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Biotech Frontiers

SPECIAL REPORT

THE BIG BIOTECH REBOUND

These Stocks Rise When Interest Rates Fall
A Basket of 10 Negative-EV Companies

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"Where are the senior bonds trading?" I asked into the phone.

It was an early morning in March 2009. I sat in a cramped office on a high floor of the Chrysler Building in New York City. Around us the financial world was burning down. But amid that burn down, I smelled opportunity. A few months earlier, I had convinced one of the titans of the hedge-fund world, Julian H. Robertson, to stake me $70 million to pursue that opportunity... principally in the domain of distressed debt.

On the other end of the phone that morning was the head trader of Deutsche Bank's distressed-bond desk. At the time, Deutsche Bank ran one of the largest, most profitable distressed desks on Wall Street.

"Four cents at four and a quarter" came his reply.

"We'd like to buy $100 million face at four and a quarter," I followed. "That's a firm order."

"Ok. Second please... Repeat: Sabretooth buying $100 million Kaupthing seniors at four a quarter."

"Yes."

"Done."

I had just bought $100 million face value of the senior bonds of Kaupthing Bank, the largest of Iceland's three banks that had gone bust during the Global Financial Crisis. At a price of 4.25 cents relative to a par value of 100, my total outlay was $4.25 million – i.e., $100 million of face value x 0.0425. We were managing just under $100 million for Julian and a few others at the time, making this a roughly 5% position for our young hedge fund.

I didn't know it that morning, but our purchase of Kaupthing senior bonds at 4.25 cents would be one of the best investments of my life. Over the next 18 months, these bonds would recover to north of 50 cents, a 12x gain. While we took profit along the way and had little left as the bonds recovered to above 50, this would nonetheless prove to be a defining investment for us.

Two centuries ago, the great financier Baron Rothschild said "buy when there's blood in the streets." That still holds true today – when most of the world is selling, due to panic, economic necessity, or both – it's often the best time to buy.

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Periods of financial distress provide you an opportunity to purchase assets for a fraction of their true value… sometimes, as in the case of the Kaupthing bonds we bought in early 2009, for literally pennies on the dollar.

"But wait a minute, Erez… I thought Porter hired the famous bond guru Marty Fridson to write about distressed bond investing… and you to write about biotech."

That's right. But what is the one thing that may be better than buying valuable bonds at 4.25 cents?

It's buying shares of valuable biotech companies trading at **negative enterprise value.** You see right now, the U.S. biotech sector is in the middle of a historic anomaly – where more U.S. biotech companies are trading at negative enterprise value than has been the case for **any** sector of the U.S. stock market in all of recorded financial history. To put it differently, the U.S. biotech sector is amid an epic fire sale. And we have to take advantage.

Defining and Finding True Value

A company's **enterprise value** ("EV") is defined as its market capitalization ("market cap") less its net cash. For example, well-known COVID-vaccine maker and molecular-medicines pioneer Moderna has an EV of $26 billion – $32 billion market cap less net cash on its balance sheet of $6 billion.

We subtract net cash in calculating EV to get at the value of the ***enterprise*** itself – the underlying business. If a company gets liquidated, any net cash can be paid out to shareholders on a pro rata basis. The cash on the balance sheet, though valuable, isn't deemed to be part of the business's intrinsic value.

It goes almost without saying that the vast majority of companies on the stock market, like Moderna, trade with a positive EV. That's because the market ascribes some worth to those businesses. When a company trades with **negative** EV, the market is saying it believes the business is worthless… or less than worthless.

It turns out the market is often wrong in that judgment. In fact, the data shows that buying the stocks of companies trading at negative EV can lead to spectacular returns.

The Historical Record on Negative-EV Stocks

The CFA Institute is one of the most prestigious organizations for finance professionals in the world, famed for its rigorous approach to security analysis. In 2013 the CFA institute sponsored a study that examined every negative EV stock that traded in the U.S. between 1972 and 2012, a 40-year span. The conclusion?

The average 12-month return for stocks in this group was **50.4%.** That's not a typo. Had you been able to find and invest in every one of these stocks over that

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time frame and held each for one year, your portfolio would have returned over 50%... **beating the market average return by over 5x.**

Let's pause to appreciate what unfolded in the world over the 40 years covered by the CFA study: the oil crisis of the 1970s... the high inflation of the 1970s and early '80s... the 1987 stock market crash... the early 1990s recession... the Russian sovereign default... the Asian financial crisis... and even the Global Financial Crisis of 2008-09. Finding a magic formula that consistently returned 50% a year through these cataclysmic events is almost unbelievable. Yet that's what buying a basket of negative-EV stocks would have done.

More recently, Broken Leg Investing – a blog for deep-value investors – updated the CFA Institute study. It looked at every U.S. negative-EV stock from 1999 to 2016. Their findings? These stocks returned **27.4%** annualized, trouncing the Nasdaq's 5.1% annual return over the same period by a similar **5x.** Notably, this more recent study encompassed both the 2001 dot-com bust and the 2008-09 Global Financial Crisis... so it, too, covered a period of economic rough sledding.

Back to Biotech and Our Current Opportunity

So if buying negative-EV stocks is a "magic formula" that crushes the market averages, why isn't it widely talked about and why don't more people do it? The answer is – because **negative-EV stocks are generally extremely rare**. Most of the time, fewer than 1% of publicly listed stocks trade with a negative EV.

In fact, finding these companies is ordinarily a sleuthing exercise done by the world's deep-value investors... the successors to Warren Buffett's mentor Benjamin Graham, who called his search for negative-EV stocks "cigar butt investing."

As Graham colorfully put it, "A cigar butt found on the street that has only one puff left may not offer much of a smoke, but the bargain purchase will make that puff all profit."

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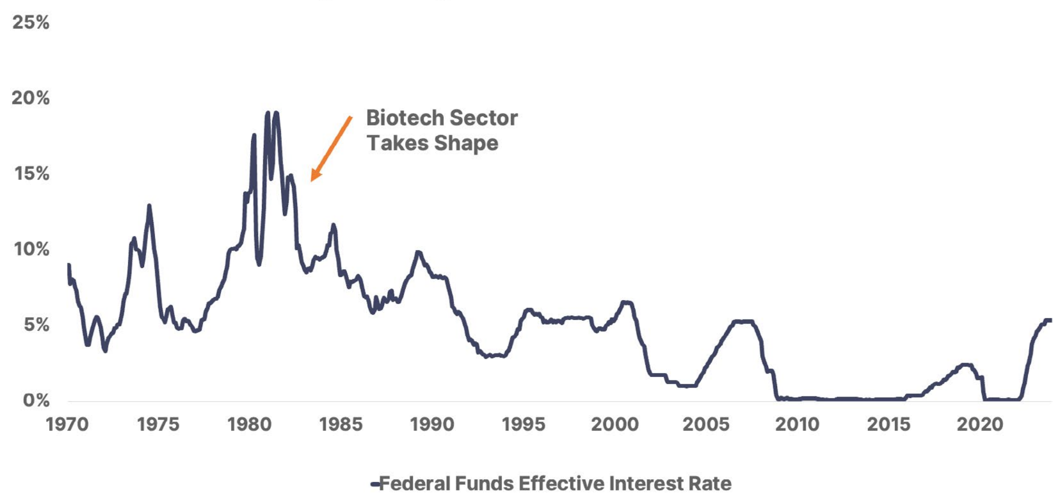
Graham, who passed away in 1976, was not talking about biotech stocks. Indeed, the “cigar butt” stocks he had a taste for were about as far removed from the biotech sector as we can imagine.

But the biotech sector today is living through a historic anomaly. Over the past two years the Federal Reserve has jacked up interest rates more aggressively than at any time since the Volcker era of the early 1980s. Biotech did not exist when Fed Chair Paul Volcker hiked rates into double digits. And as a result, the biotech sector has never before experienced a violent updraft in interest rates like we’ve seen from 2022 through today.

All Easy Money For Biotech... Until 2022



Source: Bloomberg

The 18 months of rate hikes have precipitated an unprecedented blood bath in biotech. (If you’d like to understand in greater depth why the biotech sector is so sensitive to interest rates, please read ***Exploring New Horizons: Investment Guidebook for Biotech Frontiers*** – section VI lays that out in detail.) Perhaps the craziest manifestation of the biotech bloodbath is that today, more than 20% of the biotech sector – at least 200 publicly listed biotech stocks – trade with a negative EV.

This historic dislocation gives us a historic opportunity, **one we may well never see again in our lifetimes**. We can buy a basket of the most explosive biotech stocks... at the most extreme, distressed prices – prices at which the market is saying it believes the businesses are worth *less than nothing*. So in this first issue of *Biotech Frontiers*, we are going to buy that basket.

Future issues of *Biotech Frontiers* are likely to focus on far fewer stocks – usually only one, sometimes two or three that are thematically related. In other months,

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we may make no specific buy recommendations at all, and instead add intriguing opportunities to our watchlist. But as Warren Buffett once said, “When it's raining gold, reach for a bucket, not a thimble.” In biotech, this is surely one of the times Buffett was talking about.

“Don't Own the Wrong House in Houston”

My old partner Craig had a saying that he learned from his mentor Fran Biondi, the legendary founder of hedge fund King Street Capital and one of the greatest distressed investors of all time: “Don't own the wrong house in Houston.”

What Fran meant is this: When there's an oil boom or bust, real estate prices in Houston either soar or sink. When house values are low before a boom, there are great opportunities for bargain hunters. But, Biondi cautioned: Don't get caught up trying to find the most “special snowflake” house there. Just buy a basket of homes and let the oil boom take care of the rest. The schmuck who becomes obsessed with finding the perfect house in Houston ends up buying the wrong one.

In many future issues of this letter, we are going to find the needles in the haystack... for instance, the two or three most promising genomic-medicines companies in a field of hundreds.

But that approach doesn't make sense to take advantage of the historic opportunity I've described here. Here, we want to benefit from the “mean reversion” effect – suggesting that negative-EV stocks as a group massively outperform. To seize the opportunity before us, the right answer is to build a basket of stocks.

So we will build a basket of 10 biotech companies trading at negative EV or within spitting distance of it – a large enough number of companies to offer some diversification and to capture the group-wide “snap back” I anticipate these negative-EV biotech stocks will experience... but also small enough for us to be able to execute without enormous headaches.

A Master Class From My Mentor Julian

Friends have sometimes asked me what it was like to work with Julian Robertson – the investing version of playing football with Joe Montana. Julian was remarkable in many ways. But the single quality that stood out to me was his exceptional ability to know what mattered in a specific situation and to focus on that one thing, zeroing out the rest.

Let me explain...

Julian was fluent in every aspect of finance. He could parse the most complex details of a cash flow statement... spot with X-ray vision how a company was manipulating an earnings report... imagine with prophetic clarity how

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the competitive landscape in an entire industry would evolve… or talk inside baseball on arcane currency pairs with a full-time FX trader, who would leave the conversation wondering why Julian knew more about currencies than he did…

Do you remember the Victorinox "SwissChamp" Swiss Army knife, the big one that had all the tools? That was Julian.

But Julian's most special gift of all was knowing precisely which tool to apply in any given situation.

This talent made him a fortune during the Global Financial Crisis in 2008-09, when I worked with him. In addition to managing $1 billion of his own money, Julian had also invested $4 billion of his fortune with about 30 different money managers, a famous ecosystem known as the "Tiger Cubs." Most of these money managers had reputations as stock pickers. And, in 2008, as the markets sold off, most of these money managers were running around pitching Julian on the great bargain opportunity they saw in their favorite XYZ stock.

But Julian knew better…

You see, Julian had grasped that there was a deep rot in the financial system in 2008, centered at the heart of the big Wall Street banks holding piles of toxic mortgage debt. And Julian knew that, until this rot got cleaned out, stock picking for great companies was not going to work. Instead, the right trade was to aggressively short financial stocks in anticipation of the meltdown that eventually came. So Julian assembled a basket of financial stocks and shorted them – making himself a 200% profit in 2008, a year in which most of his protégé money managers were ruined.

Then, when he spotted Fed Chair Ben Bernanke's announcement to embark on the quantitative easing program and to print money beginning in March 2009, Julian turned around and bought a basket of many of those same financial stocks he had profitably shorted – making himself another fortune.

The most important lesson I learned being at Julian's side in 2008-09 was to focus like a laser on what matters… and zero out the rest. We are going to apply that lesson to what's happening in the biotech sector now.

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Adapting Our Seven-Piece Framework

In our *Investment Guidebook for Biotech Frontiers*, I outlined seven factors that will generally guide us to find compelling opportunities:

1. The science
2. The size of the market opportunity
3. The cap table
4. The catalysts
5. The balance sheet
6. The big picture backdrop
7. The risk/reward and expected value

Most of the time, we'll study each of these factors in depth as we seek to spot the "needles in the haystack." And we will accord the appropriate weight to each factor.

But this is no ordinary time in the history of biotech. We have never seen an opportunity to buy promising biotech stocks *en masse* at negative EVs – trading for less than the value of their cash and equivalents. The 12-month return profile of owning negative-EV stocks is extraordinary. So in this issue, we are going to give major priority to the factor that matters most in the current setup: the balance sheet.

Guided by company balance sheets, I screened the entire U.S. biotech universe to create a list of stocks trading at negative EVs. That results in about 250 stocks out of roughly 1,000 biotechs. I then combed through that list name by name, applying several of our other factors as secondary filters. Specifically, I asked:

- Which of these companies are engaged in **promising science**?
- Which of these stocks have potential **catalysts** over the next 12 to 18 months?
- Which of these negative EV stocks are substantially owned by the **smart money** – elite biotech hedge funds and venture capitalists ("VCs"), large institutional capital, or Big Pharma strategic partners?

These criteria helped me narrow the list to a much smaller group. The result is a basket of biotech stocks trading at negative EV, engaged in compelling science... with catalysts on the horizon... owned by the smartest professional biotech investors in the world.

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Introducing Our Negative-EV Biotech Basket

I've summarized our 10-stock basket in this table:

The Negative-EV 10-Stock Basket

Name	Ticker	Market Cap ($m)	Cash ($m)	Debt ($m)	Enterprise Value ($m)	Share Price	Shares Outstanding (m)	Net Cash per Share	Net Cash as % of MC	Buy Up To
Vir Biotechnology	VIR	$1,365	$1,685	$128	($192)	$10.26	135	$11.57	114%	$11.00
Lyell Immunopharma	LYEL	$461	$607	$65	($82)	$1.86	252	$2.16	118%	$2.35
Nuvation Bio	NUVB	$383	$619	$5	($232)	$1.78	218	$2.82	160%	$1.80
uniQure	QURE	$262	$658	$165	($231)	$5.53	48	$10.31	188%	$7.25
Sutro Biopharma	STRO	$277	$355	$38	($40)	$4.53	61	$5.20	114%	$4.10
Atea Pharma	AVIR	$342	$595	$3	($250)	$4.16	83	$7.09	173%	$3.50
Kodiak Sciences	KOD	$267	$346	$84	$5	$5.16	52	$5.00	98%	$3.30
Sagimet Bio	SGMT	$276	$208	$0	$68	$8.25	30	$6.85	39%	$6.75
Athira Pharma	ATHA	$133	$173	$2	($38)	$3.53	38	$4.50	129%	$3.50
Chimerix	CMRX	$91	$129	$0	($38)	$1.04	89	$1.45	142%	$1.05

Price as of February 15, 2024

I've also prepared a brief description of each, which seeks to distill only the most crucial elements that helped the company make it through our filter and into our basket.

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Vir Biotechnology (VIR)	
Market Cap ($m)	$1,365
Enterprise Value ($m)	($192)
Share Price	$10.26
Net Cash Per Share	$11.57
Key Holders	
Blackrock	11.75%
Arch Ventures	9.6%
GSK	6.3%

An immunology company focused on next-generation therapies for infectious diseases, especially viral diseases, **Vir Biotechnology (Nasdaq: VIR)** has already proven the innovative mettle of its proprietary monoclonal antibody discovery platform by creating Ebanga – one of only two approved, effective medicines in the world for the dreadful Ebola virus.

Now Vir's most promising pipeline candidates are two novel treatments for chronic hepatitis B, an awful liver infection that afflicts 300 million worldwide. At the American Association for the Study of Liver Diseases meeting in 2023, one of the most important annual scientific conferences for liver disease, the interim Phase II data that Vir shared for its Hep B treatments were described by attendees as "unprecedented." Vir has several more important data releases for these drug candidates in 2024, which could trigger upward movement in the stock.

Not surprisingly, Vir has already captured the attention of smart money: BlackRock, the world's largest institutional money manager, owns 11.75% of the company, Arch Ventures, one of the most successful biotech VCs of all time, owns 9.6%, and Big Pharma giant GlaxoSmithKline is a 6.3% holder.

Action to Take: Buy Vir Biotechnology (Nasdaq: VIR) up to $11 per share.

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Lyell Immunopharma (LYEL)	
Market Cap ($m)	$461
Enterprise Value ($m)	($82)
Share Price	$1.86
Net Cash Per Share	$2.15
Key Holders	
Arch Ventures	14.5%
GSK	12.1%
Hans Bishop	1.8%

Solid tumors cause 90% of all cancer deaths, leaving victims with less than three years to live on average after a solid tumor metastasizes. Despite enormous advances in our scientific understanding of cancer over the past 50 years, resulting in several Nobel Prizes, effective treatments for solid tumors remain stubbornly elusive. **Lyell Immunopharma (Nasdaq: LYEL)** is at the leading edge of attacking this problem, with a focus on personalized T-cell therapies, one of the most promising areas of immuno-oncology medicine.

With several positive research discoveries on its lead drug candidates as well as plans to submit an Investigational New Drug ("IND") application to the Food and Drug Administration ("FDA") in 2024, Lyell has plenty ahead in the coming 12 to 18 months with potential to drive the stock.

For a relatively small, young biotech company, Lyell has also attracted a star roster of biotech talent. CEO Lynn Seely is one of the most successful biotech executives of her generation, having previously served as Chief Medical Officer of Medivation, which Pfizer acquired in 2016 for $14 billion. Meanwhile Lyell's board reads like a *Who's Who* of biotech royalty – including luminaries Bob Nelson, Hans Bishop, and Rick Klausner, all of whom own meaningful amounts of the stock.

Action to Take: Buy Lyell Immunopharma (Nasdaq: LYEL) up to $2.35 per share.

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Nuvation Bio	
Market Cap ($m)	$83
Enterprise Value ($m)	($82)
Share Price	$1.78
Net Cash Per Share	$2.16
Key Holders	
David Hung - CEO	26.%
EcoR1	8.8%
Omega	6.9%

If Lyell CEO Dr. Lynn Seely is a biotech all-star, her former colleague and boss Dr. David Hung is an MVP. Hung is the primary inventor of two major oncology drugs: Xtandi and Talzenna. He founded Medivation and guided it as CEO through Pfizer's $14 billion acquisition.

With **Nuvation Bio (NYSE: NUVB)**, we now have an opportunity to bet on Hung's "encore" in the oncology field – a company that trades at an almost 50% discount to the net cash on its balance sheet and at a negative EV of $232 million that is almost $500 million below where the company's Series A VCs first invested five years ago, back when the company had little more than a business plan. To top it off, Hung himself owns over a quarter of the company's stock, giving us an extraordinary level of alignment between the CEO and shareholders.

Nuvation has multiple strong programs in its pipeline, but the one that intrigues me the most is the company's Drug - Drug Conjugate (DDC) platform. To date, combinatorial therapies in cancer have had to rely on two distinct molecules. This approach has several disadvantages – for example, uncertainty about how the molecules will interact, and about whether they will truly complement one another. Nuvation's platform seeks to solve this problem by gluing together drugs that target different vulnerabilities of cancer into a single molecule. If successful, this approach could be revolutionary. Nuvation will be releasing several important data milestones about its DDC program in 2024, making the coming year consequential for the stock.

Action to Take: Buy Nuvation Bio (NYSE: NUVB) up to $1.80 per share.

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uniQure	
Market Cap ($m)	$262
Enterprise Value ($m)	($231)
Share Price	$5.53
Net Cash Per Share	$10.31
Key Holders	
Nantahala	6.3%
Bristol-Myers Squibb	4.9%
OrbiMed	4.3%

One of the most promising domains in all of biotech is genomic medicine, which applies insights about a patient's unique genetic information to guide clinical care. **uniQure (Nasdaq: QURE)** is a proven leader in this space – and a rare example of a company that combines a powerful genetic-medicines discovery platform with an approved, commercially launched therapy, a rich pipeline, and its own robust manufacturing capabilities.

uniQure's Hemgenix, greenlit by the FDA in 2022, is the first and only gene therapy for hemophilia B – and a best-in-class treatment for that blood disorder. The Hemgenix franchise alone could plausibly be worth multiples of uniQure's current stock price. But uniQure has a full pipeline to advance other genetic medicines targeting more prevalent diseases, including Huntington's disease and Temporal Lobe Epilepsy. The commercial ramp of the company's Hemgenix franchise, as well as clinical trials data on these pipeline candidates, offer solid catalysts over the next 12 to 18 months.

Nantahala Capital, one of the sharpest hedge funds in the world with a track record of winners in biotech, owns 6.3% of uniQure. Big Pharma giant Bristol Myers Squibb owns 3.9%. And OrbiMed, one of the most storied life sciences investors of all time, is a 4.3% holder.

Action to Take: Buy uniQure (Nasdaq: QURE) up to $7.25 per share.

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Sutro BioPharma	
Market Cap ($m)	$277
Enterprise Value ($m)	($40)
Share Price	$4.53
Net Cash Per Share	$5.20
Key Holders	
BlackRock	9.8%
Suvreta	9.6%
BVF	4.9%

In the past year, no area of biotech has seen more explosive mergers-and-acquisitions (M&A) activity than the market for antibody-drug conjugates ("ADCs"), the molecules that combine a synthetic antibody's precision targeting capability with a toxic drug payload to deliver precision strikes against cancer. Earlier in 2023, Pfizer paid $43 billion to acquire Seagen, the ADC field's pioneer... then, in November, Merck struck a $22 billion deal with Japan's Daiichi Sankyo's to license four of Sankyo's ADC candidates... followed weeks later by Abbvie's $10 billion acquisition of ImmunoGen for its ADC pipeline. Just recently, Johnson & Johnson joined the party with a $2 billion acquisition of Ambrx Biopharma, another young ADC player.

Creating safe, effective ADCs is incredibly hard, an interdisciplinary feat that combines cutting-edge immunology, synthetic chemistry, oncology, and toxicology. **Sutro Biopharma (Nasdaq: STRO)** is an emerging leader in ADC design and optimization... with a promising platform for the creation of new ADCs and its own pipeline of advanced ADC candidates. Sutro's lead ADC drug, Luvelta, benefits from FDA Fast Track designation, which the agency grants only to potential breakthrough drugs addressing serious unmet medical needs. With fresh data on Luvelta and the possibility of new partnership announcements coming in 2024, Sutro meets our aim to identify promising negative EV biotechs with catalysts.

Sutro's largest holders include BlackRock and two of the most highly respected biotech-focused smart money investors, Suvretta Capital Management and the Biotech Value Fund ("BVF").

Action to Take: Buy Sutro Biopharma (Nasdaq: STRO) up to $4.10 per share.

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Atea Pharma	
Market Cap ($m)	$342
Enterprise Value ($m)	($250)
Share Price	$4.16
Net Cash Per Share	$7.09
Key Holders	
BlackRock	10.5%
EcoR1	8.4%
Tang Capital	4.8%

While vaccines prime a person's immune system to fight infection, antiviral medicines do the fighting after a person is already sick – interfering with a virus's ability to commandeer the cell, and buying precious time for the immune system to mount a response. The COVID-19 pandemic demonstrated how clinically relevant and lucrative such drugs can be. In 2023, a year after the pandemic's end, Pfizer still generated over $10 billion in sales for Paxlovid – an antiviral cocktail given to blunt the severity of COVID infection, which I've taken with gratitude and would guess many readers have as well.

Atea Pharmaceuticals (Nasdaq: AVIR) specializes in advanced oral antiviral medicines – including new therapies directed at COVID, the broader class of coronaviruses, and other acute viral infections such as hepatitis C and RSV. With its lead drug candidate set to read out results from a Phase III pivotal trial, and other candidates with two Phase II readouts, 2024 will be a consequential year for Atea.

Notably, Atea's cap table includes a sizable investment from Tang Capital Management – an exceptionally savvy (and rare) biotech activist fund. Tang has a successful track record agitating cash-rich biotechs to return cash to shareholders if the company's management can't deliver quickly on boosting their stock. Its presence here provides us an additional path to a win.

Action to Take: Buy Atea Pharmaceuticals (Nasdaq: AVIR) up to $3.50 per share.

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Kodiak Sciences	
Market Cap ($m)	$267
Enterprise Value ($m)	$5
Share Price	$5.16
Net Cash Per Share	$5.00
Key Holders	
Baker Brothers	32.9%
Victor Perlroth - CEO	6.5%
Millennium	3.2%

Kodiak Sciences (Nasdaq: KOD) focuses on breakthrough medicines to treat the leading causes of blindness – diabetic eye disease, retinal vein occlusion, and wet age-related macular degeneration. The market opportunity to treat these three major eye diseases amounts to over $18 billion annually in the U.S. alone – but the companies looking to fight these diseases have not attracted the same caliber of scientific talent as, say, companies producing cancer medicines. Kodiak is an exception.

We saw earlier how ADCs combine cutting-edge immunology with synthetic chemistry and toxicology to create highly precise medicines targeting cancer. Alone in the retinal disease landscape, Kodiak has harnessed a similarly interdisciplinary approach to build what it calls its antibody bipolymer conjugate ("ABC") platform, which seeks to create similarly precise medicines targeting the exceptionally sensitive physiology of the retina. This platform's first drug candidate, Tarcocimab tedromer, features five Phase III studies in high prevalence retinal diseases. Kodiak will likely file its first Biologic License Application [what is this?] for Tarcocimab with the FDA in 2024.

Kodiak's founder and CEO Victor Perlroth earned MD and MBA degrees from Stanford University, and sold his prior biopharmaceutical company Avidia to Amgen for $450 million. He has partnered to build Kodiak with Baker Brothers Advisors, a legendary biotech VC and hedge fund that has over a dozen multibillion-dollar life sciences startups to its name.

Action to Take: Buy Kodiak Sciences (Nasdaq: KOD) up to $3.30 per share.

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Sagimet Bio	
Market Cap ($m)	$276
Enterprise Value ($m)	$68
Share Price	$8.25
Net Cash Per Share	$6.85
Key Holders	
NEA	18%
Kleiner Perkins	12%
Baker Brothers	4%

Metabolic disease, which can be conceived as a disorder in the body's fuel processing, is a huge and important topic in what longevity-medicine thought leader Dr. Peter Attia calls Medicine 2.0. We'll dive into this topic in future issues of *Biotech Frontiers*. One of the signature signs of metabolic disease is liver dysfunction, and specifically NASH – nonalcoholic steatohepatitis, also known as fatty liver disease, which has reached epidemic proportions in the U.S. Over 17 million Americans suffer from NASH, which will significantly reduce their life expectancy.

Sagimet Biosciences (Nasdaq: SGMT) targets NASH and other metabolic dysfunctions with Denifanstat – what would be a first-in-class oral, selective fatty acid synthase inhibitor ("FASN"). Early clinical data for Denifanstat's efficacy against NASH is compelling. Sagimet has multiple data, regulatory, and clinical trial launch milestones to look forward to in 2024.

Sagimet's roster of backers reads like a *Who's Who* of life-sciences VCs – including New Enterprise Associates, legendary Silicon Valley VC Kleiner Perkins, and Baker Brothers Advisors. The company's founder and executive chairman Dr. George Kemble is a Stanford and University of California, San Francisco-trained scientist with a distinguished track record in basic scientific research and medical entrepreneurship.

Action to Take: Buy Sagimet Biosciences (Nasdaq: SGMT) up to $6.75 per share.

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Athira Pharma	
Market Cap ($m)	$133
Enterprise Value ($m)	($38)
Share Price	$3.53
Net Cash Per Share	$1.29
Key Holders	
Perceptive Advisors	14.2%
Baker Brothers	8.3%
Richard Kayne	5.2%

Although neurodegenerative diseases such as Alzheimer's are one of Dr. Peter Attia's "four horseman" – the four major disease categories that are the largest causes of mortality for those over age 40 – they also comprise the category that medicine has, to date, made the least progress in treating. **Athira Pharma (Nasdaq: ATHA)** targets neurodegenerative diseases generally, and Alzheimer's specifically, with positive modulators of the neurotrophic hepatocyte growth factor (or HGF). The neurotrophic HGF is critical to normal brain function and plays an important role in neurodegenerative diseases. Athira's lead drug candidate, Fosgonimeton, is a first-in-class small molecule that positively modulates the neurotrophic HGF and, by doing so, is thought to protect and repair neuronal networks.

Athira has a Phase II and Phase III clinical trial read out (when they are made public) for Fosgonimeton in the second half of 2024, making the coming year a hugely important one for the stock. The company also has trials ongoing for the drug in Parkinson's and other forms of dementia.

Athira's largest shareholder – which just re-upped its investment a few weeks ago – is Perceptive Advisors, arguably the most successful biotech investor of all time. Perceptive owns more than 14% of the company. The cap table also includes legendary biotech investor Baker Brothers, which owns 8.3%. Richard Kayne, a formidably successful and astute investor in life sciences, is a 5% holder.

Action to Take: Buy Athira Pharma (Nasdaq: ATHA) up to $3.50 per share.

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Chimerix	
Market Cap ($m)	$91
Enterprise Value ($m)	($38)
Share Price	$1.04
Net Cash Per Share	$1.45
Key Holders	
RA Capital	9.9%
Dr. Peter Mol	5.1%
Monaco Asset Management	4.9%

Like several other members of our negative-EV basket, **Chimerix (Nasdaq: CMRX)** is a cancer-fighting company, which currently trades at a $91 million market cap with $129 million of cash on its balance sheet, giving the company a negative EV of about $38 million. Its lead compound, ONC-201, targets a rare and terrible form of pediatric brain cancer – where it has already shown striking results in a small handful of patients who have received the treatment on a compassionate-use basis. ONC-201 has received three important designations from the FDA: Orphan Drug Designation, Fast Track Designation, and Rare Pediatric Disease Designation.

The last of these means that, if ONC-201 is eventually approved, Chimerix will receive an FDA Priority Review Voucher – effectively, an "express lane pass" that enables any company presenting the voucher to have the FDA review a candidate drug on a significantly expedited timetable. Priority Review Vouchers are typically sold for $100 million. (Indeed, French biotech company Valneva announced it had sold its Priority Review Voucher for $103 million in early February 2024.)

Chimerix stands a good chance of receiving such a voucher, which by itself would be worth more than the entire current market cap of the company. I'm also encouraged that Chimerix's largest shareholder is RA Capital, one of the most well-respected specialist biotech venture capitalists in the world.

Action to Take: Buy Chimerix (Nasdaq: CMRX) up to $1.05 per share.

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Please note the last two of these recommendations are quite small in their market capitalization. This feature is an intentional part of our basket: I've deliberately selected a group of stocks that includes large-, medium-, and smaller-cap securities. For the smaller members of the group, be patient: If the stocks trade above our "buy up to" levels, wait a few days (or even a few weeks) for them to return. If we observe that they have permanently moved out of our range, we may consider replacing them with others.

Putting It All Together: Asset Allocation, Portfolio Construction, and Risk Management

So there you have it... our 10 stock negative-EV biotech basket.

But before you go out and buy any of these, we need to have a serious conversation about three things that play a bigger role in protecting and growing wealth than any specific stock picks: asset allocation, portfolio construction, and risk management. I've addressed each of these three in our *Investment Guidebook*... and I'd urge everyone to read it. But since this is our first issue, we'll revisit them together now.

Asset Allocation

Asset allocation is how to divide up a portfolio among the different investment categories available – for example, real estate, stocks, bonds, precious metals, digital currencies such as Bitcoin, and cash. It also refers to how to allocate capital within each category – for example, what percentage of the stock portion holds conservative investments such as Porter's "forever stocks" (the Hersheys and Microsofts of the world), and what percentage holds more "high octane" sectors such as biotech.

There is no "magic formula" nor "one size fits all" approach that solves this puzzle. The factors I consider most relevant include:

- *Investment horizon*: How long do you have to invest before you will need access to your funds – two to three years, seven to 10 years, 20 years or longer? The answer to this question matters. I don't believe anyone should make **any** stock investment with funds that will be needed in less than three years.
- *Expense coverage*: What is your net worth and how many years of expenses in your life will it cover? The longer your current net worth can cover expenses, the more aggressive an investor can be in asset allocation... the fewer years, the more conservative.
- *The opportunity set*: Asset allocation should also take into account where money is likely to be treated best. Here's a simple example: Back in the early 1980s, in the Volcker era, short-dated Treasury bonds yielded around 15%. When short-term Treasuries yielded that much, there was little reason to own anything else. The point is: Asset allocation should factor the risk/reward in different asset classes, which changes over time.

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I can't provide asset-allocation advice for any specific situation. But I can offer broad guidelines: I think the allocation to stocks should rarely exceed 50% of total net worth… and within the stock portfolio, a reasonable allocation to biotech in the current environment is anywhere from 20% to 50%. I say this because I believe the risk/reward in biotech at this moment is unusually compelling. In ordinary times, a prudent allocation to biotech could be significantly smaller.

Let's use round numbers to make this guidance concrete: For example, if an investor's total net worth is $1 million, I'd suggest that investor allocate no more than $500,000 to stocks… and within that stock portfolio, somewhere between $100,000 to $250,000 to biotech.

Portfolio Construction

An investor's portfolio should not hold more than 20 biotech stocks at a time. Holding more than 20 biotech stocks at one time becomes unmanageable. In fact, I will often press us to own *fewer* than 20 biotech stocks, so we can benefit from concentrating on our best ideas. As the late Charlie Munger, Warren Buffett's business partner, memorably put it: "It's not diversification, it's diworsification."

Again, this is an unusual time in the biotech sector… one that I strongly believe benefits from a basket approach. A basket approach is best suited to capture the snapback "mean reversion" I anticipate will benefit the entire sector… and best suited, too, to help us avoid "owning the wrong house in Houston." That's why I've started us off with a basket of 10 picks – in the issues ahead, you'll likely find us culling down this basket over time, ideally by taking profit after selling winners.

That leaves us with the question of how to size the 10-stock basket we're starting with. I'm going to suggest we make this issue's basket 50% of our total biotech portfolio – the one we'll be building together month by month over the coming year.

So to make it concrete again: Let's say an investor has $500,000 to invest in stocks – and half of that, or $250,000, gets allocated to biotech. Under this strategy, $125,000 gets invested in the 10-stock basket we've discussed in this issue.

Now a crucial final suggestion: Please equal weight each of the 10 picks by investing the same dollar amount in each. In the example we're working with, that would mean $12,500 per recommendation.

Avoid the temptation to pick your favorite and make it significantly larger… or to pick your favorite three or four and ignore the others. Why? Because I've found from hard experience that when buying a basket, the picks we think will work best, rarely do. Trust in the power of the basket to do its work for us.

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Risk Management

The final item we need to discuss together is risk management.

In general, I am a fan of stop losses.

However, we are rarely if ever going to use automatic stop losses in *Biotech Frontiers*.

Why?

Because biotech stocks are, by their nature, some of the most volatile securities that exist... and because they often trade down (and up) on low-quality information.

Let's take an example: Imagine a cancer immunotherapy company running a Phase III clinical trial. The company reports a patient death in the trial, as they're obligated to do. The FDA places a short-term hold on the trial until it can clarify what happened. The stock plummets 50% in a day based on the headline of an FDA clinical trial hold. If we were using an automatic stop loss, we'd get stopped out.

But it may be that the patient who died in the trial had failed four prior lines of therapy... was already on death's door when they enrolled in the trial... and passed away for reasons that had nothing to do with the drug under investigation. In eight weeks or less, the FDA may greenlight the trial to continue, and the stock may recover and make new highs.

We do not want to miss out on a sudden rebound in the stock.

We may well decide to exit positions, or *manually* stop ourselves out, if we decide that the risk/reward in a stock has changed adversely, or if we conclude that our investment thesis isn't playing out. But we will avoid relying on automatic stop losses.

Instead, we will rely on careful position sizing and, when appropriate, staggered entry points to help manage our risk.

Let's use our 10-stock negative-EV basket to illustrate how this approach works.

I've recommended that each stock in this basket constitute a notional 1/20 of our total biotech portfolio... the basket itself is 50% of our biotech portfolio, and each stock within the basket is equal-weighted to be 1/10 of 50%, or 5%.

Now let's imagine that I am spectacularly wrong about one of these picks, which declines by 50% a few weeks after we buy it.

For investors who followed our position-sizing guidelines, that 50% loss will cost 2.5% of the total biotech portfolio... a manageable blow, and one from which we can readily recover.

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I hope that this example also underscores the importance of my request that you equal weight the recommendations in our basket!

Conclusion

As those who have read our ***Investment Guidebook*** know, my all-time favorite issue of *Stansberry's Investment Advisory* is the September 2009 issue – "Seven Secrets of the World's Greatest Investors."

Secret #1 in that issue is: "You can time the market... You must time the market."

As Porter explains, "You can dramatically increase your returns in stocks... if you buy when stocks are cheap and most people are afraid to buy them." What we're looking for, he continues, are the "extremes."

Well, we have never seen a more extreme dislocation in biotech, or arguably in any other sector of the U.S. stock market, than a situation where more than 20% of the entire sector trades at negative EVs.

We are witnessing the biotech equivalent of the total wipeout in financials that unfolded in 2008-09 during the Global Financial Crisis... when I bought Kaupthing senior bonds for 4.5 cents.

I can't promise you that the results will be the same... But I can tell you that the setup is auspicious. We have not seen the biotech sector trade at these levels in my lifetime... and after it recovers, we may well not see it at similar levels again. Let's take advantage.

I'm excited to embark on this journey with you –

Best regards,

Erez

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