Clovis Oncology’s Rociletinib (CO-1686) Phase 2 Study Results Demonstrate Consistent and Promising Clinical Activity and Disease Control in Very Advanced Patients with EGFR-Mutant Non-Small Cell Lung Cancer (NSCLC)

May 31, 2015 9:00 AM ET

- 60% overall response rate (ORR) and 90% disease control rate (DCR) in heavily pretreated centrally confirmed tissue T790M-positive patients
- Median progression free survival (PFS) of 10.3 months observed in patients without a history of CNS metastases; median PFS of 8 months observed in overall population of 270 heavily pretreated centrally confirmed tissue T790M-positive patients, including 40% of patients with a history of CNS metastases
- Compelling activity in T790M-negative disease with 37% ORR observed
- 57% ORR and 80% DCR in heavily pretreated centrally confirmed plasma-genotyped T790M-positive patients – may allow for broader testing for mutations in patients ineligible for tissue biopsy
- Well-tolerated; only common grade 3 treatment-related adverse event (AE) observed is hyperglycemia
- Breakthrough Therapy designation granted by the U.S. FDA; U.S. and E.U. regulatory submissions to complete in July 2015

CHICAGO--(BUSINESS WIRE)--May 31, 2015-- Clovis Oncology (NASDAQ:CLVS) announced today updated findings from its Phase 2 clinical study of rociletinib (CO-1686), 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 dominant resistance mutation T790M. These data from the TIGER-X trial are being presented today in an oral presentation (Abstract #8001) at the 2015 American Society of Clinical Oncology (ASCO) annual meeting in Chicago.

“The maturing data for rociletinib confirm in a large patient population what we have seen in our early clinical experience,” said Jonathan Goldman, MD, TIGER-X investigator and Assistant Professor, UCLA Hematology & Oncology, Associate Director of Drug Development and Director of Clinical Trials in Thoracic Oncology. “Rociletinib has shown very encouraging and durable activity in the most advanced mutant EGFR lung cancer patients, including in a large population of patients with CNS metastases. Importantly, the data continue to show activity in both T790M-positive and T790M-negative patients, which gives us a potential treatment option for all patients who have progressed on their initial EGFR targeted therapy.”

“To show responses and durability of this magnitude in a very advanced U.S. patient population, of whom nearly half have a history of CNS metastases, is extremely encouraging,” said Patrick J. Mahaffy, President and CEO of Clovis Oncology. “These maturing data confirm rociletinib’s compelling activity in patients with the most advanced stage of mutant EGFR NSCLC and form the basis, along with additional data from TIGER-2, of our U.S. and E.U. regulatory filings beginning next month.”

Data presented today are from the TIGER-X trial of 456 mutant EGFR NSCLC patients treated with rociletinib tablets at each of the efficacious dose groups studied (all doses BID): 500mg (n=119), 625mg (n=236), 750mg (n=95) and 1000mg (n=6) doses. Efficacy data from 243 centrally confirmed tissue T790M-positive patients, 35 centrally confirmed tissue T790M-negative patients and 147 plasma T790M-positive patients were also presented.

The study is being conducted at sites in the U.S., Europe and Australia, with greater than 80 percent of study participants enrolled at U.S. sites.

Patients enrolled in trial were heavily pretreated prior to receiving rociletinib. Eighty-two percent of patients across all doses had immediately progressed on TKI therapy prior to rociletinib treatment. The median number of previous lines of therapy across patients at all doses was two. Seventy-two percent of patients had an ECOG performance score of one or higher.
Additionally, patients with stable CNS metastases were allowed in the trial. Forty-one percent of study participants had a history of CNS metastases, consistent with the study population being drawn largely from U.S. academic centers where more advanced patients are often referred for continuing management of progressive disease after standard therapy.

Data from this study, combined with data from the TIGER-2 study, will form the U.S. New Drug Application (NDA) and E.U. Marketing Authorization Application (MAA) submission packages in July.

**Evidence of Activity**

A total of 243 centrally confirmed tissue T790M-positive patients were evaluable in the four dose subgroups (all doses BID): 500mg (n=48), 625mg (n=114), 750mg (n=77) and 1000mg (n=4).

At the recommended dose of 500mg, a 60 percent ORR and a 90 percent DCR was observed, and across all doses, a 53 percent ORR and an 85 percent DCR was observed.

At the time of analysis, a median PFS of 10.3 months was observed in 163 heavily pretreated centrally confirmed tissue T790M-positive patients without a history of CNS metastases, while a median PFS of 8 months was observed in 270 heavily pretreated centrally confirmed tissue T790M-positive patients, of whom 40 percent had a history of CNS metastases. Clinical benefit was durable with some patients on drug for over two years without disease progression. These data continue to mature.

A total of 147 evaluable plasma T790M-positive patients were treated with rociletinib; in those treated with 500mg, a 57 percent ORR and an 80 percent DCR has been observed to date, and at all doses, a 53 percent ORR and an 82 percent DCR has been observed, which is highly consistent with the comparable tissue outcomes data. These data suggest that T790M plasma testing may be an alternative to tissue testing.

Rociletinib activity was also observed in 35 evaluable T790M-negative patients treated at all doses. A 37 percent ORR has been observed, in a range of 32 to 39 percent across doses studied. Eighty-six percent of these patients were treated with rociletinib directly after TKI therapy, so a TKI re-treatment effect cannot be the driver of this activity.

**Safety and Tolerability**

The data presented at ASCO continue to demonstrate rociletinib is well tolerated. In the 500mg dose group, the most common treatment-related AEs reported in greater than 10 percent of all patients included hyperglycemia, diarrhea and nausea.

Across all doses, most AEs were grade 1 or 2 in severity. The only common grade 3 treatment-related AE was hyperglycemia, which was observed in 17 percent of patients treated with rociletinib 500mg (20/119), 24 percent of patients treated with the 625mg dose (26/236), 36 percent of patients treated with the 750mg dose (23/65) and 33 percent of patients treated with the 1000mg dose (2/6). Most AEs appear to be dose dependent.

Hyperglycemia was readily managed with commonly prescribed oral agents and grade 3 hyperglycemia rates have decreased over time as routine monitoring was standardized in the clinical program for rociletinib. Specifically, prior to September 2014, grade 3/4 hyperglycemia was observed in 22 percent of patients treated with rociletinib at 500mg. After September 2014, by which time routine monitoring had been implemented, grade 3 hyperglycemia was observed in only eight percent of such patients.

No interstitial lung disease (ILD) was observed in the 500mg dose group. Across all doses, 1.5 percent (7/456) of patients developed ILD, and continuation of treatment with rociletinib was possible with the addition of steroid cover in recent cases. There have been no fatal cases of ILD.

No paronychia or stomatitis was observed and any observed rash was minimal. Treatment-related AEs leading to drug discontinuation were observed in 2.5 percent of cases at the recommended dose of 500mg, and in four percent of overall
Recommended Dose

TIGER-X is a large study designed to evaluate the safety and efficacy of rociletinib in three different doses, 500mg BID, 625mg BID and 750mg BID. Based on results from all dose groups, the 500mg dose clearly emerged as the best dose for patients based on its activity and safety profile. As a result, the recommended dose for rociletinib is 500mg BID and all ongoing rociletinib studies will use this dose.

Rociletinib Clinical Development

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

- TIGER-1 is a randomized Phase 2/3 registration study versus erlotinib in newly-diagnosed patients.
- TIGER-2 is a global registration study underway in both T790M-positive and T790M-negative patients directly after progression on their first and only TKI therapy.
- TIGER-3 is a randomized, comparative study versus chemotherapy in both T790M-positive and T790M-negative patients with acquired TKI resistance.
- In addition, a Phase 1 study of rociletinib in Japan has completed enrollment and a Phase 2 study in Japanese patients, agreed upon with Japanese regulatory authorities, is expected to initiate in the second half of 2015.
- Multiple combination studies planned to initiate in the second half of 2015, including inhibitors of PD-L1, PD-1 and MEK.
- For more information, please visit www.tigertrials.com.

Presentation Details

The presentation, titled “Efficacy of rociletinib (CO-1686) in plasma-genotyped T790M-positive non-small cell lung cancer (NSCLC) patients” was presented on Sunday, May 31, during the Oral Abstract Session titled “Lung Cancer: Non-Small Cell Metastatic”, from 8:00 to 11:00am Central Time (Abstract 8001). The presentation 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 31st at 6:00pm Central Time. The event will be simultaneously webcast on the Company’s web site at www.clovisoncology.com, and archived for future review.

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 of EGFR (L858R and Del19), while also inhibiting the dominant acquired resistance mutation, T790M, which develops in approximately 60 percent of patients treated with first- and second-generation EGFR inhibitors, while sparing wild-type, or “normal” EGFR at anticipated therapeutic doses. Accordingly, it has the potential to treat NSCLC patients with EGFR mutations both as a first-line or second-line treatment with a potentially reduced toxicity profile. Rociletinib was granted Breakthrough Therapy designation by the U.S. FDA in May 2014.

About Lung Cancer and EFGFR Mutations

Lung cancer is the most common cancer worldwide with 1.35 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 East Asian patients. These patients often experience significant tumor response to erlotinib, afatinib and gefitinib, which are first- and second-generation EGFR inhibitors. However, most
patients ultimately progress on these therapies, with approximately 60 percent of patients developing acquired resistance from a second, “gatekeeper” mutation, T790M. Currently, no targeted therapies are approved for treatment of this mutation.

**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

**Clovis Oncology, Inc.**

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