# The Biotech Growth Trust

ShareSoc Webinar

October 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

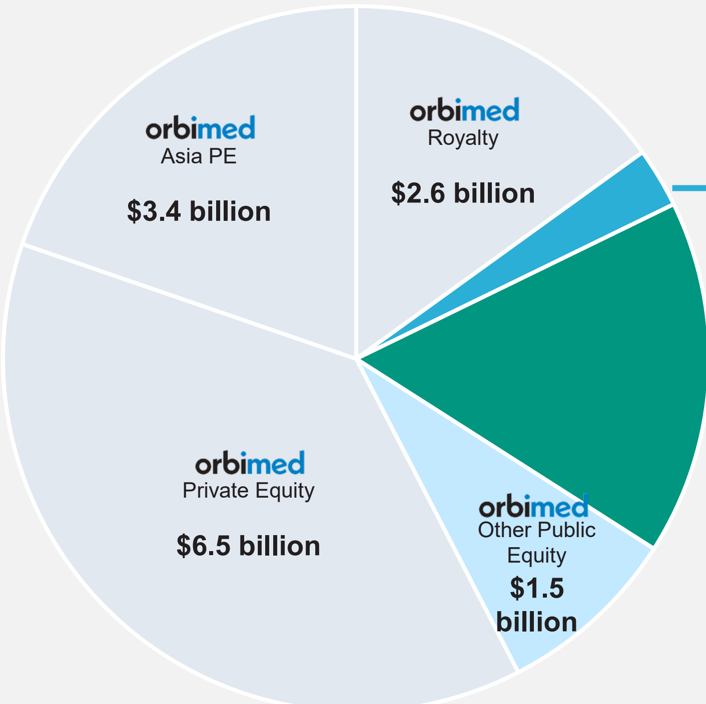
Partner

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**




THE BIOTECH GROWTH TRUST PLC — $477 million

WORLDWIDE HEALTHCARE TRUST PLC — $2.7 billion

**Total AUM: $17.1 billion**

**142** Global Employees

**300+** Years of Investment Experience

**20+** New Hires in 2023/24

**30** Colleagues with M.D. / Ph.D.

Source: OrbiMed; Data estimated as of 30 September 2024

BIOG

# Performance

# BIOG Performance for Fiscal 2024

## 31 March 2023 to 31 March 2024


Source: Frostrow, Bloomberg.

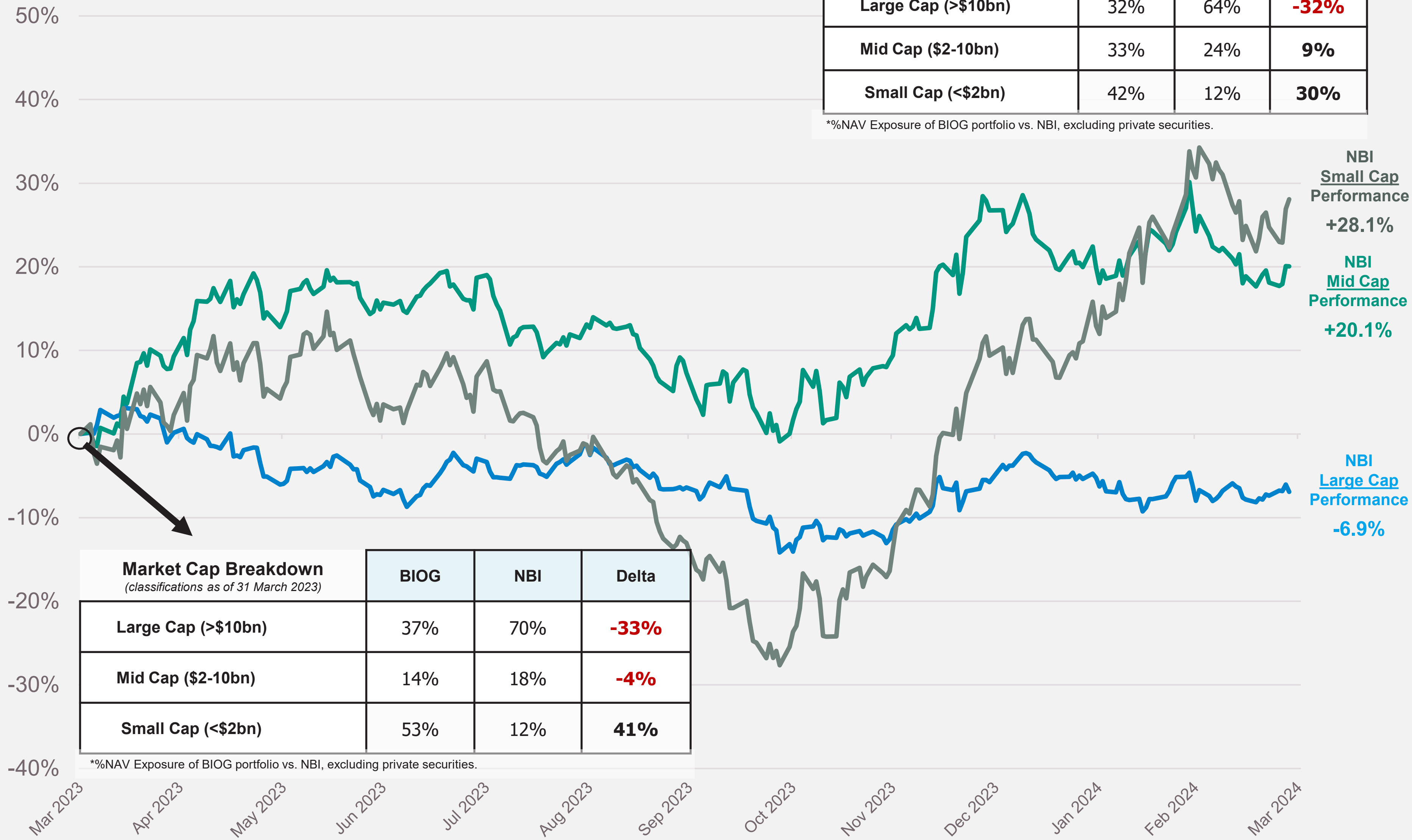
Note: See Endnotes for additional information, including with regard to the calculation of these results and the index shown above.

# Market Cap Performance Divergence in Biotech

## Small and Mid Cap Biotech Begins to Recover

| Market Cap Breakdown *(classifications as of 31 March 2024)* | 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.




| Market Cap Breakdown *(classifications as of 31 March 2023)* | BIOG | NBI | Delta |
|---|---|---|---|
| **Large Cap (>$10bn)** | 37% | 70% | **-33%** |
| **Mid Cap ($2-10bn)** | 14% | 18% | **-4%** |
| **Small Cap (<$2bn)** | 53% | 12% | **41%** |

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

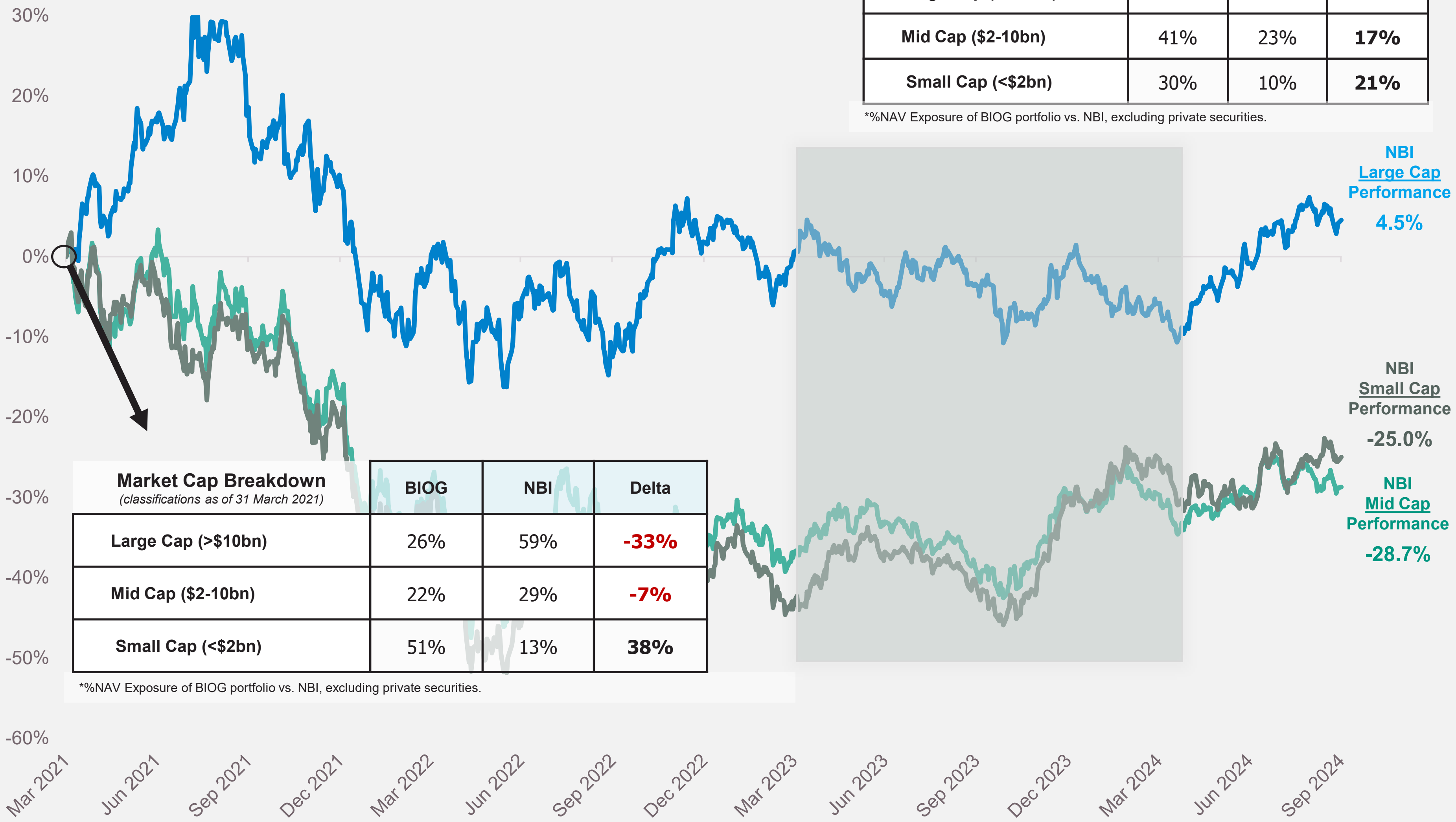
Note: Chart shows equal-weighted performance of NBI stocks in their respective market cap buckets, using market cap classifications as of 31 March 2023. Updated as of 31 March 2024, performance calculated in USD.

# Market Cap Performance Divergence in Biotech

## Performance Gap Since 2021 Has Yet to Close

| Market Cap Breakdown *(classifications as of 30 September 2024)* | BIOG | NBI | Delta |
|---|---|---|---|
| **Large Cap (>$10bn)** | 37% | 67% | **-30%** |
| **Mid Cap ($2-10bn)** | 41% | 23% | **17%** |
| **Small Cap (<$2bn)** | 30% | 10% | **21%** |

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



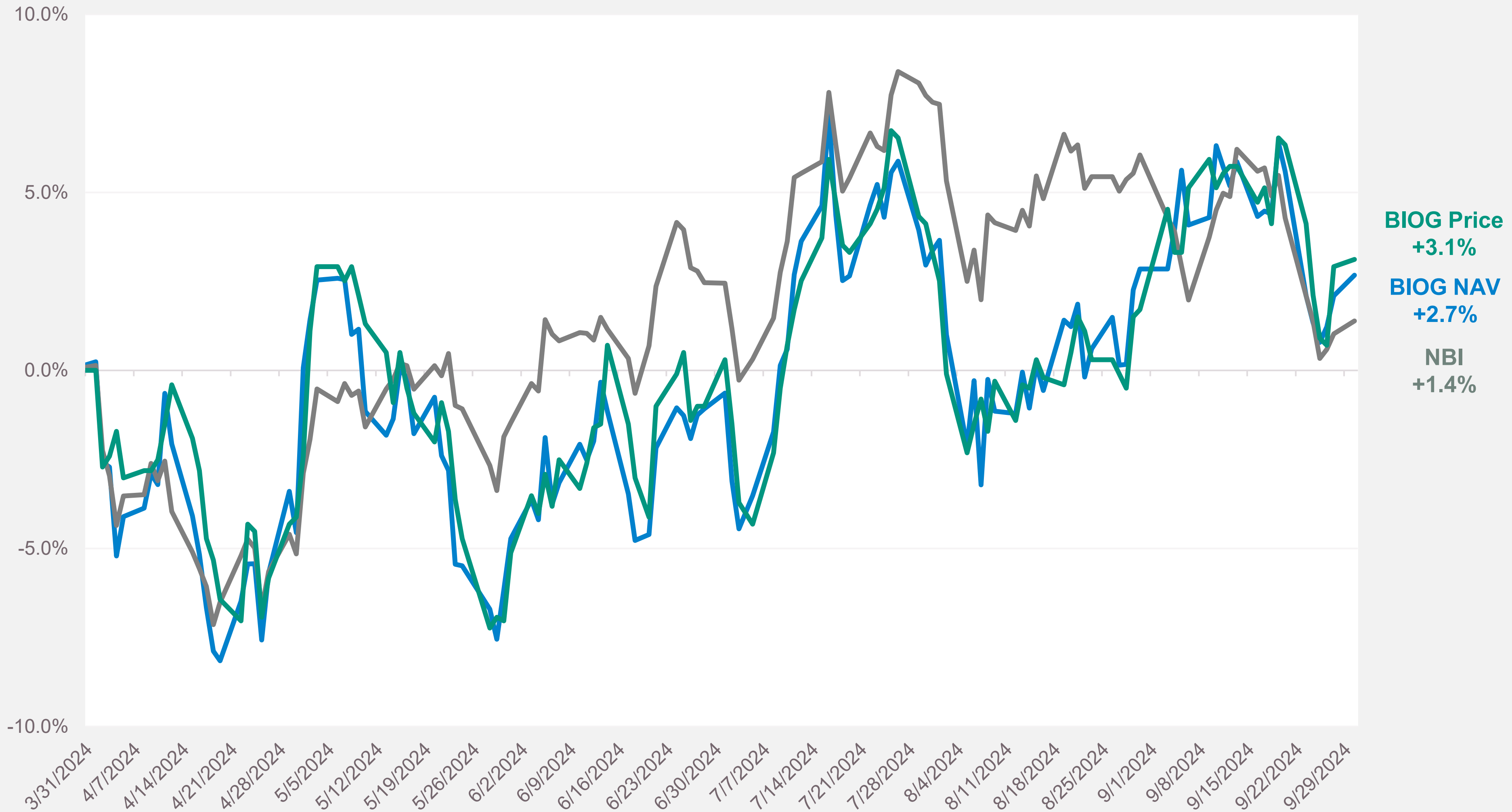

| Market Cap Breakdown *(classifications as of 31 March 2021)* | BIOG | NBI | Delta |
|---|---|---|---|
| **Large Cap (>$10bn)** | 26% | 59% | **-33%** |
| **Mid Cap ($2-10bn)** | 22% | 29% | **-7%** |
| **Small Cap (<$2bn)** | 51% | 13% | **38%** |

*%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 2021. Updated as of 30 September 2024, performance calculated in USD.

# BIOG Performance for Fiscal YTD

## 31 March 2024 to 30 September 2024



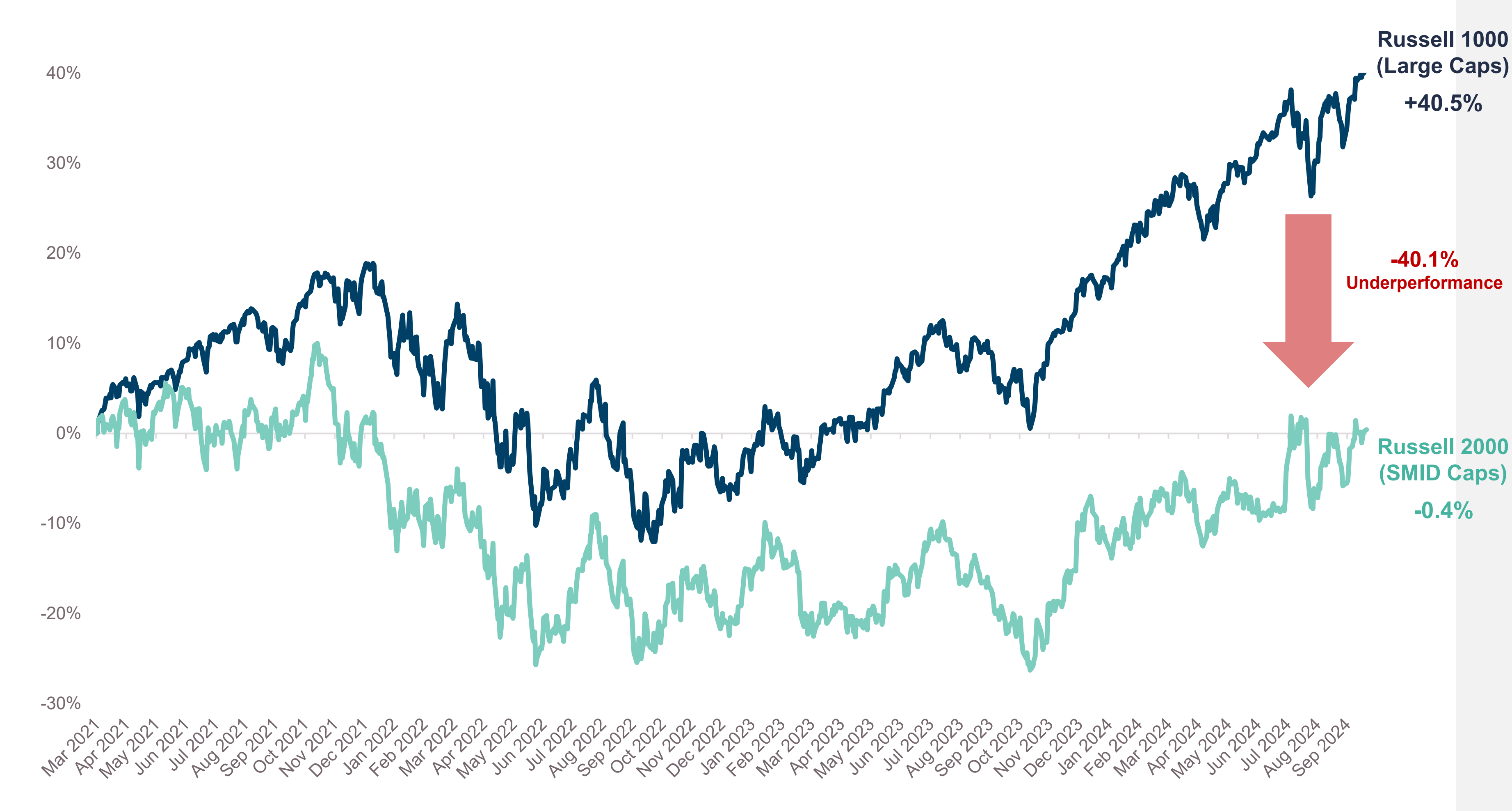

Source: Frostrow, Bloomberg.

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 September 2024)

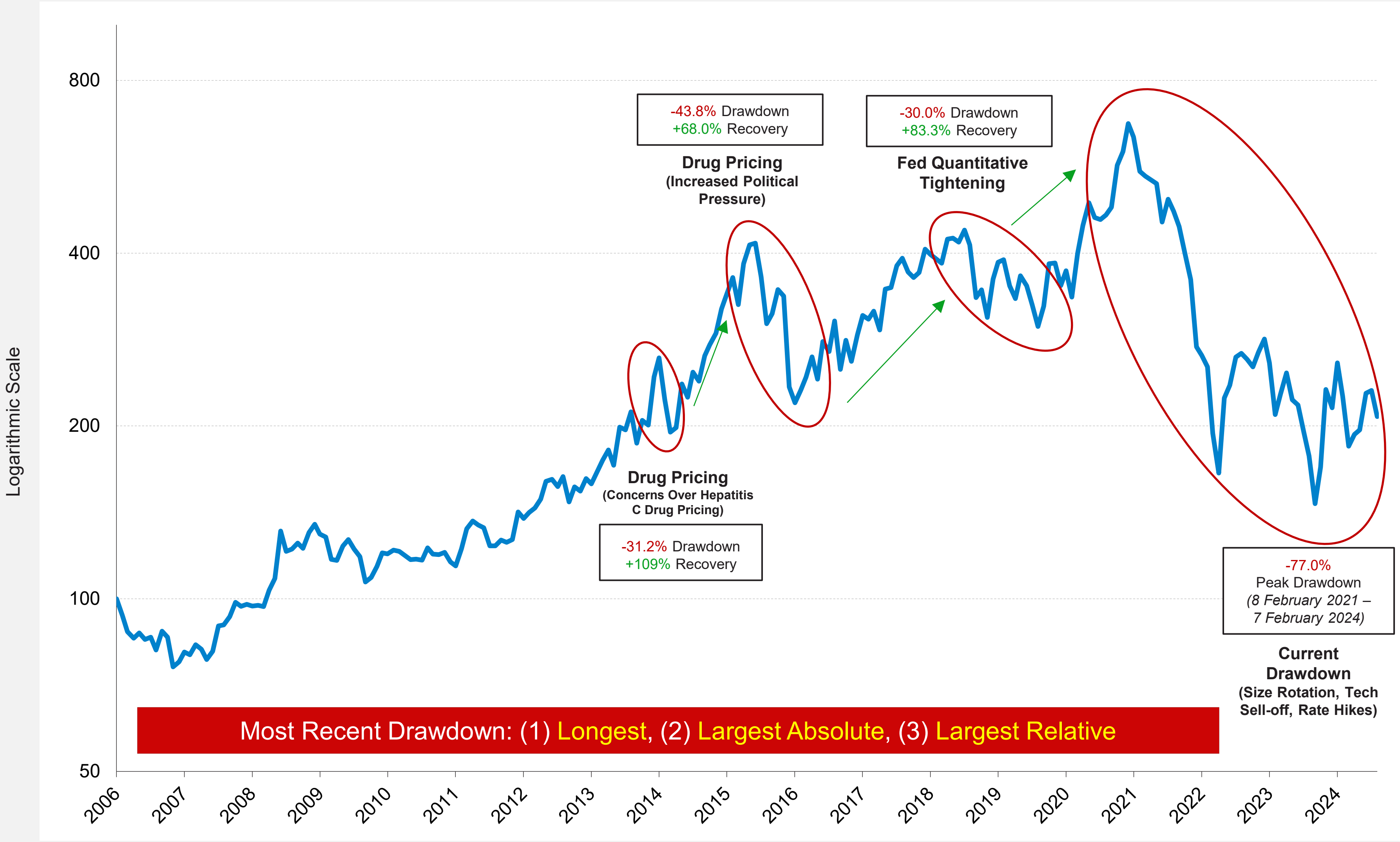
### Russell 2000 (Small/Mid Cap) vs Russell 1000 (Large Cap)




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.

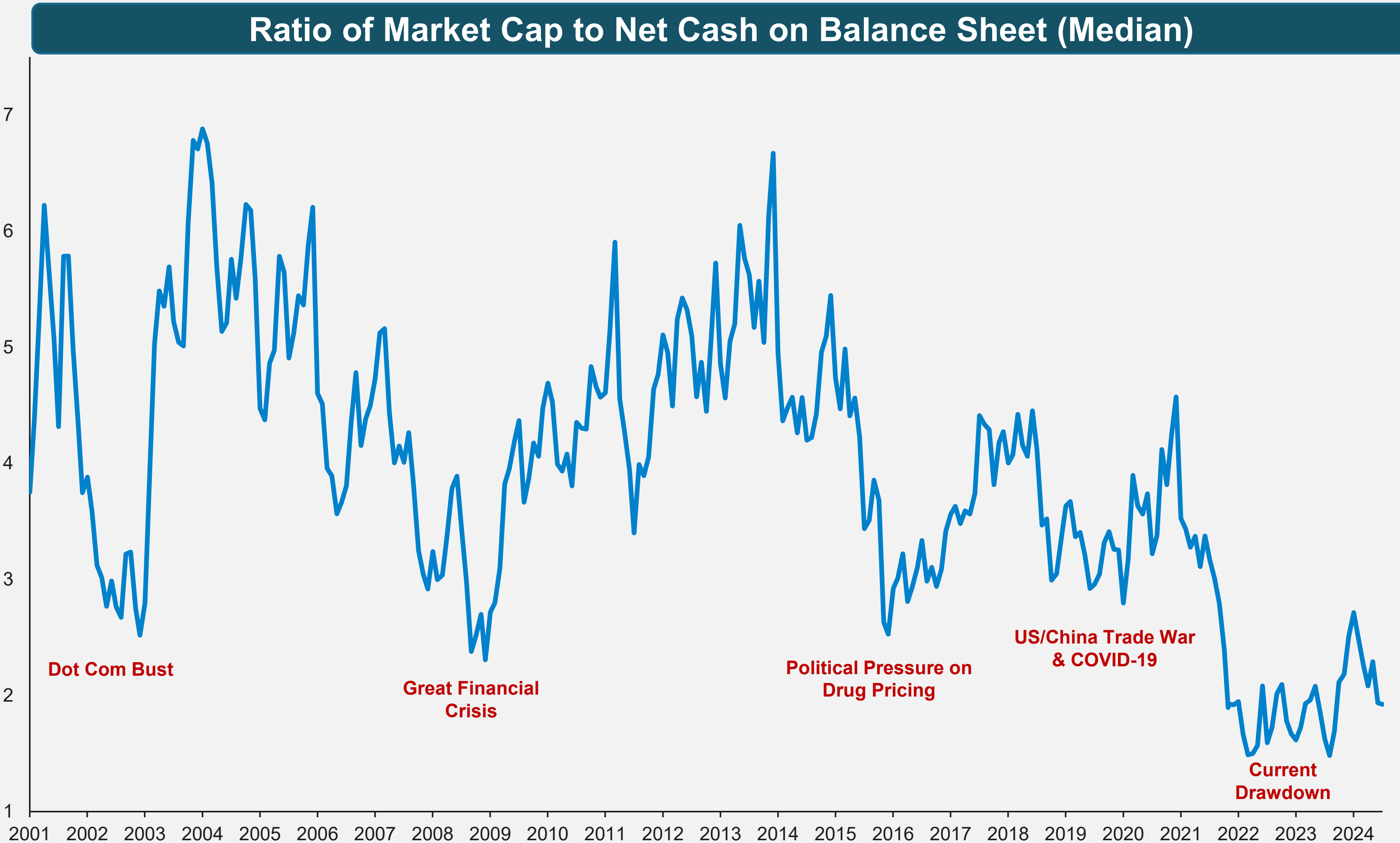
# XBI vs. S&P 500 (SPX) Spread since XBI Inception

## 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 September 2024.
Source: JPM [Drawdowns and Recoveries] | OrbiMed (XBI - SPX Spread Chart since XBI Inception).

# Biotech Valuations At Unprecedented Lows

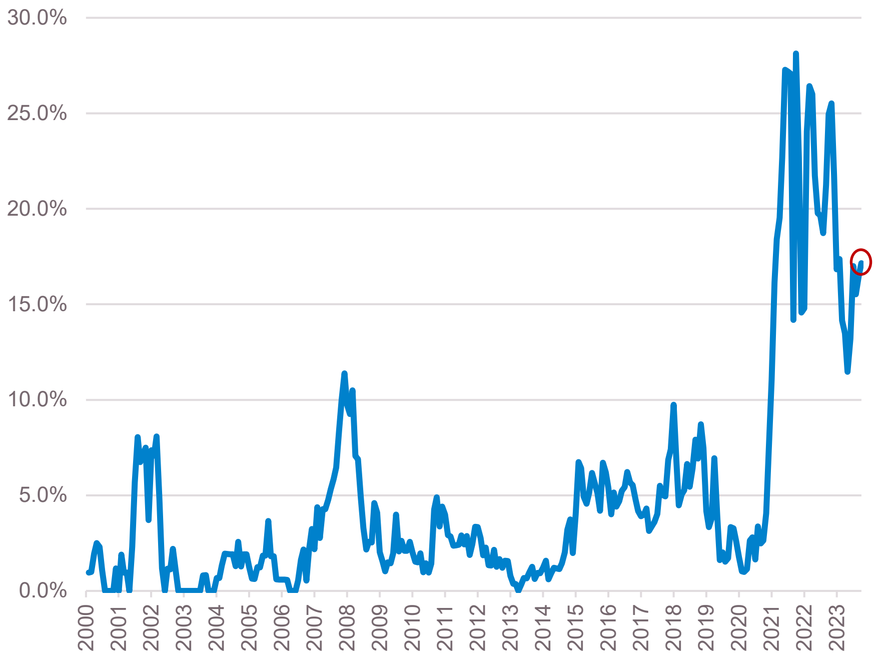



Note: Monthly chart of all GICS defined biotechnology greater than $10mm, using historical cash and debt sourced from Bloomberg, with annual GICS biotechnology universe refreshes. Updated through 30 September 2024.

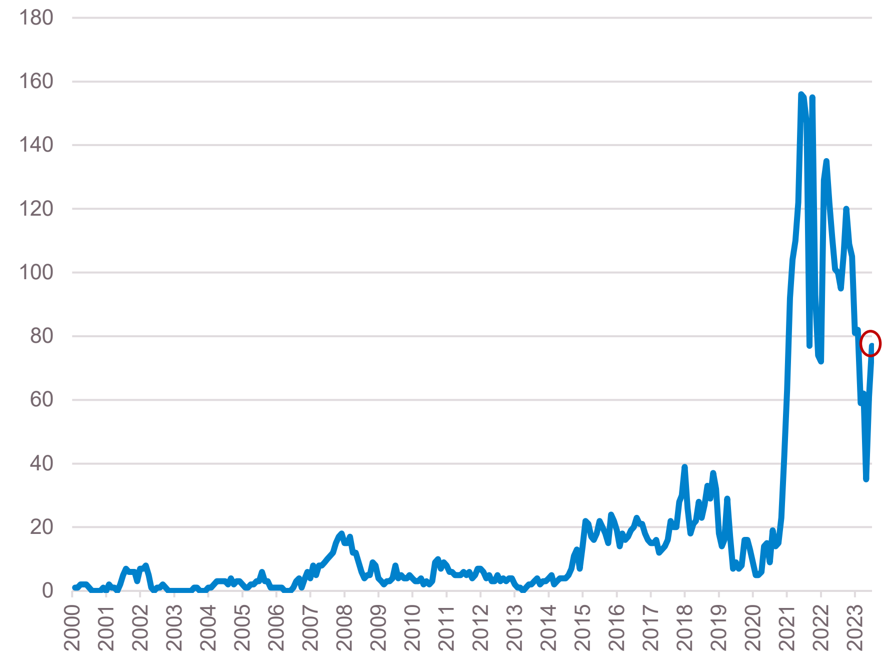
# Biotech Valuations At Unprecedented Lows

## Valuations have begun recovering from historical lows

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



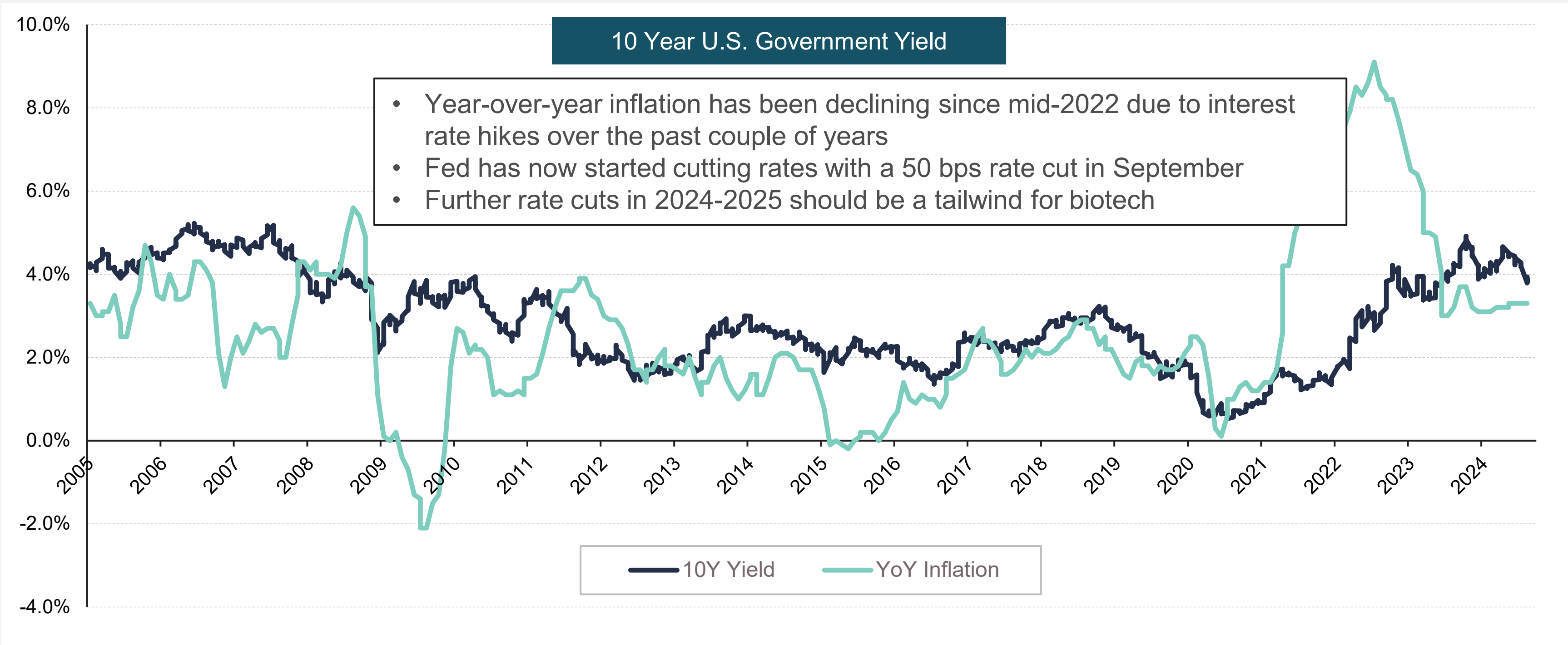

**Number of Biotech Companies Trading Below Net Cash on Balance Sheet:**

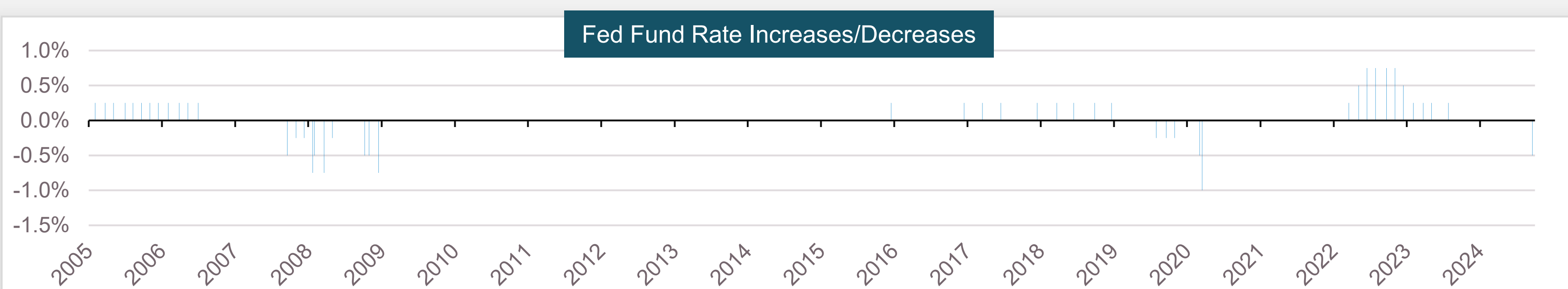



Note: Monthly chart of all GICS defined biotechnology greater than $10mm, using historical cash and debt sourced from Bloomberg, with monthly GICS biotechnology universe refreshes. Updated through 30 September 2024

# 10-Year U.S. Government Yield Poised to Decline

## (USGG10YR Index) Data as of 30 September 2024

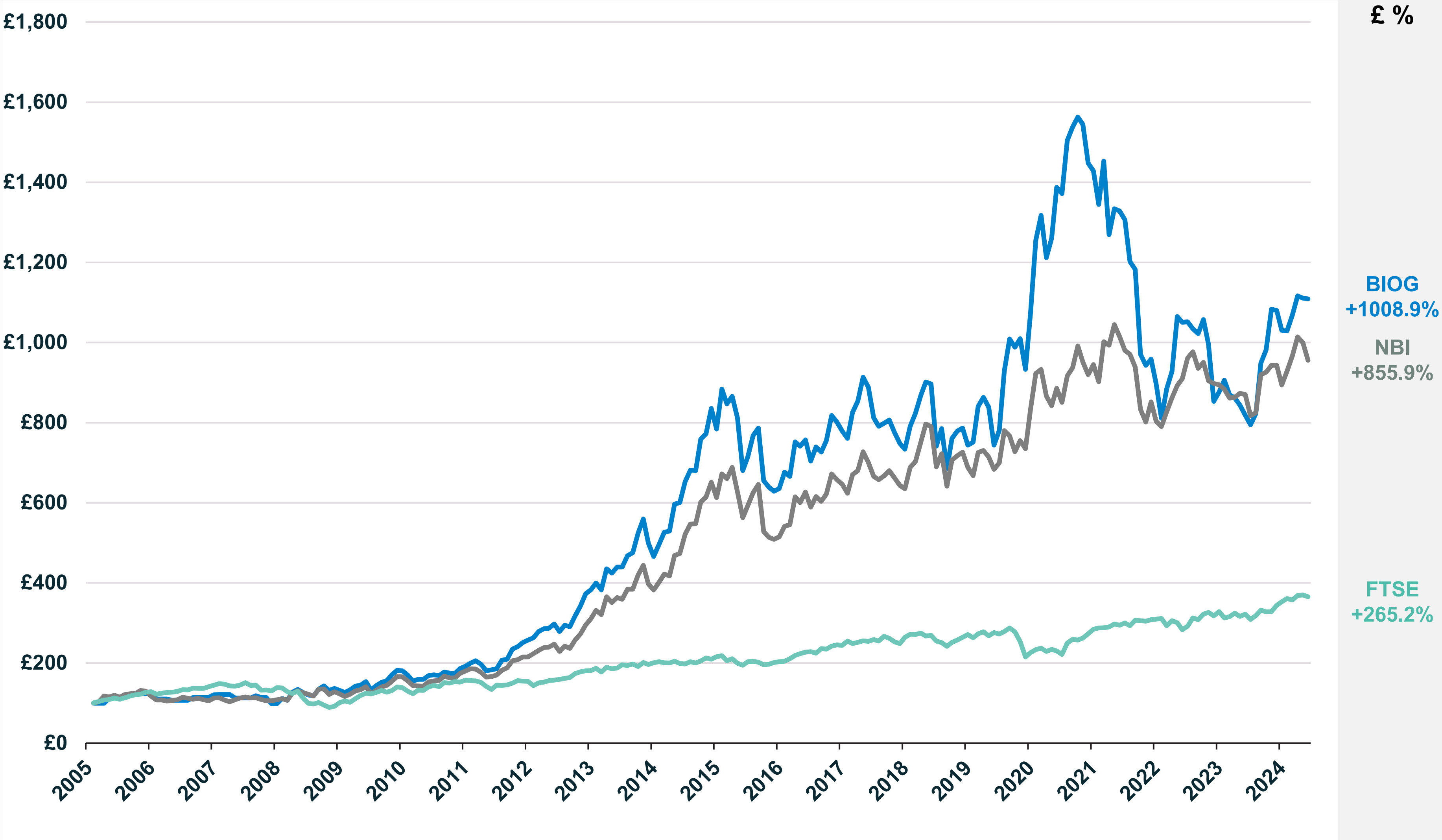



*Source: Bloomberg*

# BIOG Performance since Inception

18 May 2005 through 30 September 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 in the last 18 Months

| Company | Indication | Product (MOA) | Highlights |
|---|---|---|---|
| agios | Non-transfusion and Transfusion Dependent Adult Thalassemia | Mitapivat (PK activator) | Reported positive Phase 3 data in two trials; first oral treatment for thalassemia |
| Alnylam Pharmaceuticals | ATTR Amyloidosis with Cardiomyopathy (ATTR-CM) | Vutrisiran (siRNA) | Reported first positive ATTR-CM outcomes study with a silencer of ATTR |
| insmed | Bronchiectasis | Brensocatib (DPP1 inhibitor) | Positive Phase 3 data with 20% reduction in exacerbations over 52 weeks. First ever successful bronchiectasis study. |
| Dyne Therapeutics | 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 |
| Avidity Biosciences | 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 |
| kyverna | Autoimmune Diseases | Auto CAR-T (CD19 targeting) | Demonstrated disease modifying activity of a one-time cellular therapy in refractory autoimmune disease |
| CRISPR Therapeutics / Vertex | Sickle Cell Disease and Beta Thalassemia | Casgevy (CRISPR Cas9 gene-editing therapy) | First ever CRISPR therapy approved in the world |
| Crinetics Pharmaceuticals | 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 2024

| Company | Indication | Product (MOA) | Highlights |
|---|---|---|---|
| Iovance Biotherapeutics | Metastatic Melanoma | Amtagvi | **First** cellular therapy approved for the treatment of a solid tumor |
| Verona Pharma | Chronic Obstructive Pulmonary Disease (COPD) | Ohtuvayre | **First** novel mechanism approved to treat COPD in over a decade |
| geron | Low to Intermediate Risk Myelodysplastic Syndromes | Rytelo | **First** and only oligonucleotide telomerase inhibitor |
| AMGEN | Small Cell Lung Cancer | Imdelltra | **First** bispecific T-cell engager approved to treat a solid tumor |
| Day One Biopharmaceuticals | Pediatric Low-Grade Glioma | Ojemda | **First** therapy in its class approved for a type of pediatric brain tumor |
| Alexion AstraZeneca Rare Disease | Paroxysmal Nocturnal Hemoglobinuria (PNH) | Voydeya | **First** oral add on therapy for the treatment of PNH |
| Acceleron, Merck | Pulmonary Arterial Hypertension (PAH) | Winrevair | **First** new mechanism for the treatment of PAH in over a decade |
| Madrigal Pharmaceuticals | Non-Alcoholic Steatohepatitis (NASH) | Rezdiffra | **First** drug approved for the treatment of fatty liver disease |
| Orchard therapeutics, Kyowa Kirin | 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 |
|---|---|---|
| Gilead | Legend Biotech | Iovance Biotherapeutics |
| Bristol Myers Squibb | Arcellx | Immatics |

### Antibody-Drug Conjugates

Daiichi-Sankyo, AstraZeneca, MacroGenics, Elevation Oncology, Gilead

Antibodies with chemo attached

### Bispecific Antibodies

Antibodies that bind to 2 different targets

Amgen, Xencor, Regeneron, Merus, Janux, Genmab

### Targeted Therapies

Targeting specific genetic mutations

Syndax, Nuvalent, Revolution Medicines, SpringWorks Therapeutics, Kura Oncology, Day One Biopharmaceuticals

### Radiopharmaceuticals

Novartis, Perspective Therapeutics, Lilly, Lantheus, Actinium Pharmaceuticals, Inc., Bristol Myers Squibb, Cellectar Biosciences, AstraZeneca

Using targeted radiation to kill tumor cells

### Cancer Vaccines

Harnessing the immune system to attack cancer

Moderna, Merck, Scancell, Evaxion, Elicio Therapeutics, BioNTech

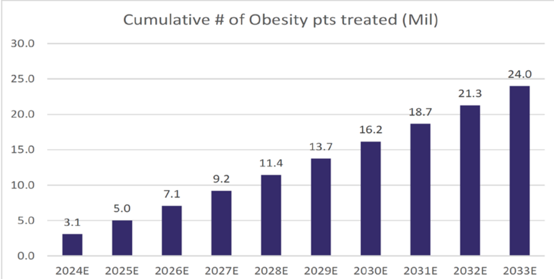
Note: companies are not necessarily representative of portfolio holdings.

**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

Lilly: zepbound, mounjaro

novo nordisk: wegovy, OZEMPIC

### Weight Loss at 1 Year

**Current Therapies**

12-18% weight loss

**Next Generation Therapies**

25%+ weight loss

### Additional Indications

Lilly

- TIRZEPATIDE MMO
- TIRZEPATIDE CV Outcomes
- TIRZEPATIDE Obstructive Sleep Apnea
- TIRZEPATIDE Heart Failure pEF

novo nordisk

- Diabetes
- CKD
- CVD
- PAD
- Obesity
- Brain disorders
- NASH
- 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

ScholarRock, altimmune, BIOAGE, STRUCTURE THERAPEUTICS, AMGEN, biohaven pharmaceuticals, VIKING THERAPEUTICS, Lexicon pharmaceuticals, REGENERON, ZEALAND PHARMA, Innovent

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.**

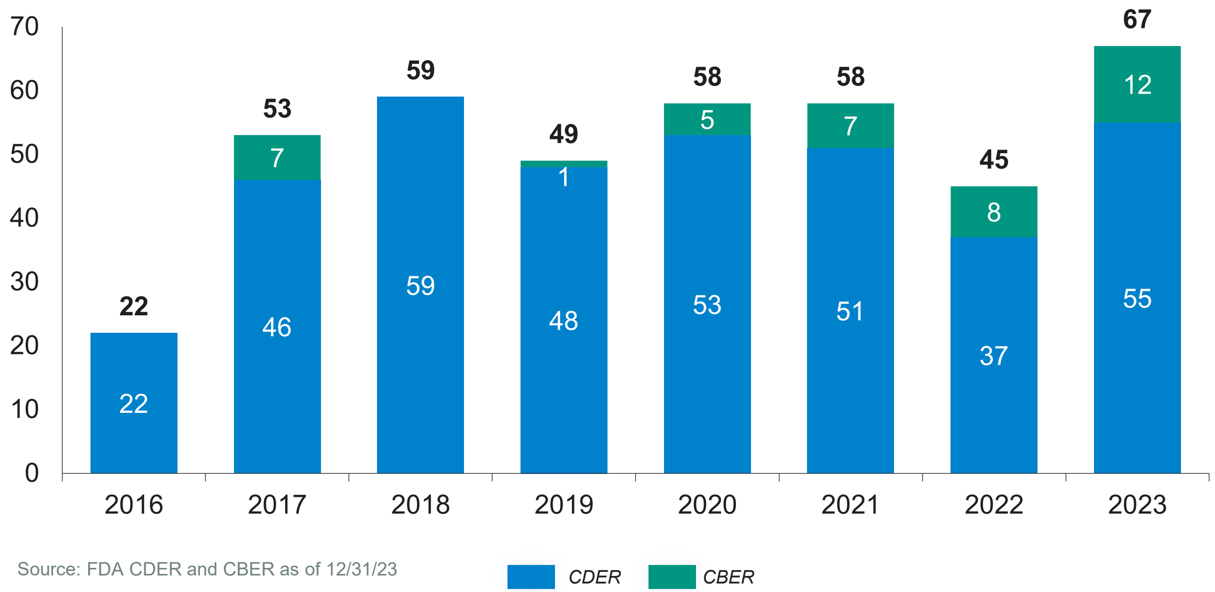
# Innovation Well Reflected in BIOG

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

| Antibody-drug conjugates | Gene Therapy Gene Editing | Cell Therapy | Multispecific antibodies T-Cell Engagers | Oligonucleotide therapeutics |
|---|---|---|---|---|
| 15.6% NAV | 12.2% NAV | 16.5% NAV | 22.9% NAV | 33.6% NAV |
| ADC THERAPEUTICS, BrightGene 博瑞医药 | Krystal, SAREPTA THERAPEUTICS, VERTEX | immatics, Fate THERAPEUTICS | AMGEN, cullinan THERAPEUTICS, Akesobio | IONIS, Dyne THERAPEUTICS, AVIDITY BIOSCIENCES |

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

# FDA New Molecular Entity Approvals



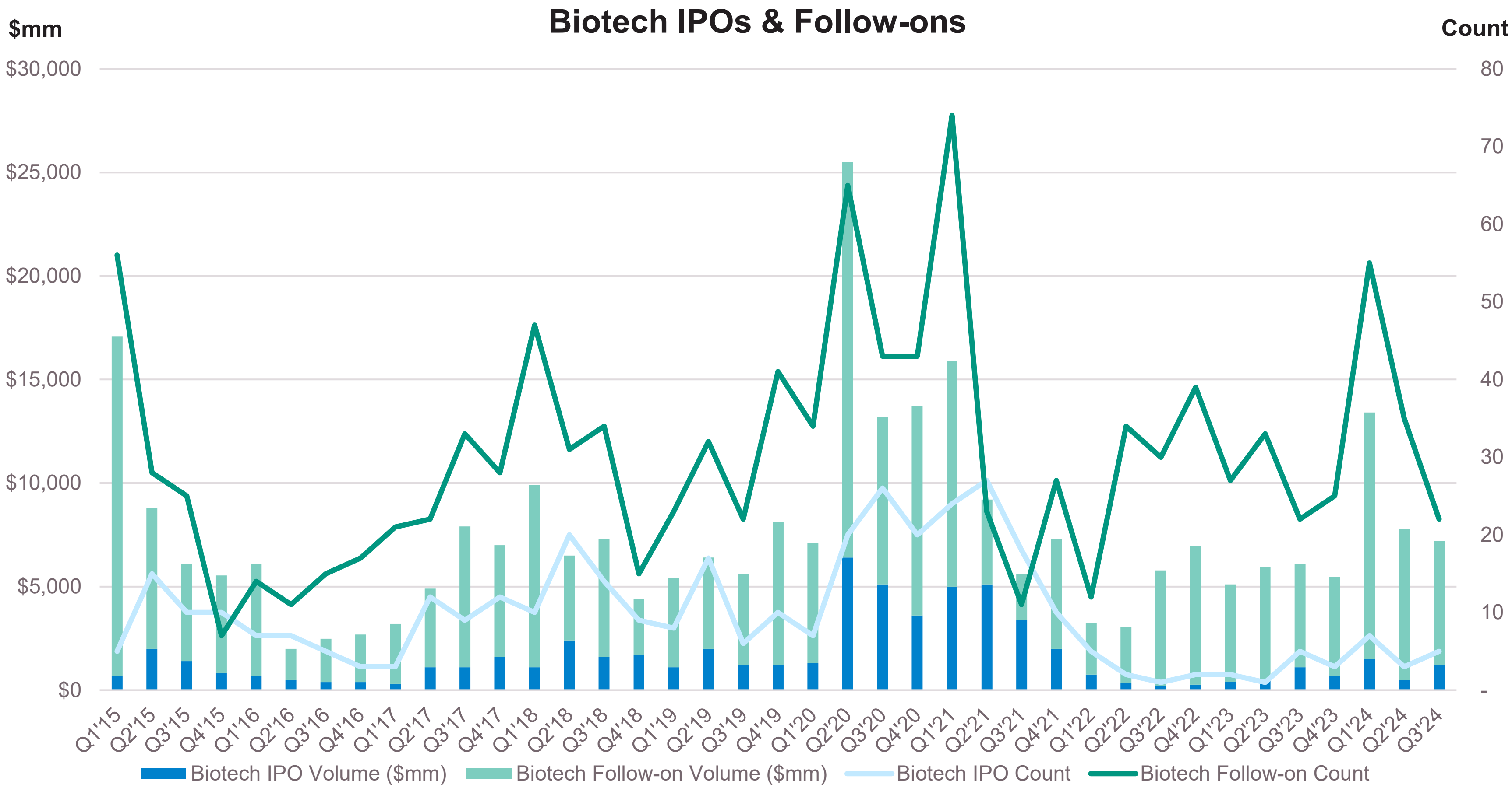

Source: FDA CDER and CBER as of 12/31/23

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

2023 was a record year for FDA approvals

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

# Financing Environment Improving

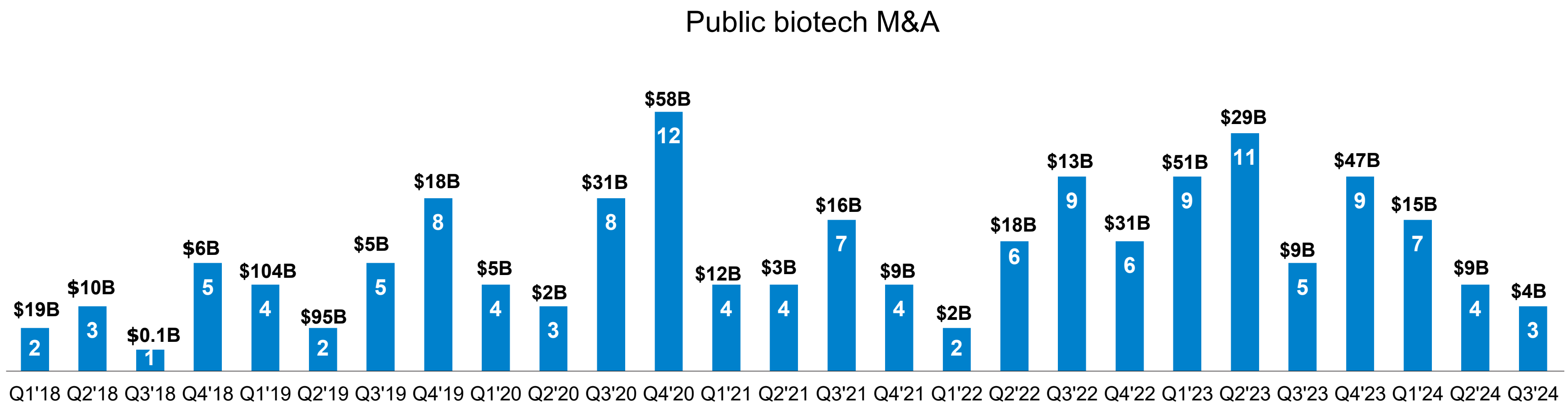



- Biotech financing volume has picked up in 2024, though the number of IPOs has remained muted
- Investor demand for follow-on financings in good companies has been strong; weaker companies still face challenges getting financed
- BIOG has been participating selectively in IPOs and confidentially marketed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

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

# M&A Activity in Biotechnology

## Announced Public Biotech M&A Transactions




Source: Factset

## Large Cap Pharma Supportive of Continued M&A

MERCK

**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"*

abbvie

**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"*

Roche

**CEO Thomas Schinecker**

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

J&J

**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

MORPHIC – Lilly

AMBRX – J&J

GRACELL – AstraZeneca

MIRATI THERAPEUTICS – Bristol Myers Squibb

DICE – Lilly

CHINOOK THERAPEUTICS – NOVARTIS

Bellus HEALTH – GSK

Seagen – Pfizer

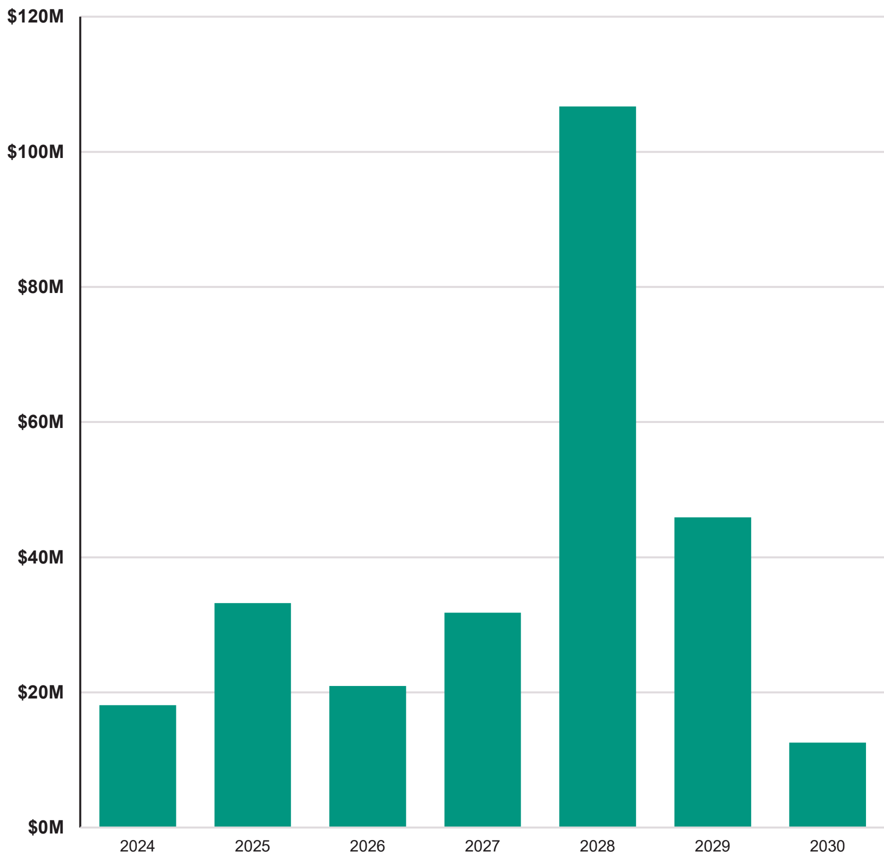
CINCOR – AstraZeneca

LONGBOARD PHARMACEUTICALS – Lundbeck

# Big Pharma Patent Cliff Drives Biotech M&A

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

**Branded Sales at Risk ($bn)**




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 (pembrolizumab) | 2028 | $25.0 |
| abbvie | HUMIRA adalimumab | 2023 | $14.4 |
| Bristol Myers Squibb / Pfizer | Eliquis (apixaban) tablets | 2026 | $12.2 |
| Johnson & Johnson | Stelara (ustekinumab) | 2025 | $10.9 |
| Johnson & Johnson | DARZALEX | 2029 | $9.7 |
| Bristol Myers Squibb | OPDIVO (nivolumab) | 2028 | $9.0 |
| abbvie / Johnson & Johnson | imbruvica | 2027 | $4.9 |
| Pfizer | IBRANCE palbociclib | 2027 | $4.8 |

Source: S&P Global report, Company Reports

# 2024 U.S. Presidential Election


## A volatile summer in election year politics; election risk for biotech appears low

- The Presidential debate on 27 June 2024 revealed Biden's weaknesses as a candidate
- Two weeks later a Trump assassination attempt on 13 July 2024 led to continued momentum for Trump
- Then history was made when Biden stepped down, passing the re-election torch to Harris on 21 July 2024
- Harris has improved chances for the Democrats, but Presidential race remains a very close call


POLITICS

A halting Biden tries to confront Trump at debate but sparks Democratic anxiety about his candidacy

AP

June 27, 2024


The New York Times

TRUMP HURT, BUT SAFE, AFTER A SHOOTING

A Suspected Gunman and a Rally Attendee Are Killed

July 13, 2024

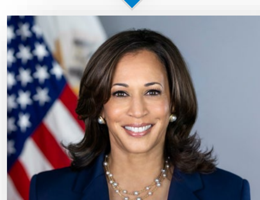

The New York Times

BIDEN BOWS OUT

LATE REVERSAL UPENDS RACE FOR WHITE HOUSE AS PRESIDENT ENDORSES HARRIS TO LEAD TICKET

Facing Pressure, He Writes, 'It's Time to Come Together and Beat Trump'

July 21, 2024



**Harris Steps In**

**July 22, 2024**

**orbimed Probabilities***

**Democrat Sweep?**

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

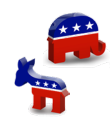
**5%** NEGATIVE

**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


 *Source: Goldman Sachs*

# 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 rates now declining rather than increasing; 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.**

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# Appendix

# BIOG Holdings

## As of 30 September 2024

| UNITED STATES | Market Price $ Millions | Pct. Value |
|---|---|---|
| **Emerging Biotechnology** | | |
| ACADIA Pharmaceuticals Inc | 11.8 | 2.5 |
| Alnylam Pharmaceuticals Inc | 15.9 | 3.3 |
| Amicus Therapeutics Inc | 6.1 | 1.3 |
| Apellis Pharmaceuticals Inc | 3.7 | 0.8 |
| Avidity Biosciences Inc | 14.0 | 2.9 |
| Bicara Therapeutics Inc | 1.0 | 0.2 |
| BioAge Labs Inc | 5.1 | 1.1 |
| C4 Therapeutics Inc | 7.3 | 1.5 |
| CG oncology Inc | 13.0 | 2.7 |
| Compass Therapeutics Inc | 6.6 | 1.4 |
| Corbus Pharmaceuticals Holdin | 5.5 | 1.2 |
| Cullinan Therapeutics Inc | 4.4 | 0.9 |
| Dyne Therapeutics Inc | 7.2 | 1.5 |
| Edgewise Therapeutics Inc | 7.1 | 1.5 |
| Enliven Therapeutics Inc | 1.1 | 0.2 |
| Exact Sciences Corp | 4.9 | 1.0 |
| Fate Therapeutics Inc | 2.4 | 0.5 |
| Instil Bio Inc | 2.3 | 0.5 |
| Ionis Pharmaceuticals Inc | 15.0 | 3.1 |
| Kezar Life Sciences Inc | 1.5 | 0.3 |
| Krystal Biotech Inc | 4.3 | 0.9 |
| Lexicon Pharmaceuticals Inc | 6.7 | 1.4 |
| Longboard Pharmaceuticals Inc | 5.7 | 1.2 |
| Lyell Immunopharma Inc | 4.0 | 0.8 |
| Milestone Pharmaceuticals Inc | 1.5 | 0.3 |
| Mineralys Therapeutics Inc | 10.2 | 2.1 |
| Neumora Therapeutics Inc | 6.0 | 1.3 |
| Neurocrine Biosciences Inc | 5.4 | 1.1 |
| Nkarta Inc | 3.7 | 0.8 |
| PepGen Inc | 4.3 | 0.9 |

Note: securities with asterisks (*) are unquoted

| UNITED STATES | Market Price $ Millions | Pct. Value |
|---|---|---|
| **Emerging Biotechnology (cont.)** | | |
| Phathom Pharmaceuticals Inc | 14.1 | 3.0 |
| Prelude Therapeutics Inc | 0.7 | 0.2 |
| Repare Therapeutics Inc | 0.2 | 0.0 |
| Rhythm Pharmaceuticals Inc | 8.6 | 1.8 |
| Sarepta Therapeutics Inc | 21.9 | 4.6 |
| Scholar Rock Holding Corp | 1.6 | 0.3 |
| Structure Therapeutics Inc | 4.7 | 1.0 |
| Syndax Pharmaceuticals Inc | 12.3 | 2.6 |
| Tyra Biosciences Inc | 9.0 | 1.9 |
| Vaxcyte Inc | 7.8 | 1.6 |
| Vera Therapeutics Inc | 10.2 | 2.1 |
| Vir Biotechnology Inc | 11.8 | 2.5 |
| Xenon Pharmaceuticals Inc | 11.1 | 2.3 |
| | **301.7** | **63.2** |
| **UNITED STATES** | | |
| **Major Biotechnology** | | |
| Amgen Inc | 41.2 | 8.6 |
| Biogen Inc | 9.5 | 2.0 |
| Gilead Sciences Inc | 12.7 | 2.7 |
| Regeneron Pharmaceuticals Inc | 7.8 | 1.6 |
| Vertex Pharmaceuticals Inc | 7.6 | 1.6 |
| | **78.8** | **16.5** |
| **United States Total** | **380.5** | **79.7** |

| INTERNATIONAL | Market Price $ Millions | Pct. Value |
|---|---|---|
| **Europe** | | |
| **Emerging Biotechnology** | | |
| ADC Therapeutics SA | 5.0 | 1.0 |
| Argenx SE | 23.0 | 4.8 |
| Immatics NV | 8.2 | 1.7 |
| | **36.1** | **7.6** |
| **Major Biotechnology** | | |
| BioNTech SE | 6.2 | 1.3 |
| | **6.2** | **1.3** |
| **Europe Subtotal** | **42.3** | **8.9** |
| **Far East** | | |
| **Emerging Biotechnology** | | |
| Akeso Inc | 10.2 | 2.1 |
| BeiGene Ltd | 10.6 | 2.2 |
| BrightGene Bio-Medical Techn | 4.9 | 1.0 |
| Gracell Biotechnologies Inc | 0.5 | 0.1 |
| HUTCHMED China Ltd | 5.0 | 1.0 |
| Innovent Biologics Inc | 9.7 | 2.0 |
| LakeShore Biopharma Co Ltd | 1.0 | 0.2 |
| Mabwell Shanghai Bioscience ( | 5.0 | 1.0 |
| New Horizon Health Ltd | 0.9 | 0.2 |
| OrbiMed Asia Partners | 1.3 | 0.3 |
| QuantumPharm Inc | 38.8 | 8.1 |
| Stemirna* | 0.3 | 0.1 |
| Suzhou Basecare Medical Corp | 0.6 | 0.1 |
| | **88.7** | **18.6** |
| **Major Biotechnology** | | |
| Sino Biopharmaceutical Ltd | 2.4 | 0.5 |
| | **2.4** | **0.5** |
| **Far East Subtotal** | **91.1** | **19.1** |
| **International Total** | **133.4** | **28.0** |
| **Cash** | **-36.7** | **-7.7** |
| **Total Portfolio** | **477.3** | **100.0** |

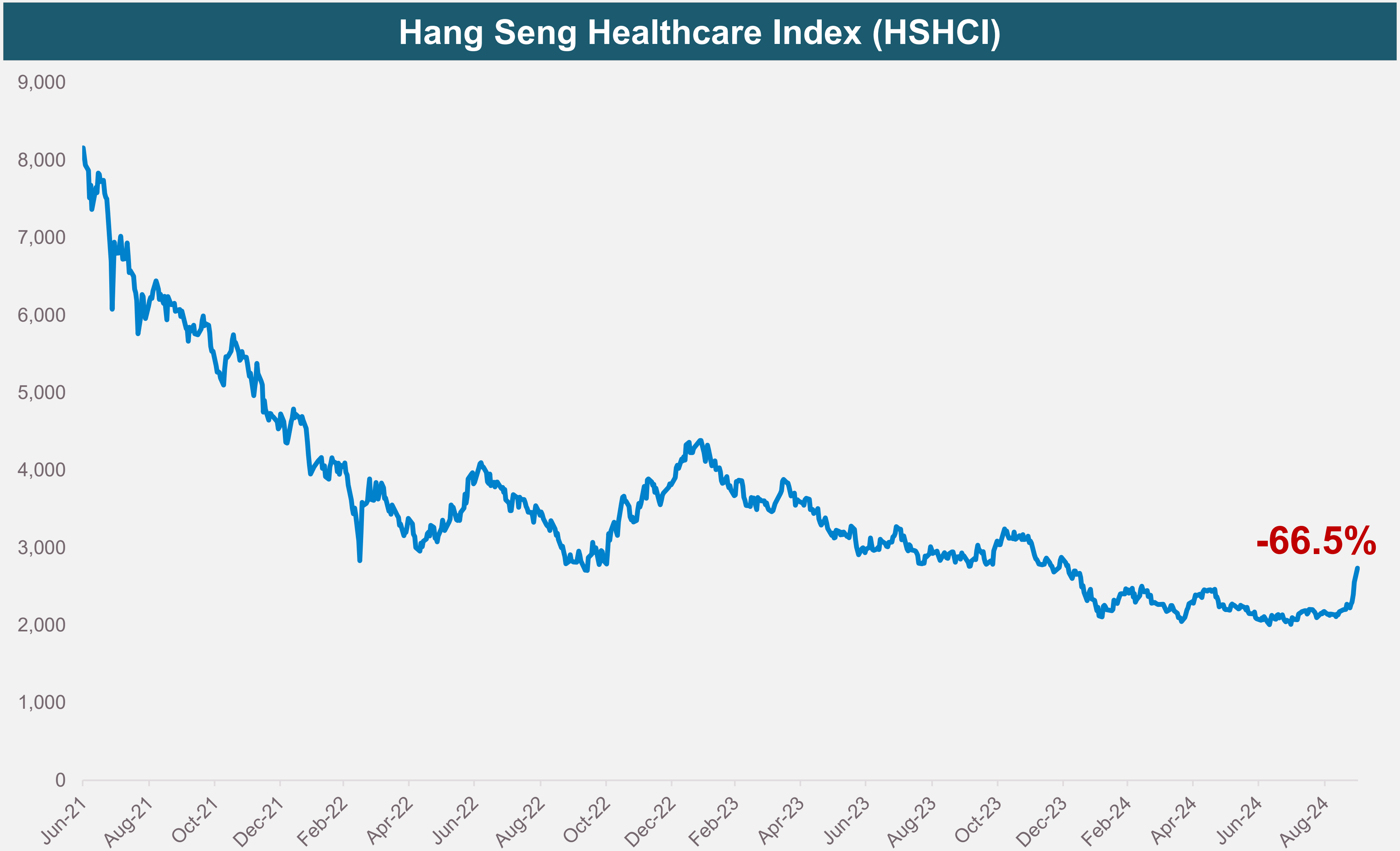
# Unprofitable Tech Has Declined Meaningfully

## 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 September 2024

# China Healthcare Near All-Time Lows

## Innovation remains strong; recovery may be starting to occur




Source: Bloomberg, OrbiMed Advisors
Note: Chart updated from 30 June 2021 through 30 September 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 October 2024 | 1 Std. Deviation |
|---|---|
| Large Cap (>$10bn) | 50.3 |
| Mid Cap ($2bn-10bn) | 65.1 |
| Small Cap (<$2bn) | 80.3 |

  - 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.

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# 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.