which targets both the activating mutations and the resistant exon 20 T790M mutation. It is our objective to prove a higher efficacy with rociletinib in the TIGER-1 study. With the high incidence of EGFR mutations in this region, I trust TIGER-1 will roar in Asia.”

“Patients with EGFR-mutant lung cancer are hungry for a new treatment option that can extend progression-free survival beyond what is seen with the first-generation EGFR inhibitors available today, particularly an option without the rash that make current treatments difficult for many patients,” said Bonnie J. Addario, founder of The Bonnie J. Addario Lung Cancer Foundation, one of the largest philanthropies (patient-founded, patient-focused, and patient-driven) devoted exclusively to eradicating Lung Cancer through research, early detection, education, and treatment. “The evident activity and clear lack of rash and other side effects associated with wild-type EGFR inhibition makes us very enthusiastic about the potential for this drug and this study. I believe the development of targeted therapies like rociletinib represents one of the most important scientific advances of this decade.”

In pre-clinical testing, rociletinib demonstrated significant reductions in tumor volume in subcutaneous xenograft and genetically-engineered mouse models with each of the two activating mutations (exon 19 deletion, L858R mutation), collectively observed in approximately 85 percent of EGFR-mutant NSCLC patients. Consistent with rociletinib sparing wild-type EGFR, there was no reduction in body weight in the animals treated with rociletinib whereas body weight loss was observed in the animals treated with erlotinib or afatinib.

In approximately 60 percent of patients with EGFR-mutant NSCLC, acquired resistance to current EGFR TKIs is driven by a secondary T790M mutation in EGFR. In a front-line PC-9 (EGFRDel19) model rociletinib and erlotinib were compared over time to determine when resistance emerged. Resistant tumors emerged around day 30 in erlotinib-treated mice whereas no tumor regrowth was observed in mice treated up to 86 days with rociletinib.

Please click here for a link to the rociletinib preclinical data described above.
The TIGER-1 study is the second of three registration studies in the program expected to initiate during 2014. The TIGER-1 study is a randomized Phase 2/3 registration study of rociletinib vs. erlotinib in newly-diagnosed EGFR-mutant patients. The Phase 2 portion of the study will enroll 200 patients. Upon completion of enrollment of the Phase 2 portion of the study, the Phase 3 portion of the study will initiate. The Phase 3 portion is a blinded study and the sizing will be determined in part by the initial data from the Phase 2 portion of the study. Study sites are currently enrolling in the U.S. and will enroll soon in Europe, Australia and Asia. For more information about the study, please visit www.tigertrials.com.

In addition to TIGER-1, Clovis is currently enrolling several studies in EGFR-mutant NSCLC:

- The TIGER-2 study is currently enrolling 125 patients with EGFR-mutant NSCLC with a centrally-confirmed T790M mutation directly after progression on their first and only TKI therapy. Patients receive rociletinib at the recommended Phase 2 dose (RP2D) of 625mg BID. The primary study endpoint is overall response rate; secondary endpoints include duration of response, progression-free survival, overall survival, and safety.
- Two TIGER-X Phase 2 expansion cohorts of its Phase 1/2 study in EGFR-mutant patients with the T790M mutation are currently enrolling; the first includes approximately 150 to 200 T790M positive patients directly after progression on their first and only TKI therapy, comparable to the population in its TIGER-2 registration study. The second cohort includes approximately 150 to 200 later-line T790M positive patients after progression on their second or later TKI therapy or subsequent chemotherapy. Both cohorts are exploring doses of 500mg, 625mg and 750mg BID.
- A Phase 1 study of rociletinib is underway in Japan.

Data from the TIGER-X expansion cohorts, combined with data from TIGER-2, are expected to serve as the basis of U.S. and E.U. regulatory submissions for rociletinib in mid-2015.

The TIGER-3 study, a randomized, comparative study of rociletinib versus chemotherapy in T790M-positive and T790M-negative patients with EGFR-mutant NSCLC and acquired TKI resistance, is expected to initiate in the next few months.

About Rociletinib

Rociletinib is an oral, potent, mutant-selective inhibitor of epidermal growth factor receptor (EGFR) under investigation for the treatment of EGFR-mutated non-small cell lung cancer (NSCLC). Rociletinib targets the activating mutations to EGFR (L858R and Del19), while also inhibiting the primary resistance mutation, T790M, which develops in 60 percent of patients treated with first- and second-generation EGFR inhibitors.

As reported at ASCO earlier this year, rociletinib has demonstrated compelling efficacy in a heavily pre-treated, Western population of patients with acquired resistance to currently available EGFR inhibitors. Rociletinib is the only EGFR-directed therapy that has been shown to spare wild-type EGFR in clinical studies. Inhibition of wild-type EGFR is associated with cutaneous (and other) toxicities such as acneiform rash, stomatitis and paronychia, all of which may significantly impact patients’ quality of life and result in treatment discontinuation and patient distress. The Company believes this aspect of rociletinib’s clinical profile represents a significant point of differentiation from approved EGFR inhibitors and those currently in clinical development. In May of 2014, the U.S. FDA granted Breakthrough Therapy designation for rociletinib as treatment for mutant NSCLC in patients with the T790M mutation after progression on EGFR-directed therapy.

About EGFR and Lung Cancer

Lung cancer is the most common cancer worldwide with 1.7 million new cases annually, with NSCLC accounting for almost 85 percent of all lung cancers. NSCLC progresses rapidly with a five-year survival rate in advanced NSCLC patients of less than five percent. EGFR activating mutations occur in approximately 10 to 15 percent of NSCLC cases in Caucasian patients and approximately 30 to 35 percent in Asian patients. These patients experience significant tumor
response currently approved EGFR inhibitors which are first-generation EGFR inhibitors. However, most patients ultimately progress on these therapies, with approximately 60 percent of patients developing acquired resistance from a second, or “gatekeeper” mutation, T790M.

**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.

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