# MTSL Issue 1018

January 18, 2024

**UPDATES:** ACAD, ALKS, CLDX, PGEN, VXRT

## IN THIS ISSUE: JP Morgan Positive Start For Biotechs in 2024

*Since Last Issue: BTK:-4.93%; NBI: -1.35%; XBI: -2.75%; Model Portfolio: 3.68%*

**BIOTECH SECTOR ANALYSIS**

SENTIMENT — M&A Lures Despite Pullback

## JP Morgan Positive Start For Biotechs in 2024

We attended the JP Morgan conference last week and the overall mood was the best we have seen since pre-COVID. The feel of general optimism for biotech was in the air as most investors expect biotech to rebound in 2024 after a brutal two years for the sector. The furious M&A we have seen lately also continued as JNJ bought Ambrx for $2 billion and was announced Monday of the JP Morgan

In our MTSL universe, VKTX is one of the most talked about buyout targets, in addition to CLDX and MDGL. In fact, VKTX rallied sharply as we went to press and Phase I oral data for '2735 is due this quarter. Technically, the XBI did see a Golden Cross, with the 50-day moving average eclipsing the longer-term 200 day MA. That is a bullish sign and one which we have not seen since the early days of 2020's pandemic bounce led by COVID stocks MRNA, BNTX and NVAX. While there has been resurgence in COVID infections and hospitalizations, the biotech stock rally has become more widespread of late with immunology, inflammation and oncology joining in the gains. With the XBI giving way to the Mega Tech stocks of late, the index has excellent support at 81 (the new 50-day) and 80 (the new 200-day). The MACD has retreated after being accumulated since November,

conference. Biotech momentum continued more or less until this week as the group pulled back after the impressive run from late last year all the way into mid-January.

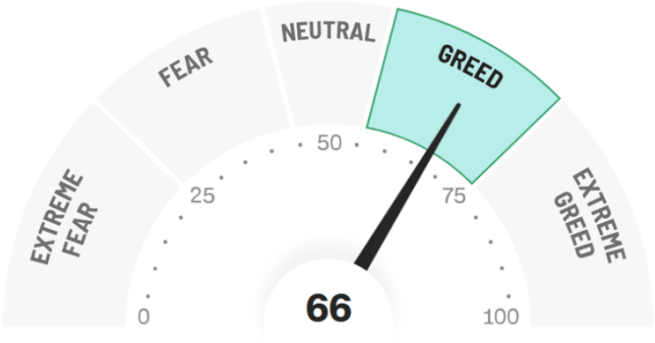
Kicking off the JP Morgan in a positive note, Johnson & Johnson announced last Monday that they are acquire Ambrx for $28 per share ($2 billion), representing an approximately 105% premium to Ambrx's closing price on January 5, 2024. The deal also has positive read through for MTSL recommendation BCYC which is a leader in developing next generation antibody drug conjugates (ADCs). ADCs are red hot as AbbVie recently bought ADC-developer ImmunoGen for $10.1 billion. Other notable deals include Pfizer's $43 billion deal for Seagen and Merck's announcement that it would pay Daiichi Sankyo $5.5 billion to jointly develop three ADCs.

Ambrx's proprietary Antibody Drug Conjugate (ADC) technology incorporates the advantages of highly specific targeting monoclonal antibodies securely linked to potent chemotherapeutic payloads to achieve targeted and efficient elimination of cancer cells without the prevalent side-effects typically associated with chemotherapy. JNJ will focus on accelerating the Phase I/II APEX-01 study of ARX517 in advanced prostate cancer, while progressing a pipeline of drug development candidates.

Merck also stepped up to the plate at JP Morgan when they bought cancer drug developer Harpoon Therapeutics for $680 million, gaining access to early-stage immunotherapies being tested for lung cancer and multiple myeloma. Global pharma companies' efforts to replace revenue from older drugs with promising new ones may have just begun in 2023, looming patent expirations and easing financing costs are setting up 2024 for a potential M&A frenzy as Big Parma scrambles to replace the over $300 billion in lost revenue to expiring patents by the end of the decade.

but to us that is healthy profit-taking after such a good run.


On a weekly basis, the XBI saw a rally that extended beyond the highs of 2023, with the 95 print on January 9th. With resistance at 101 (the 200-week MA), there is solid support at 81. The weekly RSI is still rather healthy at 59, down only slightly from last Issue's 61. That again, is quite positive as is the MACD which is showing positive fund flows since December. With a few key science meetings and FDA PDUFA dates nearing, stock picking remains key. The AAAAI abstracts are due February 5 with the conference shortly after (see CLDX below). In addition, FDA PDUFA dates in March include MTSL Recommendations MDGL (3/14) and ESPR (3/31), we believe further appreciation in those stocks is likely after the recent group pullback mentioned above. And further takeovers are probable with Big Pharma/Big Biotech in spending mode. Watch for Monday morning M&A announcements.



## Fed Not Helping Biotechs

Atlanta Fed President Raphael Bostic recently said he doesn't see the Fed cutting rates until the third quarter, later than the market's current projection for March, unless there is "convincing" evidence of inflation's decline. These comments follow pushback from several other central bank officials who pumped the brakes on market expectations for cuts in the first quarter of 2024. March was probably too early for a rate cut as the Fed needs to feel confident inflation is sustainably moving back to its 2% target. The Fed's preferred inflation gauge, the Personal Consumption Expenditures index, looks even better at 3.2% as of November. More encouraging, core PCE inflation dropped below 2% (1.9%) on a six-month annualized basis, which is under the Fed's target. The biotechs have been delivering solid news flow along with the burgeoning M&A environment. However, biotechs will need interest rate cuts to maintain momentum in 2024.


## TECHNICALS – Healthy Profit-Taking Post-JPM

After residing in overbought levels over the past month driven by strong sector fundamentals and an easing of inflation and interest rates, the XBI (87) is experiencing a well-deserved rest. The RSI is exactly at the neutral point (50), down from last Issue's 62-

## FEAR & GREED – GREED

The Fear & Greed Index has pulled back to 67 after having been in the Extreme Greed zone recently. The Index at 67 represents a healthy pull back after closing at 73 two weeks ago. Greed is also more sustainable than Extreme Greed which almost always represents market tops. We may stay in Greed for a while as the recent broad market's strength may continue.

### MTSL Events Due Near-Term

- CLDX Q1 – Barzo SubC CSU Phase II Data at American Academy of Asthma, Allergy & Immunology, Abstract released online 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 expected 1Q
- 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

63. From the 2023 low of ~64 reached on October 31, the XBI was up almost 50% to ~95 at the beginning of the JPMorgan Healthcare Conference (1/9/24), so it makes plenty of sense to see stocks pull back after such a strong run. M&A is back a feverish pace and the index and individual company takeover speculation has fallen into a familiar pattern of rallying into the weekend in hope of a Monday morning announcement, and then giving back some of the trade afterwards.

## Clinical Trials Watch

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

**COVID**

**GILD** – Study of Obeldesivir in Children and Adolescents With COVID-19

**ACAD** – ACP-204 in Adults With Alzheimer's Disease Psychosis Open Label Extension Study

**AMGN** – Effect of Repeated Oral Doses of Avacopan on the Pharmaco-kinetics (PK) of a Single Dose of Simvasta

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

**AMGN** – Olpasiran Trials of Cardiovascular Events and Lipoprotein(a) Reduction (OCEAN(a)) – Outcomes Trial

**AMGN** – A Study to Evaluate Rocatinlimab (AMG 451) in Adolescent Subjects With Moderate-to-severe Atopic De

**Genentech** – A Study to Evaluate the Efficacy and Safety of Astegolimab in Participants With Chronic Obstructiv

**INCY** – A Study to Assess the Efficacy and Safety of Ruxolitinib Cream in Children With Atopic Dermatitis (TRuE-A

**INCY** – A Study to Evaluate the Efficacy and Safety of Ruxolitinib Cream in Participants With Prurigo Nodularis (P

**PCRX** – Exparel vs. Marcaine ESP Block for Post-cardiac Surgical Pain

**SNY** – A Study to Investigate Long-term Safety and Tolerability of Itepekimab in Participants With COPD


## Company Updates

**UPDATES:** ACAD, ALKS, CLDX, PGEN, VXRT

### ACAD — Topline Pimavanserin Data from ADVANCE-2 Phase III Trial for Negative Symptoms of Schizophrenia Expected 1Q24

Topline pimavanserin data from ADVANCE-2 Phase III trial of Negative Symptoms of Schizophrenia is expected 1Q24 and positive data would serve a stock catalyst. ACAD has completed one positive pivotal study, ADVANCE-1. ADVANCE-2 leverages the optimal therapeutic dose of 34 mg in a 6-month trial designed to evaluate impact on persistent negative symptoms beyond acute psychosis period. The trial was designed to treat patients whose positive psychotic symptoms are adequately controlled, but

ACAD has two approved drugs and a pipeline of other drug development candidates in addition to a potential label expansion if ADVANCE-2 reads out positive making the company an attractive M&A candidate. That being said, potential acquirers are waiting on the ADVANCE-2 before they would make a move to acquire ACAD. In our view, ADVANCE-2 has a solid chance of success based on the ADVANCE-1 positive data which could then easily lead to a premium acquisition.

still suffer from predominant and uncontrolled negative symptoms, inhibiting their ability to live a normal, productive life. In our view, ADVANCE-2 has a solid chance of success based on the ADVANCE-1 positive data with the caveat that psychiatric trials can be tricky due to the need to use composite endpoints to prove efficacy.

**RECOMMENDATION**

**ACAD is a BUY under 28 with a TARGET PRICE of 45**

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## ALKS — ALKS Has 4 Strategic Priorities in 2024, Phase II Plan for '2680 Ready to Go

ALKS presented at JPM and provided the company's strategic priorities for 2024: (1) delivery of strong commercial growth and profitability, (2) advancement of its OX2R agonist narcolepsy program, (3) expansion of the neuroscience pipeline, and (4) planning for significant cash generation/earnings helped by winning the JNJ arbitration and spinning out oncology (MURA). ALKS decision to spin out MURA also allows them to better focus on creating shareholder value from '2680 which has more potential long term.

In our view, the Phase II trial of OX2R agonist ALKS 2680 in narcolepsy type 1 (NT1) patients has the potential to serve as a significant catalyst. '2680 has been designed for improved wakefulness duration and quality with a PK/PD profile that mirrors the natural sleep/wake cycle to control cataplexy. Recall positive Phase 1b proof-of-concept results were presented late last year which demonstrated a low therapeutic dose with once-daily oral dosing had an acceptable safety profile with a wide therapeutic window.

The placebo-controlled Phase 2 will explore 3 dose levels at 4mg, 6mg, and 8mg QD (n = 15 each; within the apparent therapeutic window of 3mg – 8mg) dosed for 6 weeks (endpoints include MWT, ESS, cataplexy) and will allow flexible dosing in a subsequent OLE portion. In 1H24E, we look for the Phase 2 NT1 trial to initiate, and also anticipate Phase 1b data in NT2 and idiopathic hypersomnia.

**RECOMMENDATION**

**ALKS is a BUY under 35 with a TARGET PRICE of 55**

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## CLDX — AAAI Abstracts/Conference Nearing, ALLK Fails In CSU/AD – BUY

Abstracts for the Annual Meeting of the American Academy of Asthma, Allergy & Immunology (AAAAI or "QuadAI") are set to be released online on February 5, 2023, followed by meeting on 2/23-2/26 to be held in Washington, D.C. (https://annualmeeting.aaaai.org/) In addition, last week ALLK's lirentelimab failed to show a benefit in two Phase II studies – one in chronic spontaneous urticaria (CSU) and one in atopic dermatitis (AD). Both events – the upcoming AAAAI meeting and the recent ALLK blow up – continue to bode quite well for Celldex' barzolvolimab. BUY

## Here Comes The AAAAI

The clinical milestones and event calendar for barzo continues. Ever since the exceptional topline data for subcutaneous (SC) barzo in CSU were released in early November, investors are eager to see the additional efficacy and safety details. These will be available next month. First, the abstracts are scheduled to be published in an online supplement to The Journal of Allergy and Clinical Immunology (JACI) on Monday, February 5, 2023 (https://www.sciencedirect.com/journal/journal-of-allergy-and-clinical-immunology). Details of the successful, 208-patient study will be further outlined as a Late-Breaker trial in an oral presentation at the AAAAI meeting in Washington, D.C. While we already have the topline results, details to look for will be the SC compound's side effect profile, including hematologic and other markers for the three dose levels (75mg at 4wks, 150mg at 4wk, and 300mg at 8wks) at 12 weeks (https://clinicaltrials.gov/study/NCT05368285?cond=Chronic Spontaneous Urticaria&term=celldex&rank=1). As we learn more, we remain steadfast that barzo is solidifying itself as the Best-in-Class KIT/mast cell inhibitor for CSU (plus CindU, and cold urticaria). We also expect the Company to hold an investor call with the drug's lead investigator, Dr. Marcus Maurer, Professor of Dermatology and Allergy and the executive Director

## ALLK Fails (Again)

Last week, Allakos announced that the Phase II lirentelimab trials in both Chronic Spontaneous Urticaria (CSU) and Atopic Dermatitis (AD) did not meet their primary endpoints. Ever since the compound's failure in eosinophil disorders (such as EoE) in late 2021, the Company has tried to position the compound as a treatment for mast cell conditions like CSU. The compound inhibits Siglec-8, an inhibitory receptor selectively expressed on human eosinophils and mast cells. However, its effects on mast cells are questionable at best and the latest data was even more disappointing that we expected. As a reminder, CLDX's barzo blocks the vast majority of mast cells via KIT/stem cell factor leading to major reductions in tryptase. Hence, we never really believed that lirentelimab was competitive to barzo. Moreover, after recent disappointments with CSU compounds from competitors NVS, AMGN, THRD and now ALLK – Barzo is the clear leader in CSU.

## With AAAAI Approaching (and even the ALLK blow-up), CLDX Prime For Acquisition

The wave of recent premium biotech takeovers by Big Pharma continues at a pace not seen in several years. With barzo being wholly-owned, the markets include various blockbusters (e.g., Dupixent like) and by far the best data around, Celldex is ripe for takeover that, in our view, may make our TARGET PRICE look conservative.

**RECOMMENDATION**

**CLDX is a BUY under 75 with a TARGET PRICE of 100**

of the Institute of Allergology at the Charité – Universitätsmedizin Berlin – likely the single Key Opinion Leader (KOL) in the field.

## ESPR — ESPR Raises $85.1 Million at $1.50 Per Share, CLEAR Label Expansion PDUFA March 31st

ESPR fresh off their $125 million settlement with Daiichi Sanyko Europe has accessed the capital markets to raise another $85.1 million at $1.50 per share. Obviously we would have liked the raise at a higher price, but ESPR had limited options. We can only hope that the book runner, Jeffries, has brought some quality institutional investors into ESPR.

Up next for ESPR are label approvals for cardiovascular risk reduction indications for NEXLETOL and NEXLIZET in the first quarter of 2024. In June 2023, the Company announced its submission of four Supplemental New Drug Applications based on the CLEAR Outcomes trial, which demonstrated that bempedoic acid, contained in both NEXLETOL and NEXLIZET, can significantly reduce cardiovascular risk across a range of primary and second endpoints.

These applications were accepted by the FDA which issued a PDUFA, or action, date of March 31, 2024. The Company's EMA applications also remain on track, with anticipated approval in the first half of 2024. We expect ESPR to receive timely label expansions in both the U.S. and EU which will allow the company to turn the corner and deliver significant sales growth going forward.

**RECOMMENDATION**

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

## PGEN — Pivotal Phase II PRGN-2012 Data in Q2

PGEN presented at JP Morgan and emphasized the progress being made with PRGN-2012. PRGN-2012 is currently in a Phase I/II pivotal single arm trial in adult patients with recurrent respiratory papillomatosis (RRP). RRP is a rare, difficult-to-treat and sometimes fatal neoplastic disease of the upper and lower respiratory tracts caused by human papillomavirus type 6 (HPV 6) or HPV type 11 (HPV 11). A Phase II data presentation is anticipated in the

PRGN-2012 has already received Orphan Drug Designation from the FDA and PGEN was the first company to receive Breakthrough Therapy Designation and an accelerated pathway for approval from the FDA for an RRP treatment. The next catalyst for PGEN will be the pivotal Phase II RRP data for PRGN-2012 in Q2 which will lead to an FDA filing

second quarter of 2024 and a planned Biologics License Application (BLA) submission under an accelerated approval pathway with the FDA is anticipated in the second half of 2024. Commercial readiness preparations are underway for a potential launch next year in both the U.S. and EU.

This week, PGEN announced that the European Commission (EC) has granted Orphan Drug Designation for the Company's first-in-class investigational medicine PRGN-2012 for the treatment of recurrent respiratory papillomatosis (RRP).

**RECOMMENDATION**

**PGEN is a BUY under 5 with a TARGET PRICE of 12**

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## VXRT — VXRT Dismisses CEO, Raises $10 Million From Industry Leader RA Capital

VXRT has made two bold moves as they have dismissed their CEO and raised important funds from the highly respected RA Capital. VXRT raised $10 million from RA Capital Management by selling 15,384,615 shares of its common stock in a registered direct offering at an offering price of $0.65 per share. The $0.65 represents a premium to the previous close of $0.56. The stock has responded positively to both the change in management and the additional funding. In our view, a change was needed as VXRT has not delivered enough progress for shareholders over the last few years. RA Capital is highly respected in the industry and their vote of confidence in VXRT and their oral/pill vaccine technology is encouraging.

VXRT's development programs currently include pill vaccines designed to protect against coronavirus, norovirus, seasonal influenza, and respiratory syncytial virus (RSV), as well as a therapeutic vaccine for human papillomavirus (HPV), the company's first immune-oncology indication.

In our view, the norovirus program has the most potential to deliver value for shareholders. VXRT is currently analyzing norovirus data to define the timing of a larger Phase IIb trial and identifying ways to reduce the size and duration of a subsequent Phase III registration trial. Importantly, RA Capital has seen all the norovirus data and has chosen to invest in VXRT. We are lowering our BUY and TARGET to more accurately reflect VXRT's current prospects

**RECOMMENDATION**

**VXRT is a BUY under 3 (was 5) with a TARGET PRICE of 8 (was 15)**

# The Back Page

| Symbol | Company | Orig.Rec. | Current | Target | Recommendation |
|---|---|---|---|---|---|
| ACAD | Acadia | 33.79 | 27.59 | 45 | BUY under $28 |
| ALKS | Alkermes | 10.13 | 27.76 | 55 | BUY under $35 |
| BCYC | Bicycle | 43.92 | 17.74 | 75 | BUY under $50 |
| BMRN | BioMarin | 12.68 | 92.53 | 150 | BUY under $100 |
| CLDX | Celldex | 10.50 | 39.66 | 100 | BUY under $75 |
| ESPR | Esperion | 24.42 | 2.15 | 25 | BUY under $10 |
| INCY | Incyte | 5.88 | 61.18 | 108 | BUY under $85 |
| IONS | Ionis | 7.63 | 50.65 | 65 | BUY under $50 |
| MDGL | Madrigal | 17.00 | 224.10 | 400 | BUY under $300 |
| PCRX | Pacira | 15.78 | 31.73 | 100 | BUY under $80 |
| PGEN | Precigen | 34.42 | 1.21 | 12 | BUY under $5 |
| SGMO | Sangamo | 4.77 | 0.42 | 15 | HOLD |
| TCRT | Alaunos | 8.00 | 1.37 | 5 | HOLD |
| VKTX | Viking | 16.83 | 20.94 | 45 | BUY under $28 |
| VXRT* | Vaxart* | 8.00 | 0.79 | 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 | 131,053 |
| Alkermes (ALKS) | 3,800 | 88,690 | 105,488 |
| Bicycle (BCYC) | 2,400 | 105,408 | 42,576 |
| Celldex (CLDX) | 15,832 | 174,993 | 627,897 |
| Esperion (ESPR) | 3,316 | 105,316 | 7,129 |
| Incyte (INCY) | 1,229 | 34,817 | 75,190 |
| Ionis (IONS) | 3,087 | 49,123 | 156,357 |
| Madrigal (MDGL) | 3,127 | 69,980 | 700,761 |
| Pacira (PCRX) | 2,375 | 63,887 | 75,359 |
| Precigen (PGEN) | 9,690 | 76,510 | 11,725 |
| Sangamo (SGMO) | 19,456 | 253,596 | 8,123 |
| Alaunos (TCRT) | 26,125 | 166,100 | 35,896 |

| | | | |
|---|---|---|---|
| Viking (VKTX) | 12,000 | 201,960 | 621,646 |
| Vaxart (VXRT) | 29,687 | 250,000 | 9,538 |
| | | | |
| *(01/18/24)* | | **Equities:** | **$2,608,736** |
| | | **Cash:** | **$ 237,884** |
| | | **PORTFOLIO VALUE:** | **$2,846,620** |

**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** | 3.6% | -4.9% | 3.7% |
| **2024 YTD** | 0.3% | 0.2% | 1.8% |
| **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

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