Clovis Oncology: CO-1686 (Phase I/NSCLC) Data Impressive at ELCC; Anti-T790M Drugs Should Move to 1st-Line; Street Underappreciates Full Market Potential

We are attending the ELCC conference in Geneva where phase 1 data for CO-1686 was presented in 53 patients who got the new HBr formulation of which 44 are still on therapy. The OR was 64% and mPFS was still not reached after > 6 months on therapy in 22 T790M+ patients. The OR was 52% if 7 patients whose T790M status was unknown (n=29) were included. Encouragingly, only 1/12 patients who is T790M- showed a response highlighting the selectivity of this drug. The reviewer called the data impressive since 10/14 of the T790M+ responders started CO-1686 immediately after failing a previous TKi. The drug was very well tolerated as only 1 patient stopped therapy due to an adverse event. The new HBr formulation has less GI side effects and better PK than the previous free base formulation. Our impression is that the audience received this data very well and that the potency and durability of the drug's efficacy is a big step forward to the field with an acceptable side effect profile.

We continue to believe that the Street is not fully appreciating the market opportunity in 1st- and 2nd-line especially since CO-1686 will likely become the standard of care and will replace the current TKi drugs. In our view, the market is lucrative for CO-1686 to share with AZN9291 as we estimate that the 1st-line market opportunity is $4B-$5B and the 2nd-line market opportunity is $1.5B.

Clearly Eyeing the 1st-Line Market. At the conference, there is a lot of discussion that patients should be carefully evaluated for T790M+ mutations at baseline and after failing 1st-line therapy. This can be done with biopsy now or by using sensitive PCR blood assays in the future. More so, there is an appreciation that there is a need for new T790M+ targeted TKis to use in both 1st-/2nd-line especially since Tarceva and Giotrif (afatinib) do not work on this mutation, which occurs in 50% of patients who fail those drugs. The TIGER-1 phase 2/3 study will test CO-1686 vs. Tarceva in 1st-line patients with EGFR mutations (not just T790M mutation). Based on the higher activity on T790M mutation and similar activity on all EGFR mutations, CO-1686 should beat Tarceva on both PFS and possible OR. This should lead to its use in 1st-line patients.

Hyperglycemia in Focus. The main side effect which was discussed at the Q&A session was asymptomatic hyperglycemia which was seen in 15%/7%/18% (gr 1/2/3). This was easily managed with dose reduction or by starting oral metformin. The side effect typically occurred during the first 1-2 weeks of initiating therapy. Only 1 patient who was pre-diabetic at baseline required insulin. In future studies, this side effect will be monitored carefully during the first month of therapy and the incidence of grade 3 will likely be reduced by starting metformin early.

CO-1686 Development Plans. Clovis will initiate 3 registration studies in 2014. The TIGER2 study, in T790M+ patients directly after progression on their first and only TKI therapy, is expected to start in Q2. TIGER1 will also start in Q2 testing CO- 1686 vs. Tarceva in 1st line EGFR mutant patients who have not had TKI therapy but who may have received one type of chemotherapy. TIGER3 will test CO-1686 vs. chemotherapy in later-line patients with or w/o the T790M mutation and will start in H2. We expect Clovis to file for approval in H2:15 and foresee approval in H2:16.

Source: Citigroup/Werber, March 27, 2014
Oncology Indication: Lung
Keyword: Clinical Trials/Pipeline