Clovis Oncology: CO-1686 (T790M+ NSCLC): Filing for Accelerated Approval Expected in 2015; Ultimate Goal is to Move into Front-Line Setting

Clovis'(CLVS) CO-1686 is very likely to receive approval and find use in a subset of lung cancer (EGFR T790M) and could ultimately provide superior efficacy with improved tolerability to marketed EGFR drugs (Roche/Astellas' Tarceva and AstraZeneca's Iressa) in the larger front-line market. **We project '1686 adjusted peak sales of $1.9bn ($3bn unadjusted).** We are positive on '1686's profile to date, but we believe risk/reward is balanced at an EV of $2.4bn, following recent performance (LTM 186% vs. NBI 59%). We look for increased visibility on '1686 as well as the competitive landscape at upcoming conferences (ELCC in March and ASCO in June).

Based on TIGER 2/3, CLVS has guided to **filing for accelerated approval in U.S. by YE15 with potential approval in 2016 (second-line label in T790M+ NSCLC)**. If successful, CLVS would then use the TIGER 5 trial (second-line or later CO-1686 vs. chemo) as the confirmatory Phase 3 trial. We assume accelerated approval filing in the US in 2015 and a potential approval in 2016. In Europe, we assume a conditional approval filing with the EMA in 2H15/2016 and potential approval and launch in 2017.

- CLVS plans to initiate a Phase 2 trial of CO-1686 in second line T790M patients (TIGER 2) in 2Q14. This single arm study will enroll approximately 125 patients directly progressing after first-line TKI. The primary endpoint will be overall response rate and we expect data in 2H15. If the ongoing Phase 1/2 T790M trial is supportive of US approval, then the primary focus of TIGER 2 will be European approval.
- CLVS is also planning the TIGER 3 trial, which will enroll about 200 patients who have progressed on second or later lines of TKI or subsequent chemotherapy. In addition, TIGER 3 will enroll both T790M positive (100 patients) and T790M-negative EGFR mutant NSCLC patients. Similar to TIGER 2, the primary endpoint will be overall response rate and data is expected in 2H15. However, given management's recent decision to expand the ongoing Phase 1/2 trial, we believe the relevance of TIGER 3 is less clear.

Moving CO-1686 to front-line setting is the ultimate goal. We expect CLVS to initiate a head-to-head Phase 2/3 trial of CO-1686 vs. Tarceva in 2Q14 (TIGER 1) in naïve EGFR+ patients. The primary endpoint will be progression free survival (PFS), but the Phase 2 portion of the trial (150 patients) will explore a number of biomarkers such as tumor growth rate or circulating tumor DNA in an effort to further refine the patient population and accelerate Phase 3 timelines. CLVS guided to initiating the Phase 3 portion of the TIGER 1 trial in 1H15 pending an internal analysis of the biomarker data.

CLVS guided to reporting data from the Phase 2 portion of the trial in 1H16 and Phase 3 in 1H17. As a benchmark, in this patient population the median PFS with approved TKIs Tarceva (EURTAC-Phase 3) and Gilotrif (LUX-Lung 3) is 10-11 months (Exhibit 9). Therefore, we would expect CLVS to power the trial to detect at least a 20% improvement (2-3 months) for CO-1686 over Tarceva.

CLVS will also be looking to identify treatment naïve patients that have the T790M mutation at baseline, who are likely to respond to CO-1686 better than Tarceva to help increase the effect size and reduce the size of the Phase 3 trial.

Source: Goldman Sachs/Flynn, March 23, 2014
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