MTSL Issue 1019

February 1, 2024

UPDATES: ESPR, IONS, VXRT

IN THIS ISSUE: VXRT Receives $9.27 Million From BARDA For 10,000 Patient Phase IIb C

Since Last Issue: BTK: -0.18%; NBI: 0.27%; XBI: 2.15%; Model Portfolio: 1.06%

BIOTECH SECTOR ANALYSIS

SENTIMENT — XBI Basing As Rate Decline Pauses

The Fed Leaves Rates Unchanged, Tempers Rate Cut Expectations

The Federal Reserve maintained its benchmark interest rate on Wednesday in a range of 5.25%-5.50%, the highest since 2001, and cautioned it won't begin lowering interest rates until it sees further progress on inflation returning to its 2% target. At this point the committee does not expect it will be appropriate to reduce the target range

TECHNICALS

XBI Basing As Rate Decline Pauses, Economy Strong – The XBI (89) has been moving sideways since the JPM Healthcare Conference ended three weeks ago. With interest rates rising a bit again after a major

until it has gained greater confidence that inflation is moving sustainably toward 2%.

The good news was Fed officials noted that the risks to achieving price stability and maintaining full employment are "moving into better balance." The Fed characterized job gains as having "moderated" over the last year, but note job gains remain "strong." The central banks also completely stripped out language from prior statements that had previously left room for rate hikes. We continue to expect rate cuts this year despite the cautious language. Rate cuts are a significant positive for biotechs and we expect a very good year for the sector.

Big Pharma & Big Biotech Are Still Shopping

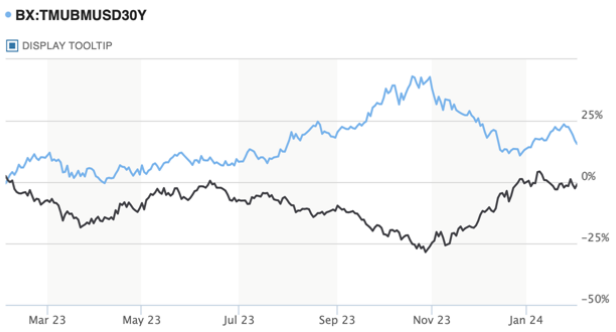
The top 20 biopharma companies have $180 billion in sales at risk from patent expirations between now and 2028 which has helped accelerate the recent boom in M&A as the pressure to replace that $180 billion is growing rapidly. Leading drugmakers are off to a good start with both AbbVie and Merck being very active as they build their drug pipelines and ink acquisitions or partnerships with other companies.

The bottom line is patent cliffs are an unavoidable issue for both Big Pharma and Big Bios and to some extent they are victims of their own success as Keytruda/Opdivo are the largest selling class of drugs in history. The cycle never ends for the Big Pharma/Big Bio as they must constantly replenish older top-selling drugs with new ones that they hope will not just sustain their sales, but also grow them. A large part of small to mid-cap biotech success is developing new drug candidates that can be acquired by the big companies.

The Big Four Patent Expirations

1. Merck's Keytruda (PD-1) treats melanoma, head and neck, lung and other certain types of

pullback coupled with the resilient strength of the U.S. economy, the inverse relationship with biotech is apparent (see 30-Year Treasury Yield below). With no recent M&A deals after a barrage of premium sector takeovers in December and early January, the group is taking what we believe is a healthy pause. We say "healthy" because the fundamentals of the biotechnology are solid once again – with new blockbuster classes (e.g., obesity) leading the way, Big Pharma/Biotech out shopping again and new drugs are on the horizon. Investors are awaiting some March FDA approvals, specifically for MTSL Recommendation MDGL (3/14, NASH) as well an important label expansion for ESPR (3/31, CV outcomes). The RSI is still in the neutral zone, with the vast majority of XBI components in the mid- or early-stages and therefore less visible during earnings season. We will, however, be getting clinical updates on many of our MTSL recommendations in the near future (e.g., CLDX, ACAD, VKTX). With a few positive IPOs, too, the group is acting better overall. The 50-day moving average is now around 84-85, up from 80-81 last Issue. Overall a strong environment and should rates resume their decline, which we believe they eventually will, then bios' rise should also resume.



The weekly XBI again is mirroring the daily as it too has leveled off for January. The weekly RSI is a little better than the daily, staying at 62 – a neutral-to-positive level. The XBI is right in between the 200-week moving average (101) and the 50-week MA (80). The MACD is still positive although peeling off a drop from the peak at the end of last year/beginning of this year. Upcoming MTSL catalysts include the FDA

cancers. Key patent expirations in 2028 with $25 billion in revenue in 2023.

2. Bristol Myers Squibb's Eliquis is a blood thinner used to prevent clotting, to reduce the risk of stroke. Key patent expirations in 2026 and 2028 representing $12 billion of revenue in 2022.
3. Bristol Myers Squibb's Opdivo (PD-1) is used to treat cancers, including melanoma and lung cancer. Key patent expirations in 2028 representing $10 billion of 2023 revenue.
4. Johnson & Johnson's Stelara is an immunosuppressive medication used to lower inflammation and treat several conditions, including plaque psoriasis and psoriatic arthritis. Key patent expirations: 2024 in Europe, 2025 in the U.S. representing $11 billion in 2023 revenue.

Merck plans to stay very active on the M&A front and their CEO recently was quoted, "It's gonna be a range of deals, but if you look in that $1 [billion] to $15 billion [range], that continues to be what we'll look for," Davis said. "We've also shown that not only are we very open to acquisition, we see collaboration as an important tool as well. Davis pointed to Merck's recent partnership with Daiichi Sankyo, paying $4 billion to co-develop three antibody-drug conjugate candidates. The urgency for Merck to diversify its portfolio are its financial figures for the fourth quarter and for 2023 overall. For the year, Merck's revenue was $60.1 billion, which was a 1% increase on 2022, with $25 billion of the sales coming from Keytruda.

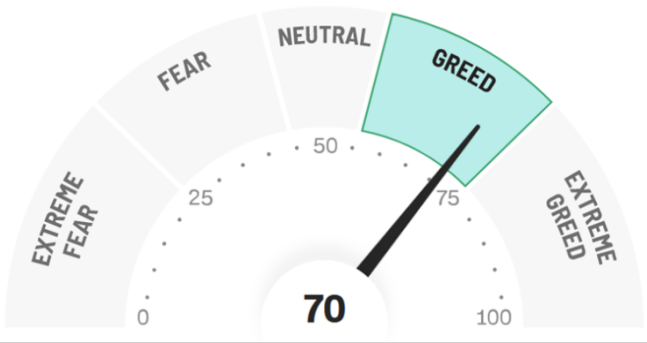
FEAR & GREED – Steady

The Fear & Greed index is up to 70 after holding very steady for most of the two weeks near 67 where it closed last Issue. The recent strength came from very strong tech earnings, not the best environment for the group as the shift into tech usually means some funds rotating out of biotechs short term.

PDUFA dates above plus the clinical updates from two favorites of ours – the oral obesity data from VKTX (Q1) and the AAAAI meeting for CLDX (2/24). Several investor conferences will also take place in February and March, with the Cowen Conference (3/4-3/6) being the most impactful and well-attended (and many of our recommended companies will be there to present). It may be feel a bit quiet after the rush of JPM, but there's still a long list of quarterly conference calls this week alone, and we expect a rather busy February and March.

MTSL Events Due Near-Term

- CLDX Q1 – Barzo SubC CSU Phase II Data at American Academy of Asthma, Allergy & Immunology, Abstract released on line on Feb. 5, 2023, followed by Late Breaker Oral presentation at meeting Feb. 23-26
- VKTX Q1-Phase I Data from Oral Formulation of VK2735 Expected in Q1.
- MDGL Q1 – March 14 PDUFA for Resmetirom for NASH
- ACAD Q1 – ADVANCE-2 Phase III study of pimavanserin in Negative Symptoms of Schizophrenia expected1Q
- ESPR Q1 – CLEAR Label expansion PDUFA March 31st
- PGEN Q2 – Pivotal Phase II RRP data for PRGN-2012 in Q2 which will lead to an FDA filing



- INCY-Q4 Earnings Call 8:00 a.m. ET, February 13

Clinical Trials Watch

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

ABBV – A Study to Assess Change in Disease Activity and Adverse Events of Oral Upadacitinib in Adult and Adoles Severe Hidradenitis Suppurativa Who Have Failed Anti-TNF Therapy

AKRO – A Study Evaluating Efruxifermin in Subjects With Non-Cir-rhotic Nonalcoholic Steatohepatitis (NASH)/M Steatohepatitis (MASH) and Fibrosis

AMGN – A Study to Investigate Efficacy and Safety of Apremilast 30 mg Twice Daily (BID) in Chinese Participants Psoriasis (PsO)

INCY – A Study to Evaluate the Safety and Tolerability of Maximal Use Ruxolitinib Cream

INCY – Ruxolitinib in Seborrheic Dermatitis

INCY – A Study to Evaluate Efficacy and Safety of Povorcitinib in Par-ticipants With Nonsegmental Vitiligo (STOI

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

NVS – A Real-world Study to Assess Safety and Effectiveness of Xolair® in Pediatric Chronic Spontaneous Urticar

PCRX – Liposomal Bupivacaine With Standard Bupivacaine Versus Dexmedetomidine With Standard Bupivacaine

REGN – Dupixent in Adults With Refractory Post-Burn Pruritus in an Ambulatory Clinic

Company Updates

UPDATES: ESPR, IONS, VXRT

ESPR — ESPR Raises $97.8 Million, Announces 2024 Promotional Calendar

ESPR recently raised $97.8 million at $1.50 per share. While we are disappointed in the low price, we believe the worst is now behind us and 2024 should be a very good year for the company. The next catalyst is the March 31 PDUFA for label expansion to include the cardio benefit in addition to lowering LDL from the CLEAR outcomes trial. The announcement of the promotional calendar is another positive for the company as we expect brand visibility to grow significantly with promotions highlighting the expanded label to include the cardio benefit in addition to lowering LDL.

Esperion 2024 Promotional Calendar

- Feb. 2: National Wear Red Day
- Feb. 6: American Heart Month video
- Feb. 8: Prize pack giveaway
- March 26-April 1: NASCAR.com race center takeover
- April 2: Stress Awareness Month video
- April 8: Buescher Appearance at ACC
- May 1: Women's Health Awareness video
- May 15-21: NASCAR.com paint scheme preview takeover
- June 3: Men's Health Awareness video

RFK Racing and Esperion Therapeutics have announced the promotional schedule for the 2024 season, highlighted by a four-race slate, and numerous accompanying campaigns and initiatives, all driving awareness of its two brands – NEXLIZET (bempedoic acid and ezetimibe) and NEXLETOL (bempedoic acid) used for adults on a statin to reduce LDL-cholesterol.

Esperion's season debut comes in the first race at Richmond this spring (March 31) on the No. 17 car of Chris Buescher. Brad Keselowski's debut with the brand comes at the All-Star Race at North Wilkesboro (May 19). Remaining races include Pocono on the No. 6 (July 14), and the fall Talladega event on the No. 17 (Oct. 6).

RFK and Esperion will collaborate to wave the red flag for uncontrolled cholesterol by promoting a myriad of campaigns, including National Wear Red Day, American Heart Month, Stress Awareness Month, Women's Health Awareness Month, Men's Health Awareness Month, a Wellness Walk, Cholesterol Education Month, World Heart Day, National Health Education Week, and Family Health History Day.

In addition, Buescher will attend the annual American College of Cardiology (ACC) session on behalf of Esperion, in April in Atlanta. RFK will also promote the brand's NASCAR Digital Media buy, which will include various graphics packages on NASCAR.com, as well as an in-car camera on the No. 6 for the second Talladega race.

Esperion is also partnering with Pocono Raceway to host a Wellness Walk the Saturday morning of its race weekend, which will invite fans in attendance to walk a secured route inside the infield alongside Keselowski, all promoting wellness and general awareness for staying in-tune to their cholesterol levels. NEXLIZET should not be used in patients who have had a previous allergic reaction to ezetimibe.

- July 9: Wellness Walk advance promotion
- July 10-16: NASCAR.com paint scheme amplification content
- July 13: Wellness Walk at Pocono Raceway
- Sept. 1: Cholesterol Education Month video
- Sept. 29: World Heart Day video
- Oct. 2-8: NASCAR.com paint scheme amplification content
- Oct. 6: In-car camera
- Oct. 21: National Health Education Week video
- Nov. 23: Family Health History Day video

While we are disappointed in the low price for the stock raise, we believe the worst is now behind us and 2024 should be a very good year for the company. The next catalyst is the March 31 PDUFA for label expansion to include the cardio benefit in addition to lowering LDL from the CLEAR outcomes trial. The announcement of the promotional calendar is another positive for the company as we expect brand visibility to grow significantly with promotions highlighting the expanded label to include the cardio benefit in addition to lowering LDL.

RECOMMENDATION

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

NEXLIZET and NEXLETOL can increase levels of uric acid in the blood which can lead to gout.

IONS — IONS Announces Positive Phase III Trial of Donidalorsen in HAE

IONS recently had good news when they announced the Phase III OASIS-HAE study of donidalorsen in hereditary angioedema (HAE) achieved its primary endpoint of reduction in attack rate in Q4W ($p<0.001$) and Q8W ($p=0.004$) arms versus placebo. Statistical significance was achieved on all secondary endpoints in the Q4W arm, but only on key secondary endpoints for Q8W arm. This leaves open questions on the profile of a bi-monthly regimen. The safety profile appeared to be benign with no SAEs, detailed data will be provided at a medical conference for the full picture. IONS will present the complete data set at a peer reviewed medical conference by mid-year, and has begun preparations for a NDA filing.

The combination of strong Phase II data, Phase III attack reduction rates, and Phase III OASIS-Plus OLE and switch cohort data – expected mid-year – will clarify the commercial profile of donidalorsen. The primary question is will the drug support broad switching from competitors or will revenue be largely be driven by newly diagnosed patients. In our view, HAE is a greater driver of economics for IONS than TTR per dollar of revenue and will increasingly take center stage 2H24. The muted share response is unsurprising as positive data was widely expected and no specific data was given on attack

RECOMMENDATION

IONS is a BUY under 50 with a TARGET PRICE of 65

VXRT — VXRT Receives $9.27 Million From BARDA For 10,000 Patient Phase IIb COVID Trial

VXRT recently announced that the Biomedical Advanced Research and Development Authority (BARDA) has awarded the Company $9.27 million to fund preparation for a 10,000 subject Phase IIb clinical study evaluating Vaxart's oral pill XBB COVID-19 vaccine candidate against an approved mRNA vaccine comparator. Project NextGen is a $5 billion initiative by the U.S. Department of Health and Human Services (HHS) to develop new, innovative

The Phase II, multicenter, randomized, double-blind, placebo-controlled single dose, dose-ranging study is designed to evaluate the safety, tolerability, and immunogenicity of orally administered bivalent GI.1/GII.4 norovirus vaccine in healthy lactating females of at least 18 years of age has completed enrollment. The study enrolled 76 subjects at five sites in South Africa. Subjects are randomized into high- or low-dose vaccine (N=30 for each arm) or

vaccines and therapeutics that provide broader and more durable protection against COVID-19 than the first generation COVID vaccines and medicines. Vaxart's oral pill vaccine platform provides many of the features desired by BARDA, such as generating mucosal immunity and providing a cross-reactive response to many COVID variants. This is a strong validation of VXRT's oral vaccine platform technology and helps explain why RA Capital has become an investor in VXRT. In our view, VXRT's pill may shine in this trial particularly if we see more variant mutations as the oral vaccine provides longer and broader protection by triggering both a systemic and mucosal response.

Norovirus Update

Next up for VXRT and their norovirus vaccine program is a Type C meeting with FDA to discuss how many patients are needed in Phase II before the company goes back to the agency for an end of Phase II meeting which is projected by year end. The company will most likely need to enroll around 400 patients their next Phase II trial before their end of Phase II meeting with the FDA. Recall that this candidate contains two genotypes, G11 and G24, both of which have caused the majority of norovirus disease in humans over the past 20 or so years. The Phase IIb dose confirmation study will use the bivalent vaccine candidate to obtain sufficient safety and efficacy data to inform an end of Phase II meeting with the FDA.

placebo (N=16). Data is expected around mid-year and will also be part of the data package presented to the FDA for the end of Phase II meeting.

VXRT is making a big come back as they now how funding and validation for their oral vaccine COVID from BARDA. This is a strong validation of VXRT's oral vaccine platform technology and helps explain why RA Capital has become an investor in VXRT. In our view, VXRT's pill may shine in this trial particularly if we see more variant mutations as the oral vaccine provides longer and broader protection by triggering both a systemic and mucosal response. While COVID vaccines have cooled off, vaccines in general have never been hotter with RSV being the latest winner.

RECOMMENDATION

VXRT is a BUY under 3 with a TARGET PRICE of 8

The Back Page

Symbol	Company	Orig.Rec.	Current	Target	Recommendation
ACAD	Acadia	33.79	26.14	45	BUY under $28
ALKS	Alkermes	10.13	26.95	55	BUY under $35

BCYC	Bicycle	43.92	17.35	75	BUY under $50
BMRN	BioMarin	12.68	88.74	150	BUY under $100
CLDX	Celldex	10.50	35.50	100	BUY under $75
ESPR	Esperion	24.42	2.07	25	BUY under $10
INCY	Incyte	5.88	59.16	108	BUY under $85
IONS	Ionis	7.63	50.97	65	BUY under $50
MDGL	Madrigal	17.00	222.23	400	BUY under $300
PCRX	Pacira	15.78	31.77	100	BUY under $80
PGEN	Precigen	34.42	1.40	12	BUY under $5
SGMO	Sangamo	4.77	0.50	15	HOLD
TCRT	Alaunos	8.00	2.03	5	HOLD
VKTX	Viking	16.83	23.95	45	BUY under $28
VXRT	Vaxart	8.00	1.20	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	124,165
Alkermes (ALKS)	3,800	88,690	102,410
Bicycle (BCYC)	2,400	105,408	41,640
Celldex (CLDX)	15,832	174,993	562,036
Esperion (ESPR)	3,316	105,316	6,864
Incyte (INCY)	1,229	34,817	72,708
Ionis (IONS)	3,087	49,123	157,344
Madrigal (MDGL)	3,127	69,980	694,913
Pacira (PCRX)	2,375	63,887	75,454
Precigen (PGEN)	9,690	76,510	13,566
Sangamo (SGMO)	19,456	253,596	9,728
Alaunos (TCRT)	26,125	166,100	53,034
Viking (VKTX)	12,000	201,960	711,004
Vaxart (VXRT)	29,687	250,000	14,400
(02/01/24)		**Equities:**	**$2,639,266**
		Cash:	**$ 237,884**

PORTFOLIO VALUE:	**$2,877,149**

**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.*

BENCHMARKS

	NASDAQ	S&P 500	MODEL
Last 2 Weeks	2.0%	-0.2%	1.1%
2024 YTD	2.3%	2.8%	2.8%
Calendar Year 2023	43.4%	24.2%	8.9%
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

Contact Info

Medical Technology Stock Letter
John McCamant, Editor
Jay Silverman, Editor
Jim McCamant, Editor-at-Large

BioInvest.com
579 Mangels Ave.
San Francisco, CA 94127
Send us an email

Download a PDF of MTSL Issue #1019

$898. You may cancel within 48 hours for a full refund. The information and opinions contained herein have been compiled or arrived at from sources believed to be reliable but no representations or warranty, express or implied, is made as to the accuracy or completeness. In no way shall this newsletter be construed as an offer to sell or solicitation of an offer to buy any securities. The publisher and its associates, directors or employees may have positions in, and may from time to time make purchases or sales of, securities mentioned herein. We cannot guarantee and you should not assume that future recommendations will equal the performance of past recommendations or be profitable.

← MTSL Issue 1018
