

**BIOTECH FRONTIERS**

ISSUE #13 | MARCH 6, 2025

# A MIRACLE DRUG FOR A DREADFUL DISEASE

A First-Of-Its-Kind Treatment For A Rare Respiratory Disorder

A Powerful Catalyst Is Only Months Away ...

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### **Powerful Catalyst Is Only Months Away . . .**

On the morning of September 11, 2001, Al-Qaeda terrorists hijacked two jets and flew them into the Twin Towers in New York City, taking the lives of 2,977 people and changing American history forever.

Raul Martinez was a sergeant with the New York City Police Department when the attacks took place. As a first responder, he rushed to the site of the disaster – and spent the next eight months at Ground Zero dealing with its aftermath. Describing those harrowing months, Martinez modestly explained, “I did what I had to do. I was just doing my job.”

Although we did not appreciate the implications at the time, the collapse of the Twin Towers unleashed a blend of jet fuel, concrete, steel, glass, paint, and other debris into the air, much of it in the form of tiny toxic matter. These particulates – which contained a multitude of known carcinogens such as asbestos, benzene, and beryllium – remained suspended in the air for weeks after. Few first responders understood the risks of breathing such air. A physician at UCLA School of Medicine would later remark, “Today, every single 9/11 recovery worker would be wearing an N-95. But nobody was wearing masks back then.”

Soon after his tour of duty at Ground Zero was complete, NYPD Sgt. Martinez – like thousands of other first responders who worked there – developed a dry, hacking cough that got progressively worse, eventually leaving him out of breath even when at rest. He was diagnosed with pulmonary sarcoidosis, a form of interstitial lung disease (“ILD”) where inflammation and scarring in the lungs can lead to devastating impairments in quality of life, and eventually to premature death.



Tragically, though both pulmonary sarcoidosis and the broader family of ILD have been known to medicine for decades, there are no cures and no truly effective therapies. Most patients are treated with corticosteroids, which can help manage symptoms in the short term and sometimes medium term but those steroids come with negative side effects in the long term. For the 9/11 first responders such as Sgt. Martinez and the hundreds of thousands of others who also suffer from ILD, the medical state of play has offered little hope.

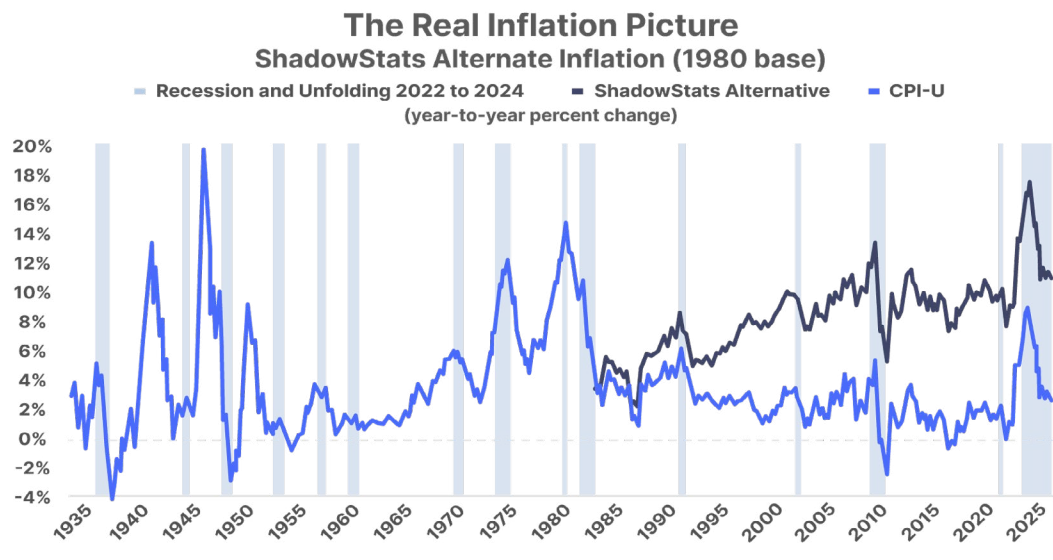
This month, we'll focus on a company that is changing all that. Its lead drug candidate promises to be a game-changing therapy both for pulmonary sarcoidosis and for the broader family of ILD to which it belongs. The company is **aTyr Pharma (Nasdaq: ATYR)**, a 20-year-old company based in San Diego, California. To better understand why it's a compelling investment, we'll be relying on our usual framework at *Biotech Frontiers*:

1. The Big Picture
2. The Science
3. The Opportunity
4. The Catalysts
5. The Balance Sheet
6. The Capitalization Table
7. The Risk / Reward

## The Big Picture

Three months ago, we warned that the U.S. economy would likely suffer from **a bout of renewed inflation**, causing the Federal Reserve to hit the brakes on its planned rate cuts. The "script" continues to play out as we cautioned. The consumer price index ("CPI") for January came in at 3% annualized, a full 50% higher than the Fed's stated 2% inflation target. On a monthly basis, CPI rose by 0.5%, equivalent to an annualized figure of 6%.

As we've observed before, the CPI is a government-manufactured index that understates the real inflation most Americans experience. The price of eggs, for example, rose 15.2% month on month in January. To more accurately track what's going on in the economy, we refer to John Williams' superb *ShadowStats* alternative CPI, which rose 10.8% annualized in January:



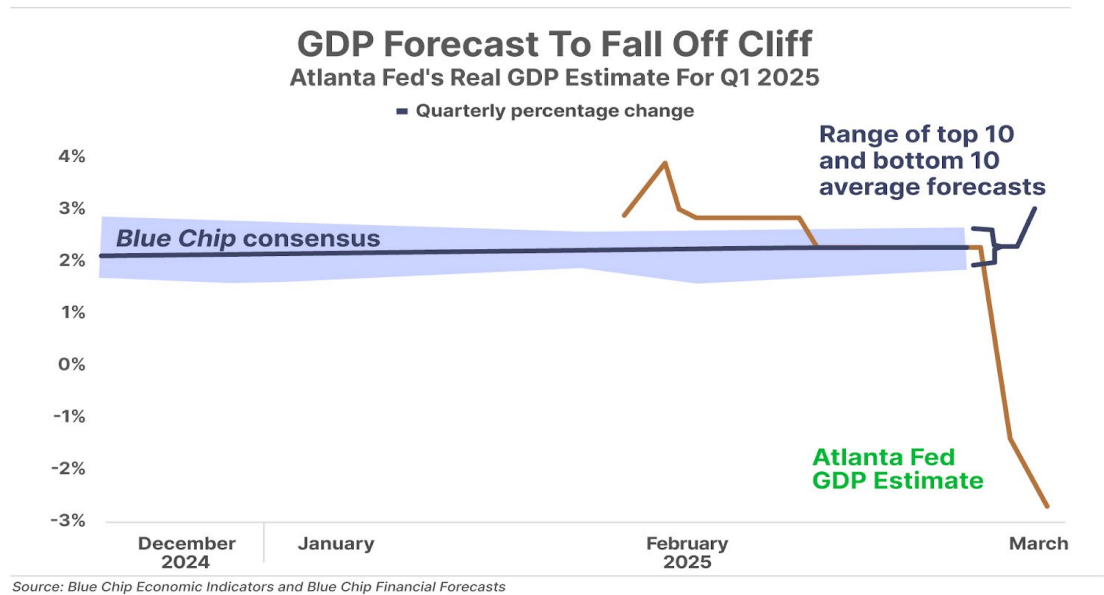
Source: Shadow Stats, Bureau of Labor Statistics

One of the most ominous aspects of this inflation data is that President Donald Trump's economic policies have yet to really take effect. Earlier this week, the Trump administration applied 25% tariffs on all goods imported from Canada and Mexico, America's two largest trading partners. It also slapped an additional 10% tariff on Chinese goods on top of the 10% tariff already in place. These moves increase the levies America imposes on foreign goods to levels not seen since World War II. They will almost surely result in higher prices for American consumers.

In the meantime, the Trump administration has yet to ramp up what it has promised will be "the largest domestic deportation operation in American history." When it does, certain critical sectors in the U.S. economy – notably agriculture, construction, and hospitality – will face a sudden supply shortage to their labor force. It would be surprising if this supply shock, too, did not result in higher prices.

But inflation isn't the only major economic problem on the horizon. In its short time in office, the Trump administration – through its Department Of Governmental Efficiency ("DOGE") – has frozen tens of billions in federal spending, including many research and development programs administered by the National Institutes of Health ("NIH") and the U.S. National Laboratories. Meanwhile, all three countries targeted by Trump's tariffs – Canada, Mexico, and China – have immediately retaliated with tariffs of their own, sparking fears of a global trade war. Not surprisingly, draconian freezes on federal spending coupled with looming anxieties about the free flow of goods into and out of the U.S. are already having a major impact on both economic confidence and economic activity.

The Federal Reserve Bank of Atlanta produces a metric called GDPNow, which aims to be an early estimate of quarterly GDP. Here is its latest GDPNow forecast for the first quarter of 2025:



The punch line: We may already be in the early innings of a severe contraction in GDP that is the telltale signal of a recession. And of course, when recession and inflation meet, we get a condition that Americans who lived through the 1970s remember with dread: *Stagflation*.

The stock market reacted with euphoria in the immediate aftermath of Trump's election, rallying to a peak gain of around 10%. But now that it has begun to weigh the consequences of Trump's policies, these gains have vanished. All four major indexes (the Dow Industrial Average, S&P 500, Nasdaq Composite, and Russell 2000) are now in the red for the period since Election Day, with the economically most sensitive Nasdaq and Russell both down more than 5%.

My sense is that we are still at the very beginning of this downturn. For those who missed the warning in [last month's issue](#), I will reiterate: I believe more pointedly today than ever that we're in for a slow-motion traffic accident in our economy and financial markets.

As is often the case, when the stock market catches a cold, the biotech sector catches pneumonia. While the S&P 500 is down about 1% since election day, the biotech sector's flagship large-cap ETF – the XBI Index – is down a sizable 16.4%. For *Biotech Frontiers* subscribers, that news contains a silver lining, because it means we have a larger bargain bin of biotech stocks to sift through to find the most compelling, extreme values. But it also puts a premium on identifying opportunities that have strong balance sheets, so that they have staying power, and strong catalysts, so that we don't need to rely on a recovery in either the stock market or the biotech sector to "get paid."

This month's recommendation fits these criteria to a T.

## The Science

ILD (interstitial lung disease), as I said earlier, refers to over 200 rare disorders characterized by inflammation and scarring (or “fibrosis”) of the supportive tissues surrounding the lung’s air sacs. This scarring leads to lung stiffness, making breathing increasingly difficult and interrupting the efficient transfer of oxygen into the bloodstream. In the beginning, ILD patients experience a persistent dry cough and shortness of breath. Over time, the disease often progresses to have a crippling effect on quality of life, leaving patients, such as Sgt. Martinez, struggling to breathe even when at rest. Many variants of ILD have survival rates worse than common cancers.

Like cancer, the causes of ILD are varied and not completely understood: exposure to environmental toxins, such as asbestos, silica dust, and radiation have been linked to ILD, as have autoimmune disorders such as rheumatoid arthritis and systemic sclerosis. But whereas many cancers today have viable treatment options that can prolong life and sometimes even deliver cures, the options for ILD are dismal: no disease-modifying therapies are available. As mentioned before, most ILD patients are treated with corticosteroids that deliver short-term relief from symptoms but result in debilitating side effects over the medium and long term, without improving patient outcomes.

ATyr Pharma’s efzofitimid holds promise to be a game-changing drug for ILD. A first-in-class biologic drug, it works by quieting the immune system’s inflammatory response locally in the lungs, thereby preventing the scarring that leads to fibrosis. Efzofitimid is derived from a naturally occurring fragment of histidyl-tRNA synthetase (“HARS”), a protein involved in protein synthesis. This fragment is then modified or “engineered” to improve its binding. The finished molecule selectively binds to neuropilin-2 (“NRP2”), a receptor highly expressed in immune cells implicated in ILD. By targeting NRP2, efzofitimid modulates the immune cells, leading to a reduction in pro-inflammatory cytokines and chemokines that are elevated in ILD patients. This immunomodulatory effect helps to resolve inflammation without broadly suppressing the immune system.

Efzofitimid’s early clinical trials have delivered home-run results. In its Phase IIa trial treating pulmonary sarcoidosis, a terrible variant of ILD, efzofitimid delivered significant improvements in multiple measures of lung function – effectively enabling patients who received it to breathe normally, without having to resort to steroids. It also exhibited a statistically significant reduction in inflammatory biomarkers, suggesting the drug works in practice the way we believe it does conceptually. Best of all, efzofitimid achieved these benefits for patients without any observed adverse side effects.

Efzofitimid’s pivotal Phase III trial for sarcoidosis is now underway. If, as we anticipate, it reproduces the efficacy and safety we saw in its Phase II, it will almost certainly earn Food and Drug Administration (“FDA”) approval and a moniker as a “miracle drug” for ILD patients.



## The Opportunity

“If you’re right, you’ve got to get paid.” We revisit my old boss Julian H. Robertson’s maxim regularly at *Biotech Frontiers* as a reminder that game-changing science isn’t enough by itself – we require any company we underwrite to have sizable opportunities that will move its stock price multiplicatively if its positive catalysts unfold favorably. To assess this factor on our investment checklist, we generally perform a back-of-the-envelope market-sizing analysis.

Here is that market-sizing arithmetic for aTyr’s efzofitimid:

The first variant of ILD that aTyr is targeting with efzofitimid – pulmonary sarcoidosis – has about 200,000 patients in the U.S. and another 200,000 in Europe and Japan. ATyr believes that, in a conservative scenario, efzofitimid will offer dramatic benefits to at least 50% of pulmonary sarcoidosis patients. A more optimistic estimate would be as high as 75%, but for our analysis here we’ll stick with the more conservative estimate.

Efzofitimid has no competitors as a treatment for ILD and would be the first novel therapy for this family of diseases in over 60 years. Because it has no direct competitors, estimating efzofitimid’s likely price is challenging. However, similar therapies for orphan diseases are priced (and reimbursed by health insurers) at \$200,000 annually. To err on the conservative side, let’s assume that efzofitimid’s price eventually settles at half of this \$200,000 benchmark – or \$100,000 per patient per year.

If efzofitimid ultimately reaches 50% of the U.S. patient population for pulmonary sarcoidosis, or 100,000 patients, at a \$100,000 annual price, this market penetration would translate into \$10 billion in annual revenue – a figure that excludes the market opportunity to treat patients in Europe and Japan (where pricing would likely be lower). It also excludes all of the other variants of ILD that efzofitimid – or sister drugs that aTyr is developing – will likely address. The market for these other variants of ILD comprises approximately 400,000 additional patients in the U.S. alone, i.e., an opportunity twice the size of the pulmonary sarcoidosis population.

What does our market-sizing analysis imply for shares of aTyr? As regular *Biotech Frontiers* subscribers know, we generally apply a rule of thumb and multiply a drug’s peak revenue by 2.5x to arrive at a conservative estimate of its value. Of course, 2.5x \$10 billion is \$25 billion. ATyr’s current market capitalization is about \$260 million – implying potential for aTyr to appreciate 95x.

To be 100% clear, I’m not predicting that aTyr’s stock will appreciate close to a hundred-fold. We perform our market-sizing analysis not to generate predictions about a future share price, but instead to “sanity check” that there’s a lot of room for a stock to appreciate if things go well. We’re searching for stocks that have a chance to generate multiplicative gains. That’s unquestionably true for aTyr, which offers us plenty of runway to “get paid” if we’re right about efzofitimid’s potential.

## The Catalysts

Amid an environment of economic and market tumult, it's more important than ever to find opportunities that feature powerful, near-term catalysts to propel a stock upward. Indeed, it is catalysts that make the biotech sector, like the high-yield bond market that Marty Fridson writes about in *Distressed Investing*, a distinctive niche that can generate winners even amid a broader market downturn. "Hope is not a strategy" – and in the biotech sector, we needn't rely on hope.

aTyr features a potent catalyst: A pivotal, Phase III clinical trial readout for efzofitimid anticipated only months from now, in Q3 2025. Success in this trial will mean aTyr will have all the data it needs to file a Biologics License Application ("BLA") with the FDA for efzofitimid's approval to treat pulmonary sarcoidosis. We would then expect the FDA to act on that BLA, likely with a green light, within six to 12 months.

Pivotal Phase III trials for new drugs are generally risky affairs with many things that can trip up the results. But here, we have two important reasons to be confident about a positive outcome.

1. Before launching this Phase III trial, aTyr held a successful end-of-Phase-II meeting with the FDA in which the agency agreed to aTyr's preferred efficacy parameters and trial design. Obtaining agreement with the FDA about trial design, and winning the FDA's consent to a company's preferred guideposts for efficacy, tend to be crucial harbingers of Phase III success.
2. The specific "primary endpoint" that aTyr negotiated with the FDA for efzofitimid's Phase II trial – a tapering of patients' reliance on corticosteroids to relieve their pulmonary sarcoidosis symptoms – is one that the efzofitimid has already demonstrated it can "knock out of the park" in its prior Phase II trial.

If, as I anticipate in our "base case," efzofitimid delivers a statistically significant, positive Phase III outcome in Q3 of this year, it would surprise me if aTyr didn't appreciate in value to \$500 million to \$1 billion – or 2x to 4x its current market capitalization. At that value, the company would still have plenty of runway to appreciate more after an FDA approval and eventual commercial launch. But a 2x to 4x appreciation would be a terrific win for a six-month (or less) holding period.

## Balance Sheet

In seasons of deep economic uncertainty with market storm clouds gathering, it becomes more important than ever for young biotech companies to have strong balance sheets that confer staying power. The best-situated companies – such as *Biotech Frontiers* portfolio company **Roivant Sciences (Nasdaq: ROIV)** – will have enough net cash on their balance sheets to fund operations for years. Short of a fortress balance sheet, we want to know that any company we underwrite has at least enough net cash to fund itself through its next major milestone.



aTyr falls into this latter category. With about \$66 million of cash, the company has enough cash to fund operations for a year without tapping the capital markets – well past aTyr’s Q3 2025 Phase III trial readout for efzofitimid’s, and likely all the way through a BLA submission for efzofitimid to the FDA. Like many young biotech companies, aTyr isn’t fully funded past financial breakeven and through to eventual positive cash flow – so it will need to raise capital again. But given our confidence about its Phase III trial result, we can accept this risk with a reasonable belief that aTyr will be able to raise its next tranche of capital at a significant premium to today’s valuation, thereby minimizing our dilution.

## The Cap Table

“Success leaves clues.” We return to this mantra of Tony Robbins, who coaches the world’s elite performers across many disciplines, as a reminder to pay attention to where the world’s best investors are putting their capital. aTyr – which, at \$260 million in market capitalization, is a tiny company in a U.S. public biotech market worth over \$1 trillion – has nonetheless drawn meaningful investments from two categories of investors we follow closely: one “Whale” and one “Smart Money” investor.

The Whale is Fidelity Investments, one of the world’s largest money managers, which manages over \$15 trillion. We watch Fidelity closely not only because of its size but also because its life sciences investment team has a storied and long track record of success in biotech. With a 10.5% ownership stake in aTyr, Fidelity is the company’s second-largest shareholder.

The Smart Money investor is Point72, which is the principal hedge-fund and family office investment vehicle of Stevie Cohen – now known to many as the owner of baseball’s New York Mets, but widely recognized on Wall Street as one of the shrewdest hedge-fund investors of all time. With a 5.8% ownership stake, Point72 is aTyr’s third-largest shareholder, right behind Fidelity. Point72 is known to prefer biotech investments with strong imminent catalysts, so the firm’s meaningful investment is a reassuring validation of our own conclusions about the company’s upcoming Phase III clinical trial readout.

Especially given aTyr’s small capitalization, the presence of these two notable investors as major shareholders lets us know some of the world’s most accomplished capital allocators share our perception of aTyr’s favorable risk/reward.

## The Risk / Reward

As regular *Biotech Frontiers* readers know, the last step in our underwriting process is always an assessment of the overall risk/reward. Three tools help us accomplish this: a Premortem, a Parade, and an Expected Value Tree.

In our **Premortem**, we imagine that our investment has not gone as planned and reverse engineer why. Here is our Premortem for aTyr: Notwithstanding the seemingly auspicious setup for aTyr's Phase III clinical trial, the results miss the trial's primary endpoint, muddying the outlook for efzofitimod's approval and delaying aTyr's plans to file a BLA. The company is compelled to raise capital at a significant discount to today's stock price, instead of a premium. Investors who hold the shares at today's levels face capital impairment of 75% to 90%.

Our **Parade** is the mirror opposite of our Premortem – it's our invitation to imagine that this investment has gone well. Our aTyr Parade goes like this: As aTyr's Phase III readout for efzofitimod draws closer – toward the beginning of Q3 2025 – the stock appreciates materially. This appreciation provides us an opportunity to take profit of between 50% to 100% even before the Phase III results are published. When the Phase III results arrive, they are a home-run success, with efzofitimod meeting its primary and secondary endpoints with statistical significance. This success prompts aTyr stock to trade at between \$500 million and \$1 billion in market cap, a 2x to 4x gain from today's level. We are able to take our original investment off the table and let the remainder ride. Over the ensuing three years, as aTyr obtains eventual approval for efzofitimod in pulmonary sarcoidosis and advances it toward approval in other variants of ILD, aTyr stock appreciates by more than 5x.

Our **Expected Value Tree** distills everything that's come before into simple arithmetic. We begin by encapsulating our entire investment thesis into a downside scenario, a base-case scenario, and an upside scenario. We assign a probability and a share price to each. And we derive our enterprise value ("EV") for the stock based on the sum of these three probability-weighted scenarios and their respective contributions. Here is our Expected Value Tree for aTyr:

**aTyr's Expected Value Tree**

Scenario	Summary	Probability	Share Price	EV Contribution
Downside	Efzofitimod experiences an unexpected Phase III trial failure	25%	\$0.50	\$0.13
Base Case	Phase III trial success and BLA approval	50%	\$10.00	\$5.00
Upside	Phase II trial success, BLA approval and eventual buyout	25%	\$15.00	\$3.75
			<b>Expected Value</b>	<b>\$8.88</b>
			<i>Change</i>	196%

Due to the adverse economic and market environment we've outlined in our discussion on the Big Picture, which has placed many stocks in the biotech market into steep downtrends, **we will be initiating our position in aTyr as a small toehold** and will wait to buy a more substantial position at what we anticipate will be lower prices. Accordingly, please buy aTyr Pharma up to \$3.50 in an amount one-tenth the size you would ordinarily allocate to a full Biotech Frontiers position. So for example, if you would typically allocate \$5,000 to a full position, buy only \$500 worth of aTyr shares. I will advise you on when to increase the position. We will track our holding in aTyr in the section of the *Biotech Frontiers* portfolio labelled "Toeholds" to reflect its smaller size.









**Action to Take: Buy aTyr Pharma (Nasdaq: ATYR) up to \$3.50 per share in an amount one-tenth the size you would ordinarily allocate to a full Biotech Frontiers position**

## Portfolio Review

BIOTECH FRONTIERS PORTFOLIO						
Ticker	Company	Entry Date▲	Entry Price	Latest Close	Total Return	Status
Open Positions						
<a href="#">SGMT</a>	Sagimet Biosciences	<a href="#">01/09/2024</a>	\$5.71	\$3.66	50.35%	Buy Up to \$5.00*
<a href="#">IOVA</a>	Iovance Biotherapeutics	<a href="#">02/05/2024</a>	\$7.92	\$4.05	26.58%	Buy Up to \$5**
<a href="#">ROIV</a>	Roivant Sciences	<a href="#">02/29/2024</a>	\$11.44	\$10.70	-6.47%	Buy Up to \$13.00
<a href="#">TGTX</a>	TG Therapeutics	<a href="#">07/03/2024</a>	\$18.79	\$35.11	86.85%	Buy Up to \$19.75
<a href="#">SGMT</a>	Sagimet Biosciences	<a href="#">09/05/2024</a>	\$2.67	\$3.66	67.04%	Buy Up to \$5.00***
Toeholds						
<a href="#">HUMA</a>	Humacyte	<a href="#">01/09/2025</a>	\$4.68	\$3.15	-32.69%	Buy Up to \$4.80
<a href="#">8473</a>	SBI Holdings	<a href="#">02/05/2025</a>	¥4,315.00	¥4,426.00	2.57%	Buy Up to ¥8,500^
<a href="#">ATYR</a>	aTyr Pharma	03/05/2025	\$3.15	\$3.15	0.00%	Buy Up to \$3.50
Portfolio Hedges						
<a href="#">LBRT</a>	Liberty Energy	<a href="#">12/04/2024</a>	\$18.32	\$15.65	-13.70%	Buy Up to \$20.00

^In order to trade SBI Holdings, you'll need to use a broker that permits you to trade specifically in Japan. See instructions in the **February 2025 issue**.

## BIOTECH FRONTIERS CLOSED POSITIONS

Ticker	Company	Entry Date	Entry Price	Exit Date ▲	Exit Price	Total Return
CYTT	Cytier Therapeutics	<a href="#">01/09/2024</a>	\$3.05	<a href="#">02/08/2024</a>	\$3.12	2.30%
STRO	 Sutro Biopharma	<a href="#">01/09/2024</a>	\$4.03	<a href="#">03/18/2024</a>	\$3.91	-2.98%
NUVB	 Nuvation Bio	<a href="#">01/09/2024</a>	\$1.51	<a href="#">03/18/2024</a>	\$2.26	49.67%
AVIR	 Atea Pharmaceuticals	<a href="#">01/09/2024</a>	\$3.45	<a href="#">03/18/2024</a>	\$4.00	15.94%
KOD	 Kodiak Sciences	<a href="#">01/09/2024</a>	\$3.16	<a href="#">03/18/2024</a>	\$5.94	87.82%
VIR	 Vir Biotechnology	<a href="#">01/09/2024</a>	\$10.18	<a href="#">03/18/2024</a>	\$10.68	4.91%
LYEL	 Lyell Immunopharma	<a href="#">01/09/2024</a>	\$2.07	<a href="#">03/18/2024</a>	\$2.08	0.48%
ATHA	 Athira Pharma	<a href="#">01/09/2024</a>	\$2.87	<a href="#">03/18/2024</a>	\$2.49	-13.09%
CMRX	 Chimerix	<a href="#">02/08/2024</a>	\$0.91	<a href="#">03/18/2024</a>	\$1.10	20.87%
VNDA	 Vanda Pharmaceuticals	<a href="#">05/02/2024</a>	\$4.68	<a href="#">10/14/2024</a>	\$4.81	2.78%
DERM	Journey Medical	<a href="#">06/06/2024</a>	\$4.68	<a href="#">12/04/2024</a>	\$5.59	19.44%
NUVB	Nuvation Bio	<a href="#">11/06/2024</a>	\$2.54	<a href="#">12/04/2024</a>	\$2.75	8.27%
QURE	 uniQure	<a href="#">01/09/2024</a>	\$6.62	<a href="#">12/10/2024</a>	\$15.30	131.12%
QURE	uniQure	<a href="#">10/02/2024</a>	\$4.54	<a href="#">12/10/2024</a>	\$15.30	237.00%

## BIOTECH FRONTIERS WATCHLIST

Ticker ▲	Company	Initial Analysis	Latest Close
Watchlist			
ADCT	ADC Therapeutics	<a href="#">04/04/2024</a>	\$1.69
DERM	Journey Medical	<a href="#">06/06/2024</a>	\$5.23
KOD	Kodiak Sciences	<a href="#">01/09/2024</a>	\$3.88
NRXP	NRX Pharmaceuticals	<a href="#">04/04/2024</a>	\$2.14
NUVB	Nuvation Bio	<a href="#">01/09/2024</a>	\$1.87
SLN	Silence Therapeutics	<a href="#">04/04/2024</a>	\$4.73
STRO	Sutro Biopharma	<a href="#">01/09/2024</a>	\$1.36

\*Total Return reflects selling 1/2 of Sagimet Bio (SGMT) on January 22, 2024 for \$18.42 per share and resuming a full position on February 8, 2024, up to \$6.75 per share.

\*\*Total Return reflects selling 1/2 of Iovance (IOVA) on February 21, 2024 for \$16 per share.

\*\*\*Total Return reflects selling 1/2 of Sagimet Bio (SGMT) on October 16, 2024 for \$5.26 per share.

Kodiak Sciences (KOD) Total Return reflects selling 1/2 of position on March 5, 2024 for \$6.20 per share.

*We cannot offer individual investment advice... but we can recommend TradeStops. TradeStops offers a customized suite of tools that can help you determine how much of a stock to buy... when to sell... when to buy more... and how much of your portfolio to dedicate to each position. As you know, we can't tell you how to handle your investments, but we can, and do, advise you to get TradeStops. [Learn more here.](#)*

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It's been a challenging month for biotech, but with a few exceptions our portfolio at *Biotech Frontiers* is holding up well.

**Sagimet Biosciences (Nasdaq: SGMT)** continues quietly searching for a strategic partner to fund the Phase III trial for its potential blockbuster denifanstat. As I remarked last month, the longer this process takes, the more bullish I become about the outcome. At this point, I estimate the probability that the company is in talks to be acquired in a buyout at greater than 50%. I say this not because I possess any actual information, but instead because a simple royalty or milestones deal wouldn't take this long to negotiate, whereas a partial or complete buyout would. Even if I'm mistaken about the buyout likelihood, I remain steadfastly confident that Sagimet will eventually negotiate an attractive deal to fund the remaining balance needed for denifanstat's Phase III trial. We re-recommended Sagimet to subscribers with an entry reference of \$2.67 per share. With the stock currently at about \$3.50 per share, we are up about 31% from that entry – having given back a fair amount of gains this past month. I still have strong conviction we have significant gains to come. With our “buy up to” price at \$5 per share, I would encourage subscribers who don't yet own Sagimet to purchase a full position below that level.

**TG Therapeutics (Nasdaq: TGTX)** is bucking the downward trend in the biotech sector with flair, as its stock recently made a new high, topping \$35 per share. *Biotech Frontiers* subscribers are up nearly 90% relative to our entry price of \$18.79 per share and well above our “buy up to” price. I expect more gains to come. TGTX is a hold.

**Roivant Sciences (Nasdaq: ROIV)** has had another quiet month with few material updates. The company remains one of my favorite holdings in our portfolio and one of the most attractive opportunities in all of biotech – a rare situation where, at these prices, investors face very limited risk of permanent capital impairment. Roivant remains a buy at up to \$13.00 per share. New subscribers can scoop it up well below that level, at about \$10.32.

**Humacyte (Nasdaq: HUMA)** began much-anticipated commercial shipments of its breakthrough ATEV synthetic blood vessel (with the brand name Symvess) in February. It's too early to tell how the commercial launch will fare, but – like much of the biotech sector – shares of Humacyte declined over the past month. That is precisely why we initiated our position in Humacyte as a “toehold,” at only one-third the size of a full *Biotech Frontiers* investment. As I remain bearish

on the market as well as the overall biotech sector at present, I think we'll likely see an opportunity to add to our Humacyte position at still lower prices (or, if you're a new subscriber, to initiate a position at a lower price as well). I remain as enthusiastic as ever about the company's long-term promise, but now is not yet the moment to add. We are moving Humacyte to a "Hold" for both existing and new subscribers. I'll let you know when I think it's time to buy.

**lovance Biotherapeutics (Nasdaq: IOVA)** has fallen to \$4 per share, making it a poster child of the extreme downside volatility we see in biotech. Shares had more than doubled above our entry reference of \$7.92 a year ago, touching \$18 – but have since declined by almost 80% from their peak. Ironically, lovance has met the upper end of the range of its first-year financial targets for lifileucel's commercial launch, delivering over \$165 million in revenue during that period. The company has also reiterated confidence in meeting its financial guidance for year two, when it anticipates lifileucel sales will grow to \$450 million. Nonetheless, the market has punished shares out of disappointment that lifileucel hasn't already achieved more and anxiety about whether the treatment will eventually achieve its \$1 billion-plus blockbuster potential. As I've said before, I don't share the market's concerns. Lifileucel is a medical game-changer that will, in time, deliver blockbuster commercial results. We remain in excellent company with our investment in lovance, as superstar biotech investor Wayne Rothbaum and legendary Smart Money hedge fund Perceptive Advisors remain among the company's top shareholders. Reflecting the stock's decline, we are lowering our "buy up to" price for lovance shares to \$5, or 25% above today's levels. I would encourage subscribers who don't own it to take advantage of the opportunity to buy it at today's \$4 level.

I have no news to share about our two portfolio hedges, **Liberty Energy (NYSE: LBRT)** and **SBI Holdings (TSE: 8473 JP)**. Please note, there was an error in last month's issue regarding the "buy up to" price for SBI, which is ¥4,500.

### **Biotech Frontiers "3 Best Buys"**

For new subscribers, we highlight three current portfolio picks that are at an attractive buy point. Our "3 Best Buys" this month are **Sagimet Biosciences**, **Roivant Sciences**, and **lovance Biotherapeutics** (all updated above), though I would also encourage new subscribers to purchase a toehold in **aTyr Pharma**.

I hope your 2025 is progressing well – I look forward to writing to you again next month.

Until then,

Best regards,

Erez