



The Biotech Growth Trust

Annual General Meeting

18 July 2024

Portfolio Managers: Geoffrey Hsu & Josh Golomb

Geoffrey Hsu, CFA

General Partner



Geoffrey C. Hsu, CFA, is a General Partner at OrbiMed and has been portfolio manager of The Biotech Growth Trust since May 2005.

Mr. Hsu joined OrbiMed in 2002 as a biotechnology analyst. Prior to joining OrbiMed, he worked as a financial analyst in the healthcare investment banking group at Lehman Brothers. Mr. Hsu received his A.B. degree summa cum laude from Harvard University and holds an M.B.A. from Harvard Business School. Prior to business school, he spent two years studying medicine at Harvard Medical School.

Josh Golomb

Partner

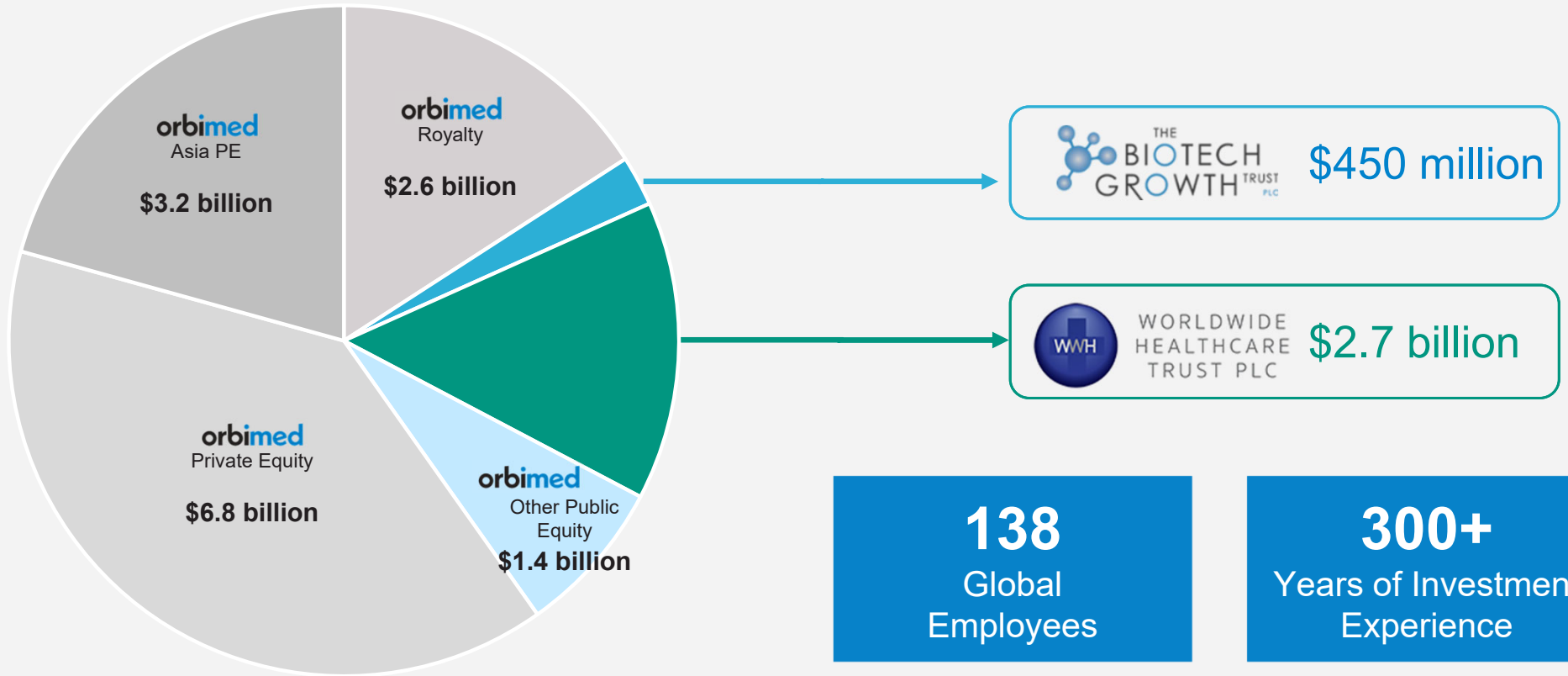


Josh Golomb is a Partner at OrbiMed focused on biotechnology. He joined the firm in 2021 and became a portfolio manager of The Biotech Growth Trust in 2023.

Mr. Golomb has covered the biotechnology and pharmaceutical sectors at investment firms since 2004. He was most recently employed at HealthCor, a healthcare-dedicated hedge fund, from 2016 to 2021 as a senior biotechnology and pharmaceutical analyst. Previously, he covered biotech at Millennium, Citadel, Diamondback and ProMed Partners. Mr. Golomb received a B.S. in Operations Research with a concentration in Engineering Management Systems from the Fu Foundation School of Engineering and Applied Science at Columbia University.

OrbiMed Corporate Update

Global Healthcare-Dedicated Investment Firm with Over 25 Years of Experience



Total AUM: \$17.2 billion

138
Global Employees

300+
Years of Investment Experience

20+
New Hires in 2023/24

35+
Colleagues with M.D. / Ph.D.

Source: OrbiMed; Data estimated as of 30 June 2024

BIOG

Performance

BIOG Performance for Fiscal 2024

31 March 2023 to 31 March 2024



Source: Frostrow, Bloomberg.

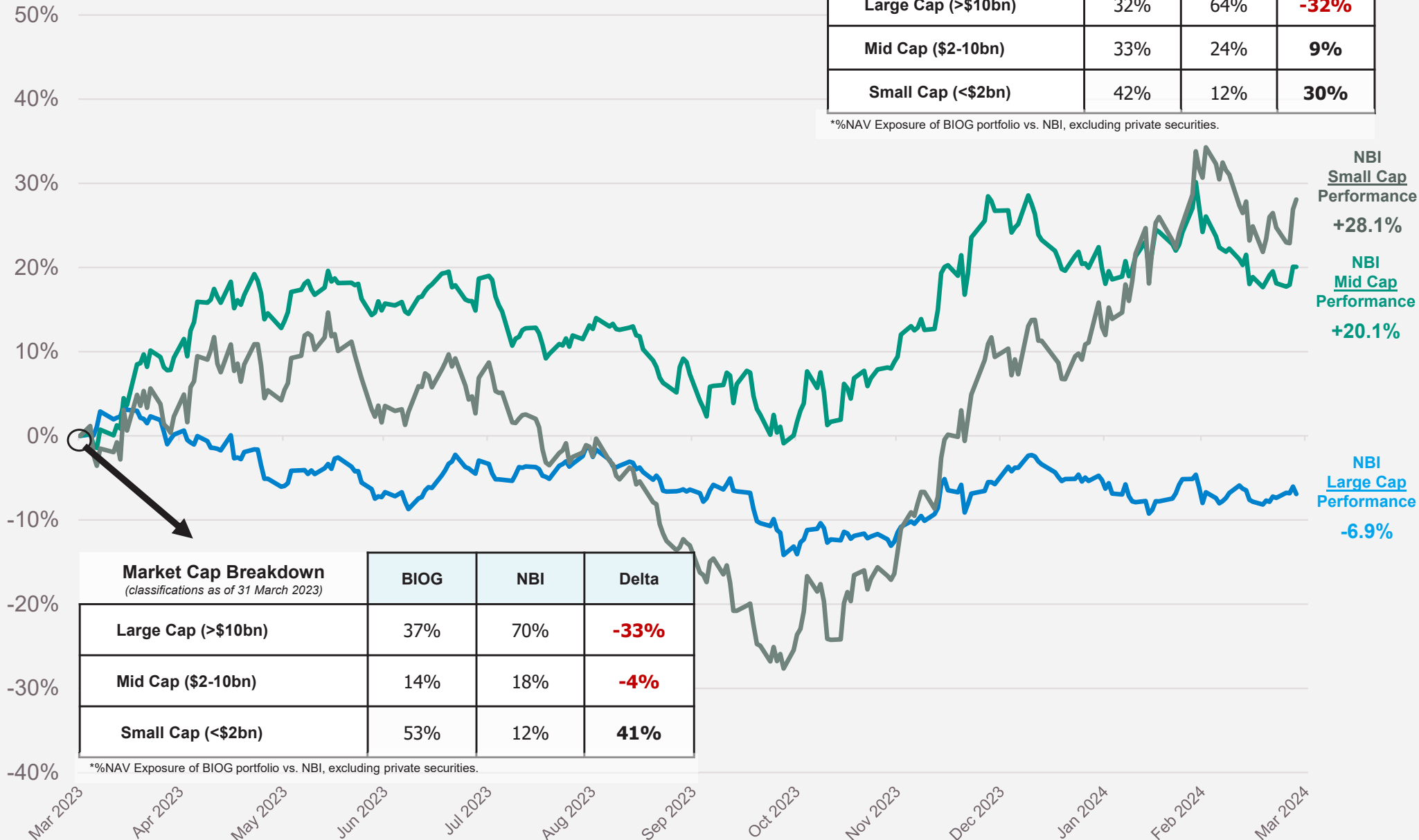
Note: See Endnotes for additional information, including with regard to the calculation of these results and the index shown above.

Market Cap Performance Divergence in Biotech

Small and Mid Cap Biotech Begins to Recover

Market Cap Breakdown <i>(classifications as of 31 March 2024)</i>	BIOG	NBI	Delta
Large Cap (>\$10bn)	32%	64%	-32%
Mid Cap (\$2-10bn)	33%	24%	9%
Small Cap (<\$2bn)	42%	12%	30%

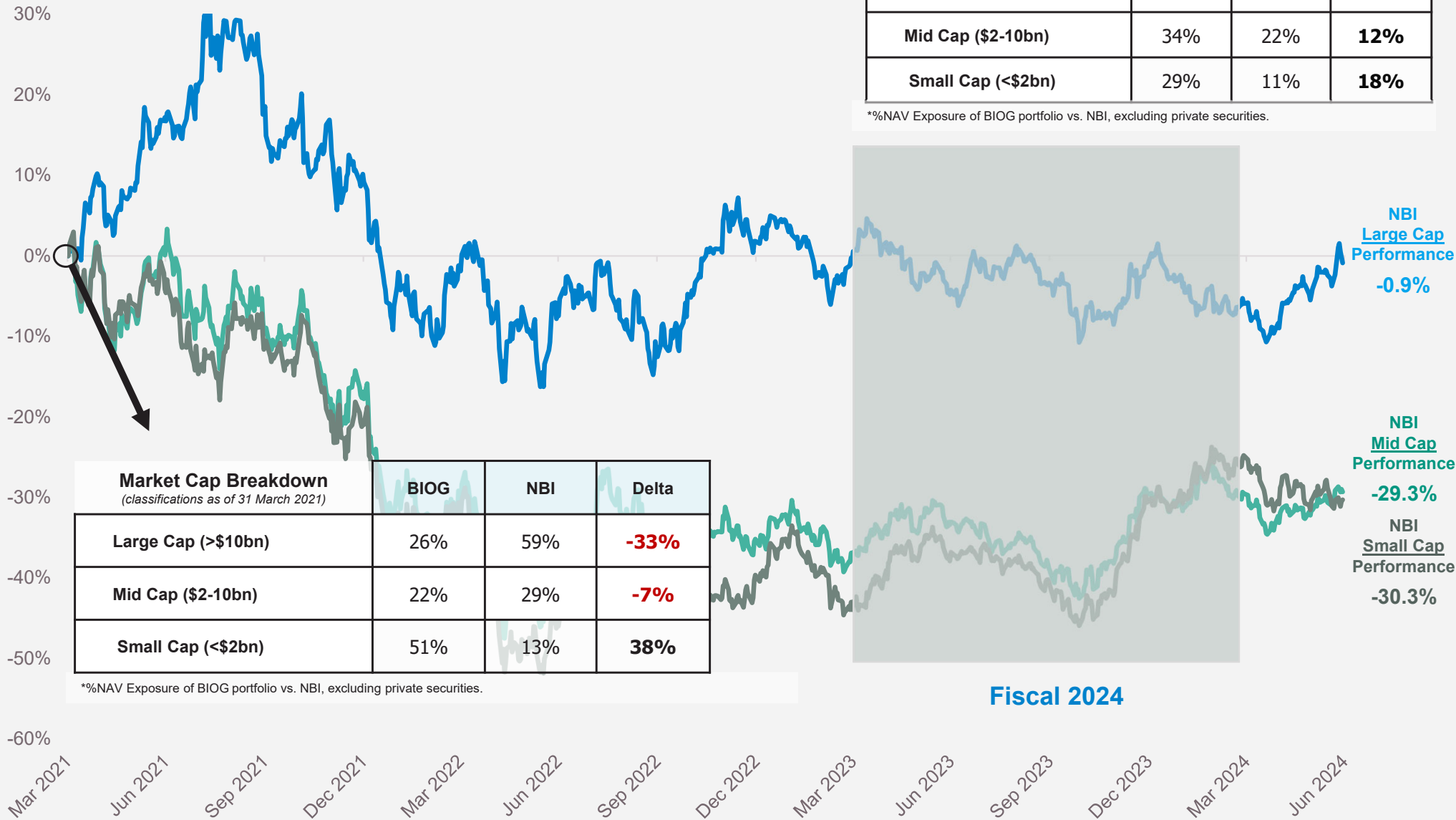
*%NAV Exposure of BIOG portfolio vs. NBI, excluding private securities.



Note: Chart shows equal-weighted performance of NBI stocks in their respective market cap buckets, using market cap classifications as of 31 March 2023. Updated as of 31 March 2024, performance calculated in USD.

Market Cap Performance Divergence in Biotech

Performance Gap Since 2021 Has Yet to Close



Note: Chart shows equal-weighted performance of NBI stocks in their respective market cap buckets, using market cap classifications as of 31 March 2021. Updated as of 30 June 2024, performance calculated in USD.

BIOG Performance for Fiscal YTD

31 March 2024 to 30 June 2024



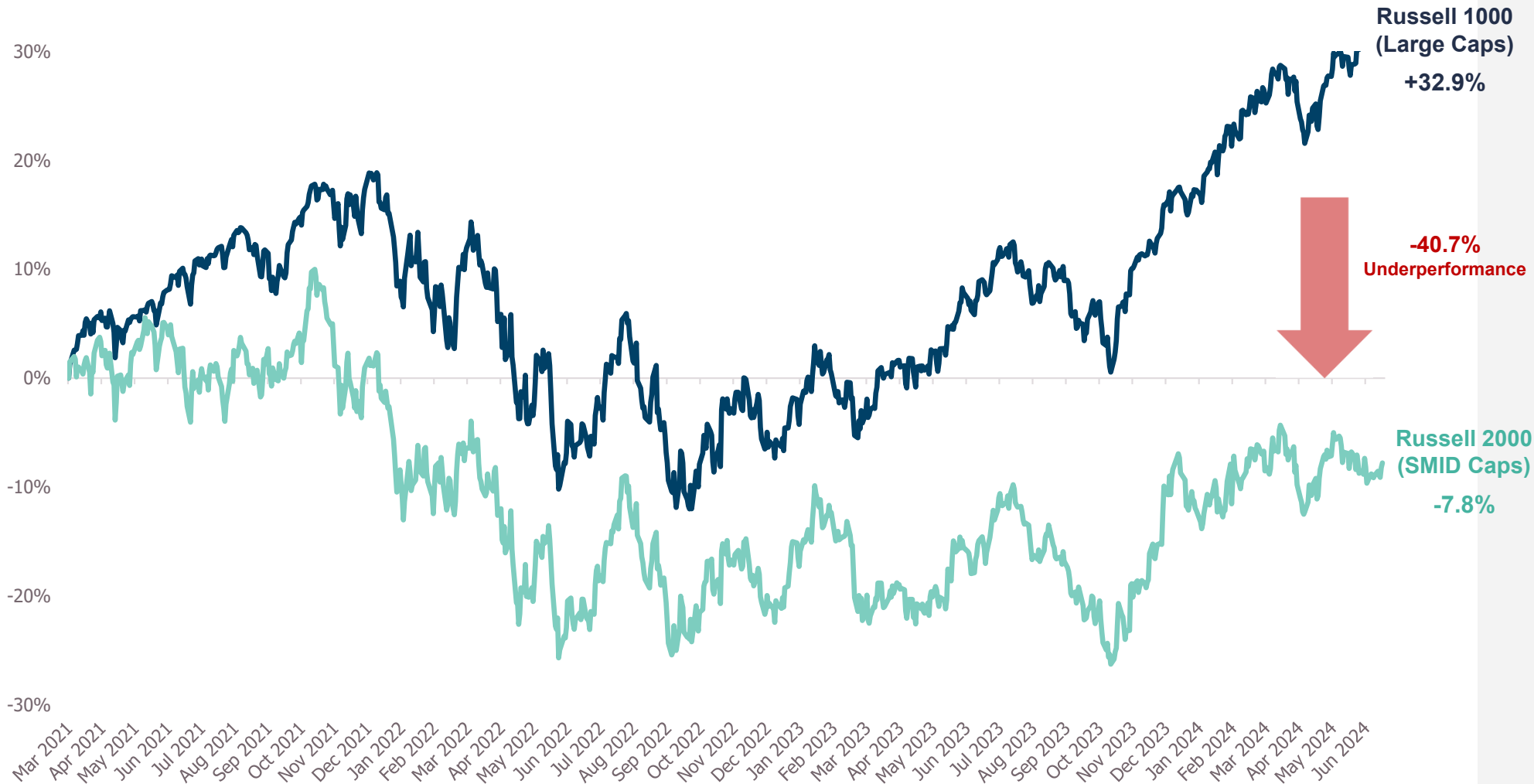
Source: Frostrow, Bloomberg.

Note: See Endnotes for additional information, including with regard to the calculation of these results and the index shown above.

Size Divergence in the Broad Market

(31 March 2021 – 30 June 2024)

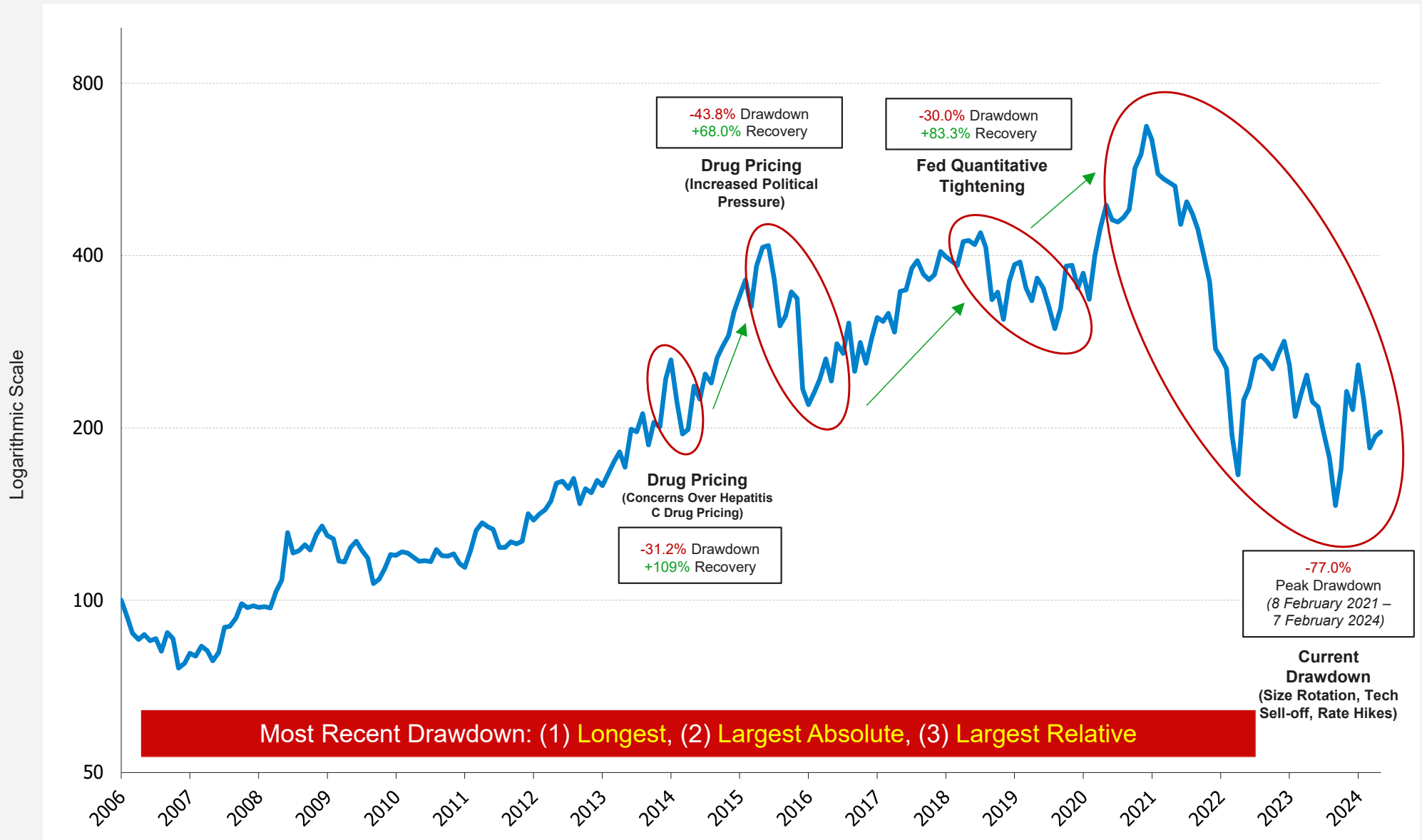
Russell 2000 (Small/Mid Cap) vs Russell 1000 (Large Cap)



Note: The Russell 2000 Index is comprised of the smallest 2000 companies in the Russell 3000 Index. The Russell 1000 Index is comprised of the largest 1000 companies in the Russell 3000 Index.

XBI vs. S&P 500 (SPX) Spread since XBI Inception

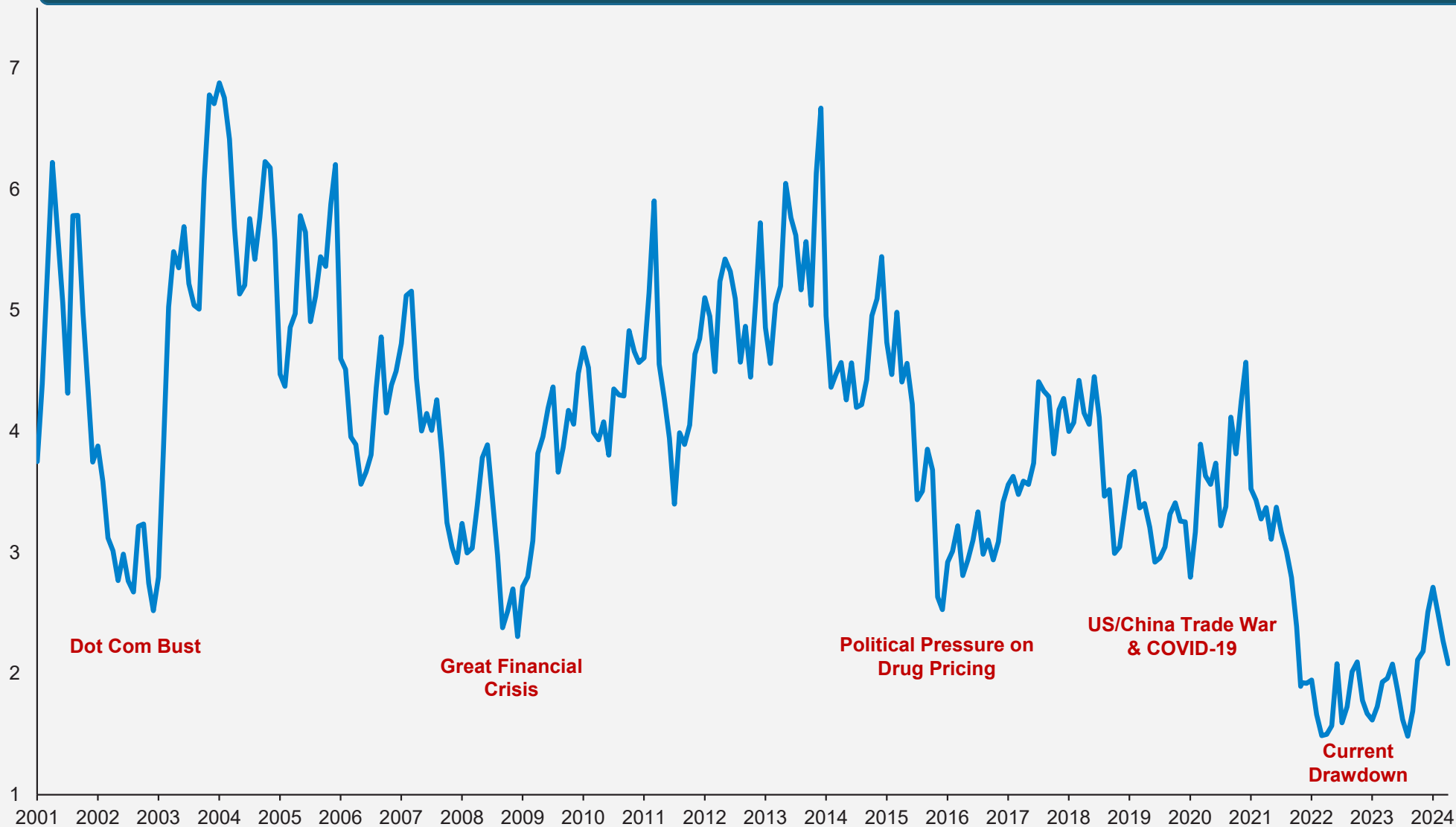
Drawdowns in spread followed by historically strong recoveries



Note: Drawdowns are calculated using daily closing prices, while chart is shown using monthly periodicity for smoothing purposes. Updated as of 30 June 2024.
Source: JPM [Drawdowns and Recoveries] | OrbiMed (XBI - SPX Spread Chart since XBI Inception).

Biotech Valuations At Unprecedented Lows

Ratio of Market Cap to Net Cash on Balance Sheet (Median)

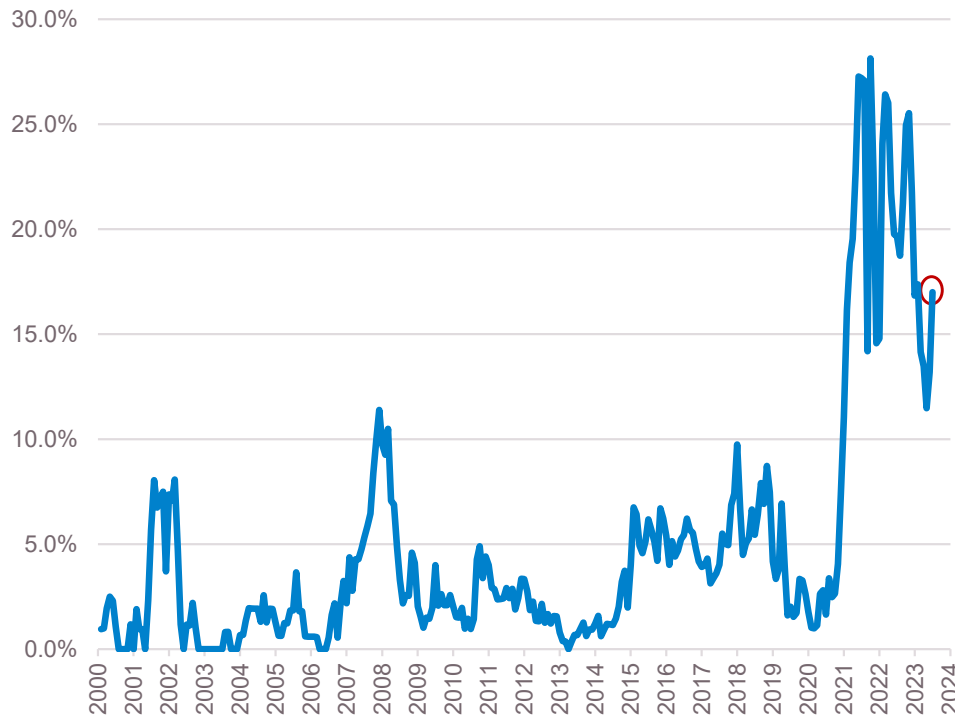


Note: Monthly chart of all GICs defined biotechnology greater than \$10mm, using historical cash and debt sourced from Bloomberg, with annual GICS biotechnology universe refreshes. Updated through 30 June 2024.

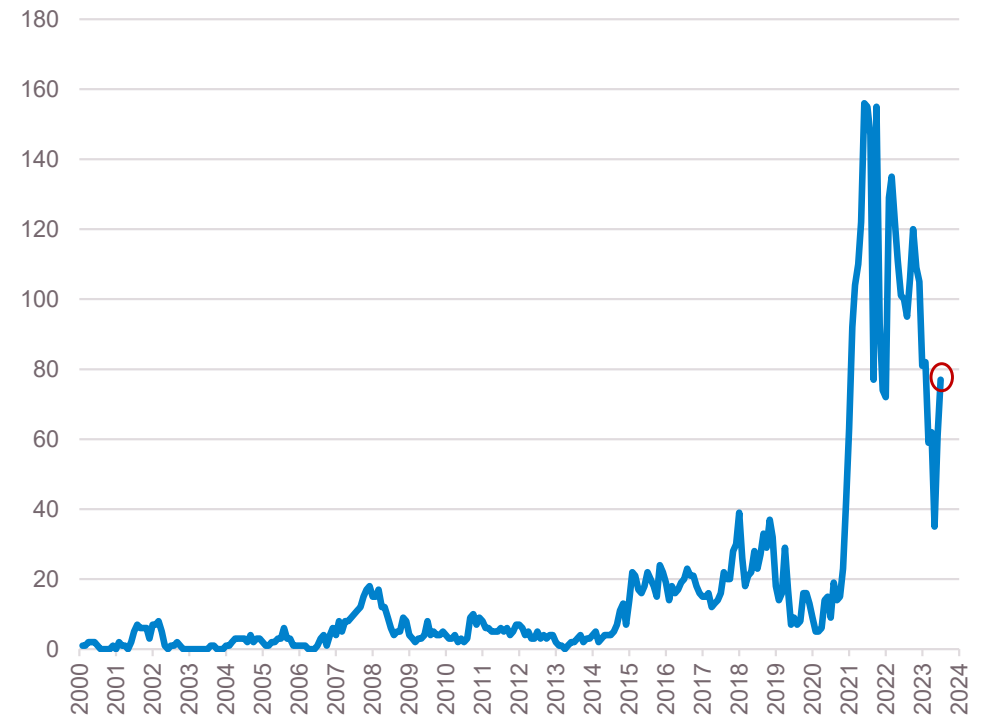
Biotech Valuations At Unprecedented Lows

Valuations have begun recovering from historical lows

Percent of Biotech Companies Trading Below Net Cash on Balance Sheet:



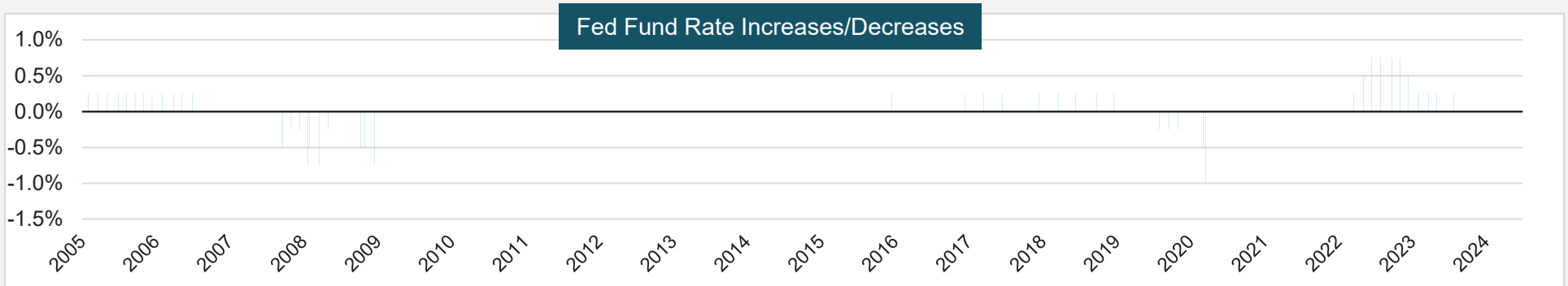
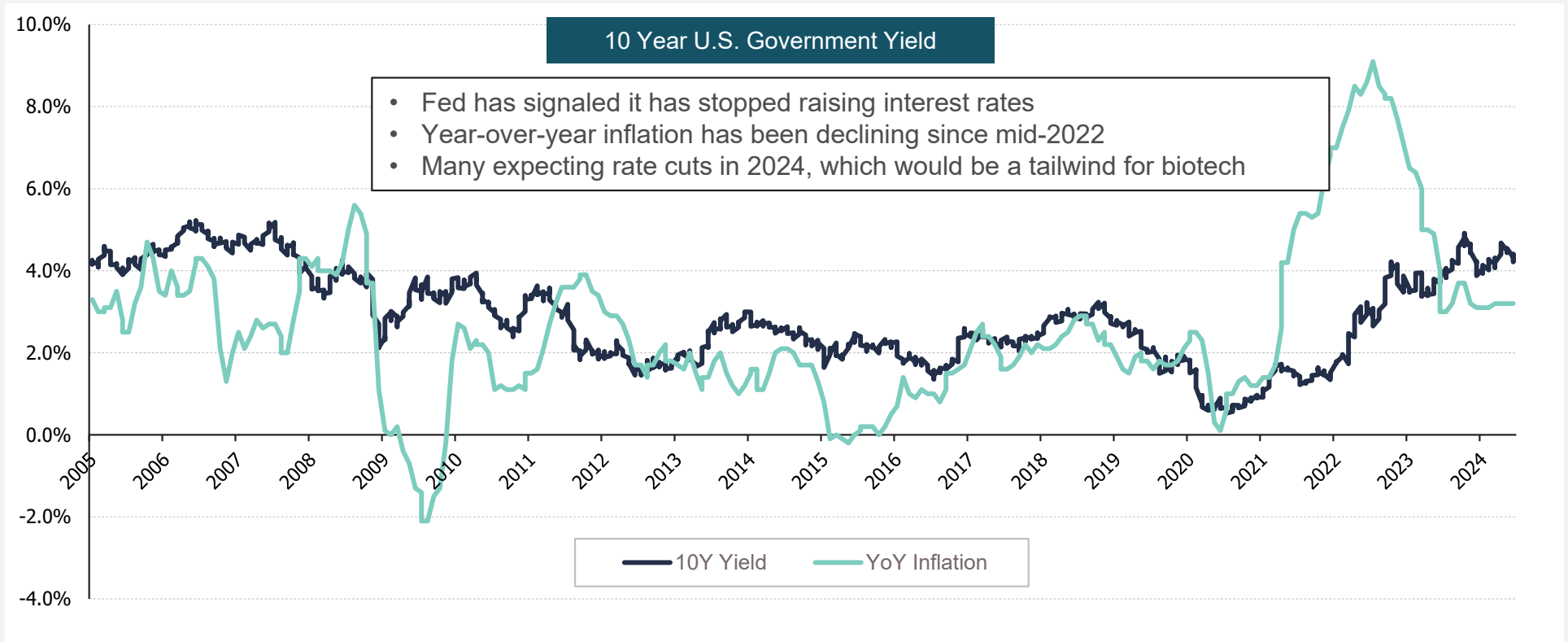
Number of Biotech Companies Trading Below Net Cash on Balance Sheet:



Note: Monthly chart of all GICs defined biotechnology greater than \$10mm, using historical cash and debt sourced from Bloomberg, with monthly GICS biotechnology universe refreshes. Updated through 30 June 2024

10-Year U.S. Government Yield Stabilizing

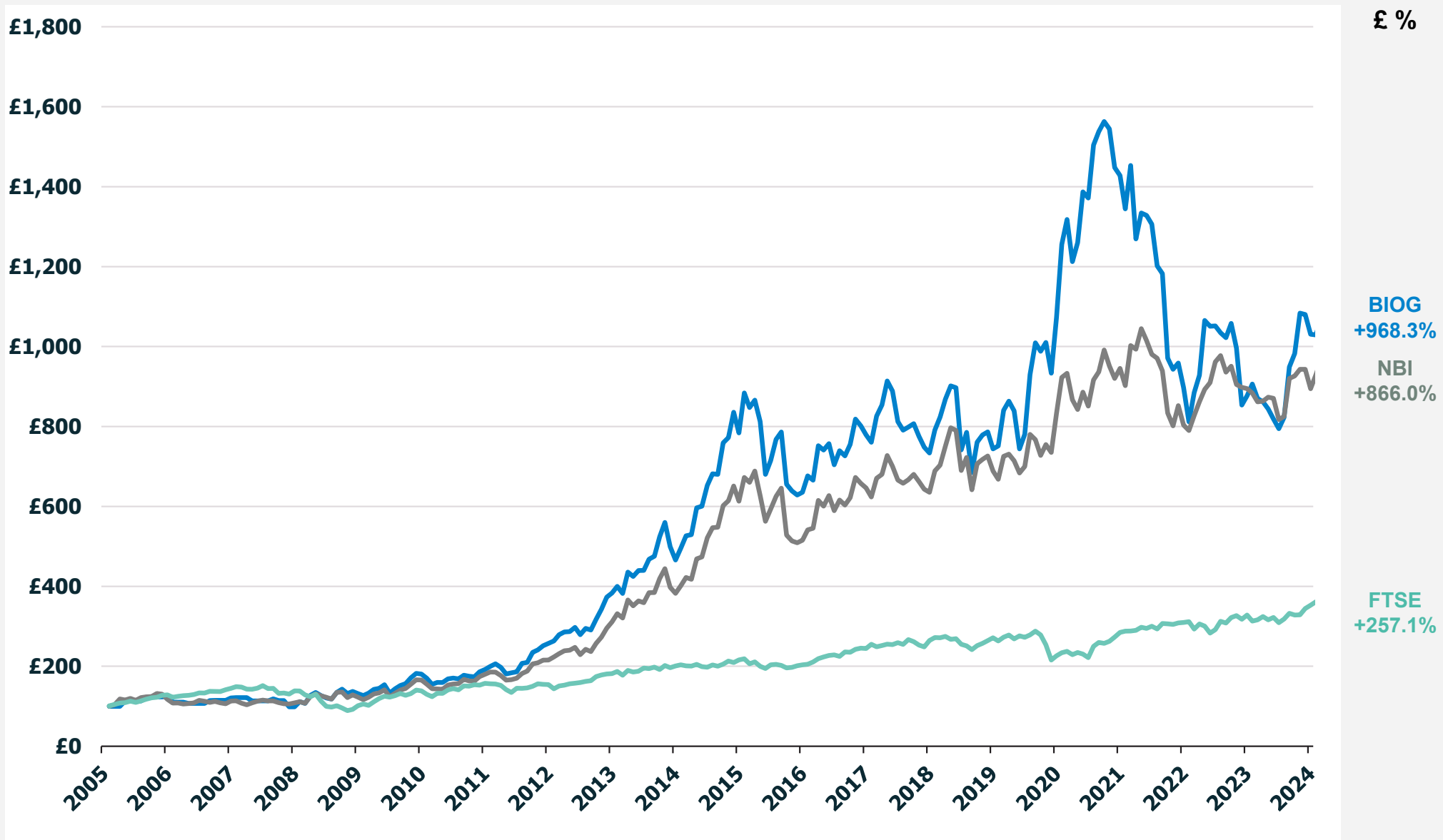
(USGG10YR Index) Data as of 30 June 2024



Source: Bloomberg

BIOG Performance since Inception

18 May 2005 through 30 June 2024











Note: See Endnotes for additional information, including with regard to the calculation of these results and the index shown above.

Source: Frostrow, Bloomberg.

BIOG










Investment Themes

Key Breakthroughs in Biotech since Last AGM

Company	Indication	Product (MOA)	Highlights
	Non-transfusion and Transfusion Dependent Adult Thalassemia	Mitapivat (PK activator)	Reported positive Phase 3 data in two trials; first oral treatment for thalassemia
	ATTR Amyloidosis with Cardiomyopathy (ATTR-CM)	Vutrisiran (siRNA)	Reported first positive ATTR-CM outcomes study with a silencer of ATTR
	Bronchiectasis	Brensocatib (DPP1 inhibitor)	Positive Phase 3 data with 20% reduction in exacerbations over 52 weeks. First ever successful bronchiectasis study.
	Myotonic Dystrophy Type 1 (DM1)	DYNE-101 (antisense oligonucleotide conjugated to a fragment antibody)	Showed best in class knockdown of DMPK resulting in splicing correction and improved function relative to placebo in a Phase 1/2 trial
	Facioscapulohumeral Muscular Dystrophy (FSHD)	Del-brax (siRNA bound to a monoclonal antibody)	First drug to ever demonstrate DUX4 knockdown and muscle function improvement in a Phase 1/2 trial
	Autoimmune Diseases	Auto CAR-T (CD19 targeting)	Demonstrated disease modifying activity of a one-time cellular therapy in refractory autoimmune disease
	Sickle Cell Disease and Beta Thalassemia	Casgevy (CRISPR Cas9 gene-editing therapy)	First ever CRISPR therapy approved in the world
	Acromegaly	Paltusotine (somatostatin receptor type 2 agonist)	Positive Phase 3 trials for first once-daily oral medication for the treatment of acromegaly

Note: Public companies shown here are not necessarily representative of portfolio holdings

Significant FDA Biotech Approvals in 1H24










Company	Indication	Product (MOA)	Highlights
	Metastatic Melanoma	Amtagvi	First cellular therapy approved for the treatment of a solid tumor
	Chronic Obstructive Pulmonary Disease (COPD)	Ohtuvayre	First novel mechanism approved to treat COPD in over a decade
	Low to Intermediate Risk Myelodysplastic Syndromes	Rytelo	First and only oligonucleotide telomerase inhibitor
	Small Cell Lung Cancer	Imdelltra	First bispecific T-cell engager approved to treat a solid tumor
	Pediatric Low Grade Glioma	Ojemda	First therapy in its class approved for a type of pediatric brain tumor
	Paroxysmal Nocturnal Hemoglobinuria (PNH)	Voydeya	First oral add on therapy for the treatment of PNH
	Pulmonary Arterial Hypertension (PAH)	Winrevair	First new mechanism for the treatment of PAH in over a decade
	Non-Alcoholic Steatohepatitis (NASH)	Rezdiffra	First drug approved for the treatment of fatty liver disease
	Metachromatic Leukodystrophy (MLD)	Lenmeldy	First gene therapy for the treatment of MLD

Note: companies are not necessarily representative of portfolio holdings.

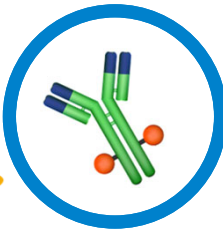
Oncology

Cancer remains #1 therapeutic area for biotech drug development given unmet need






Cellular Therapies

CD19	BCMA	Other
  	  	  

Antibody-Drug Conjugates










Antibodies with chemo attached

Bispecific Antibodies


Antibodies that bind to 2 different targets










Targeted Therapies

Targeting specific genetic mutations










Radiopharmaceuticals










Using targeted radiation to kill tumor cells

Cancer Vaccines

Harnessing the immune system to attack cancer



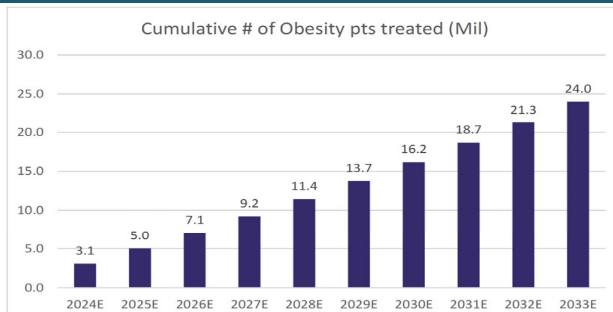
Note: companies are not necessarily representative of portfolio holdings.

Multiple innovative approaches generating clinical benefit across tumor types, giving physicians more treatment options to extend the lives of cancer patients.

Obesity

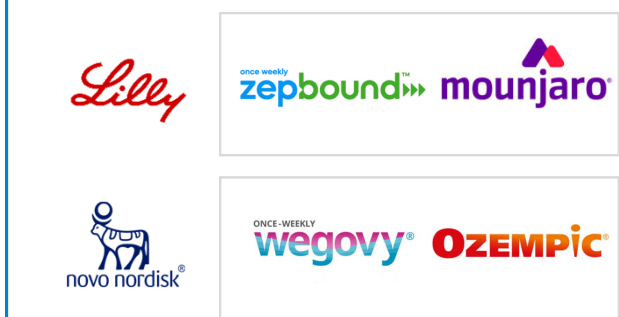
Biotech companies racing to develop next wave of therapies in potential \$200+ bn market

Substantial Growing Market



Source: Wells Fargo Securities, LLC Estimates

Current Leaders



Weight Loss at 1 Year

Current Therapies

12-18% weight loss



Next Generation Therapies

25%+ weight loss

Additional Indications

Lilly	Novo Nordisk
TIRZEPATIDE MMO	Diabetes
TIRZEPATIDE CV Outcomes	CVD
TIRZEPATIDE Obstructive Sleep Apnea	Obesity
TIRZEPATIDE Heart Failure pEF	NASH
	CKD
	PAD
	Brain disorders
	Heart Failure

Room for Improvement

- New **routes of administration** (e.g. oral)
- Novel **mechanisms of action**
- **Combination strategies** with GLP-1 agents to address shortcomings, such as loss of lean muscle mass and tolerability

Potential Solutions

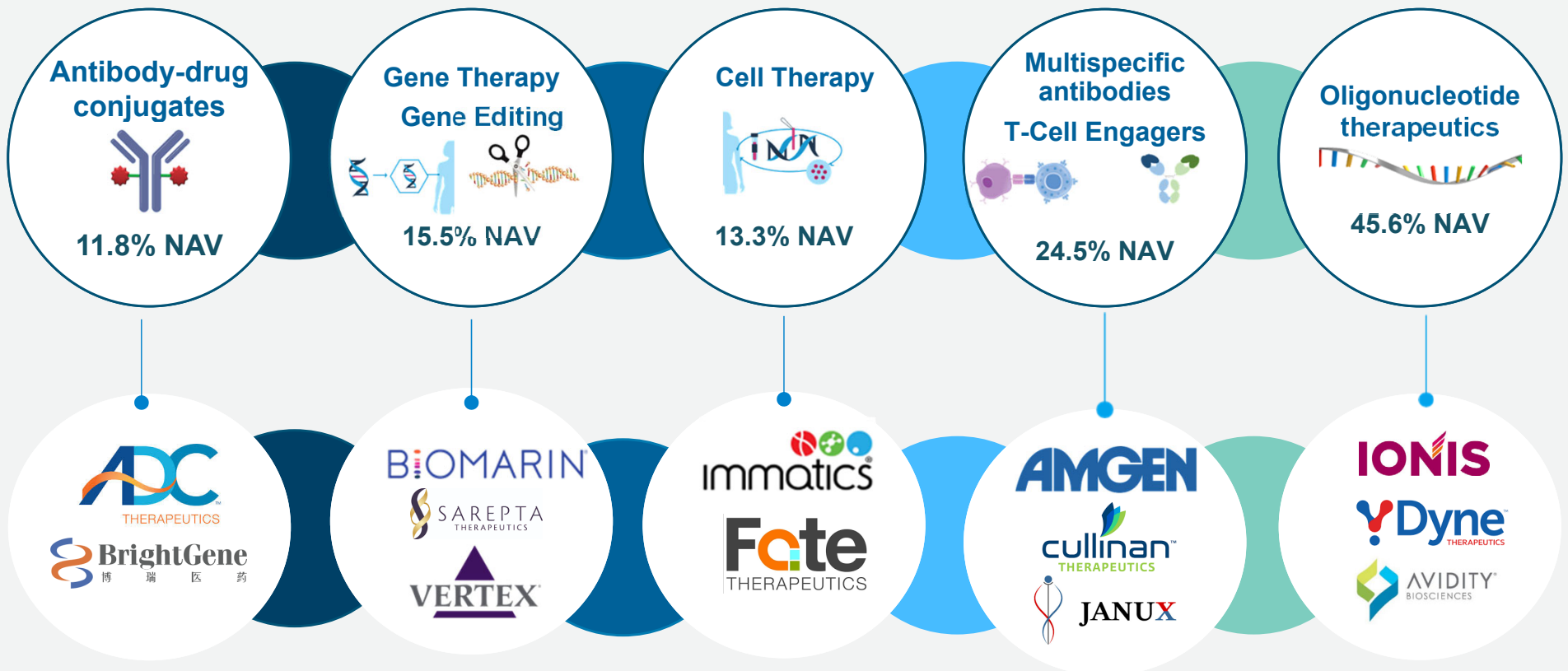


Note: companies are not necessarily representative of portfolio holdings.

Lilly and Novo have a compelling head start, but the market is large enough to support multiple players.

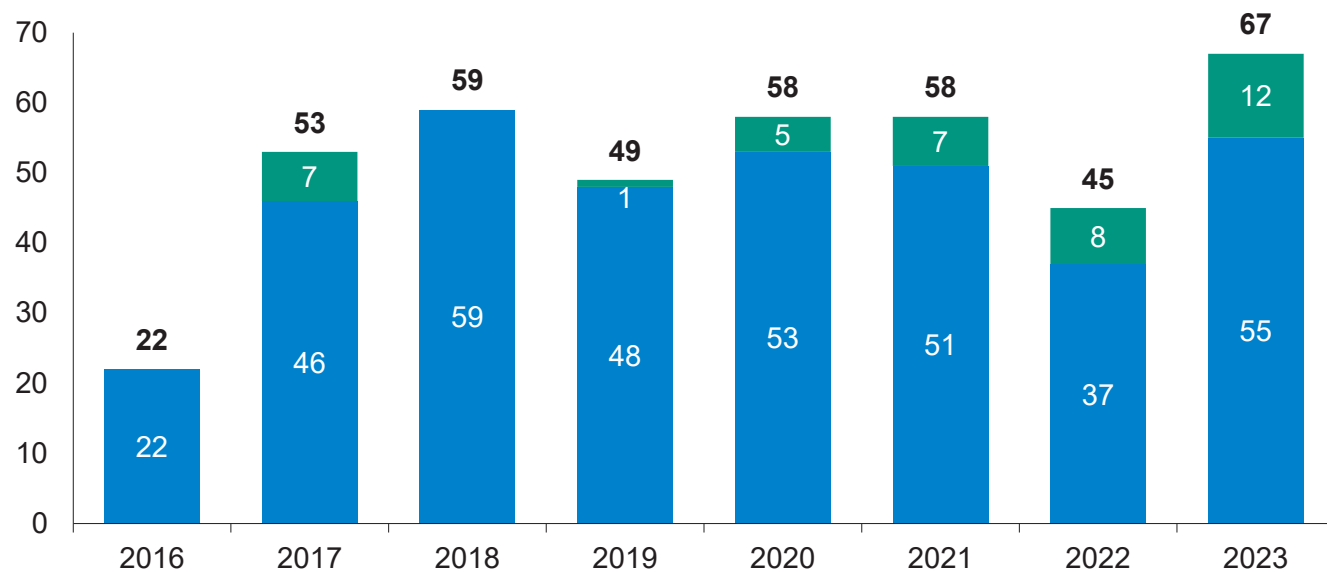
Innovation Well Reflected in BIOG

Portfolio has exposure to a wide swath of novel technologies, as shown below:



Source: OrbiMed, % of BIOG NAV as of 30 June 2024. Some positions are double-counted because they use more than one technology.

FDA New Molecular Entity Approvals



Source: FDA CDER and CBER as of 12/31/23

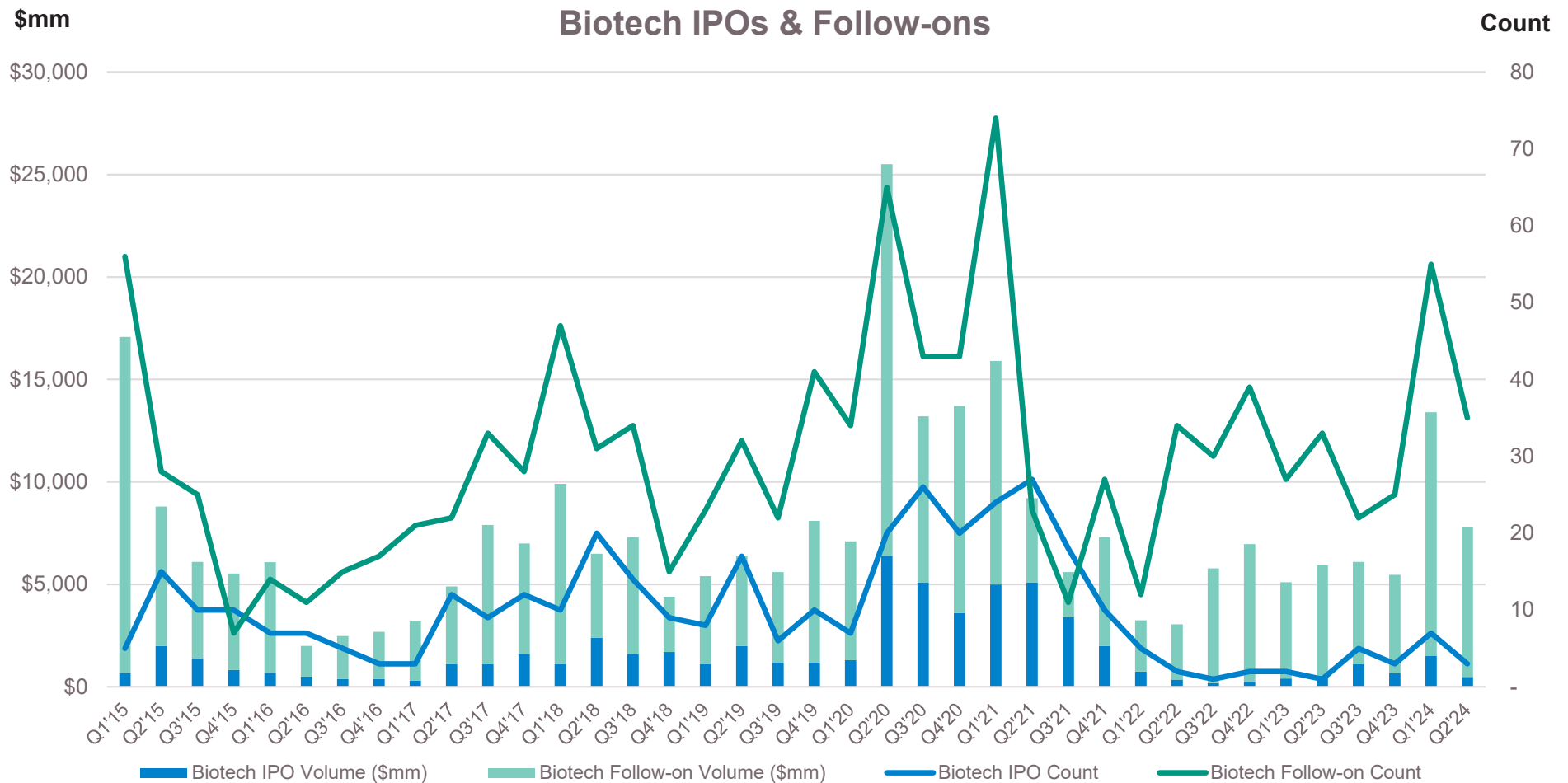
CDER CBER

✓ 2023 was a record year for FDA approvals

✓ Nearly **400** new drugs approved over the past 7 years

Dip in approvals in 2022 likely due to COVID; approval volume remains high

Financing Environment Improving

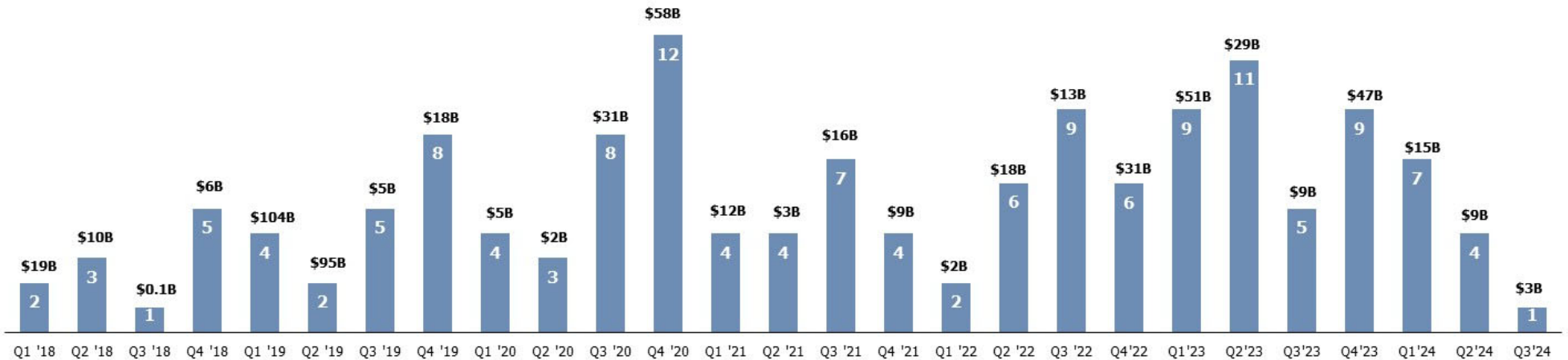


Source: BofA "Biotech ECM Activity" report as of 30 June 2024

- Biotech financing volume has picked up in 2024, though the number of IPOs has remained muted
- Investor demand for follow-on financings in good companies has been strong; weaker companies still face challenges getting financed
- BIOG has been participating selectively in IPOs and confidentially marketed follow-on offerings

M&A Activity in Biotechnology

Announced Public Biotech M&A Transactions



Source: Factset

Large Cap Pharma Supportive of Continued M&A



CEO Rob Davis

"You're going to continue to see (deals), I think both some of the smaller deals but then up to that \$15 billion range"



CEO Rick Gonzalez

"(Our) industry leadership position...affords us the ability then to really invest for growth in the next decade, which is ultimately how we're thinking about business development"



CEO Thomas Schinecker

"We are constantly looking at opportunities, both for partnering and acquisitions and yes, we are open to do more deals"



CEO Joaquin Duato

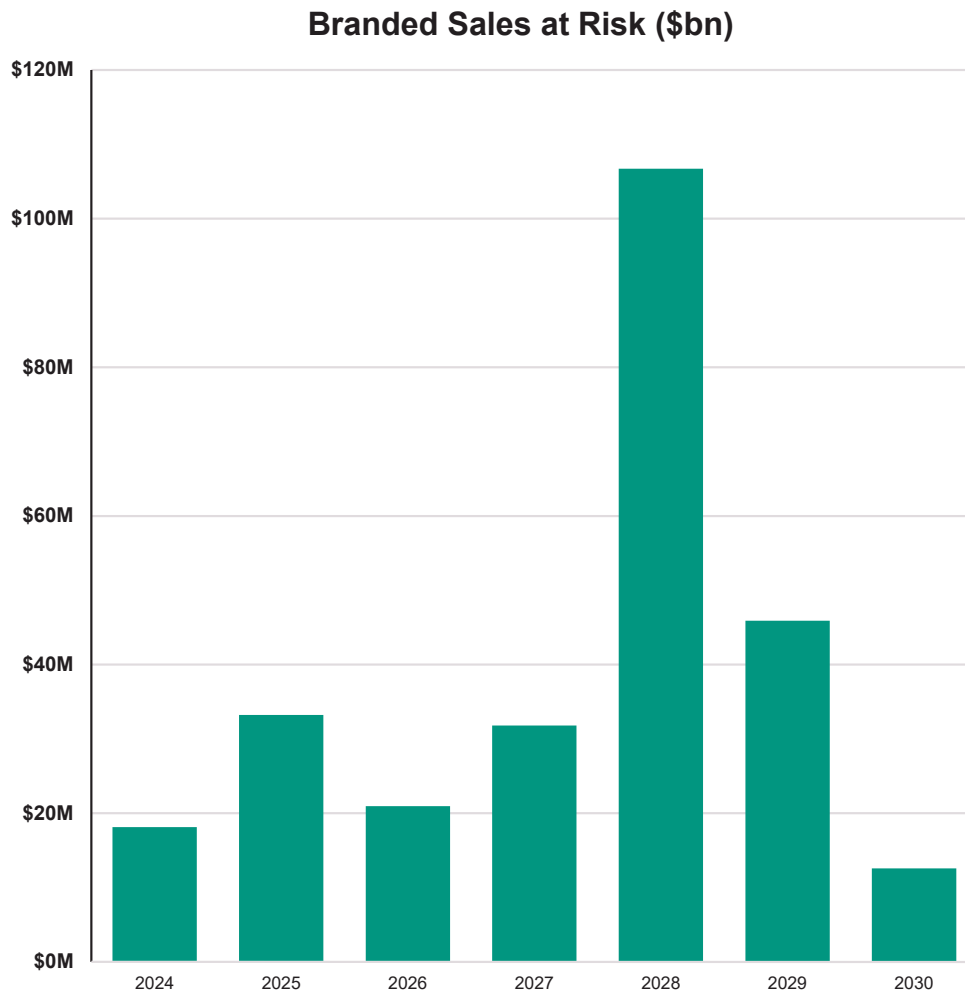
"Our capital allocation strategy will continue to be disciplined and M&A is going to remain a critical component of that, that's our M&A strategy and it's been a cornerstone of our ability to create value"

Recent M&A in BIOG



Big Pharma Patent Cliff Drives Biotech M&A

Nearly **\$270 billion** in branded sales are at risk (2024-2030)



Note: Data from Wolfe Research, OrbiMed, Visible Alpha (sales at risk represents consensus projected sales for year prior to year of expected loss of exclusivity)

Company	Drug	US Loss of Exclusivity (Projected)	'23 Global Sales (\$bn)
MERCK	KEYTRUDA <small>(pembrolizumab) injection 100mg</small>	2028	\$25.0
abbvie	HUMIRA <small>adalimumab</small>	2023	\$14.4
Bristol Myers Squibb™ Pfizer	Eliquis <small>(apixaban) tablets 25mg</small>	2026	\$12.2
Johnson & Johnson	Stelara <small>(ustekinumab)</small>	2025	\$10.9
Johnson & Johnson	DARZALEX	2029	\$9.7
Bristol Myers Squibb™	OPDIVO <small>involumab</small>	2028	\$9.0
abbvie Johnson & Johnson	imbruvica	2027	\$4.9
Pfizer	IBRANCE <small>palbociclib</small>	2027	\$4.8

Source: S&P Global report, Company Reports

2024 U.S. Presidential Election



In flux after June 27 debate but split Congress likely to continue

- The poor showing by President Biden at last month's debate has created uncertainty about the Democratic candidate, with some calling for him to step aside
- The race – as it stands today – favors the Republicans and probability of a Trump win has increased
- Prospects of further drug pricing reform likely depends on a Democratic sweep, which appears unlikely
- Of course, if Biden were to step aside, things could change materially

The screenshot shows a New York Times article page. At the top left is the NYT logo and a menu icon. Below it, the text 'PLAY THE CROSSWORD' is visible. The main headline reads 'To Serve His Country, President Biden Should Leave the Race'. Below the headline, it says 'OPINION THE EDITORIAL BOARD' and 'June 28, 2024, 5:59 p.m. ET'. The article is attributed to Thomas L. Friedman, with a sub-headline 'President Biden Is My Friend. He Must Bow Out of the Race.' and a '4 MIN READ' indicator. Below this, there are two more article teasers: one by Frank Bruni titled 'Biden Cannot Go on Like This' (4 MIN READ) and one by Patrick Healy titled 'I'm Hearing High Anxiety From Democrats Over Biden's Debate Performance' (3 MIN READ). At the bottom, there is a teaser by Nicholas Kristof titled 'President Biden, It's Time to Drop Out' (2 MIN READ).

Democrat Sweep?



- 2010: ACA passed
- 2022: IRA passed
- 2024: Nothing to do?

orbimed Probabilities*

5% **NEGATIVE**

Republican Sweep?



GOP historically "industry friendly"...may even try to revoke the most egregious parts of the IRA (drug price negotiations)

35% **POSITIVE**

Divided Government



Federal government remains in gridlock --- nothing gets passed

60% **POSITIVE**

Despite recent events in the Presidential race – split Congress expected

*OrbiMed in-house generated estimates

2024 Strategy and Outlook



Strategy to emphasize emerging biotech over large cap biotech will continue in order to fully capture sector rebound

- Will capitalize on compelling investment opportunities in companies that need to finance at low share prices
- Gearing level will generally stay between 5-10%



Unprecedented low valuations in emerging biotech suggest significant upside from current levels

- Performance drawdown of small/mid cap biotech versus the S&P 500 has been the longest and most severe we have ever seen
- Percent of biotech companies with market caps below the net cash on their balance sheets well above historical norms
- Valuation levels are lower than the Great Financial Crisis and the bursting of the Dot Com bubble
- Interest rate headwinds abating; biotech has historically outperformed during recessions



Valuation contraction is disconnected from the fundamental innovation in the sector, which remains robust



M&A activity expected to accelerate given lower valuations of biotech targets and urgent need for new products by Big Pharma



Political risk seems low given current election year outlook

OrbiMed believes this is an excellent time to invest in biotech innovation at unprecedented low valuations.

BIOG

Appendix

BIOG Holdings

As of 30 June 2024

	Market Price \$ Millions	Pct. Value		Market Price \$ Millions	Pct. Value		Market Price \$ Millions	Pct. Value
UNITED STATES			UNITED STATES			INTERNATIONAL		
Emerging Biotechnology			Emerging Biotechnology (cont.)			Europe		
ALX Oncology Holdings Inc	3.1	0.7	Prelude Therapeutics Inc	1.3	0.3	Emerging Biotechnology		
Alnylam Pharmaceuticals Inc	14.0	3.1	Repare Therapeutics Inc	0.2	0.0	ADC Therapeutics SA	4.8	1.1
Amicus Therapeutics Inc	5.7	1.3	Rhythm Pharmaceuticals Inc	12.0	2.7	Argenx SE	20.3	4.5
Apellis Pharmaceuticals Inc	6.2	1.4	Sarepta Therapeutics Inc	23.8	5.3	Immatics NV	8.4	1.9
Avidity Biosciences Inc	10.0	2.2	Scholar Rock Holding Corp	2.3	0.5	Merus NV	6.4	1.4
BioMarin Pharmaceutical Inc	2.1	0.5	Structure Therapeutics Inc	1.3	0.3		39.8	8.9
C4 Therapeutics Inc	3.2	0.7	Syndax Pharmaceuticals Inc	13.1	2.9			
Compass Therapeutics Inc	3.6	0.8	Tyra Biosciences Inc	6.1	1.4	Europe Subtotal	39.8	8.9
Cullinan Therapeutics Inc	4.6	1.0	Vaxcyte Inc	12.7	2.8			
Cytokinetics Inc	2.5	0.6	Vera Therapeutics Inc	8.4	1.9	Far East		
Dynavax Technologies Corp	1.3	0.3	Vir Biotechnology Inc	9.8	2.2	Emerging Biotechnology		
Dyne Therapeutics Inc	7.1	1.6	Xenon Pharmaceuticals Inc	9.1	2.0	BeiGene Ltd	4.7	1.1
Edgewise Therapeutics Inc	4.8	1.1		277.2	62.1	BrightGene Bio-Medical Technol	4.8	1.1
Enliven Therapeutics Inc	1.0	0.2	UNITED STATES			Gracell Biotechnologies Inc	0.5	0.1
Exact Sciences Corp	2.8	0.6	Major Biotechnology			Innovent Biologics Inc	7.5	1.7
Fate Therapeutics Inc	1.2	0.3	Amgen Inc	42.1	9.4	LakeShore Biopharma Co Ltd	0.9	0.2
Geron Corp	12.1	2.7	Biogen Inc	31.8	7.1	Mabwell Shanghai Bioscience Co	0.9	0.2
Heron Therapeutics Inc	9.0	2.0	Regeneron Pharmaceuticals Inc	24.0	5.4	New Horizon Health Ltd	1.1	0.2
Ionis Pharmaceuticals Inc	18.1	4.1	Vertex Pharmaceuticals Inc	7.6	1.7	OrbiMed Asia Partners	1.4	0.3
Janux Therapeutics Inc	13.2	3.0		105.5	23.6	QuantumPharm Inc	16.6	3.7
Kezar Life Sciences Inc	1.2	0.3	United States Total			Shanghai Runda Medical Techno	3.5	0.8
Krystal Biotech Inc	5.5	1.2		382.7	85.8	Stemirna*	0.3	0.1
Lexicon Pharmaceuticals Inc	3.5	0.8				Suzhou Basecare Medical Corp L	0.5	0.1
Lyell Immunopharma Inc	4.2	0.9					42.8	9.6
Milestone Pharmaceuticals Inc	1.3	0.3				Far East Subtotal	42.8	9.6
Mineralys Therapeutics Inc	10.0	2.2						
Morphic Holding Inc	8.1	1.8				International Total	82.7	18.5
Neumora Therapeutics Inc	4.5	1.0						
Neurocrine Biosciences Inc	10.4	2.3				Cash	-19.1	-4.3
Nkarta Inc	3.0	0.7						
						Total Portfolio	446.2	100.0

Note: securities with asterisks (*) are unquoted

Unprofitable Tech Has Declined Meaningfully

Goldman Sachs Unprofitable Tech Basket

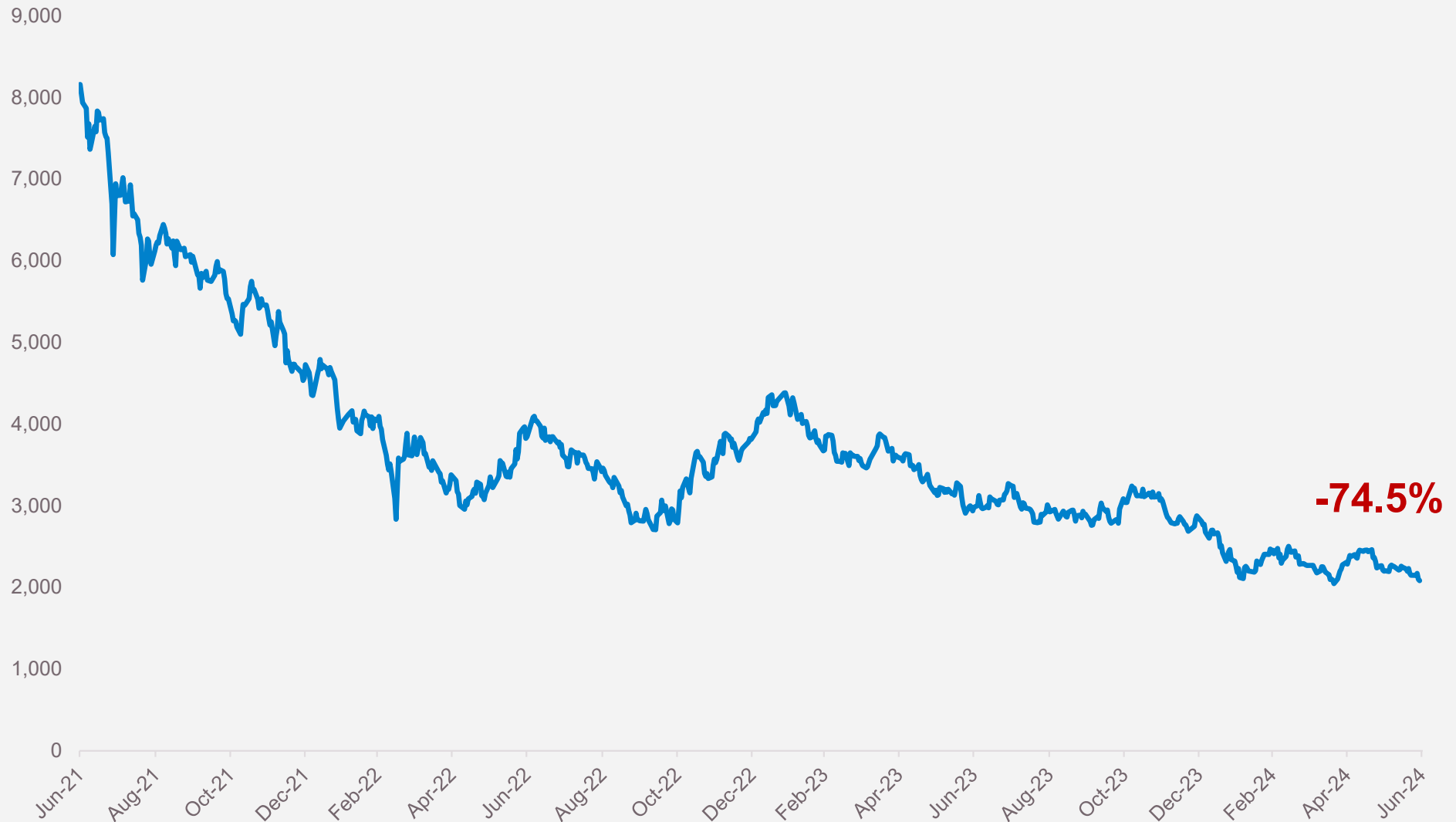


The GS Non-profitable tech basket (GSXUNPTC) consists of non-profitable US listed companies in innovative industries. Technology is defined broadly to include new economy companies across GICS industry groupings. Date range for chart is from 31 March 2021 to 30 June 2024

China Healthcare At All-Time Low

Innovation remains strong; recovery should occur eventually

Hang Seng Healthcare Index (HSHCI)



Source: Bloomberg, OrbiMed Advisors

Note: Chart updated from 30 June 2021 through 30 June 2024.

Risk Management

- Diversification across multiple parameters
 - Size and stage of company (large cap, mid cap, small cap); revenue versus pre-revenue
 - Geographical diversification (U.S., Europe, China)
 - Therapeutic area
 - Drug development technologies
- Prudent position sizing
 - Sizing depends on conviction level, liquidity of the stock, and risk/reward of the idea
 - We aim not to lose more than 100 basis points of performance on a single catalyst
 - Typical position sizes: 5-10% for large cap biotech, 1-3% for emerging biotech
 - Position sizes are actively managed to navigate the catalyst paths of emerging biotech stocks, so turnover is relatively high (~90%)
 - The fund regularly trades around positions (trimming high, adding low) to ensure position sizes appropriately reflect risk/reward, especially in advance of binary events
 - Volatility of biotech increases markedly as one descends in market cap
 - Average annual volatility of stock constituents of NASDAQ Biotech Index:

As of 10 July 2024	1 Std. Deviation
Large Cap (>\$10bn)	44.0
Mid Cap (\$2bn-10bn)	64.7
Small Cap (<\$bn)	80.9

- Fund's emphasis on emerging biotech with stock-moving catalysts means turnover will likely remain high to manage risk appropriately

Endnotes

General Notes

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An investment in the fund is speculative and involves a high degree of risk. The fund is an investment trust listed on the London Stock Exchange. Investment trusts have the ability to borrow to invest, which is known as gearing. Companies with higher gearing are subject to higher risks, and therefore the investment value may change substantially. The value and the performance of the net asset value of the fund may not be the same as its share price. In considering an investment in the fund, prospective investors should also be aware of certain other special considerations and risk factors, including those related to: the risk of deterioration in the financial markets in general and the healthcare sector in particular; the risk that the fund could incur losses due to the failure of third parties to perform their contractual commitments to the fund or financial difficulties on the part of brokerage firms, banks or other financial institutions that hold assets of the fund; risks arising from the operation of pooled investment vehicles like the fund; and tax-related risks arising from the status and operation of the fund. See the Fund Documents for more detail on those and other risks.

No guarantee or representation is made that a fund will achieve its investment objective or that the fund's risk management strategies will be successful. The fund's performance may be volatile, and investors in the fund could lose all or a substantial amount of their investment. In addition, the fees and expenses charged in connection with an investment in the fund may be higher than those charged in connection with other investments, and in some market conditions, may offset trading profits. Accordingly, shares or interests are suitable only for sophisticated investors for whom an investment in the fund does not constitute a complete investment program and who fully understand and are willing to assume the risks involved in the fund's investment program.

Prospective investors should not construe the contents of this document as legal, business or tax advice. Each investor should consult such advisors as it deems appropriate concerning a potential investment in a fund.

No securities commission or regulatory authority in the United States, the United Kingdom or in any other country has in any way passed upon the merits of an investment in any fund or the accuracy or adequacy of this document.

Endnotes

Indices

Indices are shown for comparison only, are unmanaged, do not charge fees or expenses and do not employ special techniques such as leveraging or short selling.

The volatility of indices may be materially different from the performance of the fund. In addition, the fund's portfolio holdings may differ significantly from the securities that comprise such indices.

The NASDAQ Biotechnology Index (the "NBI") includes securities of NASDAQ-listed companies classified according to the Industry Classification Benchmark as either Biotechnology or Pharmaceuticals, which also meet other eligibility criteria, and is calculated under a modified capitalization-weighted methodology. The Russell 2000 Index is comprised of the smallest 2000 companies in the Russell 3000 Index. The Russell 1000 Index consists of the largest 1000 companies in the Russell 3000 Index. The SPDR S&P Biotech ETF is an exchange-traded fund that seeks to replicate the performance of the S&P Biotechnology Select Industry Index, an equal-weighted index. The SPX includes 500 leading companies and captures approximately 80% coverage of available market capitalization. The FTSE 100 Index is a capitalization-weighted index of the 100 most highly capitalized companies traded on the London Stock Exchange. The Hang Seng Healthcare Index ("HSHCI") aims to reflect the overall performance of stocks listed in Hong Kong that are related to healthcare businesses.

Where stated as "Net" or "TR" (or total return), the index return numbers include reinvestment of dividends net of withholding taxes, as calculated by the index provider.