HealthACE Pharma Business Intelligence

Oncology Intelligence Report

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Additional Analysis

Ongoing Prostate Cancer Trials for Xtandi (MDV3100)

Study Name Design	Indication	Endpts	Estimated Completion Date
NCT00974311 Phase III; AFFIRM	CRPC (Patients Previously Treated With Docetaxel-Based Chemo)	1º: OS 2º: rPFS, Time to 1st SRE, PSA progression	November 2012 Has Results
NCT01212991 Phase III; PREVAIL	Prostate Cancer (Chemotherapy-Naive Patients, But Failed Androgen Deprivation Therapy)	1º: OS, PFS 2º: Time to 1st SRE, Time to intitiation of cytotoxic chemo	September 2014 Active; Not Recruiting
NCT02003924 Phase III; PROSPER	Prostate Cancer (Non-Metastatic Patients)	1º: MFS 2º: OS, Time to pain progression, 1st use of cytotoxic chemo, 1st use of new antineoplastic therapy, PSA progression	August 2017 Recruiting
NCT01949337 Phase III; w/o Abiraterone Acetate and Prednisone	CRPC (Metastatic Patients)	1º: OS 2º: Toxicity, PSA level, PFS, ORR, Tumor burden & bone activity	December 2019 Not Yet Recruiting
NCT01547299 Phase II	Prostate Cancer (Neoadjuvant Therapy for Patients Undergoing Prostatectomy)	1º: Pathological Complete RR; 2º: Effect on PSA, testosterone, & DHT, Rate of positive surgical margins, PD, Safety	August 2013 Active; Not Recruiting
NCT01650194 Phase II; Combo with Abiraterone Acetate & Prednisone	CRPC (Bone Metastatic)	1º: Adverse events; 2º: Effect on PSA, testosterone, & DHT, PFS, ORR, Bone scan	June 2014 Recruiting
NCT01664923 Phase II; vs. Bicalutamide	Prostate Cancer	1º: PFS 2º: Time to PSA progression, PSA response, Time to radiographic progression, Safety	July 2014 Recruiting
NCT01288911 Phase II; vs. Bicalutamide	Prostatic Neoplasms (Patients Who Have Progressed While on Luteinizing Hormone Receptor Hormone Agonist/Antagonist or After Receiving a Bilateral Orchiectomy)	1º: PFS 2º: PSA response, Time to PSA progression, Safety	November 2014 Recruiting
NCT01302041 Phase II	Prostate Cancer (Never Have Hormone Therapy)	1º: PSA level 2º: PD, PK, PSA dynamics & kinetics, Safety	December 2015 Active; Not Recruiting
NCT01534052 Phase II	Prostate Cancer (To Assess Safety of Continued Administration of MDV3100	1º: Long-term safety	December 2022 Recruiting

CRPC: Castration-Resistant Prostate Cancer
DHT: Dihydrotestosterone
MFS: Metastasis Free Survival
OS: Overall Survival
PD: Pharmacodynamic
PFS: Progression-Free Survival
PK: Pharmacokinetic
PSA: Prostate Specific Antigen
SRE: Skeletal-Related Event

Source: www.clinicaltrials.gov

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Medivation: Expects Strong Urologist Uptake of Xtandi in Long Run; Open to Other Therapeutic Areas to Maximize ROI and Drive Growth

We hosted a breakfast with David Hung (CEO) and Anne Bowdidge (Senior Director of IR) of Medivation's management team. Following PREVAIL data presented at ASCO GU, Medivation is confident in Xtandi's product profile as it offers superior efficacy (better improvement in progression free survival [PFS] and statistical significant benefit in survival), convenience (no steroids) and safety over competitor (less cardio and liver toxicity) JNJ's Zytiga. Management believes the PREVAIL data represented the best case scenario. Notably Xtandi has fewer Grade 3 cardiac and hepatotoxicity events vs. Zytiga and this appears to be most underappreciated from Medivation CEO's perspective.

Company anticipates sentiment to shift towards Xtandi when it is formally FDA approved for pre-chemo prostate cancer given urologists. This is because urologists rarely prescribe treatment off-label. Management highlighted that urologists do not use ketoconazole for the same reason Zytiga has not seen material uptake: concomitant steroid use. Rather, Casodex is heavily prescribed by urologists and Medivation foresees similar uptake trends for Xtandi because it is just a more potent version of Casodex.

Near-term focus for Medivation remains Xtandi approval for pre-chemo prostate cancer in the U.S. The company expects to complete filing in early 2014. We believe filing by end of February is possible and we continue to expect a quick turnaround from the FDA based on past timelines for Zytiga and Xtandi. Management did not provide specifics on whether Xtandi can be approved earlier based on historical timelines, but company expressed that unlike AFFIRM (phase 3 Xtandi in post-chemo prostate cancer), PREVAIL supports an indication for which there is no approved drug that claims statistically significant survival and PFS benefits in pre-chemo prostate cancer.

Medivation noted we should expect a **steady Xtandi launch trajectory early on** as urologists are primarily on-label prescribers and rely more heavily on word of mouth. Ahead of the launch, Medivation aims to expand its current urology/oncology sales force of 150 reps (Medivation: 60; partner Astellas: 90) but only modestly as urology practices have undergone consolidation.

Outside of the U.S., Medivation is also working to gain Xtandi approval for prostate cancer indication in Japan. This represents upside seeing that (1) Xtandi will be first-to-market in Japan (Zytiga is still not approved in Japan) and (2) hormonal therapies are frequently prescribed outside of the US.

Ultimately, Medivation's goal is to move Xtandi into earlier lines of prostate cancer and displace Casodex. Two studies are ongoing to support this: (1) TERRAIN which is evaluating Xtandi vs. Casodex in metastatic prostate cancer patients and (2) STRIVE which is evaluating Xtandi vs. Casodex in non-metastatic and metastatic prostate cancer patients. Both trials can lead to updated NCCN guidelines, which could encourage urologists to prescribe Xtandi over Casodex in early prostate cancer patients. TERRAIN has been enrolled for seven months and should read out in 2014. STRIVE is still enrolling patients.

Beyond Xtandi, **Medivation hopes to maximize ROI and drive growth through both internal and external opportunities. Despite its current oncology franchise, Medivation is open to other therapeutic areas.** Interestingly, the company is protected from a hostile takeaway from Astellas under its change of control provision, which commenced with the first sale of Xtandi and does not expire for multiple years (management did not specify exactly when it expires).

As supported by our physician checks and the company's commentary, we continue to believe Xtandi should emerge as the treatment of choice among urologists in the long-term given it has the best-in-class profile over Zytiga. We project Xtandi will become a blockbuster drug as early line prostate cancer opportunities will drive peak global Xtandi sales to $6.8bn.

Source: Goldman Sachs/Flynn, February 20, 2014
Oncology Indication: Prostate
Keyword: Management/Strategy/Financials

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AB Science: Starts New Phase III Trial of Masitinib in Prostate Cancer, Accessing Combination with Docetaxel for First-Line Treatment

We knew that AB Science was conducting a phase II trial in prostate cancer but this is the first time that we have data on the indication. In second-line treatment, i.e. after an initial failure with the benchmark product Taxotere, patients suffering from prostate cancer were treated with masitinib and continued to take Taxotere. This addition of masitinib enabled 50% patients to survive at least 18.4 months. This figure was not compared with a placebo arm but scientific literature shown an overall survival rate on second-line treatment of 14.4 months on average with currently available second-line treatments.

The most effective of these treatments on the market is Xtandi, which has a similar median survival rate of 18.4 months. Masitinib + Taxotère therefore match the performance of Xtandi, a drug that the consensus forecasts reaching $3bn in sales in 2018. AB Science's drug could therefore potentially provide an attractive second-line. But the company is ambitious, and as masitinib is combined with the first-line-treatment Taxotere, AB hopes to make the masitinib + Taxotere combination the new benchmark first-line treatment in prostate cancer.

On the commercial front, the first-line treatment is clearly more attractive as it addresses a wider population than a second-line treatment. Phase III will therefore compare with masitinib + Taxotere vs. Taxotere alone. The phase III study is likely to take three years and involve 550 patients. The total cost is likely to be €5.5m (i.e. just under €2m in additional R&D spending per annum). Results will be available mid-2017, on our estimates.

Note that this is the fourth time that masitinib has demonstrated a benefit regarding patient survival. In GIST, the increase was 12 months (a virtual doubling vs. Sutent), for pancreatic cancer, it also rose in two patient categories (+3 months for patients in pain, +8 months at patients with a genetic marker of aggressiveness) and in colorectal cancer the increase is two months. Note that in colorectal and prostate cancer, these benefits are still theoretical as it is not a case of a comparison vs. a placebo but a comparison with what is admitted in scientific literature, although it remains highly encouraging.

Another key point, AB Science is making progress in understanding the workings of masitinib which would appear to be particularly suitable for treating aggressive cancers. The drug does not directly act on cancer cells but on the neighboring immune cells which apparently controls the aggressiveness of the tumor. These elements are part of the arguments which the company will underscore in calls with the EMS.

Source: Oddo Securities/Malafosse, February 21, 2014
Oncology Indication: Prostate
Keyword: Clinical Trials/Pipeline

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Exelixis: Market Penetration for Cometriq Beginning to Slow Given Small Size of MTC Market; Focus Remains on Upcoming CRPC Data

4Q Cometriq sales of $4.3M were below our $5.7M estimate. Market penetration is beginning to slow as expected given the small size of the MTC market. OpEx were $64M vs. JPMe of $64M. Exelixis reiterated their broad guidance for top-line COMET data in 2014 and remained tightlipped on progress with the studies. We continue to see cabo's potential in CRPC as the key value driver, thus data from these trials (specifically OS data from COMET-1) will be the key catalyst in 2014. Pivotal trials in RCC and HCC are also enrolling with data expected in 2015 and 2016/17 respectively.
On cobimetinib, partnered with Roche/Genentech, data and regulatory filings are still expected in 2014.

Focus remains on upcoming data from the COMET-1 and COMET-2 trials in 2014. Recall that COMET-1 (OS endpoint) completed enrollment (~960pts) in Sept. 2013, and an interim analysis will take place after 387 survival events; the final analysis will occur after 578 events. The retrospective OS analysis (presented at ASCO) in patients with bone scan and pain responses could have positive read through for COMET-1, though we once again note that the bar has been raised in prostate cancer given recent successes from other products. In the pre-chemo setting, a Phase 2 RCT in combo with Zytiga is also up and running, and a second DDI/PK/Safety trial in combo with Xtandi is planned for 1H14.

Source: JPMorgan/Kasimov, February 20, 2014
Oncology Indication: Multiple
Keyword: Management/Strategy/Financials

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Pharmacyclics: Imbruvica Sales Ahead of Expectations, 2014 Consensus Too Conservative; Off-Label Use to Drive Upside; Competition Immaterial in 2014

Pharmacyclics (PCYC) Q4 sales at $13.6M were higher than consensus at $3.8M. Demand was $10M while inventory was $3.6. We believe consensus 2014 at $217M might be conservative as it represents average 2700 patients on treatment (duration 10 months) in 2014 while our calculation indicates average ~760 patients on treatment in 6-7 weeks of launch. Also previous transformational therapies such as Rituxan & Revlimid sold $163M (1997) & $321M (2006), respectively, in the first full year of launch. We model 2014 Imbruvica sales at $310M.

Demand suggests IMS capture rate at ~70-80%. PCYC shipped 931 120-cap bottles (MCL) & 584 90-cap bottles (CLL). CLL actual share at 38% is in line with our IMS-based calculation at ~37%. Our IMS calculation suggested ~$7-8M demand in Q4 vs. $10M actual. This suggests the capture rate could be ~70-80%.

Uptake in CLL driven by favorable NCCN guidelines to drive growth in 2014. PCYC has reached out to all the practicing hematologists at least once post MCL launch and they plan to do that again with the launch in CLL. The company noted that inclusion of CLL, MCL, SLL and WM in NCCN guidelines could get them access to 45K treated patients annually. According to PCYC, 91% of oncology use is driven by these guidelines and is used as a reference by oncologists.

Off-label use could drive further upside; Competition may be immaterial in 2014. Our checks indicate some off-label use in elderly unfit treatment naïve CLL patients. They also noted the likelihood of use in unfit DLBCL patients based on early data. We model ~30% of 2014 sales from off-label use. Our doc checks see minimal impact of off label Idelalisib use in CLL. Idelalisib PDUFA in iNHL is in Sep 2014.

Detailed data from RESONATE trial next key catalyst in CLL. The company would share detailed data from RESONATE trial in an upcoming medical meeting it would unlikely be at AACR. Next big phase 3 readout in CLL would be RESONATE-2 in naïve elderly patients in 2H15 (this trial is fully enrolled now). In our view, we could see data from ongoing phase 2 follicular lymphoma trial some-time this year. JNJ is running this trial and the timelines have not been disclosed. The company is also conducting a combo trial in treatment naïve DLBCL patients but data may not be available in near term. We expect to see Phase 1 durability and Rituxan combo data for ABT-199 (competition) at ASCO.

New BTK moving to clinics in autoimmune disorders. PCYC is also moving a new BTK inhibitor in clinics for autoimmune diseases. The co, in coming months, will initiate dose escalation study in healthy volunteers & then in RA patients. The patent for this compound lasts til 2035.

Source: Deutsche Bank/Karnauskas, February 20, 2014
Oncology Indication: Hematologic
Keyword: Management/Strategy/Financials

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Pharmacyclics: Independent Investigators to Begin Two Key Studies of Imbruvica in CLL; Trials Beyond CLL Progressing

Management provided incremental clinical and regulatory updates in the conference call:

- Pharmacyclics' strategy in auto-inflammatory indications is shaping up, with a (long awaited) IND for a second Btk inhibitor accepted by the FDA last week. The Btk compound will be tested in a dose escalation phase I study in healthy volunteers, set to begin in the coming months. The company's plan is to then evaluate this agent in patients with rheumatoid arthritis (and presumably other indications) in a phase IIa trial.
- Results from the RESONATE study will be presented at a "congress", most likely at the ASCO meeting (May 30th-June 4th). Imbruvica is currently under review at the EMA for relapsed MCL and CLL, and management expects that it could be approved by the end of 2014.
- The RESONATE-2 study of Imbruvica in elderly treatment naïve patients completed enrollment in early 2014. With 12-15 months follow up period, the study is expected to report out in 2H15. We anticipate that Imbruvica will be superior to the control treatment chlorambucil in this study and could be approved in this indication in late 2016. We expect that Imbruvica will face competitive challenges in this indication from Roche's Gazyva.
- Two key studies of Imbruvica in CLL are being conducted by independent investigators.
    1. An ECOG study of Imbruvica in combination with Rituxan compared to FCR could provide an avenue for the use of Imbruvica in lieu of the current standard of care in the younger and more-fit CLL patients. The study is expected to enroll 519 patients, and the primary endpoint is improvement in PFS. Based on the median PFS of 30.6 months achieved by patients on FCR in the REACH phase III trial, PCYC's management conceded that the ECOG 1912 study may not read out until 2018-2019.
    2. A second study is being conducted by the German CLL group and is testing Imbruvica in patients that would typically be recommended for "watchful waiting" but who nevertheless harbor intermediate and high risk disease. A positive outcome in this study may represent the catalyst for patients in the prevalent pool to initiate active therapy. Similarly to the ECOG study, we anticipate that the duration of this study could be 5 years or longer.

Beyond CLL, there were few updates on the progress of Imbruvica development in diffuse large B-cell lymphoma (DLBCL), indolent non-Hodgkin lymphoma (iNHL), Waldenström's and multiple myeloma:

- In MM, the first two cohorts of an ongoing phase II study did not achieve responses. While data from cohorts 3 and 4 (Imbruvica 840 mg single agent and Imbruvica 840 mg in combination with dexamethasone) are currently being analyzed and the outcome is expected in 1H14, management appeared rather reluctant to comment on any signs of efficacy or whether data would be presented at the ASCO conference. We remain lukewarm on the potential of Imbruvica in MM and we currently do not include this indication in our revenue projections.
- In addition to the FLR3001 phase III study of Imbruvica monotherapy in relapsed indolent NHL, two phase II studies are evaluating Imbruvica combinations in frontline and relapsed follicular lymphoma. As the primary endpoint of these phase II trials is overall response rate (ORR), we expect that the FLR2002 in relapsed FL could read out this year, potentially at the ASH conference in December. We anticipate that Gilead's idelalisib will be approved in relapsed iNHL in 3Q14, and will likely dominate this indication for at least 1-2 years before the potential approval of Imbruvica. PCYC's management noted combinations with their HDAC inhibitor abexinostat as an incremental opportunity for Imbruvica in iNHL. We view this comment as somewhat surprising, given the scarce clinical data supporting the use of HDAC compounds in follicular lymphoma or any clinical data supporting the safety and efficacy of the Imbruvica-abexinostat combination.
- Results from the ongoing phase III PHOENIX study of Imbruvica in combination with R-CHOP in frontline DLBCL are unlikely to emerge for several years. A phase II study of Imbruvica in non-GCB subtype DLBCL reported out initial results from the 560 mg cohort. No improvement in ORR or duration of responses was seen with the higher 840mg dose and the higher dose cohort was discontinued.

Source: Bernstein Research/Porges, February 21, 2014
Oncology Indication: Hematologic
Keyword: Clinical Trials/Pipeline

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Chugai: High Expectations for Immunotherapy Drug for Cancer; Roche's PD-L1 Antibody Could Launch in Japan in 2017 and Drive Earnings

Our Roche analyst forecasts peak global sales of the PD-L1 antibody (MPDL3280A) cancer treatment Roche is developing at over ¥700bn. We believe the drug will be launched in Japan in 2017 and drive Chugai earnings as well.

Our global pharma research team believes immunotherapy is a game-changer in cancer treatment that will lead to innovative drugs being launched and a substantial change in the earnings outlook for pharmaceutical companies. The leaders in this field are Bristol-Myers Squibb (BMS), from which Ono has licensed a PD-1 antibody, and Chugai's parent, Roche.

Here, we factor the longer-term sales prospects of the PD-L1 antibody into our estimates for Chugai, as with Roche coordinating joint international clinical trials we anticipate an NDA filing in 2016 and a launch in 2017. As a result, while existing antibodies face the risk of declining sales on the launch of biosimilars, we think Chugai has entered a growth trajectory for the medium term with the PD-L1 antibody likely to become a blockbuster and contributions likely from other new drugs as well.

$1.00 = ¥102.19

Source: Citigroup/Yamaguchi, February 20, 2014
Oncology Indication: Multiple
Keyword: Partnerships/Business Developments

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Pfizer: Streamlined R&D Efforts and Focus on Oncology Will Help Company to Create Value and Sustain Business Growth

Pfizer's fourth quarter results were a reminder of the continued growth pressure that the company faces due to declining revenues from its legacy drugs. For the full year 2013, the sales decline in the U.S. and international markets was roughly the same, implying that the revenue split remained unchanged. Going forward, we believe that **international markets will become more important for Pfizer as the company taps into opportunities that exist in emerging markets of China and India**. At the same time, we believe that **most of the revenue growth will be driven by the expected ramp-up in the company's oncology drug sales**.

We expect further R&D cuts as Pfizer restructures its business to divert resources to certain key growth areas such as oncology (cancer treatment) and reduces spending in other therapeutic areas. The company is reorganizing its business into innovative and value segments, which would lead to better focus and efficient resource allocation. The innovative segments are likely to be allocated proportionally more of the R&D budget, and we believe that oncology (cancer treatment) comes under this category.

Oncology and immunology are going to be the key growth areas for the pharmaceutical industry. Oncology can help Pfizer command better pricing as primary care areas such as cardiovascular get flooded with generics. The company's focus in this area is evident from the fact that 3 out of 6 drugs in its late stage program are intended for cancer treatment. These include Palbociclib for breast cancer, Inotuzumab Ozogamicin for aggressive non-hodgkin's lymphoma and acute lymphoblastic leukemia, and Dacomitinib for non-small cell lung cancer.

Source: Trefis, February 19, 2014
Oncology Indication: Multiple
Keyword: Management/Strategy/Financials

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Merck KGaA: Increases Investment for Existing Cancer Product in EMs; Look to Acquisitions in the U.S. to Enhance Its Pipeline

Merck KGaA is increasing investment in existing products for cancer and fertility in emerging markets while waiting for its drug pipeline to mature, said Belen Garijo, head of its prescription drug unit.

There is "significant growth potential" for fertility products such as Gonal-f in China, where the government is easing its one-child rule, as well as in Turkey and Russia, Merck Serono CEO Garijo said. The company also plans to "fully exploit" cancer drug Erbitux in Asia, particularly for head-and-neck cancer in Japan and China where smoking rates are high.

While the company isn't planning any new studies of Erbitux, Garijo pointed out that a recent analysis of clinical trials showed patients with advanced non-small-cell lung cancer who took Erbitux in combination with chemotherapy lived an average of a month longer than those who received chemotherapy alone. Merck KGaA withdrew an application to market the drug to this group of lung cancer patients in Europe in 2012 after regulators asked for more data.

Erbitux has been approved in Japan for head-and-neck cancer and is still in the registration process for the indication in China. The company is also developing what Garijo calls a "super Erbitux" dubbed Sym004, which licensed from Symphogen A/S in 2012. Sym004 and Erbitux are both designed to work on a subset of patients who carry a normal form of a gene called KRAS and the company believes that Sym004 may be effective.

Merck KGaA is scouting acquisitions in the U.S., particularly in oncology, to beef up its pipeline, Garijo said. Our aspiration is to become a significant player in highly-specialized diseases and a leading player in emerging markets," she said.

Source: Bloomberg/Connolly, February 21, 2014
Oncology Indication: Head & Neck
Keyword: Management/Strategy/Financials