Oncology Intelligence Report

March 25, 2014 Tuesday

Today's Intelligence at a Glance

1. Exelixis: EU Approves Cometriq for MTC; Launch Could Pave Way for Future Infrastructure Development
Stifel/Sendek, March 25, 2014
HealthACE Abstract *Indication: Thyroid*

2. Clovis Oncology: CO-1686 Durability Will Be the Focal Point at ELCC; PFS Results Could Provide a Preview into Potential Efficacy in 1st-Line EGFRm+ NSCLC
Credit Suisse/Mehrotra, March 25, 2014
HealthACE Abstract *Indication: Lung*

3. Clovis Oncology: CO-1686 (T790M+ NSCLC): Filing for Accelerated Approval Expected in 2015; Ultimate Goal is to Move into Front-Line Setting
Goldman Sachs/Flynn, March 23, 2014
HealthACE Abstract *Indication: Lung*

4. Endocyte: Vynfinit Approval in Ovarian Cancer a Nice Win; Phase II Signal in NSCLC Remains Modest; OS Benefit Will Be Key for Approval
Leerink/Liang, March 24, 2014
HealthACE Abstract *Indication: Lung*

5. Curis: Erivedge (Phase II/Operable BCC) Fails to Meet Pre-Defined Efficacy Criteria, Likely Limiting Usage to Non-Operable or Operationally Difficult Disease
Stifel/Klein, March 23, 2014
HealthACE Abstract *Indication: Skin*

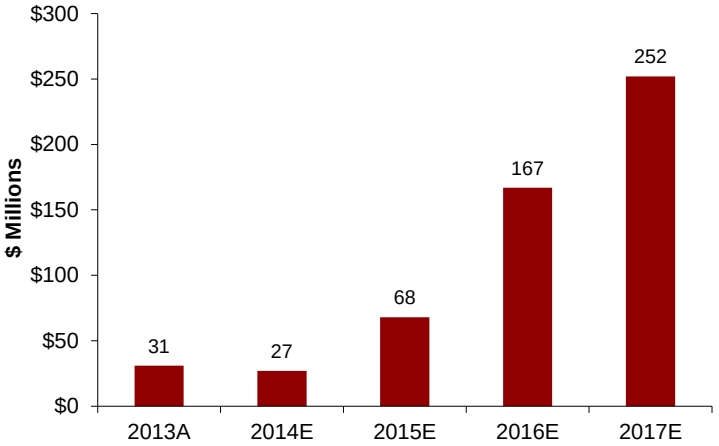
6. Johnson & Johnson: Releases One Batch of Doxil in the U.S.; Timing for Market Re-Entry with FDA-Approved Product Unclear
Morgan Stanley/Baisiwala, March 25, 2014
HealthACE Abstract *Indication: Multiple*

7. Pfizer: Xalkori (Phase III) Can Delay Progression of Lung Cancer Longer Than Chemo in Previously Untreated Patients
Reuters/Pierson, March 25, 2014
HealthACE Abstract *Indication: Lung*

8. Sanofi: U.K. NICE Rejects Zaltrap for Colorectal Cancer, Stating It is Not Cost-Effective
Bloomberg/Bennett, March 25, 2014
HealthACE Abstract *Indication: Colorectal*

Additional Analysis

Exelixis - Annual Revenues Forecast



Sources: Company Reports; 5+ Brokerage Analyst Reports

Phase III Clinical Trials for Cabozantinib (XL184)

Study Name Design	Indication	Endpts	Estimated Completion Date
NCT00704730 EXAM	Medullary Thyroid Cancer (Advanced)	1º: PFS 2º: OS, ORR, Safety and tolerability	March 2013 Ongoing
NCT01605227 COMET-1; vs. Prednisone	CRPC (Previously Treated with Docetaxel & Abiraterone or MDV3100)	1º: OS 2º: Bone scan response	March 2014 Ongoing
NCT01522443 COMET-2; vs. Mitoxantrone + Prednisone	CRPC (Previously Treated)	1º: Pain response; 2º: Bone scan response	June 2014 Recruiting
NCT01865747 METEOR; vs. Everolimus	RCC (Metastatic)	1º: PFS 2º: OS, ORR	August 2016 Recruiting
NCT01908426 CELESTIAL; vs. Placebo	HCC (Patients Who Have Received Prior Sorafenib)	1º: OS 2º: PFS, ORR	October 2016 Recruiting

CRPC: Castration Resistant Prostate Cancer
HCC: Hepatocellular Carcinoma
ORR: Objective Response Rate
OS: Overall Survival
PFS: Progression Free Survival
RCC: Renal Cell Carcinoma

Source: www.clinicaltrials.gov

Back to Front Page

Exelixis: EU Approves Cometriq for MTC; Launch Could Pave Way for Future Infrastructure Development

In-line with our expectations, the European Commission approved Cometriq in unresectable locally advanced or metastatic MTC (medullary thyroid carcinoma). We estimate 2014/2015 Cometriq EU sales of $10M/$17M.

We see a relatively low impact on Cometriq prescribing due to RET mutation language in the EU label as only ~17% of patients in the EXAM MTC study were RET negative. We note the approved indication in the EU states for patients in whom RET mutation status is not known or is negative, a possible lower benefit should be taken into account. In addition, based on the EXAM study we see a relatively small difference in the response rate by RET mutation as 32% of RET positive patients respond versus 25% of RET negative patients. These patients also have limited alternative treatment options despite RET status.

Cometriq EU launch in MTC paving the way for the development of a potential future commercial infrastructure. We expect Swedish Orphan Biovitrum (Sobi) to provide distribution and commercialization of Cometriq for MTC in the EU for 2014 and 2015. If up-coming prostate cancer results are positive, we believe Exelixis would develop their own EU infrastructure for the commercialization and distribution of Cometriq and would no longer require Sobi's services beyond 2015. In the current arrangement with Sobi, Exelixis pays Sobi an undisclosed management fee to sell Cometriq in MTC in the EU.

Source: Stifel/Sendek, March 25, 2014
Oncology Indication: Thyroid
Keyword: FDA/Regulatory Issues

Back to Front Page

Clovis Oncology: CO-1686 Durability Will Be the Focal Point at ELCC; PFS Results Could Provide a Preview into Potential Efficacy in 1st-Line EGFRm+ NSCLC

Updated PI data on Clovis' (CLVS) CO-1686 in EGFRm-T790M+ NSCLC will be provided in an oral presentation at ELCC. Focus will likely be on more mature data on PFS in the 9 evaluable patients treated with 900mg BID freebase (transitioned to 500mg BID HBr) especially on the potential efficacy impact in "first-line" EGFRm+ NSCLC. Further interest could be on early efficacy and safety data for CO-1686 HBr.

CO-1686's PFS could provide a glimpse into the potential efficacy in "first-line" EGFRm+ NSCLC. We estimate that a PFS of ≥6 months in EGFRm-T790M+ NSCLC will likely be needed in order for CO-1686 to show a "clinically meaningful" benefit (25% improvement) in PFS over Tarceva in "first-line" EGFRm+ NSCLC. This estimate assumes that 50% of EGFRm+ NSCLC patients develop the T790M mutation. We flag that the percentage of patients who develop T790M+ will be an important sensitivity. The PFS benefit may need to be higher/lower depending on whether T790M occurs in less/greater than 50% of the time respectively.

Receiving early data of efficacy/safety of CO-1686 HBr. CLVS has dosed patients at 500mg BID, 625mg BID, 750mg BID, and 1000mg BID CO-1686 HBr. CLVS has already selected the 750mg BID dose for PII trials. We expect that the focus will be on how improved dose-proportional and tighter pharmacokinetics as well as higher exposures impacts efficacy and safety.

Source: Credit Suisse/Mehrotra, March 25, 2014
Oncology Indication: Lung
Keyword: Clinical Trials/Pipeline

Back to Front Page

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
Oncology Indication: Lung
Keyword: Clinical Trials/Pipeline

Back to Front Page

Endocyte: Vynfinit Approval in Ovarian Cancer a Nice Win; Phase II Signal in NSCLC Remains Modest; OS Benefit Will Be Key for Approval

Endocyte/Merck & Co. (ECYT/MRK) announced a positive CHMP opinion for EU conditional approval of Vynfinit (vintafolide)/Folcepri (etarfolatide, companion diagnostic imaging agent)/Neocepri (IV folic acid) for the treatment of folate receptor positive (FR100), platinum resistant ovarian cancer in combination with pegylated liposomal doxorubicin (PLD). The early approval on arguably quite limited and mixed Phase II data is a nice win.

We believe top-line TARGET Phase II data showing progression free survival (PFS) benefit (HR of 0.75) in non-small cell lung cancer (NSCLC) provides the valuable second randomized trial supporting activity of Vynfinit for which data had been inconsistent in our view. However, the signal in NSCLC as announced is relatively modest as there are a number of historical examples where the magnitude of the PFS benefit in this range failed to produce a significant overall survival (OS) benefit, which is needed for approval. While a favorable trend to date in OS from TARGET is encouraging, data are based on a small number of patients and are immature.

In addition, we believe the treatment paradigm for lung cancer is rapidly evolving and immunotherapy as well as highly effective targeted agents for specific molecular oncogenic drivers will likely take an increasingly prominent role. Lilly's ramucirumab, for which positive Phase III data from REVEL in the same setting (2nd-line NSCLC in combination with Taxotere) but an all-comer population were recently announced, also presents a hurdle as presumably Vynfinit would need to show superior efficacy for physicians to screen for FR100 patients.

Source: Leerink/Liang, March 24, 2014
Oncology Indication: Lung
Keyword: Clinical Trials/Pipeline

Back to Front Page

Curis: Erivedge (Phase II/Operable BCC) Fails to Meet Pre-Defined Efficacy Criteria, Likely Limiting Usage to Non-Operable or Operationally Difficult Disease

Recently investigators presented final results from a Phase 2 trial of Erivedge in operable BCC patients, finding that the therapy did not meet its primary endpoint of complete histological clearance (CHC) or achieve durable results. Corporate partner Genentech/Roche is continuing to evaluate Erivedge in this indication utilizing alternative dosing schedules and in combination therapies. We anticipate Erivedge sales will not be negatively impacted by these data as forecast continued middling sales consistent with the current trajectory.

Newly diagnosed operable BCC patients were treated using three regimens: Cohort 1, 12 weeks treatment then surgery (n=24, 33% discontinued early); Cohort 2, 12 week treatment, 24 weeks observation, then surgery (n=25, 44% discontinued early) and Cohort 3, 8 weeks treatment, 4 week break, second 8 weeks treatment then surgery (n=25, 24% discontinued early), with Cohorts 1 & 3 requiring a >50% CHC rate and Cohort 2 requiring a 30% CHC rate. The pre-defined efficacy criteria were not met in any cohort, with CHC rates in Cohorts 1 and 3 of 42% and 44%, respectively, and just 16% of patients achieving a durable responses in Cohort 2.

We note that 25 patients total achieved complete histological clearance, with 17 CRs, 7 PRs, and 1 SD, suggesting Erivedge is having a beneficial effect in some patients. Regarding safety, we note a high rate of side effects, including muscle spasm, alopecia, and others, which likely led to treatment discontinuations. While Erivedge did not meet the defined efficacy criteria, Erivedge was never likely to be a viable therapy for small operable BCC given the high success rates with surgery and we believe Erivedge could still gain some usage for larger tumors to improve outcomes, as well as in non-operable disease. However we do not expect royalties derived from Erivedge will ever lead Curis to profitability.

Source: Stifel/Klein, March 23, 2014
Oncology Indication: Skin
Keyword: Clinical Trials/Pipeline

Back to Front Page

Johnson & Johnson: Releases One Batch of Doxil in the U.S.; Timing for Market Re-Entry with FDA-Approved Product Unclear

Janssen has released one batch of Doxil ($180m market size) in the U.S. market. The drug has not yet approved by the FDA, but the FDA has allowed distribution of one lot on request by Janssen. The company's supplier (BI, Ben Venue) has been facing manufacturing issues with this product for the last 2-3 years and it had discontinued the supplies in October 2013.

Notably, Sun is the only generic player in this market: Therefore, it was enjoying no competitive market dynamics. Janssen had leased the Ben Venue facility in December 2013 for six months to commence manufacturing. Presently, it is manufacturing bulk active (doxorubicin) from this site and another supplier is formulating it (alternative manufacturing approach). Also, Janssen is planning to get Doxil manufactured by TTY (Taiwan-based pharmaceutical company).

We believe that Janssen's re-entry into Doxil in a sustainable way is still nebulous: The company may be exploring two options – Ben Venue leasing and TTY – as a way to get back into the market. It is unclear when Janssen will be able to re-enter the market with FDA-approved product and from which site. We have assumed Janssen entry in F3Q15 and projected flat U.S. revenues yoy for F15 at $120m. In F14, Sun shared the Doxil market with Janssen for 7-8 months and enjoyed the market exclusively for the remaining months.

Source: Morgan Stanley/Baisiwala, March 25, 2014
Oncology Indication: Multiple
Keyword: FDA/Regulatory Issues

Back to Front Page

Pfizer: Xalkori (Phase III) Can Delay Progression of Lung Cancer Longer Than Chemo in Previously Untreated Patients

Pfizer's Xalkori delayed progression of lung cancer longer than chemotherapy in patients who had never previously been treated for the disease, according to results of a late-stage study released on Tuesday (3/25).

The drug had shown in a previous Phase III trial that it significantly delayed disease progression among those who have already undergone chemotherapy for non-small-cell lung cancer.

Xalkori is used among patients who have a mutation in the so-called ALK gene, as determined by an approved diagnostic test. The mutation only occurs in a small percentage of patients with lung cancer, but makes them good candidates for treatment with Xalkori.

Xalkori had global sales of $89 million in the fourth quarter. Pfizer is also developing an array of other cancer medicines that work through new mechanisms, with the aim of becoming a major player in the oncology field.

Source: Reuters/Pierson, March 25, 2014
Oncology Indication: Lung
Keyword: Clinical Trials/Pipeline

Back to Front Page

Sanofi: U.K. NICE Rejects Zaltrap for Colorectal Cancer, Stating It is Not Cost-Effective

Sanofi's cancer drug Zaltrap was rejected by England's cost regulator, which said the drug isn't cost effective even after the company offered a discount.

The treatment, also known as aflibercept, is clinically effective against colorectal cancer but exceeded the threshold at which a drug can be considered a cost-effective use of government funds, the National Institute for Health and Care Excellence (NICE) said today (3/25). The agency rejected Sanofi's appeal of the decision, it said.

Governments are pushing back on high prices of new drugs as they seek to rein in health-care spending. Sanofi effectively cut the price of the $11,000-a-month treatment in half in the U.S. after doctors from Memorial Sloan-Kettering Cancer Center wrote in the New York Times that they had decided not to use the medicine because it was more costly than Roche's Avastin and no more effective.

"We have already recommended six treatments for various stages of colorectal cancer and are disappointed not to be able to add aflibercept as another treatment option for this stage of the disease," Andrew Dillon, NICE's chief executive officer, said. "However, we have to be confident that the benefits that drugs offer patients really do justify what the NHS will have to pay for them."

Scotland, which does its own review of the cost effectiveness of new drugs, recommended the treatment, Sanofi said.

A 100-milligram vial of the drug has a list price of about 296 pounds ($488), while a 200-milligram vial is priced at 591 pounds, the agency said. The cost per patient will vary depending on the dose and length of treatment, NICE said. The agency declined to say how much of a discount the company offered.

Source: Bloomberg/Bennett, March 25, 2014
Oncology Indication: Colorectal
Keyword: FDA/Regulatory Issues