Today’s Intelligence at a Glance

1. **Infinity**: IPI-145’s (Phase III) Efficacy Unlikely to Outcompete Rivals, Trial Recruitment Likely to Be Slower-Than-Expected; May Have a Role in Smaller iNHL & PTCL Settings
   
   Wedbush/Nierengarten, March 5, 2014
   HealthACE Abstract
   
   **Indication**: Hematologic

2. **Gilead**: Betting Big on Sintuzumab with Phase II Studies Ongoing in Six Indications for Cancer and Fibrotic Diseases; However Targeting LOXL2 in Cancer May Face Significant Hurdles
   
   Bernstein Research/Porges, March 6, 2014
   HealthACE Abstract
   
   **Indication**: Multiple

3. **Johnson & Johnson**: Imbruvica Launch Early But Encouraging, Should Turn Profitable in 2015; Zytiga TRx Uptake to Remain Robust in 2014
   
   Wells Fargo Securities/Biegelsen, March 5, 2014
   HealthACE Abstract
   
   **Indication**: Multiple

4. **ArQule**: Tivantinib: Enrollment for METIV-HCC Trial Expected to Complete in Mid-2016; Roche’s MetMab Failure Could Impact Decision in NSCLC
   
   Leerink/Liang, March 6, 2014
   HealthACE Abstract
   
   **Indication**: Liver

5. **Bristol-Myers**: Reiterates Its Approach to Evaluate All Options of Immune Therapies: Mono, Combo, & Biomarkers
   
   Cowen and Company/Scala, March 5, 2014
   HealthACE Abstract
   
   **Indication**: Multiple

6. **AstraZeneca**: AACR Preview: Abstract Suggests Updated Phase I Data for 3rd Gen. TKI (AZD9291) in NSCLC
   
   Leerink/Fernandez, March 6, 2014
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   **Indication**: Multiple

7. **AstraZeneca**: Establishes a New Oncology Research Program with Korea Health Industry Development Institute; Will Support 12 Early-Stage Translational Projects
   
   Genetic Engineering & Biotechnology News, March 6, 2014
   HealthACE Abstract
   
   **Indication**: General

8. **BIND Therapeutics**: AACR Abstracts Reveal Details of AZN Collaboration and BIND-014 Phase I Data in Solid Tumor
   
   Cowen and Company/Schmidt, March 6, 2014
   HealthACE Abstract
   
   **Indication**: Solid Tumors

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**Additional Analysis**

**Study Name**

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<th>Design</th>
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**Ongoing Clinical Trials for IPI-145**

- **CLL**: Chronic Lymphocytic Leukemia
- **iNHL**: Indolent Non-Hodgkin Lymphoma
- **DOR**: Duration of Response
- **ORR**: Overall Response Rate
- **OS**: Overall Survival
- **PFS**: Progression-Free Survival

**Infinity - Annual Revenues Forecast**

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Sources: Company Reports; 5+ Brokerage Analyst Reports
Infinity: IPI-145’s (Phase III) Efficacy Unlikely to Outcompete Rivals, Trial Recruitment Likely to Be Slower-Than-Expected; May Have a Role in Smaller iNHL & PTCL Settings

Infinity’s (INFI) lead asset, IPI-145, is over two years behind rival therapies, and we do not believe it is sufficiently differentiated in efficacy to outcompete with drugs that will have an established market presence by IPI-145’s potential 2017 launch. In particular, we believe treatment of chronic lymphocytic leukemia (CLL), where INFI has begun a Phase III program, will become increasingly competitive.

Clinical trial recruitment into INFI’s CLL program is likely to be slower than expected, given the entry into the market of highly efficacious new therapies, such as Imbruvica and idelalisib. Given long duration of responses with these drugs, the available patient pool for INFI’s clinical trial will likely shrink dramatically, delaying recruitment into its pivotal DUO Phase III trial in relapsed/refractory CLL.

We do, however, see a role for IPI-145 in the smaller indolent non-Hodgkin’s lymphoma (NHL) and peripheral T-cell lymphoma (PTCL) settings. The strong clinical responses IPI-145 demonstrated in PTCL is tempered by the small size of the market, while expected approval for both Imbruvica and idelalisib in the iNHL setting before IPI-145 is likely to limit the commercial opportunity for ‘145.

A partnership for IPI-145 is possible, but in our view, doesn’t change the game. An alternative to an equity financing would be to find a pharmaceutical partner to share development costs for ‘145. While this would defray the multiple financings we have modeled, the upside from commercialization would be capped, leading to the same price target of $10, according to our estimates.

Management has guided to a 2014 cash burn of $170-$180M, and a similar burn rate is likely in 2015 given the expenses associated with running multiple clinical studies. We do not anticipate a catalyst likely to increase share price significantly before the company will require a dilutive equity financing in 2015 (in addition to drawing down its $100M credit line). Given the competition in the space, we believe that the clinical catalysts in 2015 are likely to be delayed.

Oncology Indication: Hematologic
Keyword: Clinical Trials/Pipeline
Gilead: Betting Big on Simtuzumab with Phase II Studies Ongoing in Six Indications for Cancer and Fibrotic Diseases; However Targeting LOXL2 in Cancer May Face Significant Hurdles

Simtuzumab targets LOXL2, an enzyme involved in collagen remodeling. The drug is being tested in several cancers but also in idiopathic pulmonary fibrosis (IPF) and fibrosis associated with non-alcoholic steatohepatitis (NASH), two indications with high unmet need. These two indications have recently caught investors' attention as Intercept (ICPT) and InterMune (ITMN) have enjoyed explosive ~500% and ~170% market cap growth respectively after the announcement of positive results in NASH and IPF. Should animal model data for simtuzumab be recapitulated in the clinic, our expert consultants believe this drug could complement ICPT's and ITMN's agents in the respective diseases. Beyond the potential utility of simtuzumab in combination with other anti-cancer agents in Gilead's pipeline, it is not implausible that the company may deploy some of the substantial near term cash inflows towards acquiring smaller players such as ICPT or ITMN to better position themselves in fibrotic diseases.

Gilead is betting big on simtuzumab, phase II studies ongoing in six indications. The company obtained the rights to simtuzumab (formerly GS-6624/AB0024) with the acquisition of privately held Arresto Therapeutics in December 2010. The humanized anti-LOXL2 antibody simtuzumab had demonstrated promising anti-tumor and anti-fibrotic efficacy in preclinical models. As Gilead took over simtuzumab development, the oncology program started by Arresto was expanded to three phase II studies in pancreatic and colon cancer and in myelofibrosis. Additional randomized double blind phase II studies are testing this antibody in fibrotic diseases (idiopathic pulmonary fibrosis, advanced fibrosis associated with non-alcoholic steatohepatosis and primary sclerosing cholangitis, PSC) and in patients with liver fibrosis caused by HIV/HCV coinfection. This broad phase II program is targeting enrollment of ~1,700 patients, suggesting that Gilead has a high level of confidence in the potential of this product.

Simtuzumab appears best suited to development in fibrotic diseases rather than cancer indications. The rationale of targeting LOXL2 in fibrosis is that this enzyme functions as a key mediator of collagen cross-linking. Targeting the collagen cross-linking mechanism may help clear fibrotic tissue in liver, bile duct or lung. Our expert consultants believe that this approach may be complementary to other therapies currently in development (such as ITMN's Esbriet in IPF or ICPT's obethicolic acid in NASH). Gilead may get an early read into the activity of simtuzumab in NASH patients with advanced liver fibrosis or cirrhosis and in patients with PSC as the primary endpoint of these three phase II studies is change in collagen levels as measured by biopsy. According to management's guidance, the two NASH studies are expected to complete enrollment by mid-2014 and report out before mid-2015.

Targeting LOXL2 in cancer may face significant hurdles. LOXL2 is abundantly present in the microenvironment that surrounds tumor cells known as stroma, in colorectal, pancreatic and gastric cancers. Its collagen-modifying properties are hijacked to remodel the tumor environment and help promote the survival of cancer cells. High levels of LOXL2 are generally associated with a higher propensity for metastasis, higher tumor grade and poorer prognosis of these cancers. However, our expert consultants believe that inhibition of LOXL2 may be offset by de novo activation of other alternative pathways. Based on the scientific literature and this opinion, our outlook about the likely efficacy of simtuzumab in pancreatic and colon cancer is tepid at best. Our advisers suggest that the product is much better suited for development in cancers where clinical manifestations are linked to fibrotic progression, such as myelofibrosis or neuroectodermal gastrointestinal tumors. A phase II study of simtuzumab +/- Jakafi is ongoing in myelofibrosis. Should simtuzumab demonstrate any signs of activity in MF in combination with Jakafi, it is likely that Gilead may move on to test in combination with their in-house JAK agent, momelotinib. We expect initial data for this combination to report out at ASH in December 2014.

Source: Bernstein Research/Porges, March 6, 2014
Oncology Indication: Multiple
Keyword: Clinical Trials/Pipeline
Johnson & Johnson: Imbruvica Launch Early But Encouraging, Should Turn Profitable in 2015; Zytiga TRx Uptake to Remain Robust in 2014

Most of Johnson & Johnson’s (JNJ) key drugs launched since 2011 performed in-line with or better than expected in 2013, with outperformers including Zytiga (prostate cancer), Xarelto (DVT, SPAF, VTE treatment) and Stelara (plaque psoriasis). We believe the recently launched Olysio (simeprevir) for Hep C and Imbruvica (ibrutinib) for MCL in the U.S. will also be focal points for investors this year. In our view, the new pharma products launched in recent years, if successful, should help to drive JNJ’s pharma sales growth in the long run. We expect sales for JNJ’s portfolio of new products to grow to over $6.0B or nearly 40% of JNJ’s U.S. pharma sales in 2014.

**Imbruvica (ibrutinib) launch early but encouraging:** R/R CLL U.S. approval should accelerate uptake: The drug was FDA approved for relapse-remitting (R/R) MCL (mantle cell lymphoma) in November 2013 and was promptly launched by JNJ’s partner Pharmacyclics (PCYC). The subsequent R/R CLL (chronic lymphocytic leukemia) approval in mid-February presents a larger market opportunity and should accelerate commercial ramp of the drug in 2014. OUS, JNJ filed for R/R MCL and CLL in October 2013, suggesting approval possible in later 2014.

Recall that PCYC books all U.S. sales while JNJ books OUS sales and the partners split profits 50-50 on a global basis. PYCY reported 4Q13 Imbruvica end-user sales of $10MM ($14MM including inventory stocking) but did not provide 2014 guidance due to early nature of the launch. Even prior to R/R CLL approval, Imbruvica usage was estimated one-third in R/R CLL off-label and two-thirds in R/R MCL (based on bottle size). For PCYC, Wells Fargo biotech analyst Matthew J. Andrews estimates U.S. Imbruvica sales of $240MM in 2014 growing to $452MM in 2015 and nearly $1.2B by 2017 (probability weighted for different indications). For JNJ, we assume that the drug will turn profitable in 2015 and conservatively estimate that JNJ will record its share of U.S. profits as revenue of $21MM in 2015 growing to $141MM in 2017. OUS, we assume R/R MCL/CLL approvals in Europe in late 2014 with sales of $8MM growing to $275MM in 2017.

**Zytiga TRx uptake expected to remain robust in 2014:** U.S. sales and Rx growth for the prostate cancer drug in 2013 was driven by increased use in pre-chemo setting. Third-party data continued to point to solid share gain by Zytiga for pre-chemo use despite share loss, as expected, in post-chemo setting amid increasing competition such as MDVN/Astella’s Xtandi. We expect Zytiga’s growth momentum to remain strong in 2014 with further pre-chemo uptake despite Xtandi’s expected approval in pre-chemo use in 2H14. We estimate U.S. Zytiga sales growing to $958MM in 2014 from $750MM in 2013 and peaking at $1.2B in 2016 (assuming generic competition starting in 2017 following patent expiration). On its 4Q13 earnings call, MDVN guided to 2014 U.S. Xtandi sales of $500-535MM assuming mid-single-digit qtr/qtr sales growth until pre-chemo approval in late Q3. Midpoint of the sales guidance range of $517MM is just above annualized 4Q13 U.S. sales of $504MM, although MDVN management pointed to certain headwinds such as Medicare donut and inventory destocking expected in 1Q14.

Source: Wells Fargo Securities/Biegelsen, March 5, 2014
Oncology Indication: Multiple
Keyword: Management/Strategy/Financials
ArQule: Tivantinib: Enrollment for METIV-HCC Trial Expected to Complete in Mid-2016; Roche’s MetMab Failure Could Impact Decision in NSCLC

Development continues in HCC, METIV study expected to complete enrollment in mid-2016. Management provided an update on its tivantinib program in HCC, highlighting the two ongoing Phase III trials. In the US and EU, the METIV-HCC trial is progressing using the 120 mg tablet formulation (which has shown comparable plasma exposure to the 240 mg capsule with a neutropenia rate deemed acceptable by the data monitoring committee). Management estimated that enrollment should be completed by mid-2016, but would depend on screening failure rates. There is an interim efficacy analysis planned after approximately 60-65% events, which the company expects to occur shortly before the completion of enrollment. Partner Kyowa Hakko Kirin also initiated the JET-HCC trial in January, which aims to enroll 160 MET-high patients in Asia who have been previously treated with a Nexavar (sorafenib)-containing regimen. This trial has progression-free survival as the primary endpoint, while METIV-HCC is using overall survival.

MetMab failure could impact decision to move tivantinib forward in NSCLC. ArQule had previously stated that it would need to evaluate the rapidly changing environment in NSCLC before deciding whether to pursue further development of tivantinib in this indication, specifically citing upcoming data from Roche’s MetMab, the PD-1 inhibitors, and new agents for EGFR mutants. While management stated that the full results of the MetMab trial will need to be explored to determine the impact the failure will have on this decision, we believe this makes it more likely that ARQL will move forward with tivantinib in NSCLC than if the data had been positive. The company is also awaiting full results from the ATTENTION study (expected at a medical meeting this year) and a subgroup analysis of the MARQUEE trial based on EGFR status (timing uncertain, but possibly by the end of 2014) to further inform this decision.

Source: Leerink/Liang, March 6, 2014
Oncology Indication: Liver
Keyword: Clinical Trials/Pipeline
Bristol-Myers: Reiterates Its Approach to Evaluate All Options of Immune Therapies to Determine Optimal therapy for Particular Tumor: Mono, Combo, and Biomarkers

Management indicated that while they are still evaluating all the data from the Phase I trial of Nivolumab in various combinations (12 different arms that include ipi, TKI, Avastin, others), they now expect to initiate a Phase III trial of nivo + ipi in NSCLC by year end 2014. Phase III mono trials of nivo in 1st-line NSCLC are well underway and report in H2:14. Data from the Phase II trial in stage 3 squamous NSCLC (n=120) will be available in H1:14.

The company reiterated its approach to Immune Therapy will be to evaluate all options – mono, combo, biomarkers – to determine optimal therapy for a particular tumor. The endpoint for many studies is overall survival. Bristol currently is evaluating nivo in 11 different tumors with 35+ studies in progress, and is looking at other immune-acting targets as well, including LAG3, anti-KIR, anti-CD137, and has a preclinical effort on IDO inhibition. BMY knows of no significant differences between Yervoy and AZN’s similar drug. BMY’s PD-L1 program targets chronic virologic conditions such as HIV and hepatitis B. BMY notes that both its PD1 and PD-L1 are well behaved molecules and are somewhat similar. BMY’s PD1 partner Ono filed PD1 in Japan.

Source: Cowen and Company/Scala, March 5, 2014
Oncology Indication: Multiple
Keyword: Clinical Trials/Pipeline
Abstract suggests AACR will include updated Phase I data for 3rd Gen. TKI, AZD9291. Presentation #4744, though focused on the discovery and development of AZD9291, suggests that it will include "an update of recent data from ongoing AZD9291 Phase I clinical studies in NSCLC patients," though the company has not been able to confirm novel clinical data will be available. While additional clinical information would not be surprising given MEDACorp KOLs' feedback that they expect data for AstraZeneca (AZN) and Clovis' (CLVS) 3rd Gen tyrosine kinase inhibitors (TKIs) at "every meeting possible" in 2014, in either case, we continue to emphasize the impressive pace of development for these agents - AZN followed 26 patients of data at ESMO 2013 (9/6 cutoff) with 34 patients of data at IASLC (9/27 cutoff). We continue to be bullish on the class and are also interested in early research suggesting potential combinations with other pathway inhibitors (Presentation #1722).

Further review of tremelimumab in mesothelioma. Though full Phase II data are not expected until ASCO, Presentation LB-228 will focus on the pharmacokinetics of tremelimumab in subjects with unresectable malignant mesothelioma and may continue to establish clinical faith in this until-recently overlooked anti-CTLA4 antibody ahead of monotherapy (in mesothelioma) and combination therapy (with MEDI4736 in NSCLC) at ASCO.

Clinical trial symposium will discuss moxetumomab in pediatric acute lymphoblastic leukemia (ALL). Recall impressive Phase I efficacy (88% response rate; 55% complete response rate) in niche hairy cell leukemia moved the compound directly to Phase III in that indication. Thus the antibody drug conjugate's (ADC's) effect in broader indications (Presentation CT230) could, if promising, continue to build the foundation for Medimmune's ADC platform.
AstraZeneca: Establishes a New Oncology Research Program with Korea Health Industry Development Institute; Will Support 12 Early-Stage Translational Research Projects

AstraZeneca (AZN) signed a memorandum of understanding with the Korea Health Industry Development Institute (KHIDI) to establish a new Oncology Research Program, under which AZN will support 12 early-stage translational research projects headed by Korean investigators focused on cancer.

AZN and KHIDI will be inviting oncology investigators based at Korean research hospitals to submit research project applications. Proposed topics should be focused on oncology translational research, and the deadline for pre-proposals, which should be submitted to KHIDI's website, is April 15th. AZN's Oncology iMed will review and select four pre-proposals by May, and the researchers who make the shortlist will each receive funding for their research from AZN through their institutes and also gain priority access to a list of AZN compounds for preclinical testing. Those researchers will also have the opportunity to collaborate, network, and get advice with AZN's own oncology scientists.

AZN, which already has open innovation collaborations in the U.S., U.K., and Taiwan, says it is thrilled to bring its open innovation platform to Korea, where cancer research is sorely needed. "Cancer is the number one cause of death in Korea and the incidence rate is growing," Liz Chatwin, country president of AstraZeneca Korea, said in a statement. "We hope this program will provide momentum to develop new medicines to help improve the health of cancer patients in the future – both in Korea and globally."

Source: Genetic Engineering & Biotechnology News, March 6, 2014
Oncology Indication: General
Keyword: Partnerships/Business Developments
BIND Therapeutics: AACR Abstracts Reveal Details of AZN Collaboration and BIND-014 Phase I Data in Solid Tumor; Early Data Support Accurins to Provide for Differentiated Therapeutic Profile

Early data suggest BIND-014 is differentiated from docetaxel, and ongoing trials could produce data in H2:14 to support an improved efficacy profile. Should BIND-014 achieve its target profile of superiority to docetaxel, the rewards to Bind, which owns 100% rights, could be enormous: docetaxel sales peaked at over $3B in 2009. Following a September 2013 IPO that raised over $70MM in gross proceeds, Bind has $81MM in cash, enough to fund operations well into 2015.

Aurora B Kinase: BIND began a partnership with AstraZeneca (AZN) to develop an accurin in April 2013. Today, BIND unveiled barasertib (an Aurora B kinase inhibitor prodrug; AZD1152) as the active pharmaceutical ingredient along with preclinical data to be presented at AACR. Barasertib previously completed a randomized Phase 2 trial in elderly AML. In 2010, Barasertib demonstrated a statistically significant improvement in overall CR rates and trended towards an overall survival benefit following 7 days of continuous infusion. However, high levels of neutropenia and stomatitis were detected. Consequently, AZN collaborated with BIND to improve the therapeutic index via accurization.

In a nude rat tumor model, AZD1152-hQPA accurins increased the PD inhibition of p-histone H3, improved the anti-tumor effect and reduced the bone marrow pathology compared to barasertib. Therefore, in an animal model BIND's accurin platform has meaningfully impacted barasertib's therapeutic index. Consequently, BIND's platform has been further validated and we are hopeful that AZ will exercise its option, providing BIND with an additional clinical candidate.

BIND-014 Q1W: An abstract for the Phase I Q1W administration of BIND-014 was also released. Dose limiting toxicities of mucositis and febrile neutropenia occurred at 40mg/m2. This compares to an MTD of 60mg/m2 for BIND-014's Q3W regimen. Of the 28 enrolled patients, 2 PRs were observed along with 4 disease stabilizations >12 weeks. Therefore, Q1W MTD increases the average weekly exposure to docetaxel compared to free docetaxel or Q3W but no major effect on efficacy was observable in this limited data set.

Source: Cowen and Company/Schmidt, March 6, 2014
Oncology Indication: Solid Tumors
Keyword: Clinical Trials/Pipeline