BioInvest
Medical Technology Stock Letter

MTSL Issue 876

April 26, 2018

UPDATES: ACAD, ALKS, BMRN, INCY, IONS, MDCO, NKTR

IN THIS ISSUE: IONS/BIIB Neuro Program – BIIB Commits Another $Billion

Since Last Issue: BTK: -1.8%; NBI: -1.3%; Model Portfolio: -9.4%; Trader's Portfolio: -14.4%

BIOTECH SECTOR ANALYSIS

SENTIMENT — It Is What It Is

As the IBB approached resistance levels at the last Issue, it was up to the industry specific fundamentals to give that and the other biotech indices a helpful boost to break above their respective moving average. Unfortunately, that did not happen after some disappointing clinical, regulatory and earnings events having occurred, and biotech stocks once more retreated along with the broader market (see IBB below). Therefore, we remain stuck in a trading environment with a negative bias. Despite the increase in the amount of cash and funds available for investment, there has been no follow up takeovers to the NVS/AVXS deal. Although Japan's Takeda has made a $64 billion offer for Shire, to us that is less of a classic biotech M&A transaction and more of a Big Pharma deal. The beginning of earnings, however, may have started a rotation back into the Big Caps.

Bluebird bio's (BLUE) interim data was published in the *New England Journal of Medicine (NEJM)* from two separate two-year clinical studies investigating the potential for LentiGlobin gene therapy to eliminate or reduce chronic blood transfusions in patients with transfusion-dependent β-thalassemia (TDT). Both studies, Northstar (HGB-204), which recently was completed, and HGB-205, which is ongoing, are evaluating the safety and efficacy of one-time treatment with LentiGlobin gene therapy and the interim results showed that a majority of the 22 patients in the two Phase 1/2 studies followed for two years or longer remained free from transfusions.

Interim results also showed that all but one patient with a non-β0/β0 genotype (12 of 13 patients) stopped receiving regular red blood cell (RBC) transfusions, with a median time since last transfusion of 27 months. In the nine patients with a β0/β0 genotype or similar severity, median transfusion volume decreased by 73 percent, and RBC transfusions were stopped in three patients. Treatment with

ASCO abstract titles were also released last week (4/25). We are closely monitoring the IBB, which still is on the downward trend, although sentiment may have hit a near-term trough. The 100 mark (touched on 4/6) has been the recent bottom level, so traders will be eyeing the indices' ability to hold support there before turning around. Q1:18 results appear to have been the needed stimulus.

Even before the mixed BIIB Q1:18 results were announced (Biogen is the first of the Big Caps to announce earnings), in our view, expectations for Big Bio results were extremely low. The fact that BIIB shares have bounced sharply off a rather weak opening after the quarterly call provides some solace that all is not lost and, maybe, the worst might be behind. AMGN and ALXN have followed suit with a solid first quarter reports. Additional Q1 calls from CELG and GILD will give further insight into current corporate updates, strategies for the changing global marketplace amid President Trump's recent drug pricing proposals. As the market digests these reports and low P/E multiples, the burgeoning cash positions has provided these undervalued leaders with a bid in this crazy market. Big Bios sentiment may finally be improving.

The FDA gave a surprising about face for MTSL's ALKS depression drug, ALK-5461, allowing the LentiGlobin requires an autologous stem cell transplant. The safety profile of LentiGlobin has been consistent with myeloablative conditioning with the chemotherapy agent busulfan. *Our beta-thal play is MTSL's SGMO, partnered with Bioverativ/SNY, where SNY recently mentioned its increasing priority of that program – expected to dose the first patient in this current quarter (https://clinicaltrials.gov/ct2/show/NCT03432364?term=Bioverativ+Beta-thalassemia&rank=1).*

The FDA placed EPZM's tazemetostat on a partial clinical hold. On the data side, PRTA's NEOD001 for AL amyloidosis was discontinued after a failed Phase IIb trial and the Phase III trial was also shutdown after an independent assessment of futility.

DEALS – IONS/BIIB Expand Neuro Deal

Investors' are beginning to recognize the breadth of the collaboration between Biogen and Ionis – as the compounds associated with the deal will now comprise the brunt of BIIB's long-term neuro pipeline (see IONS below). Ironically, investors' have warmed to BIIB's stock recently based on the pipeline driven by IONS.

REGULATORY – GWPH AdCom Unanimous Recommendation for "Pot For Seizures"

The FDA Peripheral and Central Nervous System Drugs Advisory Committe (PCNSDAC) reviewed GWPH's lead drug Epidiolex (cannabidiol) for approval in orphan seizure disorders Lennox-Gastaut and Dravet syndromes (LGS/DS). With impressive efficacy, use of blood monitoring to identify liver enzyme elevations and positive impact on patient/caregiver quality of life, the AdCom recommended Epidiolex for approval in a unanimous 13-0 panel vote ahead of the June 27 PDUFA and noted that they "have not identified any obstacles to approval." Final

Company to move forward with it's application. Interestingly, as the agency had requested additional clinical trials when issuing the recent RTF letter, the two-week turnaround included no new trial requests and also included a PDUFA date (see ALKS below). On the other hand, LLY and MTSL's INCY's baricitinib got a lukewarm response from an Advisory Committee, recommending the lower of two dosages (2mg yes, 4mg no) to treat rheumatoid arthritis. Both doses have been approved in the EU and Japan, so the domestic home stretch of that drug's regulatory path has not gone smoothly (see INCY below).

DATA – AAN, World Congress & ASCO Abstract; AMGN's Migraine Drug Looks Great

The American Academy of Neurology (AAN) took place this week and MTSL recommendations IONS presented positive HTT-Rx data from their Huntinton's disease program and ACAD presented positive safety data for Nuplazid (see ACAD below).

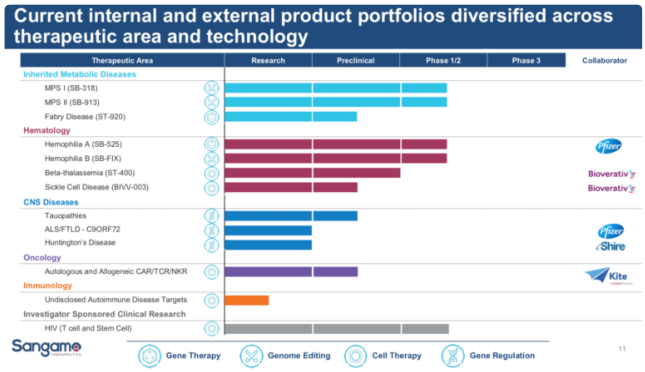
Amgen announced final data from its Phase IIIb LIBERTY clinical trial of Aimovig (erenumab), with positive results likely to lead to a blockbuster drug for migraine sufferers. Aimovig decreased migraine days by about 50% in about a third of patients receiving it. In the trial, 246 patients who had two to four previous treatments that didn't work were randomized to receive monthly subcutaneous injections of either 140 mg of Aimovig or placebo for 12 weeks.

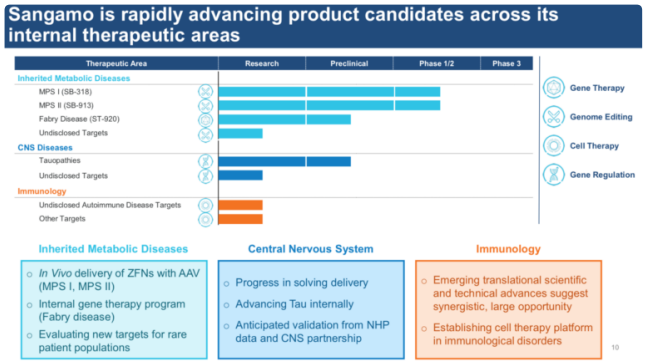
Patients treated with Aimovig also met all secondary endpoints, including reduction in monthly migraine days, decreased migraine-specific drug use per month, a reduction of 75% or more in monthly migraine days, and a 100% reduction in monthly migraine days. The patients also showed improved physical function and ability to conduct everyday activities as measured by the Migraine Physical Function Impact Diary (MPFID).

approval will lead to what is likely to become the first approved cannabinoid therapy.

FINANCING – SGMO Goes To Fund Pipeline With GILD's Participation

SGMO raised $200 million to additionally pay for its wholly-owned R&D pipeline. We believe investors have yet to realize the true power of the ZFNs and the depth of their therapeutic reach. With GILD taking up to $50 million of the deal, SGMO is extremely well-funded for the present and future, as clinical data nears (mid-year) and the pipeline expands for the early but underappreciated CNS and autoimmune programs (see below).





The PDUFA date is May 17, 2018. The European Medicines Agency (EMA) has validated the Marketing Authorization Application (MAA) for the drug as well.

Clinical Trials Watch

Relevant New Studies or Changes Posted on ClinicalTrials.gov for our MTSL Portfolio and/or Related Comp

ABBV – Expanded Access to Rovalpituzumab Tesirine

CELG/JUNO – BCMA-Specific CAR T-Cells Combined With a Gamma Secretase Inhibitor (LY3039478) Multiple Myeloma

IONS – Study of ISIS 681257 in Patients With Renal Impairment Compared to Healthy Patients

NCI/INCY – Phase I/II Study of Immunotherapy Combination BN-Brachyury Vaccine, M7824, ALT-803 a

PCRX – Post-Mastectomy Analgesia Using Exparel (Liposomal) Versus Standard Bupivacaine or Place

PCRX – Hip Fracture Exparel Administration Trial Capsule During Hemiarthroplasty (HEAT)

REGN – PCSK9 Inhibition in Patients With Symptomatic Intracranial Atherosclerosis

REGN – Effect of Evolocumab on Coronary Endothelial Function (EVOLVE)

Company Updates

UPDATES: ACAD, ALKS, BMRN, INCY, IONS, MDCO, NKTR

Acadia Pharmaceuticals **announces presentation of clinical experience data for NUPLAZID 2018 AAN**

- Researchers at Vanderbilt University Medical Center performed a retrospective chart review of patients treated with

ACAD – Both Acadia and The FDA Respond to CNN Hit Piece

ACAD has responded to a second bear attack on CNN that questions the safety of ACAD's Nuplazid and the FDA for approving the drug. The company has issued the following comments and data at AAN.

- "ACADIA's top priority has been, and continues to be, patient safety. NUPLAZID was approved and launched in 2016. As the manufacturer of a newly launched drug, we are routinely in contact with the FDA regarding requests for additional information on NUPLAZID, including post-marketing safety surveillance information as part of the FDA's ongoing safety monitoring.
- In a statement released to the media on April 10, the FDA stated, "The FDA continues to monitor adverse events reported with NUPLAZID that are submitted to the FDA Adverse Event Reporting System (FAERS).
- We have noted that the cases typically involve geriatric patients with advanced-stage Parkinson's disease, as well as numerous medical conditions, who are frequently taking concomitant medications with risks for serious adverse events, including death.
- Based on these data, the FDA has, at this time, not identified a specific safety issue that is not already adequately described in the product labeling."

NUPLAZID. In this study, the researchers identified a total of 102 patients who were prescribed NUPLAZID between May 2016 and March 2018. Data from the study show:

- 70% of all patients treated with NUPLAZID reported clinical improvement, while 88% of patients treated longer than four weeks improved.
- 67% of patients have remained on NUPLAZID for an average of 10+ months.
- Only 11% of patients were unable to tolerate NUPLAZID due to adverse events.
- NUPLAZID was effective in both treatment naïve and prior antipsychotic failure patients.
- For those who failed NUPLAZID, improvement with a subsequent antipsychotic was uncommon.
- There was no increase in mortality detected in users of NUPLAZID.
- 6 of the 88 patients treated with NUPLAZID died.

ACAD is doing about all they can do given the pressure from the recent CNN articles by releasing the above comments and data at AAN. The company is also actively communicating with the FDA to resolve the situation. It appears to us that CNN backed the FDA into a corner and the agency had to respond. Our expectation is the drug remains on the market due to its efficacy and the safety profile will be exonerated.

RECOMMENDATION

ACAD **is a BUY under 35 with a TARGET PRICE of 45**

- On April 25, the FDA stated that its evaluation does not mean the Agency has determined the medicine has a new risk and does not suggest healthcare providers should not prescribe it nor that patients should stop taking the medication. The Agency also has confirmed this statement does not represent a change from the safety review and monitoring activities the FDA referred to in its statement of April 10. As always, we will continue to work with the FDA and medical community to answer any questions related to NUPLAZID.
- Because NUPLAZID is distributed through a specialty distribution channel, we have frequent (in most cases monthly) contact with patients and caregivers through our distribution partners.
- This increased interaction naturally results in dramatically higher adverse event collection and reporting compared to products without such a distribution method.
- Approximately 93% of the reported adverse events associated with NUPLAZID are considered “solicited” due to this direct interaction with patients and caregivers, while only approximately 7% of these events are considered “spontaneous” reports, which are voluntary reports originating from consumers or healthcare professionals. In contrast, most other antipsychotics are distributed through retail channels, which rely almost entirely on “spontaneous” reporting. Consequently, only a small fraction of actual adverse events are collected for these drugs.

ALKS recently held the quarterly conference call and provided an interesting update on their IL-2 drug candidate, ALKS-4230, that is in the same drug class as NKTR-214. ‘4230 is currently in a Phase I/II dose escalation and is about to be tested in combination with PD-L1s where we have seen

ALKS — FDA Reverses Course and Accepts ALKS' NDA For '5461

In a completely unexpected turn of events, ALKS announced that the FDA has accepted the ALKS-5461 NDA for review for major depressive disorder (MDD). It was just two weeks ago that the agency issued a strongly-worded Refuse to File (RTF) letter. '5461 now has a target PDUFA date of 1/31/2019 and an AdCom meeting is expected in Q4:18. The company remains confident in the overall profile and potential approvability of '5461 while providing little additional detail as to what was discussed with FDA that led to the 180-degree turnaround. The unexpected positive development is a clear win for ALKS as they were strong in their own defense two weeks ago. In our view, the approvability of '5461 has improved versus two weeks ago despite the initial negative reaction from the FDA. ALKS' experienced management has already "pulled a rabbit out of the hat" by getting the FDA to reverse course so quickly. We are still cautious that ALKS can "pull *another* rabbit in the hat" and can get '5461 over the goal line, but the rapid about face by the FDA is no doubt a positive. The overall data package is still mixed at best, so we will look for additional information on the '5461 filing.

significant responses with NKTR-214. Importantly, ALKS has developed a sub-q version of '4230 as the current version has been slow to enroll patients due to the onerous 5 day IV infusion. We are intrigued by the potential for '4230 and its unique mechanism of action.

RECOMMENDATION

ALKS **is a BUY under 55 with a TARGET PRICE of 75**

A Phase /II study of the 6e13 vg/kg high dose (n=10) in AAV5 seropositive patients with pre-existing antibodies (<10%) is set to begin this quarter. Enrollment in the 6e13 vg/kg cohort is ongoing expected to complete by mid-2018

BMRN – Q1 Results Solid – Pegvaliase PDUFA May 28

Biomarin reported Q1 revenue of $373 million, above consensus of ~$350 million. The difference was due to a change in revenue recognition for Aldurazyme. The Company is set to deliver several clinical and regulatory catalysts including updated BMN 270 Ph1/2 gene therapy data in hemophilia A at the World Federation of Hemophilia 2018 World Congress (May 20-24); pegvaliase AdCom, subsequent US approval (May 28 PDUFA); and additional pipeline updates (first look at Phase I/II trial of BMN 290 in Friedreich's ataxia and potentially PKU gene therapy and Phase III val-rox (hemophilia A gene therapy) and vosoritide (achondroplasia) results.

Pegvaliase May 28 PDUFA

Approval for pegvaliase after the PDUFA date is highly likely. The Company notes that at launch a bolus of ~200 patients will shift from clinical trials to commercial drug. BMRN estimates ~11,400 adult PKU patients exist in the U.S., of which 2.500 will be initially targeted. Of the 125 PKU clinics, 32 have been involved in pegvaliase studies, and BMRN will apply their experience to the remaining ~90 inexperienced centers. Consensus forecasts are ~$20 million for 2018. Management expects pegvaliase to be priced at a modest premium to current adult Kuvan of ~$150,000.

Gene Therapy Momentum Building

followed shortly by the 4e13 vg/kg dose – with press releases to be issued. *We look to val-rox Phase II one-year follow up data at the 4e13 vg/kg dose and two-year follow up data at the 6e13 dose at the World Federation of Hemophilia 2018 World Congress (May 20-24).* BMRN expects to file an IND for its first PKU gene therapy candidate in 2019, which has demonstrated pre-clinical data in mice supporting normalization of Phe levels without hypophenylalanemia out to 53 weeks at the last observation.

Pipeline Progresses in 2018; Key Pipeline for 2019

The global Phase III vosoritide for achondroplasia (dwarfism) program will complete enrollment in mid-2018 (the feeder study in the U.S. is fully enrolled) with top-line data expected in H2:19. Updated BMN 250 Phase I/II data in MPS3B will help guide the development and regulatory strategy. BMN 250 may have a best-in-class profile given it is the only clinical drug that is able to achieve normalization of CSF GAG levels vs. ERT and gene therapies that achieve partial knockdown. IND filing for BMN 290 in Friedreich's ataxia is expected in H2:18 and enter the clinic by YE:18.

Solid momentum continues. BioMarin has historically been a buyer of technology etc, but we believe in this current environment, they can always be bought themselves.

RECOMMENDATION

BMRN **is a BUY under 100 with a TARGET PRICE of 130**

BMRN's gene therapy investment is growing, led by their hemophilia A compound, BMN 270. Currently underway are two studies (n=40 per study), a 52-week trial for filing with a 4-year follow-up; primary endpoint is the FVIII level, with secondary endpoints of annualized bleed rate and FVIII use.

INCY – Incyte/LLY's Baricitinib Receives Split Decision From FDA, Yea 2mg Dose, Nay 4mg Dose; Upcoming ASCO Meeting May Offer Some Help

INCY got a split decision from the FDA at their recent panel meeting with a 10-5 vote in favor for the 2-mg dose and a vote of 10-5 against the 4-mg dose. While the panel voted overwhelmingly in favor of the drug's efficacy—14-1 on 2mg and 15-0 on 4mg—they split on safety, voting against the 4mg dose and in favor of the 2mg dose. In our view, Bari still has potential to be a significant drug given that it is a pill that has shown to be as effective as powerful biologics (Humira) that are delivered as injectable drugs. The PDUFA date is expected in June and although the panel's lukewarm vote has cast a shadow on bari for now, the final approval will at the very least approve the 2 mg dose. The fact both bari doses are approved in the EU and Japan gives us some cautious optimism that Lilly can get both doses through. Either way, the stock now reflects little value for bari.

Immuno-oncology abstracts

Clinical Data from the DeCidE[1] trial: Assessing the First Combination of DPX-Survivac, Low Dose Cyclophosphamide (CPA), and Epacadostat (INCB024360) in Subjects with Stage IIc-IV Recurrent Epithelial Ovarian Cancer. (Abstract #5510, clinical science symposium)

Sunday, June 3, 2018, 9:45 – 11:15 a.m. CT, S406

Epacadostat (E) Plus Pembrolizumab (P) Versus Pembrolizumab Alone in Patients (pts) with Unresectable or Metastatic Melanoma: Results of the Phase 3 ECHO-301/KEYNOTE-252 Study. (Abstract #108, clinical science symposium)

Sunday, June 3, 2018, 9:45 – 11:15 a.m. CT, Hall D1

Pilot Trial of an Indoleamine 2,3-dioxygenase-1 (IDO1) Inhibitor Plus a Multipeptide Melanoma Vaccine in Patients with Advanced Melanoma. (Abstract #3033, poster session)

Monday, June 4, 2018, 8:00 – 11:30 a.m. CT, Hall A, Poster Board #247

Epacadostat Plus Nivolumab for Advanced Melanoma: Updated Phase 2 Results of the ECHO-204 Study. (Abstract #9511, poster discussion session)

ASCO Might Show More INCY Bright Spots Than ECHO-301

INCY data at ASCO 2018 will include oral presentations from a Phase 1 study of ruxolitinib (Jakafi®), lenalidomide and methylprednisolone in patients with relapsed and refractory multiple myeloma, the DeCidE1 trial assessing the combination of DPX-Survivac, cyclophosphamide and epacadostat in patients with recurrent epithelial ovarian cancer, and the Phase 3 ECHO-301/KEYNOTE-252 study evaluating the safety and efficacy of epacadostat in combination with pembrolizumab in patients with unresectable or metastatic melanoma.

Select key abstracts and presentations include:

Targeted therapy abstracts

A Phase 1 Trial of Ruxolitinib, Lenalidomide, and Methylprednisolone for Relapsed/Refractory Multiple Myeloma Patients. (Abstract #8005, oral abstract session)

Friday, June 1, 2018, 2:45 – 5:45 p.m. CT, E450

Monday, June 4, 2018, 1:15 – 4:45 p.m. CT, Hall A, Poster Board #338; Discussion at 4:45 – 6:00 p.m. CT, E451

Full session details and data presentations at the ASCO 2018 annual meeting can be found here. While ASCO will bring up the recent IDO disappointment with the presentations listed above, there is still some potential for positive developments in the IDO program. Importantly, the company also has an interesting early stage cancer pipeline that will gain further visibility later in the year. The split FDA vote for Bari is a modest disappointment. However, the key is to get the drug on the market and compete, and in our view, Bari will receive FDA approval by the June PDUFA date.

RECOMMENDATION

INCY **is a BUY under 75 with a TARGET PRICE of 95**

IONS — Ionis and Biogen Ink Large Neuro Extension

IONS and BIIB recently announced a one billion dollar cash deal, including a $375 million upfront payment and anoterh $625 million IONS equity purchased at $54.34 per share. This deal has

Other positives this deal for IONS include the fact that BIIB has to opt-in earlier at the completion of IND-enabling studies compared to clinical POC under the current agreement. In addition, BIIB will assume all development responsibilities at the identification of the product candidate stage and will be responsible for and pay for non-clinical toxicology studies, clinical development, manufacturing, and commercialization. IONS will also receive up to $270 million in milestone payments per program skewed toward late-stage events.

The drug development candidates already known are: SOD1-Rx (ALS), C9-Rx (ALS) and MAPTRx (Alzheimer's). Disease areas under the agreement

been in the works as for many months in anticipation of the current collaboration was due to expire in September 2019. This is a rather strong vote of confidence by BIIB in the IONS antisense platform as they are clearly pleased with Spinraza, and which has exceeded $1 billion in sales already. Safety has been very important to BIIB and they referenced the safety for neuro conditions as a reason they struck the lucrative extension. The deal also includes improved economics with tiered royalties starting in the mid-teens up to 20% on net sales. We would note that this is an improvement to the current royalty rate under the prior BIIB agreement with tiered royalty rates in the low to mid-teens.

include dementia, neuromuscular diseases, movement disorders, ophthalmology, diseases of the inner ear, and neuropsychiatry. This is an excellent deal for IONS as BIIB is one of the world's leaders in neurology and is strong validation of IONS' cutting edge antisense drug development platform. Their collaborations keep getting bigger and their terms better.

RECOMMENDATION

IONS **is a BUY under 55 with a TARGET PRICE of 70**

MDCO – Q1 Report – ORION Trials' Pace & Reassuring Timelines

The key update on the call was the speed of the enrollment in the ORION trials for iclisiran. Furthermore in March, the ORION DSMB met for the second time to review data from the ORION Pivotal Trials and recommended that they continue without change or modification. With the entire company focus on the execution of these studies, all four Phase III trials are on pace to report clinical data as well as file both the NDA and MAA submissions in H2:19. While that may seem far away in today's hyper-demanding stock market, that timeline is ahead of the initial schedule and will be here before you know it.

In the meantime, AMGN and REGN/SNY continue to prime the PCSK-9 market for the unparalleled value proposition that is MDCO's inclisiran. The investment of both of the behemoths into the PCSK-9 market has only increased the market as they form creative ways to increase access to patients that continue to be denied insurance coverage. We still firmly believe that MDCO's inclisiran will change that substantially. Both management and activist investors remain focused on the goal line which gets closer every day.

RECOMMENDATION

MDCO **is a BUY under 40 with a TARGET PRICE of 65**

NKTR – Expands Combo Development For '214 With Takeda's '659

NKTR has entered into a new clinical collaboration with Japan's Takeda to evaluate NKTR-214, with Takeda's TAK-659, as a potential combination treatment regimen in multiple cancer settings. NKTR-214 is a developmental immuno-stimulatory therapy designed to expand specific cancer-fighting T cells and natural killer (NK) cells directly in the tumor micro-environment and increase expression of PD-1 on these immune cells. TAK-659 is a dual kinase inhibitor affecting both spleen tyrosine kinase (SYK), a kinase involved in cell proliferation and FLT-3, a cytokine receptor in the receptor tyrosine kinase class III.

NKTR and Takeda will each maintain global commercial rights to their respective investigational medicines and will split the costs related to the clinical trial and each company will contribute their respective compounds to the clinical collaboration. The first trial is expected to start in H2:18 and will evaluate the combination of an every three-week schedule of NKTR-214 with oral daily doses of TAK-659 in patients with Non-Hodgkin Lymphoma.

NKTR-214 is unique in that it can stimulate tumor-killing T-cells in the tumor micro-environment itself. By combining with TAK-659, the goal is to target different stages of the cancer immunity cycle in a combination regimen. NKTR-214 is an investigational immuno-stimulatory therapy designed to expand specific cancer-fighting CD8+ effector T cells and natural killer (NK) cells directly in the tumor micro-environment and increase expression of PD-1 on these immune cells. TAK-659 is an orally-available investigational reversible dual SYK/FLT-3 inhibitor. SYK is a non-receptor cytoplasmic kinase that binds to phosphorylated immuno-receptor tyrosine-based activating motifs and mediates cellular proliferation and survival. Mutations in FLT-3 genes can result in the constitutive activation of the FLT-3 receptor and result in acute myeloid leukemia and acute lymphoblastic leukemia. TAK-659 demonstrates both direct- and immune-mediated tumor cell kill mechanisms. It is currently being explored in clinical studies as a single agent and in combination in solid and hematological malignancies.

NKTR continues to execute at a high level by expanding the potential market opportunities for '214. This deal is similar to the INCY IDO deals which allow NKTR to retain all the economics for '214 in this combination with Takeda until they see data. Next up for NKTR is the NDA filing for NKTR-181 with the FDA around the end of April. Following that we expect Nektar to have a major presence at ASCO with positive Phase I/II PIVOT data testing '214 with BMS' Opdivo and the Phase I/II PROPEL study, which is testing '214 with Merck and AZ's PDL-1 inhibitors.

RECOMMENDATION

NKTR **is a BUY under 95 with a TARGET PRICE of 120**

The Back Page

Symbol	Company	Orig.Rec.	Current	Target	Recommendation
ACAD	Acadia	33.79	15.12	45	BUY under $32
ALKS	Alkermes	10.13	46.05	75	BUY under $55
BMRN	BioMarin	12.68	82.51	130	BUY under $100
CELG	Celgene	24.97	92.08	130	BUY under $105
ESPR	Esperion	24.42	68.78	100	BUY under $75
FPRX	Five Prime	16.29	16.76	45	BUY under $30
INCY	Incyte	5.88	62.61	95	BUY under $75
XON	Intrexon	34.42	18.08	45	BUY under $25
IONS	Ionis	7.63	43.48	70	BUY under $55
MDGL	Madrigal	17.00	114.75	190	BUY under $160
MDCO	Medicines Company	31.98	29.98	65	BUY under $40
MYOV	Myovant	13.74	19.93	25	BUY under $17
NKTR	Nektar	4.66	84.19	120	BUY under $95
NVAX	Novavax	2.44	1.62	4	BUY under $2
PCRX	Pacira	15.78	34.45	50	BUY under $35
SGMO	Sangamo	4.77	16.25	40	BUY under $30

ZIOP	Ziopharm	8.00	4.41	18	BUY under $12

**new recommendation*

THE MODEL PORTFOLIO*

COMPANY	SHARES OWNED	TOTAL COST	TODAY'S VALUE
Long Positions			
Acadia	3,000	102,417	45,360
Alkermes	2,500	32,695	115,125
Esperion	3,491	105,316	240,111
Five Prime	3,250	91,136	54,470
Incyte	1,294	34,817	81,017
Intrexon	2,200	76,510	39,776
Ionis	3,250	49,123	141,310
Madrigal	5,387	105,595	618,158
Medicines Co	2,600	19,380	77,948
Myovant	6,500	103,853	149,475
Nektar	6,500	63,277	547,235

Novavax	27,000	60,984	43,740
Pacira	1,500	23,907	51,675
Sangamo	7,190	53,597	116,838
Ziopharm	12,500	101,000	55,125
(04/29/18)		**Equities:**	**$2,377,363**
		Cash:	**$11,683**
	PORTFOLIO	**VALUE:**	**$2,389,046**

**The Model Portfolio is designed to reflect specific recommendations. We began the Model Portfolio on 12/23/83 with $100,000. On 4/13/84, we became fully invested. All profits are reinvested. Stocks recommended since then may be equally attractive, but may not be in the Model Portfolio. Transactions and positions are valued at closing prices. No dividends are created, and a 1% commission is charged. We don't use margin. Interest income is credited only on large cash balances.*

THE TRADER'S PORTFOLIO**

COMPANY	SHARES OWNED	TOTAL COST	TODAY'S VALUE
Long Positions			
Acadia	3,000	102,417	45,360
Alkermes	2,000	27,189	92,100
Esperion	4,075	100,005	280,279
Five Prime	4,020	70,679	67,375

Incyte	2,229	51,176	139,558
Intrexon	2,170	75,472	39,234
Ionis	3,300	53,501	143,484
Madrigal	2,910	49,964	333,923
Medicines Co	1,250	40,375	37,475
Myovant	7,410	102,831	147,681
Nektar	6,000	36,411	505,140
Novavax	25,000	58,025	40,500
Pacira	1,000	15,938	34,450
Sangamo	7,190	53,597	116,838
Ziopharm	12,500	101,000	55,125
(04/29/18)		**Position Total:**	**$2,078,520**
		Margin:	**–$690,793**
	PORTFOLIO	**VALUE:**	**$1,387,727**

***The Trader's Portfolio joined the Model Portfolio on 1/6/05 with $500,000 and is designed to take advantage of short-term opportunities throughout the biotech sector. The Trader's Portfolio will hold both long and short positions in stocks, trade-in options, and use margin. These strategies increase risk. Although there is no limit on the time any purchase can be held, the time frame for most investments will be weeks to months.*

BENCHMARKS

	NASDAQ	S&P 500	MODEL	TRADER'S
Last 2 Weeks	-0.2%	0.1%	-9.4%	-14.4%
2018 YTD	3.1%	-0.2%	19.9%	23.9%
Calendar Year 2017	29.3%	19.9%	65.6%	98.9%
Calendar Year 2016	7.5%	9.5%	-29.6%	-30.5%
Calendar Year 2015	-0.1%	-0.1%	25.1%	27.9%
Calendar Year 2014	13.4%	11.4%	29.2%	45.0%
Calendar Year 2013	38.3%	29.6%	103.4%	214.7%
Calendar Year 2012	13.4%	15.9%	25.7%	68.7%

New Money Buys

NEW MONEY BUYS

(Based on Market Cap when under our limit)

1st Tier: ALKS, BMRN, CELG, INCY, IONS, NKTR

2nd Tier: ACAD, ESPR, MDGL, MDCO, MYOV, PCRX, XON, SGMO

3rd Tier: FPRX, NVAX, ZIOP

Contact Info

Medical Technology Stock Letter
John McCamant, Editor
Jay Silverman, Editor
Jim McCamant, Editor-at-Large
Connie Hammond, Associate
Joan Wallner, Associate

BioInvest.com
PO Box 40460
Berkeley, CA 94704
510-843-1857
Send us an email

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