HealthACE Pharma Business Intelligence

Oncology Intelligence Report

March 12, 2014 Wednesday

Today's Intelligence at a Glance

1. Geron: Imetelstat (Phase II/PV) Placed on Clinical Hold; No Impact to Incyte, Key Drivers Shifted to Jakafi in Pancreatic Cancer & IDO1 Inhibitor in Melanoma
Goldman Sachs/Singh, March 12, 2014
HealthACE Abstract *Indication: Hematologic*

2. Geron: Imetelstat: FDA Concerns with Persistent Low-Grade Liver Function Tests Abnormalities; Planned Phase II MF Trial Likely to Be Delayed
JPMorgan/Kasimov, March 12, 2014
HealthACE Abstract *Indication: Hematologic*

3. Threshold: Intends to Start a 3rd Registrational Study of TH-302 in Coming Months; Interim Analysis for TH-302 Phase III Sarcoma Study On-Track in Mid-2014
PiperJaffray/Duncan, March 10, 2014
HealthACE Abstract *Indication: Sarcoma*

4. NewLink Genetics: Algenpantucel-L (Phase III/Pancreatic Cancer) IMPRESS 2nd Interim Readout in 2H14, Positive Outcome on Final Analysis Expected in 2015
Jefferies/Amin, March 12, 2014
HealthACE Abstract *Indication: Pancreatic*

5. OncoGenex: Custirsen (Phase III/CRPC) SYNERGY Trial On-Track to Report Top-Line By Mid-2014; 2nd-Line Study (AFFINITY) Could Still Be Relevant Even If SYNERGY Fails
Leerink/Liang, March 12, 2014
HealthACE Abstract *Indication: Prostate*

6. Peregrine: Continues to Seek Partner for Bavituximab, Possibly for Breast and/or Liver Cancer; Moving Forward in NSCLC
PiperJaffray/Duncan, March 10, 2014
HealthACE Abstract *Indication: Lung*

7. Onconova: Phase III Oral Rigosertib Trial in Lower-Risk MDS Planned for 2H14 with a Biomarker Component; Approval of IV Rigosertib in High-Risk MDS Unlikely
Leerink/Liang, March 11, 2014
HealthACE Abstract *Indication: Hematologic*

8. Oxigene: Zybrestat & Avastin Combo Shows PFS Improvement in Phase II Ovarian Cancer; May Advance into Phase III, But Funding Could Be an Issue
FierceBiotech/Garde, March 12, 2014
HealthACE Abstract *Indication: Ovarian*

Additional Analysis

Phase II Trials for Imetelstat

Study Name Design	Indication	Endpts	Estimated Completion Date
NCT01242930 vs. Standard of Care	Multiple Myeloma	1º: Respone rate improvement; 2º: PFS, Safety and tolerability	December 2013
NCT01243073 vs. Standard of Care	ET/PV	1º: Hematologic response; 2º: Safety and tolerability	January 2016

ET: Essential Thrombocythemia
PV: Polycythemia Vera
PFS: Progression-Free Survival

Source: www.clinicaltrials.gov

Phase III Trials for Jakafi

Study Name Design	Indication	Endpts	Estimated Completion Date
NCT00952289 COMFORT-I	Myelofibrosis	1º: Proportion of subjects achieving ≥ 35% reduction in spleen volume; 2º: Duration of maintenance, OS	June 2015 Has Results
NCT00934544 COMFORT-II	Myelofibrosis	1º: Proportion of subjects achieving ≥ 35% reduction in spleen volume; 2º: Duration of maintenance, PFS, LFS, OS, Histomorphology	February 2015 Has Results
NCT01243944 RESPONSE; vs. Best Available Care	PV (Resistant to or Intolerant of Hydroxyurea)	1º: Proportion of subjects achieving a response at Week 32; 2º: Proportion of subjects achieving complete hematologic remission at Week 32	March 2014 Ongoing
NCT01632904 The Relief Study	PV (Switch Study From Hydroxyurea to Ruxolitinib)	1º: Proportion of subjects with ≥ 50% reduction in a cluster of PV-related symptoms; 2º: Proportion of subjects with ≥ 50% reduction in individual PV-related symptoms at Week 16, Duration of symptomatic improvement	November 2013 Recruiting

LFS: Leukemia Free Survival
PFS: Progression-Free Survival
PV: Polycythemia Vera
OS: Overall Survival

Source: www.clinicaltrials.gov

Back to Front Page

Geron: Imetelstat (Phase II/PV) Placed on Clinical Hold; No Impact to Incyte, Key Drivers Shifted to Jakafi in Pancreatic Cancer & IDO1 Inhibitor in Melanoma

This morning (3/12), Geron announced its investigational new drug (IND) application for imetelstat has been placed on clinical hold by the FDA. Although the FDA has not formally submitted a written notice, the FDA verbally communicated to Geron that liver toxicity issues observed in the phase 2 imetelstat in essential thrombocythemia (ET)/polycythemia vera (PV) study warranted the clinical hold.

The clinical hold by the FDA impacts all ongoing Geron-sponsored trials, including a potentially planned phase 2 imetelstat in myelofibrosis (MF) study. In our view, even if Geron were able to resolve these liver toxicity issues and make it to the market, these safety concerns could potentially harm imetelstat's future market uptake.

Incyte's Jakafi has been on the market with a potential filing to expand the Jakafi label for PV in 2014. Recall, Jakafi previously had its own set of safety concerns surrounding thrombocytopenia but Incyte has made strides in educating physicians on Jakafi's safety profile and dose-escalating accordingly.

In our view, the key drivers of Incyte has shifted away from Jakafi in blood cancers and to (1) IDO1 inhibitor + Yervoy phase 1 data in melanoma and (2) Jakafi phase 3 data in pancreatic cancer. Both datasets are expected at ASCO 2014 in June. Our analysis indicates that the current share price factors in ≥$3bn in non-risk adjusted IDO1 sales.

Source: Goldman Sachs/Singh, March 12, 2014
Oncology Indication: Hematologic
Keyword: FDA/Regulatory Issues

Back to Front Page

Geron: Imetelstat: FDA Concerns with Persistent Low-Grade Liver Function Tests Abnormalities; Planned Phase II MF Trial Likely to Be Delayed

Geron received verbal notice from the FDA that imetelstat has been placed on full clinical hold based on concerns around persistent low-grade liver function test (LFT) abnormalities. Specifically, the FDA expressed concern that the changes were not reversible. On their call, Geron noted some of the acute, higher grade LFT abnormalities were reversible on dose reductions/modifications, but many patients have experienced persistent low-grade LFTs, which are the cause for concern.

Enrollment in the Mayo Clinic IST was stopped in January, although Geron noted that it had nothing to do with LFTs. As discussed at ASH 2013, the main toxicity concern in the MF study had been myelosuppression (recall that Arm B and C in the Mayo Clinic IST were discontinued due to toxicity). The FDA has requested LFT data from this study (in addition to further info from the company-sponsored trials). Geron noted that at this stage, it has little insight into the specifics of the LFT abnormalities in that trial.

Geron expects to receive the official letter from the FDA soon and will then assimilate any information/concerns into its analysis to formulate a response. Management noted that the start of the planned Phase II MF trial is likely to be delayed, although timing of next steps/potential resolution are uncertain. Recall that Geron had intended to start a Phase II multi-center study in June 2014, with data ~mid/late 2015.

Source: JPMorgan/Kasimov, March 12, 2014
Oncology Indication: Hematologic
Keyword: FDA/Regulatory Issues

Back to Front Page

Threshold: Intends to Start a 3rd Registrational Study of TH-302 in Coming Months; Interim Analysis for TH-302 Phase III Sarcoma Study On-Track in Mid-2014

An interim for Threshold's pivotal sarcoma study of TH-302 remains on track for the 50% triggering event mid-'14 and final data possibly in 2H15. The Phase III in pancreatic cancer continues to enroll patients. This study is being conducted by partner Merck KGaA. Threshold intends to start a 3rd registrational study for an undisclosed solid tumor in "coming months." Other development programs appear to be progressing well; data from the myeloma and glioblastoma studies may be presented this year (we guess ASCO).

2014 guidance for the Phase II study in melanoma is for continued enrollment and additional study sites. As reported at ASH'13, Threshold believes evidence for TH-302's activity may warrant further investigation in advanced multiple myeloma and in combination with other agents in advanced leukemias. In myeloma, Threshold is currently assessing '302's activity in combination with dexamethasone and intends to start a 3rd part of the Phase I/II study to assess the feasibility of adding in a proteasome inhibitor. This indication remains as upside to our current projections pending additional clinical data, though we believe there have been provocative signals of activity and sound rationale for the setting given the platform's hypoxia-targeted trigger.

The Phase I combo study with Sutent in gastrointestinal/kidney/pancreatic neuroendocrine tumors is expected to complete enrollment in 2H14. The Phase I/II of '302 + Avastin in glioblastoma is enrolling at a 670 mg/m2 dose level for '302. The company is still considering future plans for '302 plus Votrient, which completed a Phase I study in various solid tumors last year. This program also currently remains as upside to our projections.

Management is guiding to higher R&D expenses for 2014 vs. 2013 on continuing and new clinical trials, and is also indicating increased SG&A expenses. Note that Merck KGaA is responsible for 70% of the TH-302 development cost.

Source: PiperJaffray/Duncan, March 10, 2014
Oncology Indication: Sarcoma
Keyword: Clinical Trials/Pipeline

Back to Front Page

NewLink Genetics: Algenpantucel-L (Phase III/Pancreatic Cancer) IMPRESS 2nd Interim Readout in 2H14, Positive Outcome on Final Analysis Expected in 2015

IMPRESS 2nd Interim Readout in H2 2014: On March 7th, NewLink (NLNK) reported that DSMC has recommended the continuation of the Phase III IMPRESS trial unchanged upon the review of 222 events required for the first interim analysis. The Phase III IMPRESS trial is evaluating the efficacy of algenpantucel-L+SOC (gemcitabine+5FU/radiation) v. SOC in surgically-resected pancreatic cancer patients. The second interim analysis will occur upon reaching 333 events, which we believe will occur in H2 2014. The second interim analysis of the trial needs to observe a +30% improvement in OS for trial to stop, which we believe may be a high bar. The final analysis will occur upon reaching 444 events, which we expect in 2015 and could report HR ~0.80 on final data, sufficient to drive a positive outcome.

Clinical Program Updates: NLNK initiated the Phase I trial of IDO inhibitor NLG919 in solid tumors in late 2013 and expects the preliminary data by YE 2014/early 2015. Preliminary data from the Phase II trial of indoximod + docetaxel in metastatic breast cancer is expected by YE 2014/early 2015. HyperAcute immunotherapy programs are progressing with the second Phase III trial (PILLAR) continuing to enroll patients with borderline resectable/locally advanced pancreatic cancer evaluating algenpantucel-L with FOLFIRINOX (data expected in 2016), a Phase IIb trial in NSCLC expected to report in 2014. NLNK disclosed that it has initiated Phase I trial of HyperAcute program in renal cell carcinoma in late 2013 and expects to launch the Phase I trial in melanoma in 2014.

Source: Jefferies/Amin, March 12, 2014
Oncology Indication: Pancreatic
Keyword: Clinical Trials/Pipeline

Back to Front Page

OncoGenex: Custirsen (Phase III/CRPC) SYNERGY Trial On-Track to Report Top-Line By Mid-2014; 2nd-Line Study (AFFINITY) Could Still Be Relevant Even If SYNERGY Fails

SYNERGY on track to report top line by mid-2014, complete data expected at an upcoming medical conference. After the recent announcement in February that the SYNERGY Phase III trial reached the pre-specified number of events for final analysis, management reiterated that the analysis of the trial results is on schedule and top-line OS data is expected to be released "by mid-2014". At our recent conference, management commentary appeared to suggest that the typical time lag of 2-3 months from reaching triggering event to data may be a reasonable expectation. Detailed analysis beyond the top-line OS data, which should include secondary endpoints such progression free survival (PFS) and prostate specific antigen (PSA) levels, will likely be presented at upcoming medical conferences in 2H14 (likely at ESMO, abstract submission May 7, 2014).

AFFINITY could still be of interest after SYNERGY. Management noted that SYNERGY by itself can support approval as there is an SPA, and in the case that SYNERGY failed to achieve the intended hazard ratio (HR), depending on how far the actual HR and p-values are from the pre-determined result, AFFINITY could either be used as a confirmatory trial for SYNERGY or considered independently for approval of custirsen in second-line prostate cancer setting.

The Phase II trials for apatorsen (OGX-427) are all on schedule, with BOREALIS-1 for bladder cancer expected to have an OS readout in 2H14. If BOREALIS-1 successfully meets the OS endpoint, management plans to meet with the FDA to discuss Phase III trial design and approval prospects on the basis of a single Phase III trial.

Source: Leerink/Liang, March 12, 2014
Oncology Indication: Prostate
Keyword: Clinical Trials/Pipeline

Back to Front Page

Peregrine: Continues to Seek Partner for Bavituximab, Possibly for Breast and/or Liver Cancer; Moving Forward in NSCLC

Management appears to be continuing to pursue a potential partnership for bavituximab (bavi'), though indicated a shift towards possibly breast and/or liver cancer. The need to partner NSCLC is less acute following the recent financing. Pending the outcomes of ISTs in liver, rectal, and 1st-line NSCLC, we could see a partnership for those indications. The cancer immunotherapy space continues to evolve rapidly and is complicated (as evidenced by recent Keystone abstracts), however we believe bavi' may prove well positioned to integrate with emerging treatment paradigms in the coming years and management is taking the right steps to enable these potential synergies.

The Phase III for bavi' in 2nd-line NSCLC (SUNRISE) has begun enrolling patients and management reiterated a target 2 year enrollment timeframe. The study will monitor biomarkers, we expect PD-1, EGFR status to be among those; however enrollment is not restricted by these markers. The remainder of calendar 2014 should help investors gain perspective on bavi's potential as we expect a number of ISTs to provide at least early data, including the planned combo study with Yervoy in metastatic melanoma.

Source: PiperJaffray/Duncan, March 10, 2014
Oncology Indication: Lung
Keyword: Clinical Trials/Pipeline

Back to Front Page

Onconova: Phase III Oral Rigosertib Trial in Lower-Risk MDS Planned for 2H14 with a Biomarker Component; Approval of IV Rigosertib in High-Risk MDS Unlikely

Details of the Phase III trial in lower-risk MDS will be announced following SPA discussion with the FDA. Onconova (ONTX) announced that it has designed a randomized, double-blind, placebo-controlled Phase III trial for oral rigosertib in lower-risk MDS patients who are transfusion-dependent and do not respond to erythropoietin-stimulating agents (ESAs). The company expects to finalize the details through the SPA process, which could take several months, and aims to initiate the trial in 2H14. A validation cohort of 20 patients is also being enrolled in a Phase II trial to assess the prognostic methylation marker, and ONTX intends to include this biomarker in the Phase III trial, pending discussion with the FDA. While we await the final trial design, we continue to view the chances of Phase III success in lower-risk patients to be largely independent of ONTIME failure in higher-risk MDS.

ONTX plans to start Phase II dosing of oral rigosertib in combination with azacitadine in first-line MDS in 2H14. Following the completion of the dose-finding portion of the Phase I/II trial, the company expects to begin an enrollment of an expanded cohort in the selected dose. A total of 40 patients will be enrolled in the whole study, with additional updates provided in the second half of this year.

FDA approval of IV rigosertib in high-risk MDS based on subgroup analysis of ONTIME does not seem probable to us. ONTX plans to hold discussions with the FDA to determine next steps following the failure of the ONTIME trial to show a survival benefit in the intent-totreat (ITT) population. In what the company described as a hierarchical analysis, a significant OS improvement was seen in a subset of 184 patients who had not responded to prior hypomethylating agents (HMA) (either failed or progressed while on treatment). However, we believe that the FDA will likely be quite strict in considering this analysis. Full data from the ONTIME trial is expected at ASCO 2014.

Source: Leerink/Liang, March 11, 2014
Oncology Indication: Hematologic
Keyword: Clinical Trials/Pipeline

Back to Front Page

Oxigene: Zybrestat & Avastin Combo Shows PFS Improvement in Phase II Ovarian Cancer; May Advance into Phase III, But Funding Could Be an Issue

In a Phase II trial on 107 patients, a zybrestat-Avastin combo beat out the Roche's drug alone in progression-free survival, Oxigene said, meeting its primary endpoint. The zybrestat arm failed to reach statistical significance in a secondary goal of objective response, and the company said it needs more time before it can pool data on the all-important overall survival. Oxigene didn't disclose safety results from the trial, which was sponsored by the National Cancer Institute.

After years of cash concerns and start-and-stop development, Oxigene has some momentum heading into a possible Phase III trial for zybrestat.

That's a welcome reversal of fortunes for Oxigene, which in 2011 had to hit the brakes on planned late-stage studies on zybrestat in anaplastic thyroid cancer because it simply couldn't afford to continue. The year before, the biotech sacked half of its staff and moved to focus on the drug's potential in non-small cell lung cancer, a study which has since been scuttled.

Despite the top-line Phase II promise, cash will likely still be an issue for Oxigene as it weighs zybrestat's future. The company closed 2013 with $7 million, and is unlikely to fund a Phase III trial alone.

Zybrestat is a vascular disrupting agent, designed to selectively seal off abnormal blood vessels and thereby starve tumors of the oxygen they need to survive. Oxigene's pipeline also includes OXi4503, a Phase I vascular disrupter for leukemia.

Source: FierceBiotech/Garde, March 12, 2014
Oncology Indication: Ovarian
Keyword: Clinical Trials/Pipeline