



The Biotech Growth Trust

Investor Update

November 21, 2023

The Biotech Growth Trust - Introduction

The Biotech Growth Trust is a closed-end investment trust designed to generate capital appreciation through investing in the global biotechnology industry.

The biotech universe can be classified into two major categories:

- **Major biotech** – large, profitable, valued on traditional metrics like P/E and earnings growth
- **Emerging biotech** – not yet sustainably profitable, may not have any revenues, require financing to fund clinical trials

The Trust invests in companies across all stages of development, with an emphasis on emerging biotech. Investments are made across geographies, therapeutic areas, and drug development technologies.

Investments are made based on scientific appraisal of drugs in development as well as financial analysis of the future revenue and earnings potential of companies.

Closed-end fund structure allows the manager to make investments in private companies as well as use gearing to enhance returns, all with oversight from a board of directors.

OrbiMed, a healthcare specialist, has managed the Trust since May 2005.

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

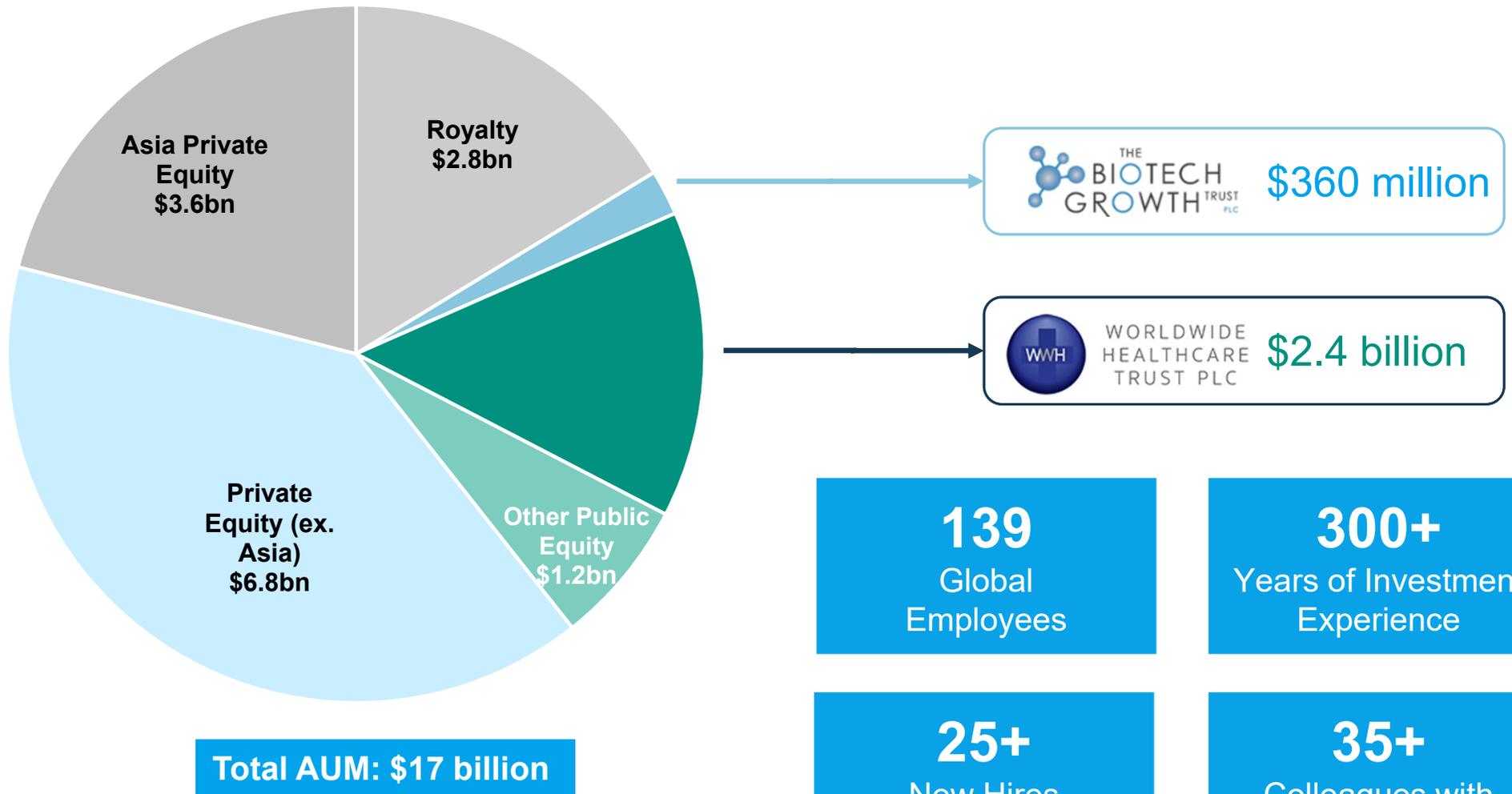


Josh Golomb is a Partner at OrbiMed focused on biotechnology. He joined the firm in 2021 and became a portfolio manager of The Biotech Growth Trust in 2023.

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



Source: OrbiMed; Data updated as of 30 September 2023

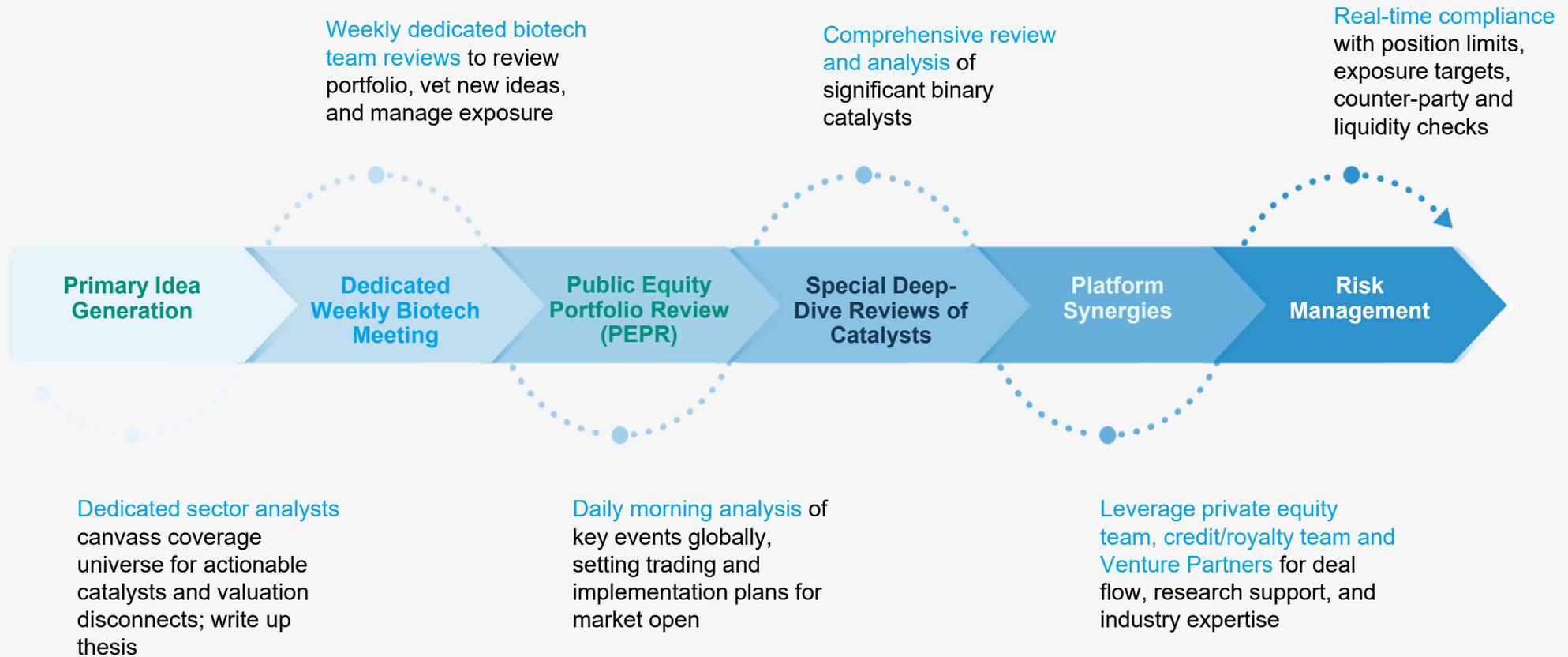
OrbiMed Has Extensive Resources to Invest in Biotech

Differentiated platform capable of delivering strong returns

OrbiMed's capabilities are well-suited to achieving the fund objective of generating capital appreciation by investing in biotech companies worldwide:

- **Global footprint**
 - 12 locations worldwide including New York, San Francisco, Hong Kong, Shanghai, and London
 - can invest in the U.S., Europe, and Asia; provides geographic diversification
- **Large research team**
 - 7 dedicated biotech analysts (including 2 PMs), with 60+ years of collective experience
 - additional expertise from 12 other public equity analysts covering other healthcare sectors
- **Preferential access to deal flow**
 - firm gets wall-crossed on 3-4 deals per week (not all investors have access to this deal flow)
 - potential opportunity to invest based on confidential information before public release
 - in some cases, warrants and other deal sweeteners can be present to enhance returns
- **Private equity business**
 - dedicated team of 51 professionals provides preferential access to crossover opportunities and IPOs in OrbiMed companies; BIOG has the option, but not the obligation, to participate
 - private equity team aids in diligence for both IPOs and other publicly-traded names
 - regular interactions with large pharma provide insight into areas of M&A interest
- **Extensive experience**
 - healthcare specialist firm with over 25 years of experience investing in biotech

Disciplined Investment Process



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:

	1 Std Deviation
Large Cap (>\$10 bn)	31%
Mid Cap (\$2-10 bn)	62%
Small Cap (<\$2 bn)	84%
 - Fund's emphasis on emerging biotech with stock-moving catalysts means turnover will likely remain high to manage risk appropriately

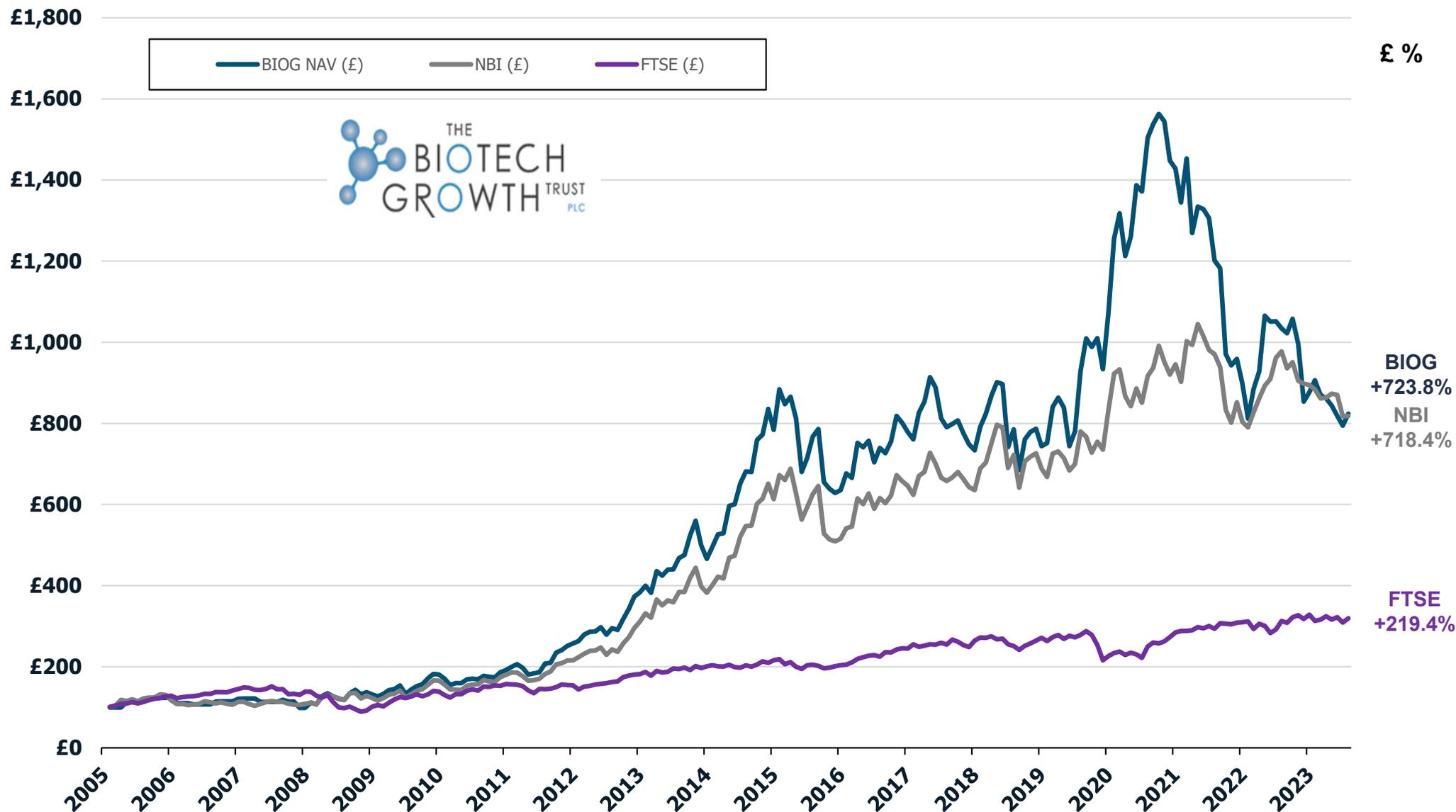


BIOG

Fund
Performance

BIOG Performance since Inception

18 May 2005 through 15 November 2023

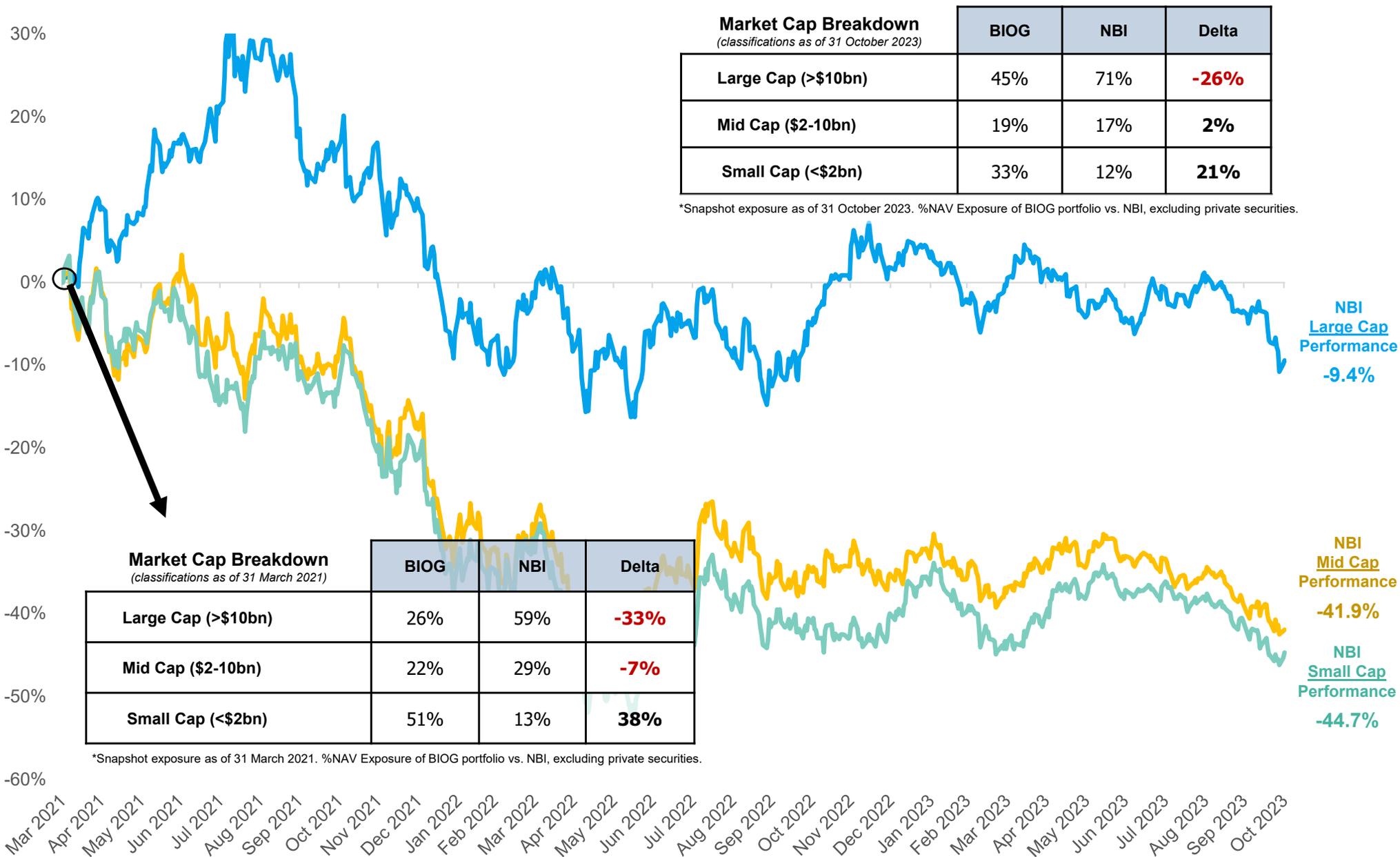


Note: See Endnotes for additional information, including with regard to the calculation of these results and the index shown above.

Source: Frostrow, Bloomberg.

Market Cap Performance Divergence in Biotechnology

Small and Mid Cap Biotech Overdue For a Recovery

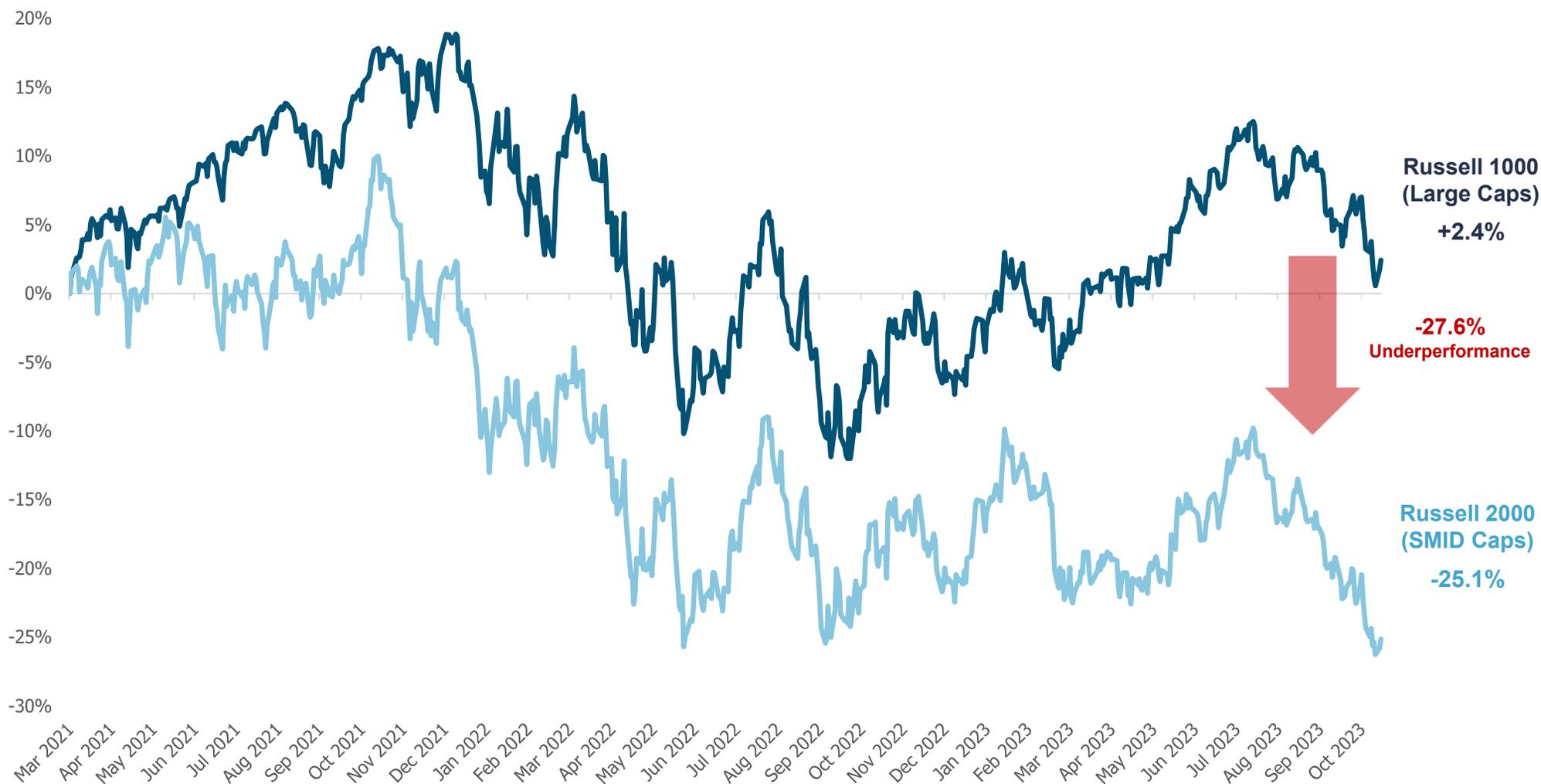


Note: Chart shows equal-weighted performance of NBI stocks in their respective market cap buckets, using market cap classifications as of 31 March 2021. Updated as of 31 October 2023, performance calculated in USD.

Size Divergence in the Broad Market

(31 March 2021 – 31 October 2023)

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



Note: Chart updated from 31 March 2021 to 31 October 2023. 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.

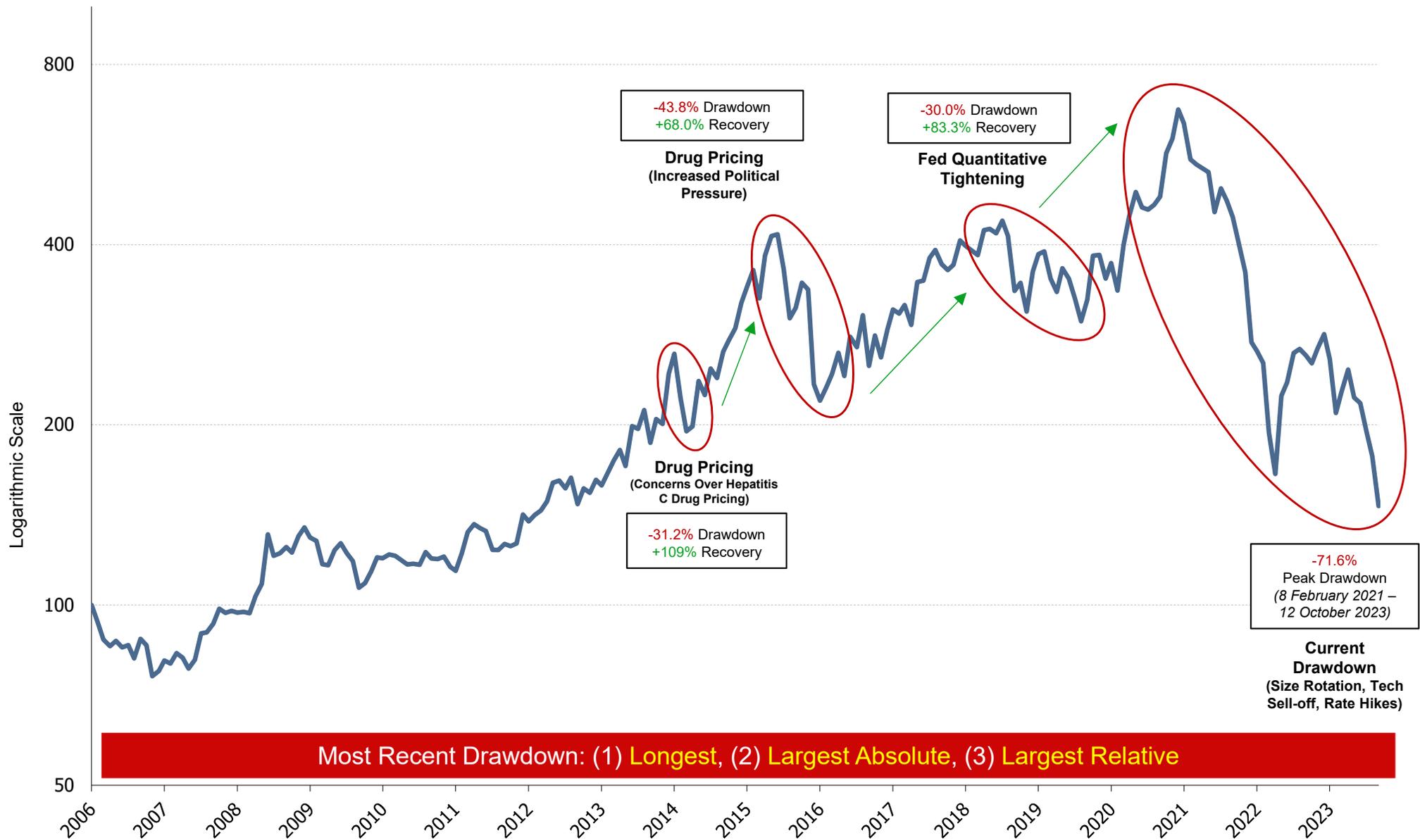


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Investment
Opportunity

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

Drawdowns in spread followed by historically strong recoveries

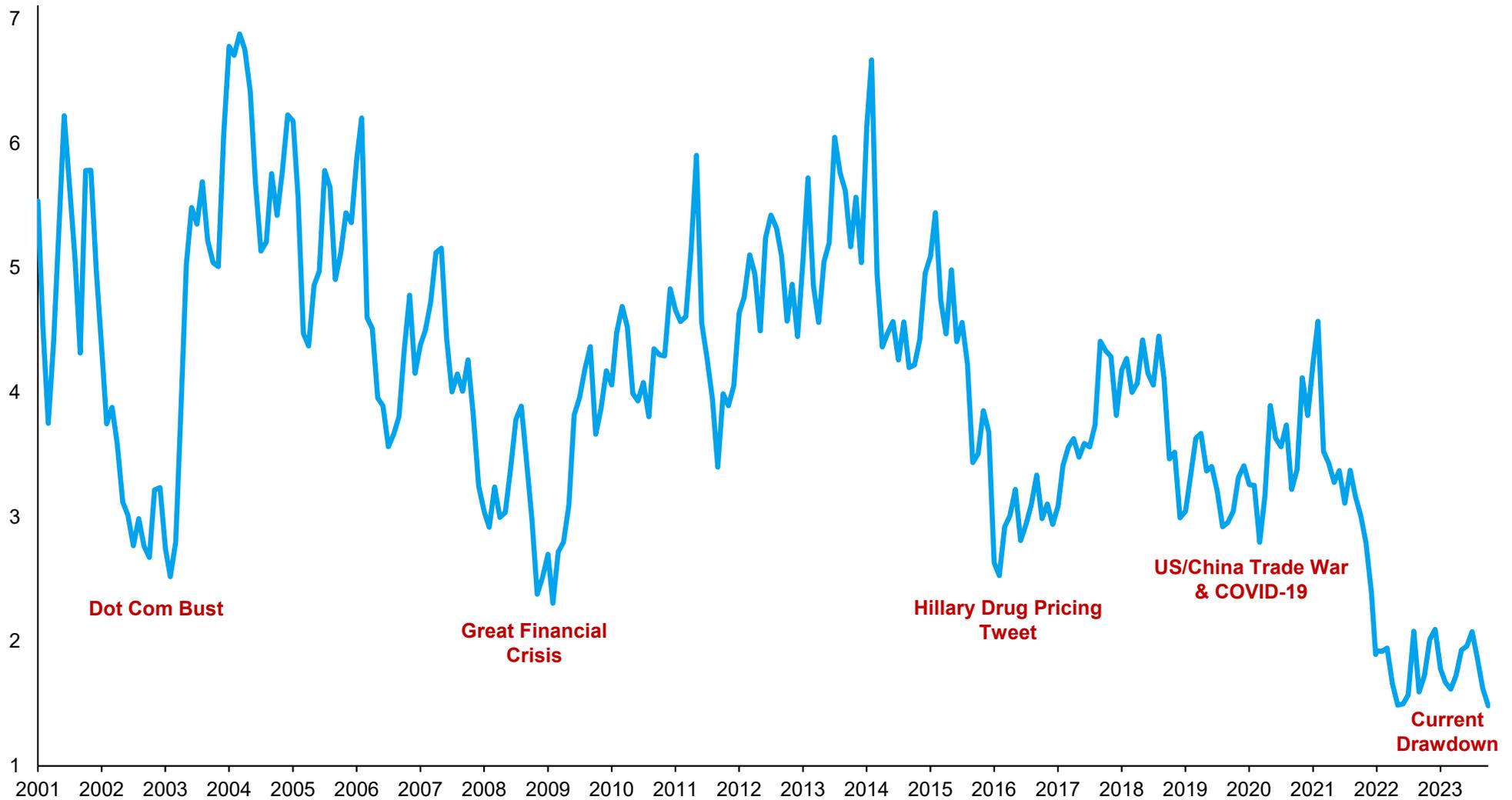


Note: Drawdowns are calculated using daily closing prices, while chart is shown using monthly periodicity for smoothing purposes. Updated as of 31 October 2023.

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

Biotech Valuations at Unprecedented Lows

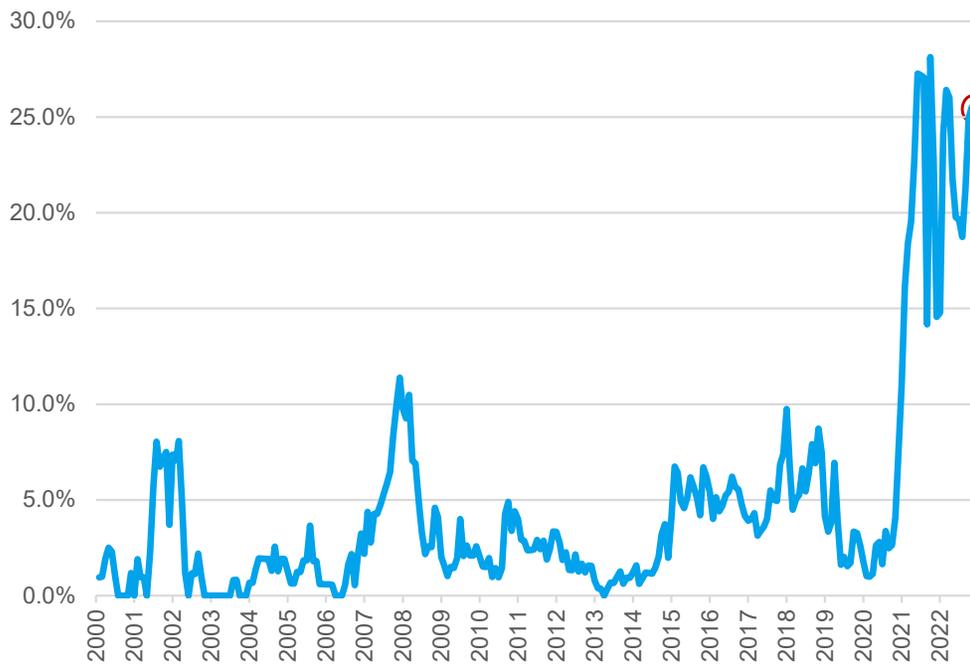
Ratio of Market Cap to Net Cash on Balance Sheet (Median)



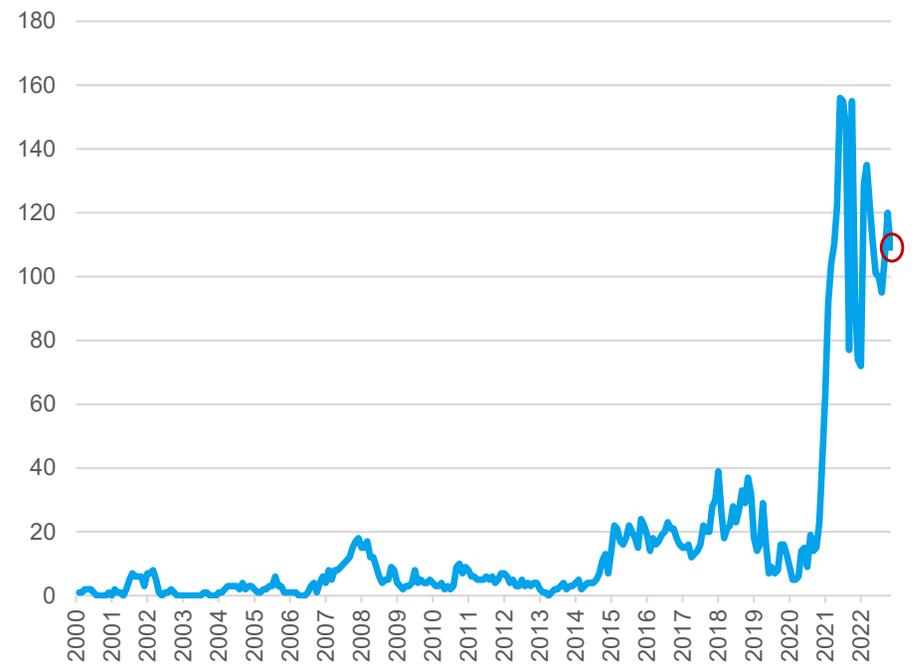
Note: Monthly chart of all GICs defined biotechnology greater than \$10mm, using historical cash and debt sourced from Bloomberg, with annual GICS biotechnology universe refreshes. Updated through 31 October 2023.

Biotech Valuations at Unprecedented Lows

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



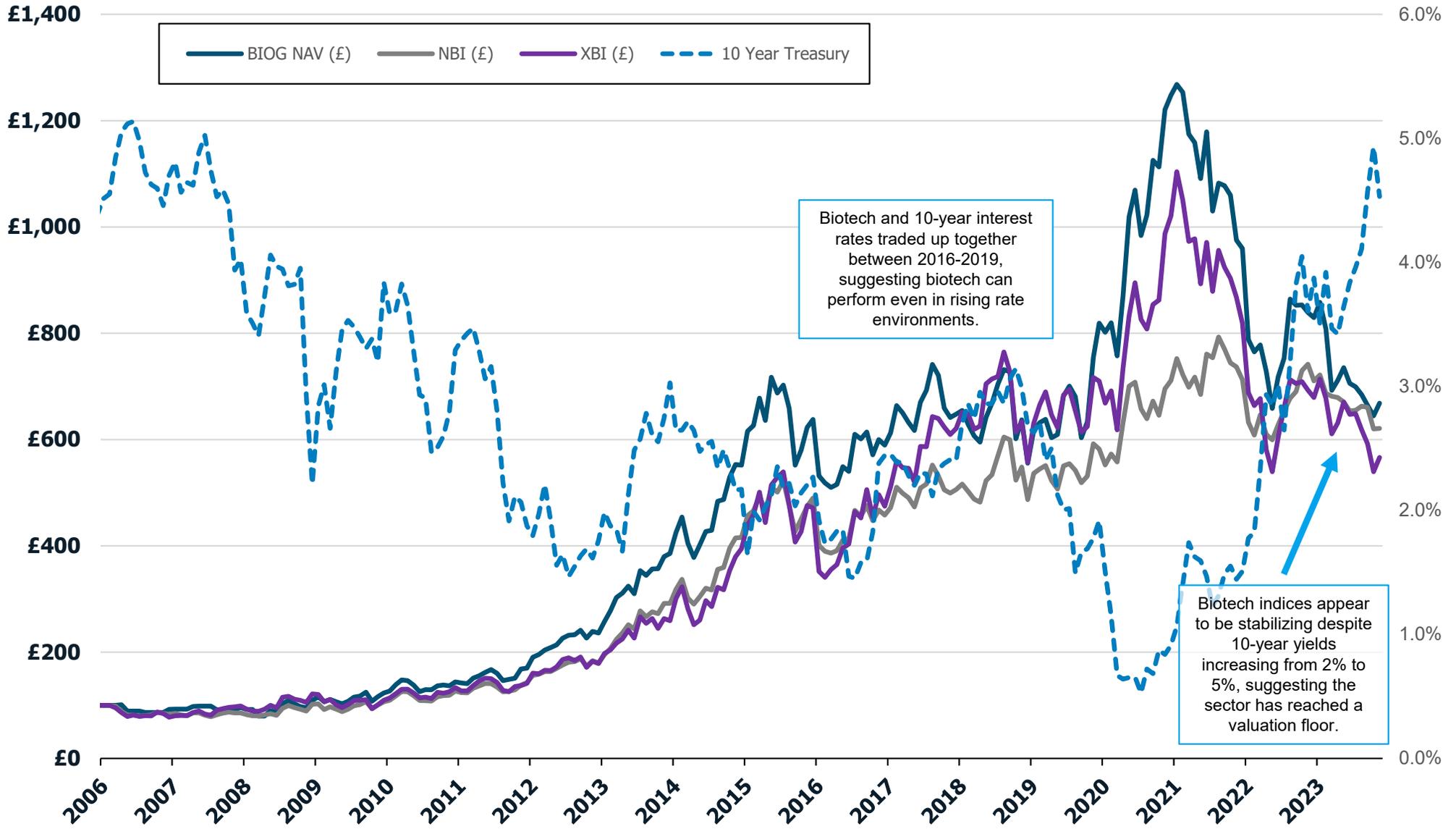
Number of Biotech Companies Trading Below Net Cash on Balance Sheet:



Note: Monthly chart of all GICs defined biotechnology greater than \$10mm, using historical cash and debt sourced from Bloomberg, with annual GICS biotechnology universe refreshes. Updated through 31 October 2023.

Interest Rate Impact on Biotech Abating

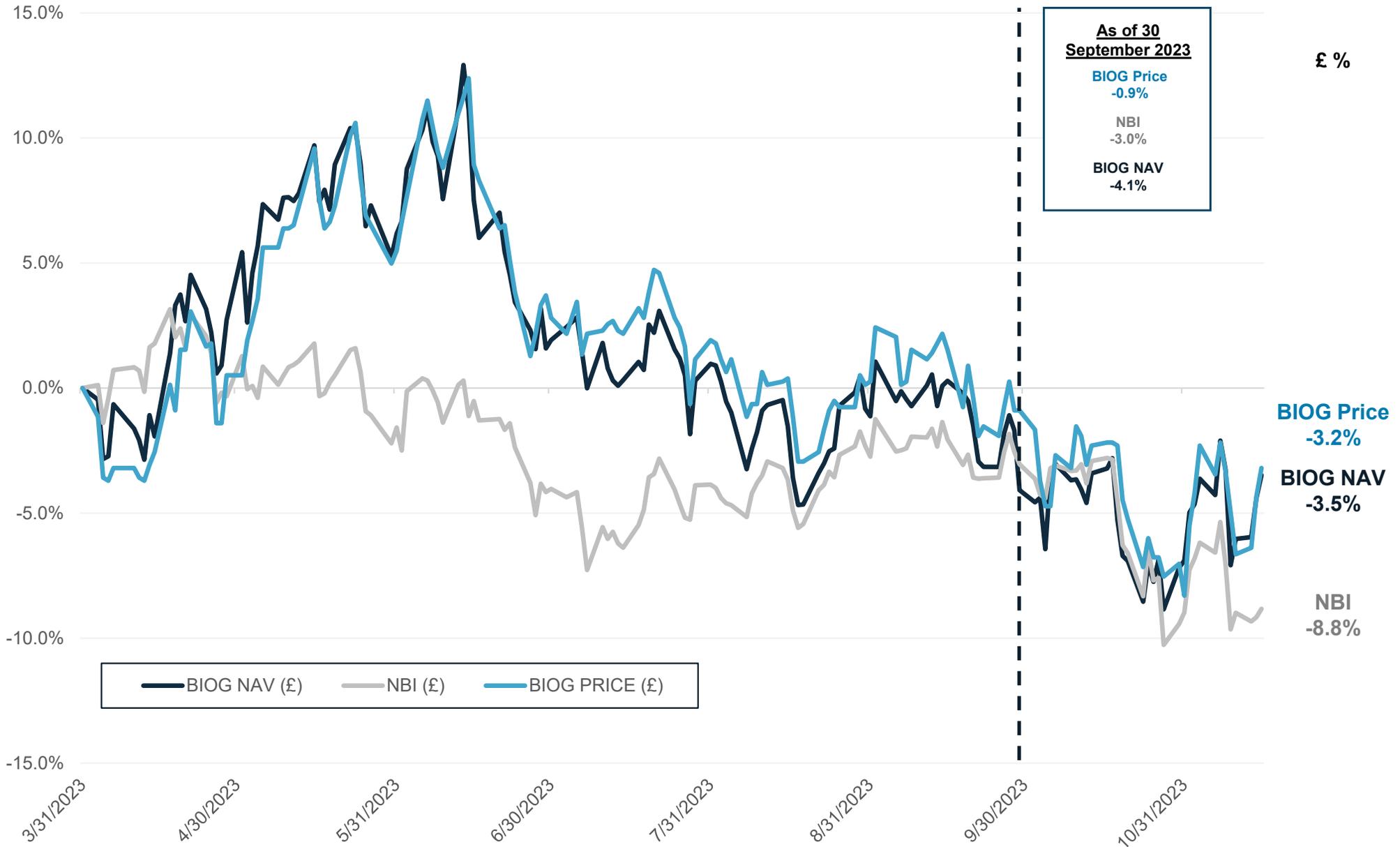
Biotech has performed in rising interest rate environments previously



Note: See Endnotes for additional information, including with regard to the calculation of these results and the index shown above. Chart begins on 2/28/06 (First month-end of XBI Inception). Updated as of 30 October 2023.

BIOG Performance for Fiscal 2024

31 March 2023 to 15 November 2023



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

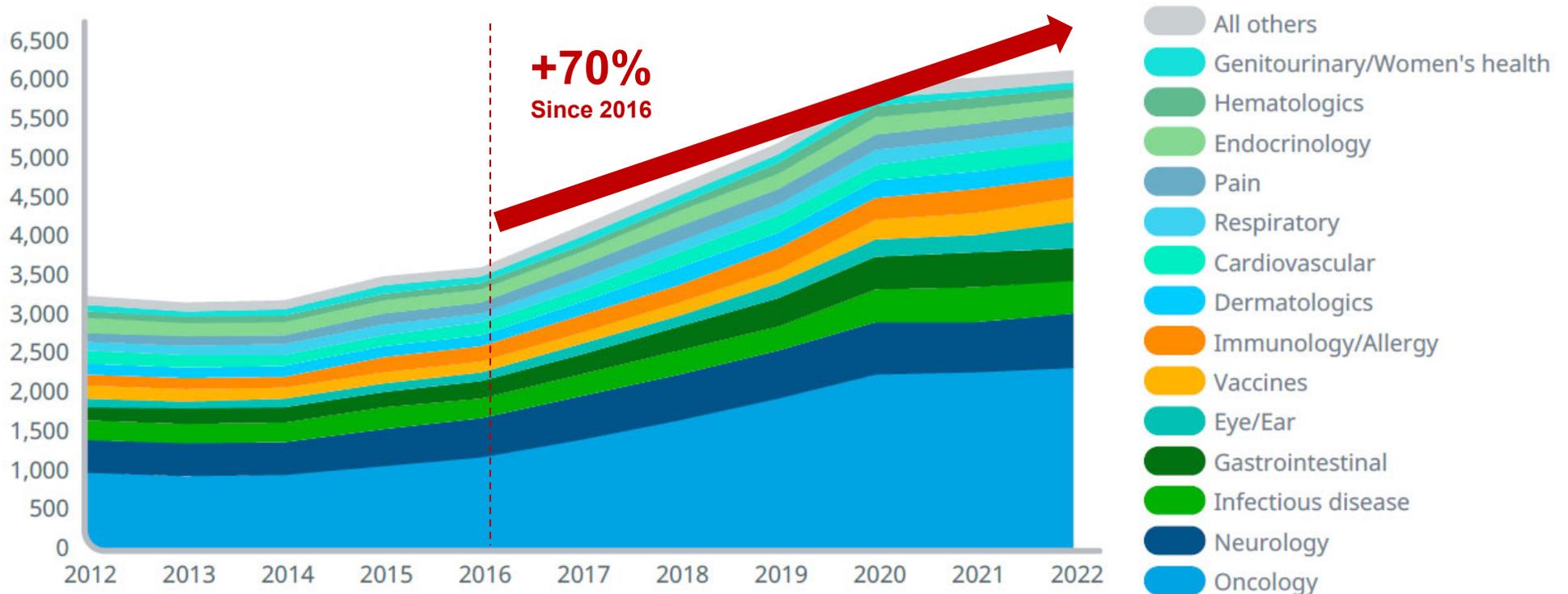
Innovation – Pipeline as Full as it's Ever Been



“Golden era” of innovation increasing number of drugs in development



Number of pipeline products Phase I to regulatory submission by therapeutic drug class, 2011-2022:

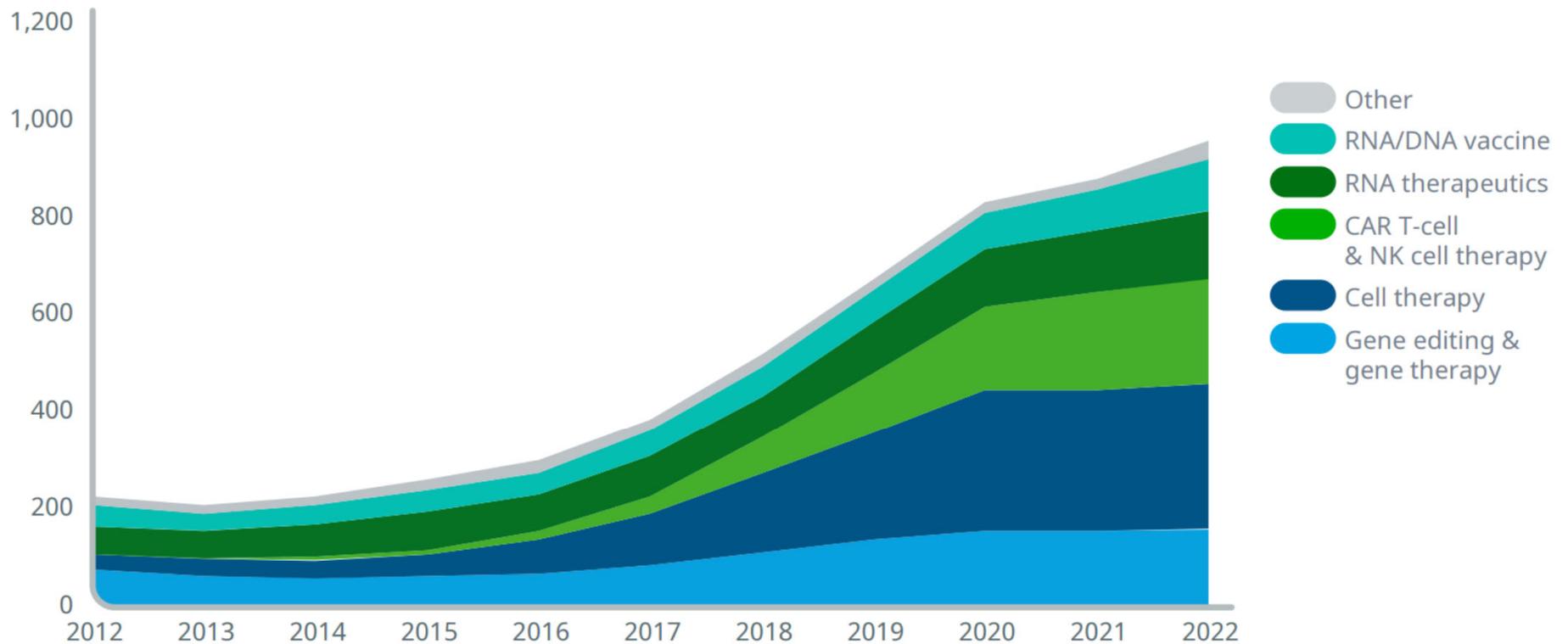


Source: IQVIA Pipeline Intelligence, Dec 2022; IQVIA Institute, Jan 2023.

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Novel Technologies Driving R&D Pipeline Growth

Next-Generation Biotherapeutics Phase I to Regulatory Submission Pipeline by Mechanism, 2011–2022:



- Emerging technologies still in the early stages of reaching their full potential, with hundreds of candidates now in clinical trials
- We expect dozens more of these next-gen products to reach the market over the next several years

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Notable New Drug Approvals Address Large Markets

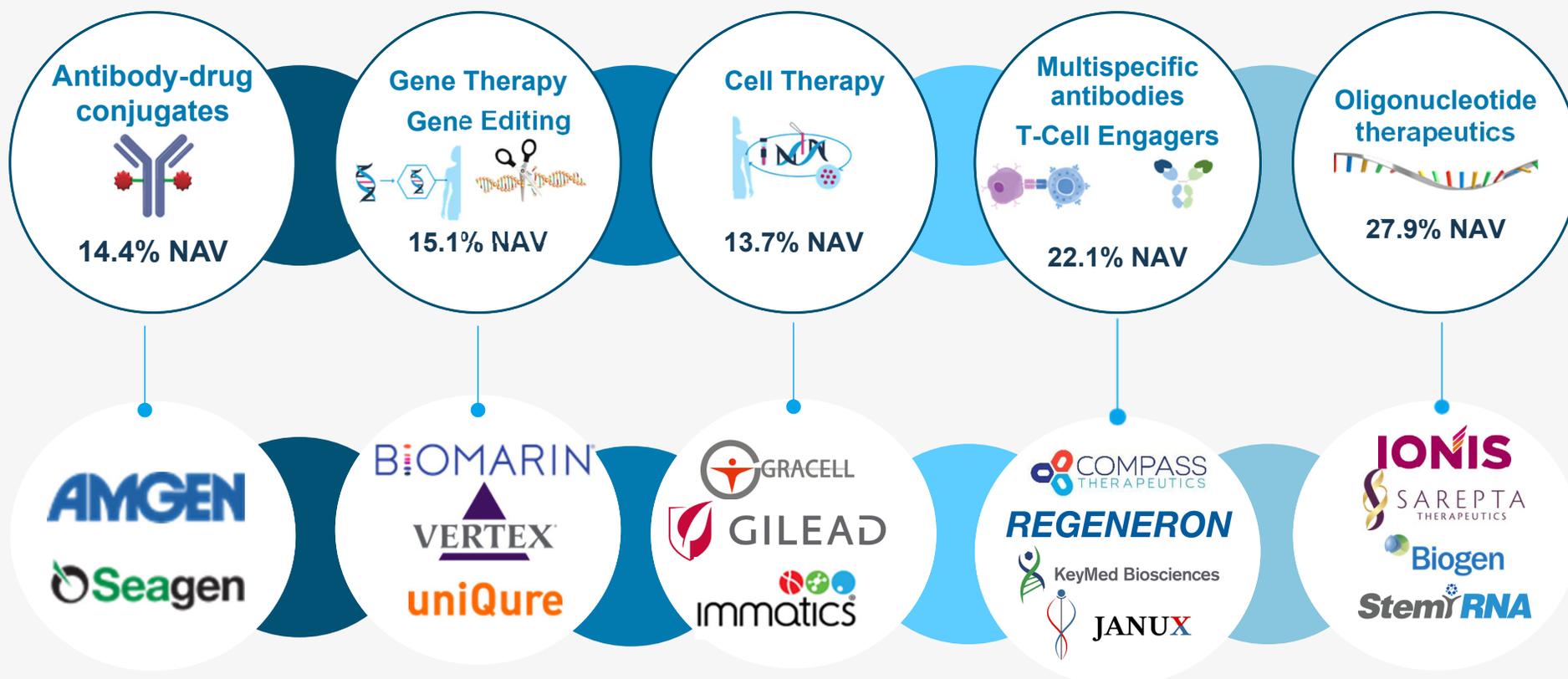
 <p>Gene Therapy for Spinal Muscular Atrophy</p>  <p>\$2.0bn peak sales</p> 	 <p>Protein Modulation for Cystic Fibrosis</p>  <p>\$10 bn peak sales</p> 	 <p>Antibody for Alzheimer's Disease</p>  <p>\$10.9bn peak sales</p> 	 <p>Antibody Drug Conjugate for Breast Cancer</p>  <p>\$3.4bn peak sales</p> 	 <p>Antibody Fragment for Myasthenia Gravis</p>  <p>\$6.6bn peak sales</p> 
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 <p>Polymerization Inhibitor for Sickle Cell Disease</p>  <p>\$1.1bn peak sales</p> 	 <p>Fusion Protein for Beta-Thalassemia</p>  <p>\$2.8bn peak sales</p> 	 <p>Peptide for Achondroplasia</p>  <p>\$1.5bn peak sales</p> 	 <p>Antibody for Thyroid Eye Disease</p>  <p>\$3.6bn peak sales</p> 	 <p>Antibody Drug Conjugate for Bladder Cancer</p>  <p>\$4.1bn peak sales</p> 
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Note: examples may not be representative of fund holdings, estimates as of Jan 2023.
 Source: peak sales estimates are from various sources including company reports, Bloomberg, Visible Alpha, and First Order Analytics

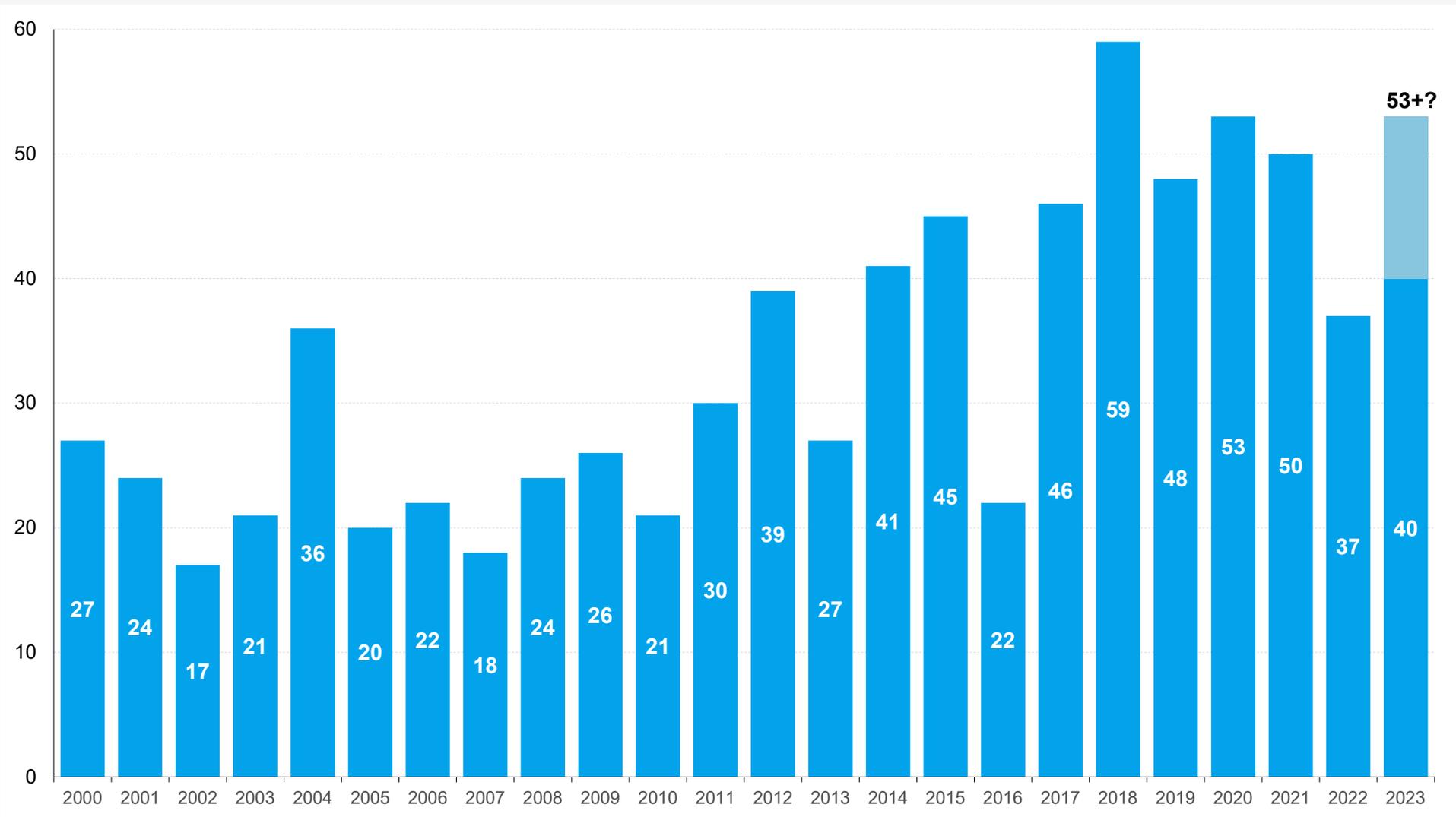
Innovation Well Reflected in BIOG

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



Source: OrbiMed, % of BIOG NAV as of 30 October 2023. Some positions are double counted because they use more than one technology.

FDA New Molecular Entity Approvals



Dip in approvals in 2022 likely due to COVID; run rate YTD remains high

Note: 2023 figures represent YTD New Molecular Entities (NME) approvals through 9/30/23. There were 26 NME approvals in the first half of 2023, and the 50+ figure is an extrapolation based on this data, projecting potential approvals through the end of 2023.

Significant FDA Biotech Approvals in 2023

Company	Indication	Product (MOA)	Highlights
	Pompe Disease	Pombiliti + Opfolda (enzyme replacement + oral chaperone)	First treatment approved in Pompe disease patients not showing improvement on current enzyme replacement therapy
	Postpartum Depression	Zyzyvae	First and only oral treatment for postpartum depression
	SOD1 Amyotrophic Lateral Sclerosis	Qalsody (antisense)	First approval for a specific genetic subset of ALS
	Friedreich's Ataxia	Skyclarys	First approved drug for treatment of Friedreich's ataxia
	Rett Syndrome	Daybue	First approved therapy to treat Rett syndrome
	Duchenne Muscular Dystrophy	Elevidys (gene therapy)	First gene therapy for Duchenne muscular dystrophy
	Geographic Atrophy	Skyfovre	First approved therapy for treatment of GA, a leading cause of blindness
	Hemophilia A	Roctavian (gene therapy)	First gene therapy approved in hemophilia
	Alzheimer's disease	Leqembi (monoclonal antibody)	First disease-modifying therapy approved to treat Alzheimer's

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

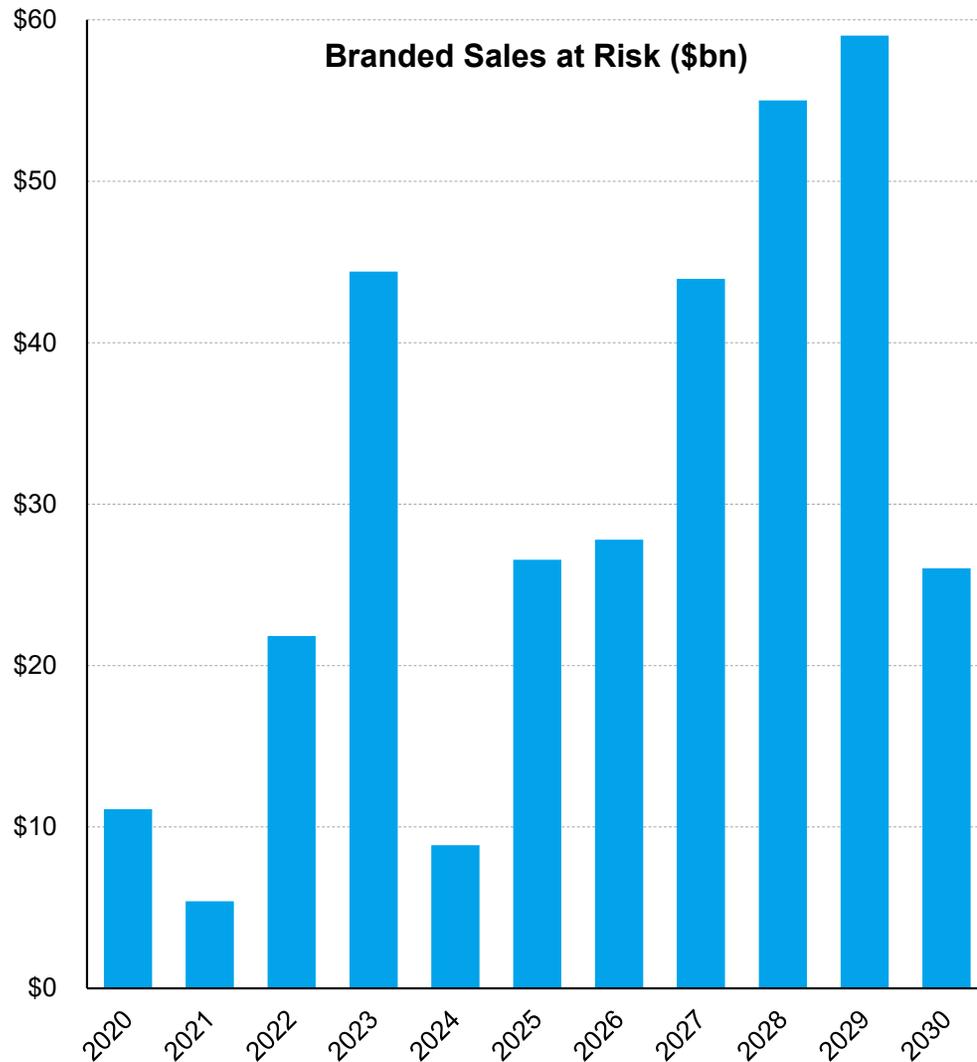
Recent Technology Breakthroughs in Biotech

Company	Indication	Product (MOA)	Highlights
	Chronic Inflammatory demyelinating polyneuropathy (CIDP)	Vyvgart (anti-FcRN)	Reported positive Phase 3 data; first novel treatment for CIDP in over 10 yrs
	Hidradenitis suppurativa (HS)	Sonelokimab (anti-IL17/ AF nanobody)	Reported best in class Phase 2 efficacy and safety data in HS
	Chronic obstructive pulmonary disease (COPD)	Ensifentrine (PDE3/PDE4 inhibitor)	Positive Phase 3 data with 36% reduction in exacerbations over 52 weeks; first-in-class dual PDE3/4 inhibitor
	Sickle Cell Disease and Beta Thalassemia	Casgevy (CRISPR Cas9 gene-editing therapy)	First ever CRISPR therapy approved in the world (in the UK)
	Pneumococcal infection	VAX-24 (vaccine)	First 24-valent pneumococcal conjugate vaccine to show Phase 2 efficacy in adults
	Schizophrenia	KarXT (dual M1/M4 muscarinic agonist)	First drug with novel mechanism of action for schizophrenia in decades
	Acromegaly	Paltusotine (oral SST2 agonist)	Positive Phase 3 trial for first once-daily oral medication for the treatment of acromegaly
	Nonalcoholic steatohepatitis (NASH)	Resmetirom (THR-Beta selective agonist)	First successful Phase 3 trial showing NASH resolution and improvement in liver fibrosis relative to placebo

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

Big Pharma Patent Cliff Drives Biotech M&A

Nearly **\$250 billion** in branded sales are at risk (2025-2030)



Source: Evaluate, "The Patent Winter is Coming", May 25, 2022.

Company	Drug	US Loss of Exclusivity (Projected)	'22 Global Sales (\$bn)
abbvie	HUMIRA adalimumab	2023	\$21.2
MERCK	KEYTRUDA [®] pembrolizumab (injection) 100mg	2028	\$20.9
Bristol Myers Squibb [™] Pfizer	Eliquis. [®] (apixaban) tablets 5mg/25mg	2026	\$11.8
abbvie Johnson & Johnson	imbruvica [®]	2027	\$5.8
Johnson & Johnson	Stelara [®] (ustekinumab)	2023	\$9.7
Bristol Myers Squibb [™]	OPDIVO [®] (nivolumab)	2028	\$8.2
Pfizer	IBRANCE [®] palbociclib	2027	\$5.1
Johnson & Johnson	DARZALEX [®]	2029	\$8.0

Source: S&P Global report, data as of 2/17/22; Company Reports

M&A Activity Picking Up

2022 Acquisitions			
Date	Target	Acquirer	% Premium
11/29/22	HORIZON	AMGEN	48%
11/29/22	neo ^{gene} THERAPEUTICS	AstraZeneca	\$320m (private)
11/21/22	IMAGO	MERCK	107%
10/23/22	MYOVANT SCIENCES	Sumitomo	50%
10/18/22	AVEO ONCOLOGY	LG Chem	43%
10/18/22	AKVOOS	Lilly	121%
10/03/22	LogicBio THERAPEUTICS	AstraZeneca	667%
09/01/22	forma THERAPEUTICS	novo nordisk	49%
08/08/22	GBT	Pfizer	102%
08/04/22	CHEMOCENTRYX	AMGEN	116%
08/04/22	mirco ^{bio}	GILEAD	\$405m (private)
07/11/22	VIACYTE	VERTEX	\$320m (private)
07/11/22	La Jolla PHARMACEUTICAL	INNOVIVA	84%
07/05/22	TeneoTwo	AstraZeneca	\$1,270 (private)
06/17/22	Seagen	MERCK	Rumored
06/03/22	Turning Point THERAPEUTICS	Bristol Myers Squibb [®]	122%
05/31/22	Affinivax	GSK	\$2,650 (private)
05/10/22	biohaven PHARMACEUTICALS	Pfizer	79%
04/13/22	SIERRA ONCOLOGY	GSK	39%

2023 Acquisitions			
Date	Target	Acquirer	% Premium
10/08/23	MIRATI THERAPEUTICS [®]	Bristol Myers Squibb [®]	63% [^]
10/05/23	Orchard therapeutics	OYOWA KIRIN	109%*
10/3/203	POINT BIOPHARMA	Lilly	87%
09/26/23	Intercept	ALFASIGMA	82%
08/14/23	Zynerba PHARMACEUTICALS	H3 HARMONY BIOSCIENCES	226%
08/09/23	Decibel THERAPEUTICS	REGENERON	169%*
07/28/23	REATA PHARMACEUTICALS	Biogen	59%
6/29/23	sigilon therapeutics	Lilly	~380%
6/20/23	DICE	Lilly	~40%
6/12/23	CHINOOK THERAPEUTICS	NOVARTIS	83%*
5/22/23	VectivBio	Ironwood [®]	80%
5/10/23	CTI	sobi	89%
04/30/23	IVERIC	astellas	23%
04/25/23	SPECTRUM PHARMACEUTICALS	ASSERTIO	~94%*
04/18/23	Bellus HEALTH	GSK	>100%
04/16/23	Prometheus Biosciences	MERCK	75%
03/27/23	Jounce THERAPEUTICS	Concentra Biosciences	75%
03/13/23	Seagen	Pfizer	42%
03/13/23	preventionbio	sanofi	278%
01/19/23	CoNcert Pharmaceuticals Inc. [*]	SUN PHARMA	~67%*
01/09/23	CINCOR	AstraZeneca	>200%*
01/09/23	Albireo	IPSEN Innovation for patient care	>100%
01/08/23	AMRYT	Chiesi	>100%

Sources: FactSet, Company Websites. The above is a subset of 2022 acquisitions. Companies shown may not be representative of portfolio holdings. Shading denotes BIOG holding at acquisition announcement. Sources: Pitchbook data as of 9/30/23. William Blair, "The Quarterly Rx: Q2 2023 U.S. Biopharma Recap," July 2023. Note: M&A activity includes biopharma deals with disclosed total deal value of \$20M+.

[^] Premium to unaffected share price; with CVR
* With CVR

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

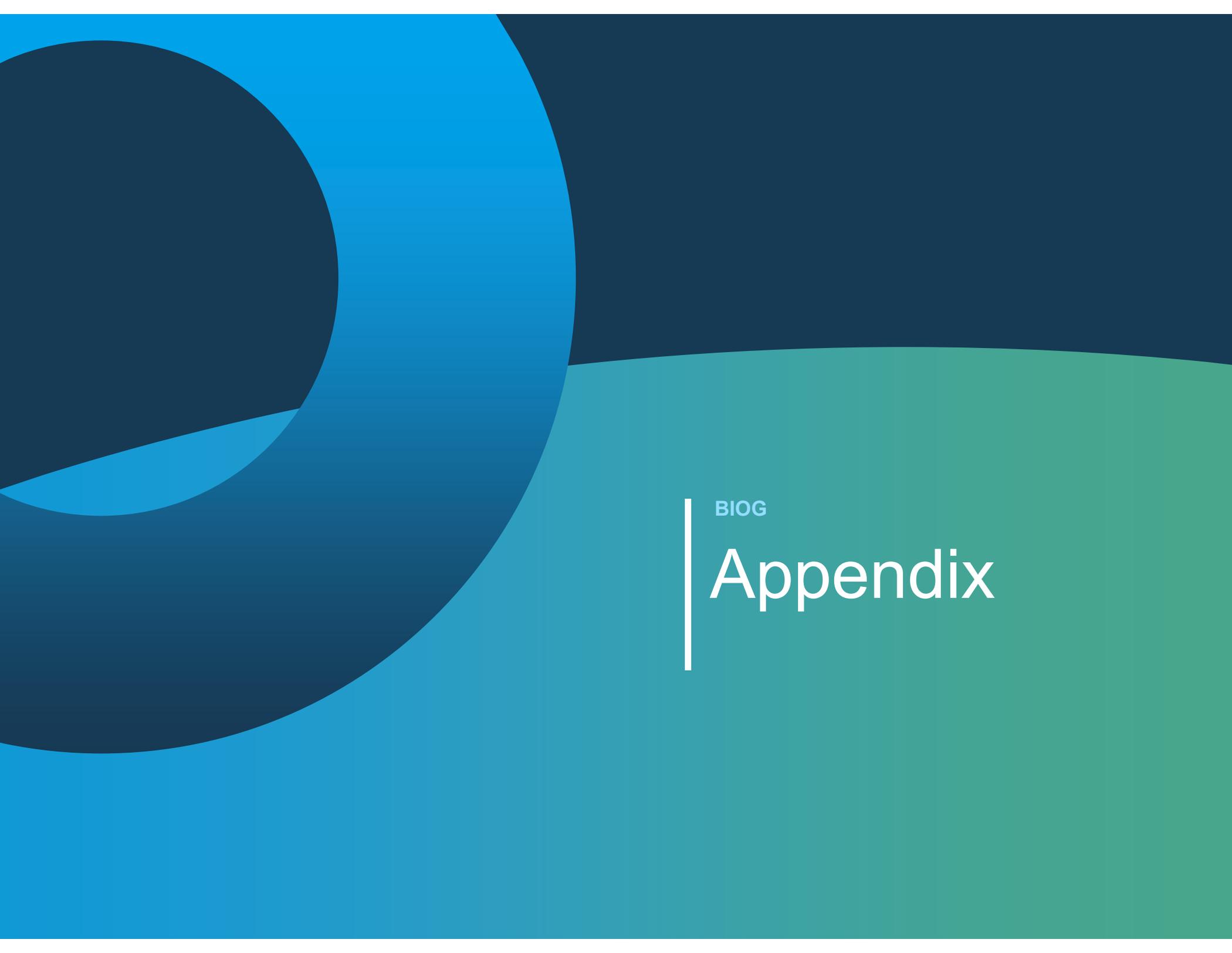


Valuation contraction is disconnected from the fundamental innovation in the sector, which remains robust



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

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



BIOG

Appendix

BIOG Holdings

As of 31 October 2023

	<u>Mkt Cap \$ mm</u>	<u>Pct Value</u>		<u>Mkt Cap \$ mm</u>	<u>Pct Value</u>
United States - Emerging Biotechnology	\$181.4	52.8%	United States - Major Biotechnology	\$96.2	28.0%
ALX Oncology Holdings Inc	\$7.9	2.3%	Amgen Inc	\$32.6	9.5%
Aerovate Therapeutics Inc	\$5.7	1.7%	Biogen Inc	\$24.0	7.0%
Apellis Pharmaceuticals Inc	\$6.0	1.8%	Gilead Sciences Inc	\$7.9	2.3%
Arrowhead Pharmaceuticals Inc	\$2.8	0.8%	Regeneron Pharmaceuticals Inc	\$10.5	3.1%
AWAKN Life Sciences*	\$0.3	0.1%	United Therapeutics Corp	\$13.1	3.8%
BioMarin Pharmaceutical Inc	\$20.2	5.9%	Vertex Pharmaceuticals Inc	\$8.1	2.4%
Compass Therapeutics Inc	\$6.4	1.9%			
Crinetix Pharmaceuticals Inc	\$3.0	0.9%	United States Subtotal	\$277.6	80.8%
Edgewise Therapeutics Inc	\$1.7	0.5%			
Enliven Therapeutics Inc	\$0.6	0.2%	Europe - Emerging Biotechnology	\$30.6	8.9%
Heron Therapeutics Inc	\$0.5	0.1%	Argenx SE	\$20.5	6.0%
Ionis Pharmaceuticals Inc	\$20.6	6.0%	Immatics NV	\$4.0	1.2%
Janux Therapeutics Inc	\$3.4	1.0%	MoonLake Immunotherapeutics	\$2.6	0.8%
Karuna Therapeutics Inc	\$2.3	0.7%	uniQure NV	\$3.5	1.0%
Keros Therapeutics Inc	\$7.0	2.0%			
Kezar Life Sciences Inc	\$1.4	0.4%	Far East - Emerging Biotechnology	\$44.6	13.0%
Morphic Holding Inc	\$1.1	0.3%	BeiGene Ltd	\$6.7	2.0%
Neumora Therapeutics Inc	\$5.0	1.5%	Gracell Biotechnologies Inc	\$2.5	0.7%
Prelude Therapeutics Inc	\$0.6	0.2%	Innovent Biologics Inc	\$9.4	2.7%
RAPT Therapeutics Inc	\$5.6	1.6%	Keymed Biosciences Inc	\$4.6	1.3%
Repare Therapeutics Inc	\$0.2	0.0%	OrbiMed Asia Partners	\$1.9	0.6%
Rhythm Pharmaceuticals Inc	\$7.3	2.1%	Stemirna*	\$1.6	0.5%
Sarepta Therapeutics Inc	\$3.5	1.0%	Suzhou Basecare Medical Corp	\$0.8	0.2%
Scholar Rock Holding Corp	\$21.8	6.3%	Xtalpi Pfd*	\$15.9	4.6%
Seagen Inc	\$9.1	2.6%	YS Biopharma Co Ltd	\$1.0	0.3%
Syndax Pharmaceuticals Inc	\$4.8	1.4%			
Vaxcyte Inc	\$14.2	4.1%	Far East - Major Biotechnology	\$1.7	0.5%
Vera Therapeutics Inc	\$9.1	2.6%	Wuxi Biologics Cayman Inc	\$1.7	0.5%
Xencor Inc	\$0.3	0.1%			
Xenon Pharmaceuticals Inc	\$8.8	2.6%	International Subtotal	\$76.9	22.4%
			Cash	(\$11.1)	-3.2%
			Total	\$343.3	100.0%

Note: securities with asterisks (*) are unquoted or include unquoted securities

Unprofitable Tech Has Declined Meaningfully

Goldman Sachs Unprofitable Tech Basket

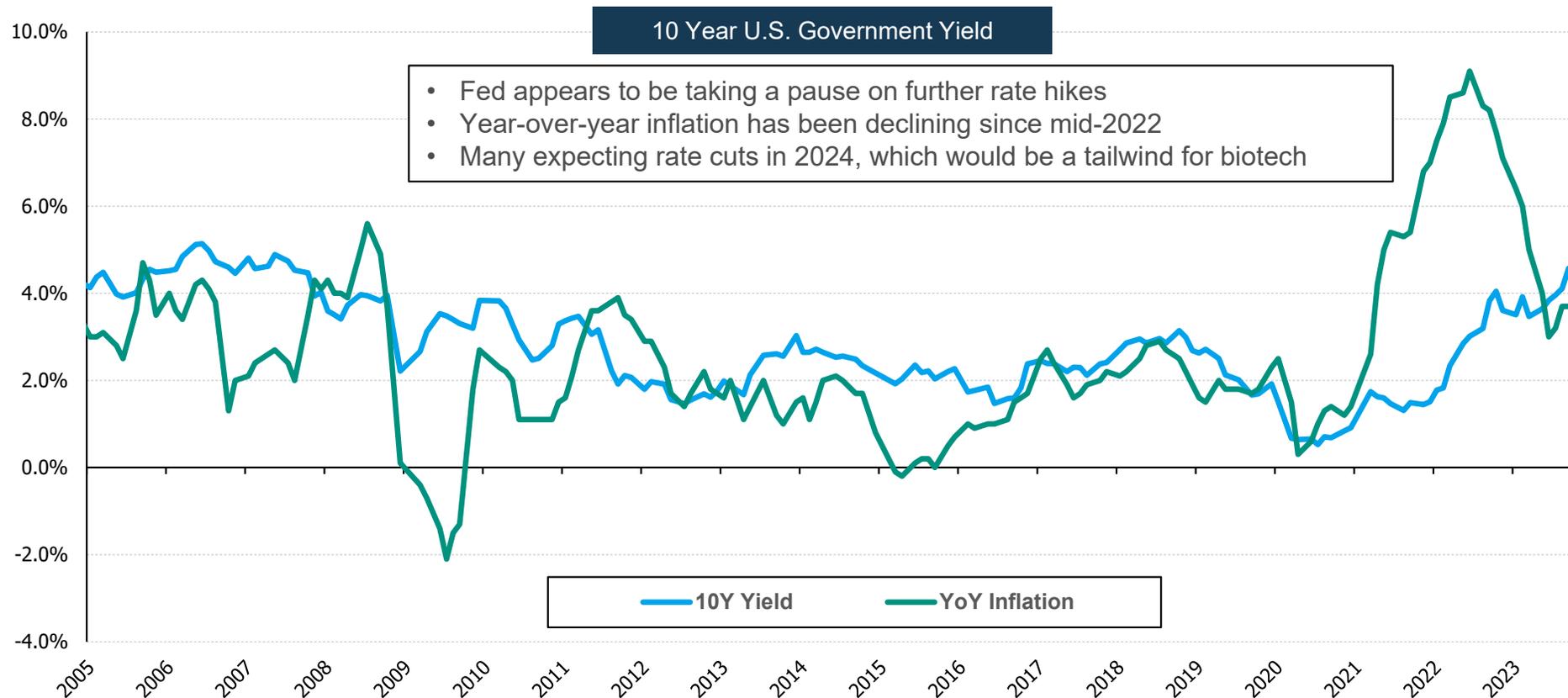


**GS Unprofitable
Technology Basket**
-67.7%

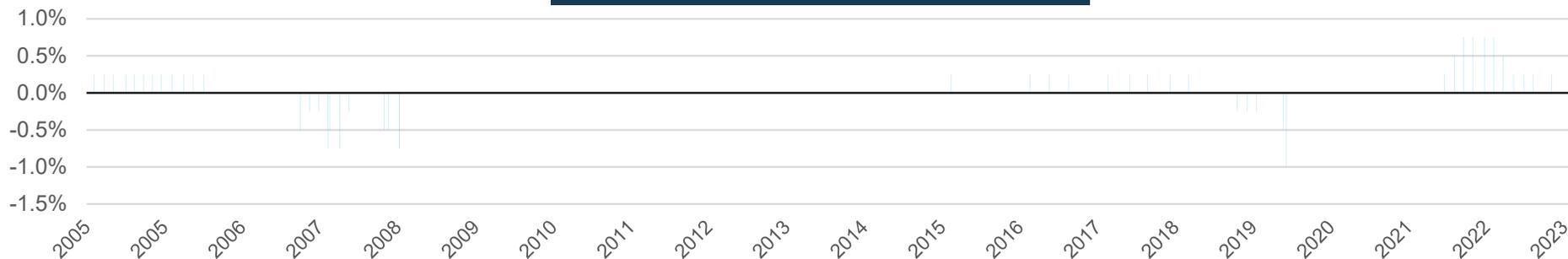
The GS Non-profitable tech basket (GSXUNPTC) consists of non-profitable US listed companies in innovative industries. Technology is defined broadly to include new economy companies across GICS industry groupings. Date range for chart is from 31 March 2021 to 31 October 2023

10 Year U.S. Government Yield Stabilizing (USGG10YR Index)

Data as of 31 October 2023



Fed Fund Rate Increases/Decreases

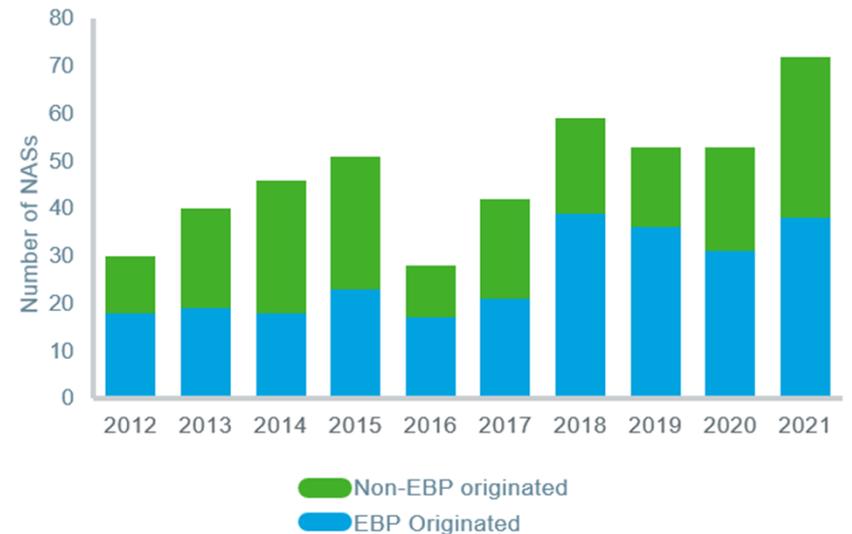
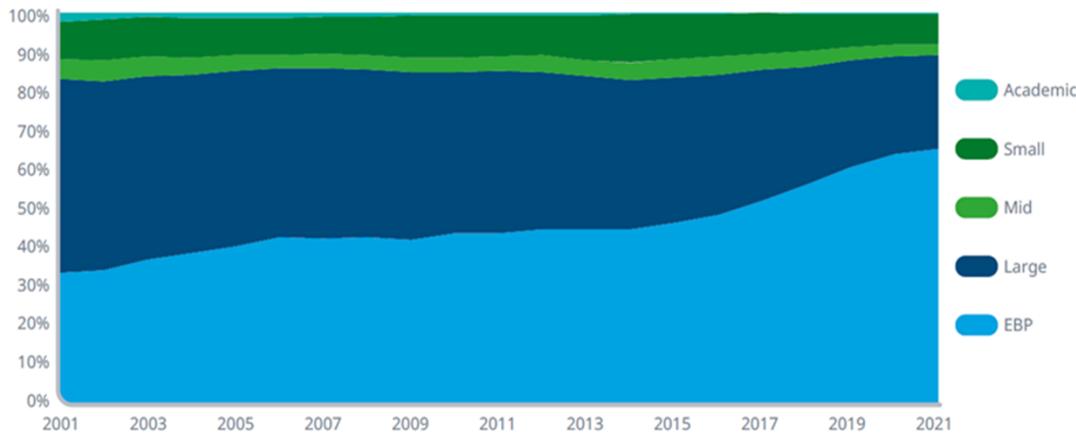


Source: Bloomberg, data as of 31 October 2023

Majority of Industry Drug Pipeline and Approved Novel Drugs Originated by Emerging Biotech Companies

Share of Industry R&D Pipeline by Company Type:

Source of Origination for Novel Active Substances (NASs) Launched:



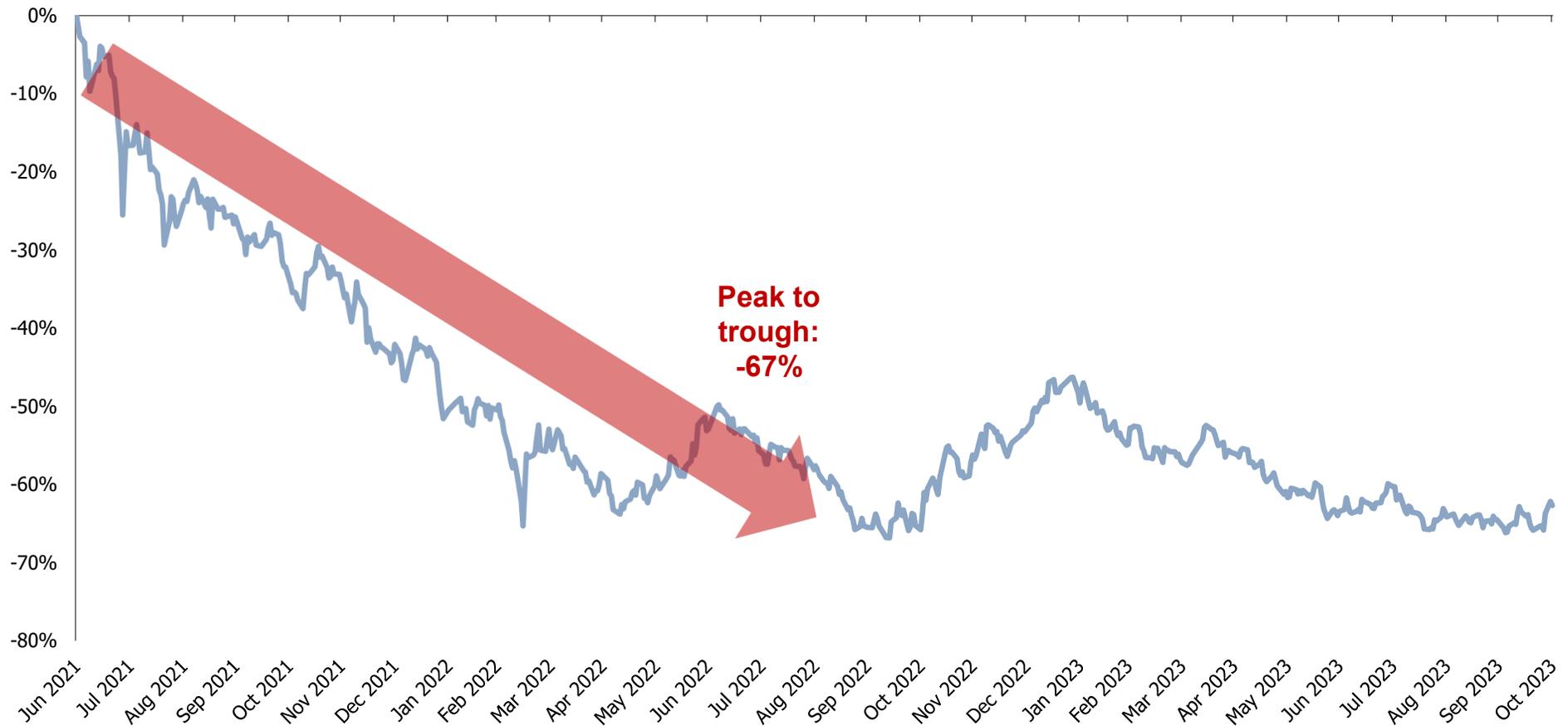
- Emerging biopharma companies (EBPs)* are now responsible for nearly two-thirds of the drug industry’s R&D pipeline
- EBPs originated 53% of new drugs launched in 2021
- These emerging biopharma companies are well reflected in the portfolio, consistent with the growing share of innovation occurring in this company segment

Source: IQVIA Institute, IQVIA Global Trends in R&D 2021, February 2022, Copyright IQVIA. All rights reserved.

* EBPs defined as companies with less than \$500 mm in annual sales and R&D spending less than \$200 mm per year

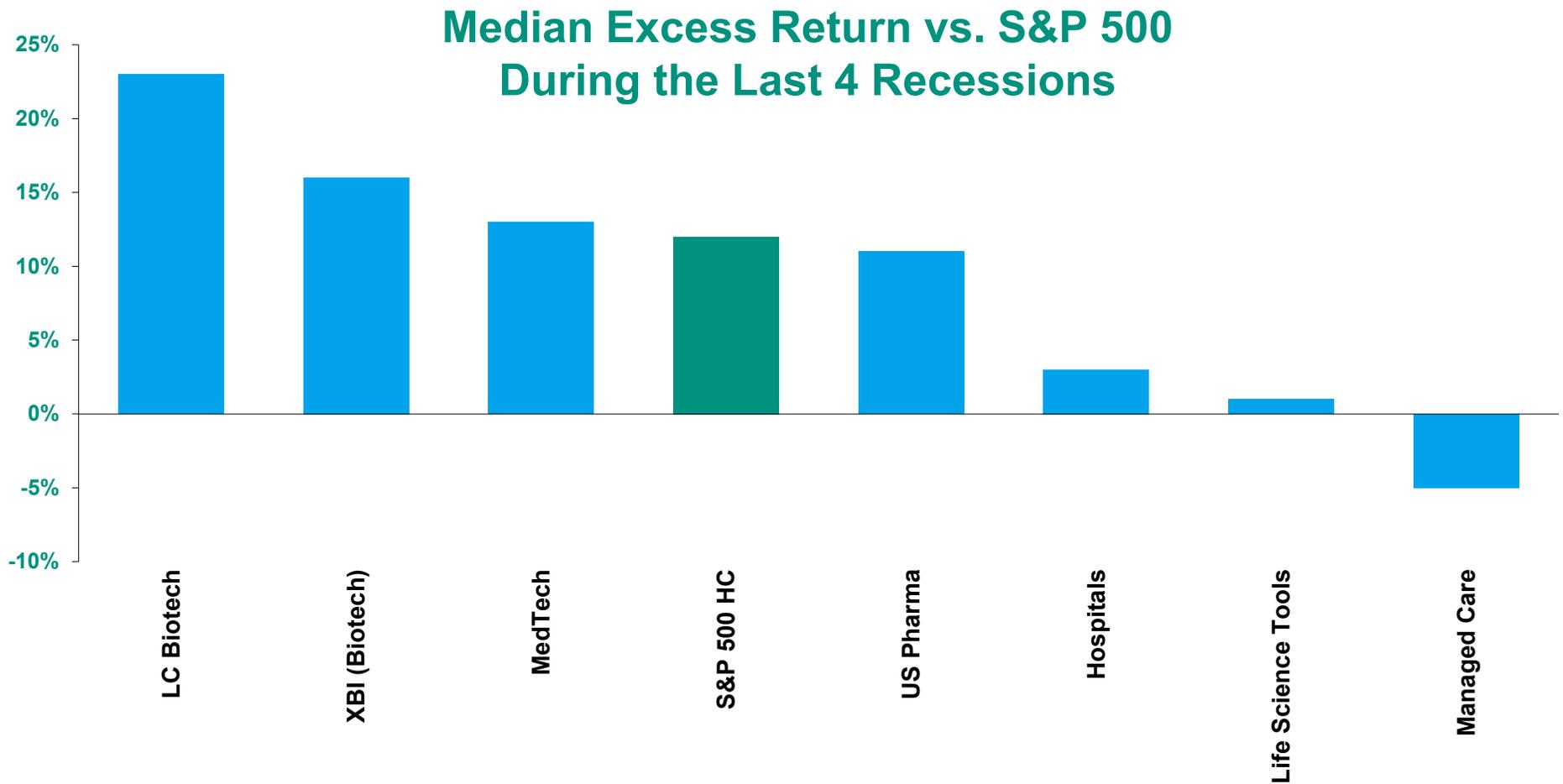
China Recovery Yet to Occur After “Re-opening”

Hong Kong Healthcare Index (HSHCI)



China healthcare stocks hit all-time lows last fall but should eventually rebound with post-COVID recovery and economic stimulus

What Could a Recession Mean for Biotech Stocks?



**Biotech returns have been the most robust across
Healthcare during recessionary periods**

Source: Goldman Sachs. Assessing Recession Impact Across Subsectors. 7.20.22

Endnotes

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Endnotes

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