MTSL Issue 1023

March 28, 2024

UPDATES: ESPR, SGMO, VXRT, VKTX

IN THIS ISSUE: VK2735 Oral Data For Obesity Has Best-In-Class Potential

Since Last Issue: BTK: 1.51%; NBI: 1.69%; XBI: 0.47%; Model Portfolio: 10.61%

BIOTECH SECTOR ANALYSIS

SENTIMENT — XBI Forming a Base

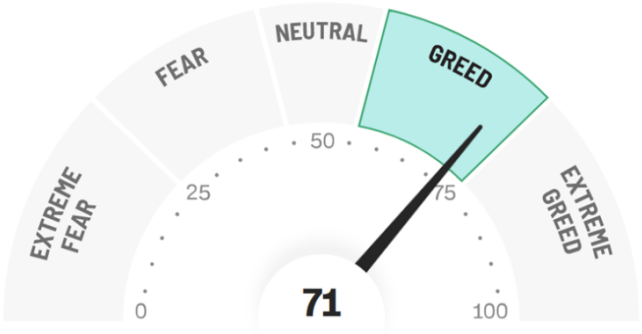
The biotechs have been relatively quiet since the last Issue with two MTSL recommendations, ESPR and VKTX, bucking the trend with both delivering excellent news. With no major M&A deals to feed the biotech froth, we have to be content with some smaller deals, AbbVie will acquire Landos and AZN is acquiring Amoylt. In our view, MTSL has a very large list of potential take out candidates. VKTX with possible Best-in-Class Phase I obesity data for VKTX's oral VX2735 has to top the list. Following close behind are MDGL and ESPR with approved drugs; MDGL is poised to serve pent up demand in MASH/NASH with a strong

On a weekly basis, the XBI also looks favorable. The weekly RSI is at 60, down a bit from the past few Issues but still neutral/positive overall. March was not a very good month versus the fun we had in January and February, but the sector did end relatively better than the overall tape. Interest rates will decline sometime this year – even Powell said about 3 times – and as a result the market rally has continued with a much wider breadth than just the Big Tech stocks. We still see excellent biotechnology fundamentals. While the index is flat since the last Issue, the 50-week MA is higher and that gives us a higher level of support on the charts. The resistance remains for the 200-week at 101. With quarterly calls mostly behind us, eyes will be on the upcoming launch of Rezdiffra (April) and whatever else happens to the GLP market. The ACC conference will include ESPR's new label and data. Then we'll get closer to the May/June key science

launch and ESPR is about to explode sales with a new Outcomes label enabling broader insurer coverage. Importantly, both drugs have been validated in major peer reviewed publications like the *New England Journal of Medicine* which are powerful sales tools.

FEAR & GREED – Greed Again

The F&G Index has remained in Greed for March as a strong overall market with significant strength in tech/AI has fueled investor expectations. The Fed remains a positive as all signs point to lower inflation which will allow Powell to cut interest rates multiple times. A lower rate environment is a net positive for biotechs and will help the group continue its strong 2024 performance.



TECHNICALS – XBI Basing In Time For Baseball Season

Pardon the pun but for the past two weeks the XBI (95) has been forming a base with a wide band between 92 and 96 as the first quarter comes to a close. With the official and broad FDA approval of MDGL's Rezdiffra, the impressive and possibly Best-in-Class Phase I obesity data for VKTX's oral VX2735 and the other broad FDA label expansion for ESPR's NEXLETOL/NEXLIZET – the Medical Technology Stock Letter recommendations had an exceptional Q1:24. While most of the stocks have had strong quarterly performance, every one of the companies took advantage of the positive fundamental news and favorable market to raise capital. As a result, many of the stocks gave back some of their respective gains events – ASCO and ADA. In addition, we will see the more specific company catalyst for MTSL stocks CLDX, PGEN, SKYE, SGMO, IONS, INCY, ALKS…….No rest for the weary. Play BALL!!!

MTSL Events Due Near-Term

- CLDX Q1 – Initiate Phase II study of barzolvilumab in prurigo nodularis (PN)
- VXRT Q2 – World Vaccine Congress 2024, Dr. Sean Tucker, April 3, 3:10 p.m. ET. Title: Moving the needle: Blocking transmission and boosting existing vaccines by oral tablet vaccination.
- BCYC Q2 – American Association for Cancer Research (AACR) in San Diego on April 5-10, Three Abstracts:
  - Bicycle Toxin Conjugates for the treatment of solid tumors, Tuesday, April 9, at 1:30 p.m. PT
  - Modulation of the natural killer cell immune response to tumor with a synthetic tumor-immune cell agonist, NK-TICA, Monday, April 8, at 9 a.m. PT
  - Tumor-targeted activation of CD137 using Bicycles: New insights into mechanism of action and discovery of BT7455, a clinical candidate for the treatment of EphA2-expressing cancers, Tuesday, April 9, at 1:30 p.m. PT
- PGEN Q2 – Pivotal Phase II RRP data for PRGN-2012 in Q2 which will lead to an FDA filing.

but still remain well above levels since the beginning of 2024. The RSI has stayed neutral over this two week period, closing right at 50. The 50-day moving average is flattening (after rising for months) and the 200-day MA is still heading higher. The index is holding steadily above the 50-day MA of 93 and the 200-day of 82 – both still higher than the last Issue. We also got a few albeit small but premium takeovers recently (ABBV/LAPB, AZN/Amoylt)- more signals of Big Pharma shopping. In addition, the MACD went negative and hit a trough in early March and is now at break-even and heading into positive territory – a sign that profit-taking is mostly behind us. To us, it's a good sign of both a healthy sector and market.

PGEN will host the first RRP Awareness Day on June 11 where Phase II data could be released/discussed.

Clinical Trials Watch

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

ABBV – Crohn's Disease: Efficacy, Safety, and Pharmacokinetics of Upadacitinib in Pediatric Subjects With Moderate

ABBV – A Study to Learn How Safe and Effective Risankizumab is When Compared to Deucravacitinib to Treat Partic and Who Need to Try Systemic Treatment (Works Throughout the Whole Body)

ABBV/INCY – Study of Oral Navitoclax Tablet in Combination With Oral Ruxolitinib Tablet to Assess Change in Splee Relapsed/Refractory Myelofibrosis

AMGN – Study to Evaluate Avacopan in Combination With a Rituximab or Cyclophosphamide-containing Regimen, of Age With AAV

AMGN – https://clinicaltrials.gov/study/NCT05581303?term=amgen

GILD – A Study to Evaluate the Efficacy and Safety of Astegolimab in Participants With Chronic Obstructive Pulmona

INCY – A Study of INCB099280 in Combination With Adagrasib in Adults With Advanced Solid Tumors Harboring a K

INCY – A Study to Evaluate INCA033989 Administered in Participants With Myeloproliferative Neoplasms

INCY – A Study to Evaluate the Relative Bioavailability of Ruxolitinib Extended Release (XR) Tablets Compared With Tablets Administered Orally in Healthy Participants

INCY – A Study to Evaluate the Long-Term Safety and Efficacy of Povorcitinib in Participants With Moderate to Sever

SNY/REGN – Observational Study of Patients Receiving Dupixent® for Atopic Dermatitis (AD) (GLOBOSTAD)

Company Updates

UPDATES:ESPR, SGMO, VXRT, VKTX

ESPR — FDA Approves CLEAR Outcomes LABEL, EU Issues Positive Opinion, ACC Up Next

ESPR has had a great two weeks with early positive Outcomes labeling news from both the FDA and the EU. The FDA has approved broad new label expansions for NEXLETOL® (bempedoic acid) Tablets and NEXLIZET® (bempedoic acid and ezetimibe) Tablets based on positive CLEAR Outcomes data that include indications for cardiovascular risk reduction and expanded LDL-C lowering in both primary and secondary prevention patients. In addition, the enhanced labels support the use of NEXLETOL and NEXLIZET either alone or in combination with statins.

Additionally, the Company will participate in a moderated session in partnership with UT Southwestern Medical Center, host an industry expert theatre, and have a commercial and medical information booth during ACC.24. The posters will highlight the commitment to underserved populations and present subset analyses in women and Hispanic/Latinx patients as well as in patients with obesity.

They also include new indications for primary hyperlipidemia, alone or in combination with a statin, and are the only LDL-C lowering non-statin drugs indicated for primary prevention patients.

The Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) has adopted positive opinions for the label update of both bempedoic acid and the bempedoic acid / ezetimibe fixed dose combination (FDC), recommending their approval as treatments to reduce low-density lipoprotein cholesterol (LDL-C) and cardiovascular risk. The actual label approval is expected in Q2.

ESPR has announced the acceptance of three CLEAR Outcomes subgroup analyses as poster presentations at the 2024 American College of Cardiology's Annual Scientific Session (ACC.24) in Atlanta, Georgia.

ESPR is poised for a strong 2024 with the recent Outcomes label approvals. ACC is the perfect venue for the company to educate/market the new Outcomes label which will help fuel the anticipated growth of insurance coverage for the LDL lowering drugs. In addition, the odds of a premium acquisition are very high given that ESPR owns 100% of the U.S. rights to a new drug poised for significant growth.

RECOMMENDATION

ESPR is a BUY under 10 with a TARGET PRICE of 25

SGMO — SGMO Adds $24 Million

SGMO has raised $24 million by selling 24,761,905 shares of its common stock and pre-funded warrants to purchase up to an aggregate of 3,809,523 shares of common stock, together with accompanying warrants to purchase up to an aggregate of 28,571,428 shares of common stock. The combined offering price of each share of common stock and accompanying warrant is $0.84, priced at-the-market under Nasdaq rules. The combined offering price of each pre-funded warrant and accompanying warrant is $0.83. The warrants will become exercisable six months from issuance, expire five and a half years from the issuance date and have an exercise price of $1.00 per share.

As we said in the last Issue, SGMO needs to address their low cash position. This funding certainly helps and should take us into early 2025 when the Phase III Hem A data from Pfizer is expected. We believe that SGMO needs to deliver some shareholder value by adding partnerships during 2024 that both fund and validate their zinc finger technology platform

RECOMMENDATION

SGMO is a BUY under 2 with a TARGET PRICE of 5

VXRT — VXRT Will Start Two Phase IIb Trials Shortly, World Vaccine Congress April 3rd

VXRT recently held their quarterly conference call and much of the focus was on the January $9.27 million contract from BARDA to prepare for a 10,000-subject Phase IIb clinical trial evaluating VXRT's oral pill XBB COVID-19 vaccine candidate against an approved mRNA vaccine comparator. The company believes that the milestones in this contract will put them in a position to receive additional funds. We should expect this Phase IIb trial to start as early as Q2. VXRT is poised to start two Phase IIb trials, one each for COVID and Noro virus respectively. Either of the upcoming Phase IIb trials has the potential to provide proof of concept data which would be a significant stock catalyst and also provide positive read through for VXRT'S oral vaccine technology.

Noro Virus: VXRT plans to meet with the FDA during the second quarter of 2024 to discuss data on potential correlates, a Phase IIb dose confirmation study, and potentially a G24 challenge study. The company currently believes a Phase IIb study would generate sufficient safety data to have an end-of-Phase II meeting with the FDA. That said, the type and timing of our next clinical study will be determined following our meeting with the FDA in Q2.

VXRT recently announced that Dr. Sean Tucker, Founder and Chief Scientific Officer, will present at the World Vaccine Congress Washington 2024 in Washington, D.C. on Wednesday, April 3, 2024. The Company has appeared repeatedly at the annual event in Washington, D.C.

- **Title**: Moving the needle: Blocking transmission and boosting existing vaccines by oral tablet vaccination
- Dr. Sean Tucker, Wednesday, April 3, 2024, 3:10 p.m. ET, Room 207A

VXRT is poised to start two Phase IIb trials, one each for COVID and Noro virus respectively. We are encouraged by the company's recent progress and their new CEO as we will finally get to see if VXRT's proprietary oral vaccine platform can deliver solid data. Either of the upcoming Phase IIb trials has the potential to provide proof of concept data which would be a significant stock catalyst and also provide positive read through for VXRT'S oral vaccine technology.

RECOMMENDATION

VXRT is a BUY under 2 with a TARGET PRICE of 5

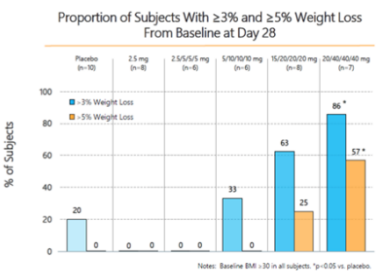
VKTX — (3/27/24 Update) Significantly Undervalued After Roche Pays $2.7 Billion For Competitor

In a widely anticipated clinical trial in the blockbuster GLP class, VKTX released excellent Phase I data for Oral '2735 at 28 days in obese patients. The company reported both excellent efficacy of 5.3% weight loss at the highest dose in just one month along with a clean safety profile. Despite the small trial size, VKTX was able to demonstrate dose-dependent and statistical significance at the top dose of 40mg vs. a placebo group which performed unusually well (5.3% vs. 2.1%; p=0.0006), with no signs of plateau at the highest dose tested. Importantly, the safety profile was very good, with all GI events mild or moderate and no difference in overall GI tolerability between oral VK2735 and placebo. Based on these promising initial results, VKTX will continue dose escalation in this trial, starting patients at the 40mg dose and could go as high as 60-90mg or higher depending on safety/tolerability. At first glance, Viking may have another Best-In-Class oral GLP to go with its potential Best-In-Class injectable one. BUY

Clear Dose Response

VK2735 showed a classic and imposing dose response even in this small trial (n=45).

- Dose response shows increased proportion of subjects with 3% and 5% at higher doses with increasing VK2735 dose
- Potential to improve with higher dose and/or longer dosing period



VIKING

Impressive Safety

The impressive safety data – which is critical for a potentially chronic use pill where A/Es but not lack of efficacy lead to discontinuation – further supports dose-escalation of oral '2735 that VKTX is currently conducting, and VKTX plans to start the first dose at 40mg for the additional cohorts. This is excellent news for the potential best in class drug as we may see even better efficacy at higher doses.

Common GI related TEAEs Number of subjects reporting (%)	Placebo (n=10)	VK2735 2.5 mg (n=8)	VK2735 5 mg (n=7)	VK2735 10 mg (n=6)	VK2735 20 mg (n=8)	VK2735 40 mg (n=8)	VK2735 Combined (n=37)
GERD	2 (20%)	0 (0%)	0 (0%)	0 (0%)	1 (13%)	0 (0%)	1 (3%)
Nausea							
Mild	0 (0%)	0 (0%)	1 (14%)	0 (0%)	2 (25%)	2 (25%)	5 (14%)
Moderate	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Severe	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Vomiting	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Abdominal pain	3 (30%)	0 (0%)	1 (14%)	1 (17%)	0 (0%)	1 (13%)	3 (8%)
Diarrhea	2 (20%)	0 (0%)	0 (0%)	0 (0%)	1 (13%)	0 (0%)	1 (3%)
Constipation	2 (20%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)

GERD: Gastroesophageal reflux disease

- All GI-specific TEAEs among VK2735 subjects were mild or moderate (79% mild)
- No clinically meaningful difference in overall GI AEs compared with placebo

VIKING

In our view, the top line Phase I oral data exceeded all expectations and reinforces the best-in-class potential for VK2735. This is particularly encouraging after market leader Novo Nordisk (NVO) recently cherry-picked a small data cohort to announce positive results from the first trial of its own oral GLP version. We have been excited to see the oral VKTX data ever since the subQ version of the same drug significantly exceeded expectations in Phase II with a 14.7% weight loss after 13 weeks. VKTX is planning to start a Phase II trial for oral '2735 in 2H24 (IND planned for mid-year), which could mirror the development of the subQ '2735 Phase II development program with additional titration/doses tested. With a potential best in class drug for oral and injectable use, VKTX has to be on many Big Pharma/Bio acquisition wish lists as the Company represents a very scarce asset in the $100 billion market for weight loss drugs.

We are particularly encouraged by the safety profile, as all TEAEs appear to be mild and moderate and only a low rate of common GI AEs (like nausea and diarrhea), with no vomiting or constipation observed and no difference in overall GI tolerability between oral VK2735 and placebo.

RECOMMENDATION

VKTX is a BUY under 100 with a TARGET PRICE of 145

The Back Page

Symbol	Company	Orig.Rec.	Current	Target	Recommendation
ACAD	Acadia	33.79	18.49	45	BUY under $28
ALKS	Alkermes	10.13	27.07	55	BUY under $35
BCYC	Bicycle	43.92	24.90	75	BUY under $50
BMRN	BioMarin	12.68	87.34	150	BUY under $100
CLDX	Celldex	10.50	41.97	100	BUY under $75
ESPR	Esperion	24.42	2.68	25	BUY under $10
INCY	Incyte	5.88	56.97	108	BUY under $85
IONS	Ionis	7.63	43.35	65	BUY under $50
MDGL	Madrigal	17.00	267.04	400	BUY under $300
PCRX	Pacira	15.78	29.22	100	BUY under $80
PGEN	Precigen	34.42	1.45	12	BUY under $5
SGMO	Sangamo	4.77	0.67	5	BUY under $2
SKYE	Skye	17.00	15.64	40	BUY under $24

TCRT	Alaunos	8.00	1.81	5	HOLD
VKTX	Viking	16.83	82.00	145	BUY under $100
VXRT	Vaxart	8.00	1.30	8	BUY under $3

**New recommendation.*

THE MODEL PORTFOLIO*

COMPANY	SHARES OWNED	TOTAL COST	TODAY'S VALUE
Long Positions			
Acadia (ACAD)	4,750	156,557	87,828
Alkermes (ALKS)	3,800	88,690	102,866
Bicycle (BCYC)	2,400	105,408	59,760
Celldex (CLDX)	15,832	174,993	601,094
Esperion (ESPR)	3,316	105,316	8,887
Incyte (INCY)	1,229	34,817	70,016
Ionis (IONS)	3,087	49,123	133,821
Madrigal (MDGL)	3,127	69,980	768,274

Pacira (PCRX)	2,375	63,887	69,398
Precigen (PGEN)	9,690	76,510	14,051
Sangamo (SGMO)	19,456	253,596	13,036
Skye (SKYE)	13,500	229,500	211,140
Alaunos (TCRT)	26,125	166,100	47,286
Viking (VKTX)	12,000	201,960	984,000
Vaxart (VXRT)	29,687	250,000	38,593
(03/28/24)		**Equities:**	**$3,210,049**
		Cash:	**$ 8,384**
		PORTFOLIO VALUE:	**$3,218,433**

**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 we don't use margin. Interest income is credited only on large cash balances.*

**Model Portfolio Update: Purchased $229,500 of SKYE.*

BENCHMARKS

	NASDAQ	S&P 500	MODEL

Last 2 Weeks	1.6%	2.0%	10.6%
2024 YTD	7.4%	8.0%	36.4%
Calendar Year 2023	43.4%	24.2%	-3.5%
Calendar Year 2022	-33.1%	-19.4%	-12.7%
Calendar Year 2021	21.3%	26.9%	-15.2%
Calendar Year 2020	43.6%	16.3%	13.8%
Calendar Year 2019	35.2%	28.8%	10.7%
Calendar Year 2018	5.7%	6.6%	4.5%
Calendar Year 2017	29.3%	19.9%	65.6%
Calendar Year 2016	7.5%	9.5%	-29.6%
Calendar Year 2015	-0.1%	-0.1%	25.1%
Calendar Year 2014	13.4%	11.4%	29.2%
Calendar Year 2013	38.3%	29.6%	103.4%

New Money Buys

BioInvest

(Based on Market Cap when under our limit)

1st Tier: ACAD, ALKS, BMRN, INCY, IONS, MDGL

2nd Tier: BCYC, CLDX, PCRX, VKTX

3rd Tier: TCRT, ESPR, PGEN, SGMO, VXRT

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← Viking Therapeutics (VKTX) – Oral VK2735 Delivers Excellent Phase I Weight Loss of 5.3% at 28 Days; Highest Dose Not Reached Yet Due to Outstanding Safety

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