



# Frostrow Investment Seminar

10 May 2023



WORLDWIDE  
HEALTHCARE  
TRUST

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## Proven

20+ year strong returns across public and private equity and debt markets

## Global

11 locations, including New York, San Francisco, Hong Kong, Shanghai, Mumbai, Herzliya

## Health

100% healthcare: biopharma, devices, diagnostics, digital health, and services

## Leader

\$17.1 billion AUM  
138 professionals  
100% employee-owned

## Flexible

Investing across stages, sub-sectors, geographies and capital structures



**OrbiMed**  
Healthcare Fund Management

Leading Global Healthcare Investment Firm

# Portfolio Managers

**Sven Borho, CFA**  
Managing Partner



**Trevor M. Polischuk, PhD**  
Partner

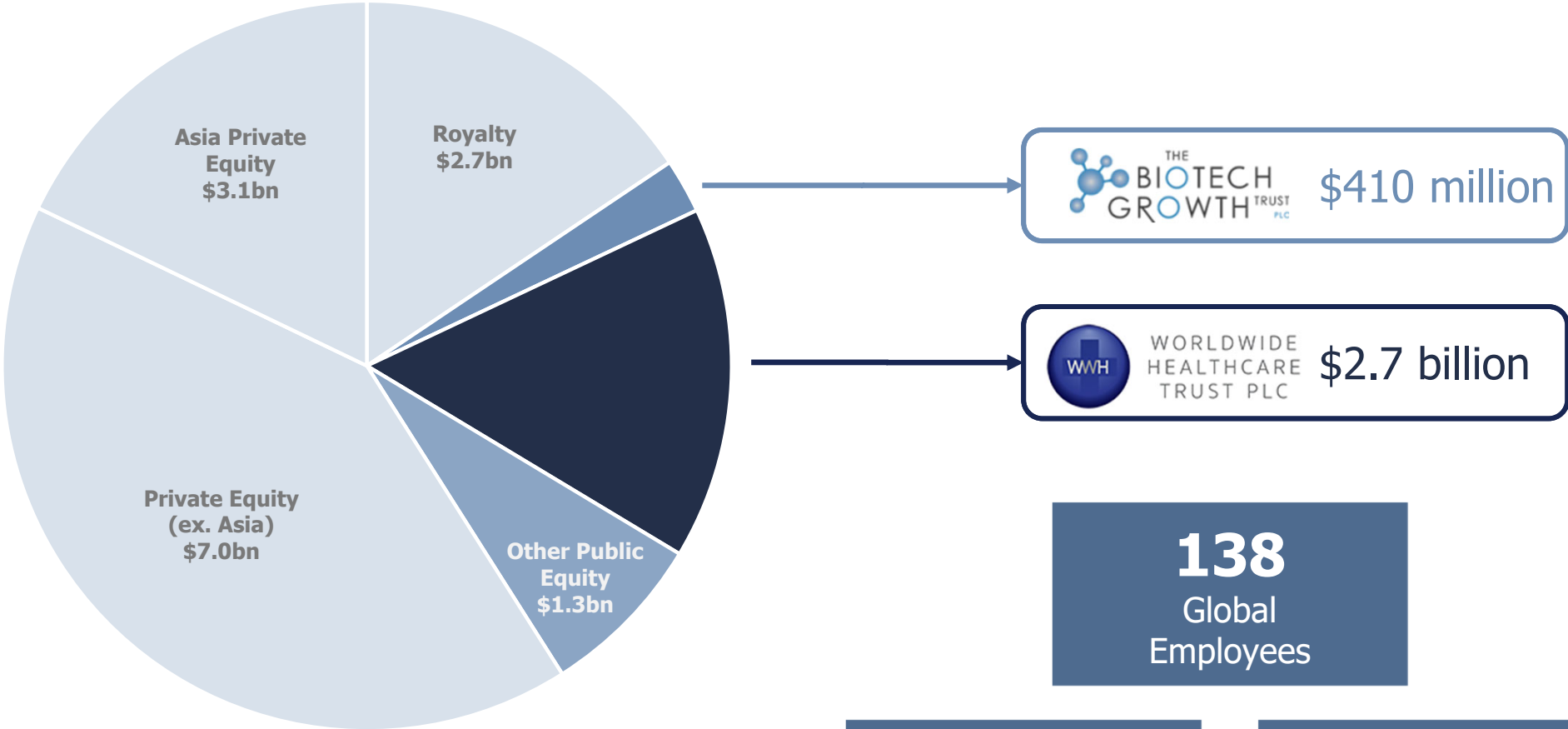


**Geoffrey Hsu, CFA**  
Partner



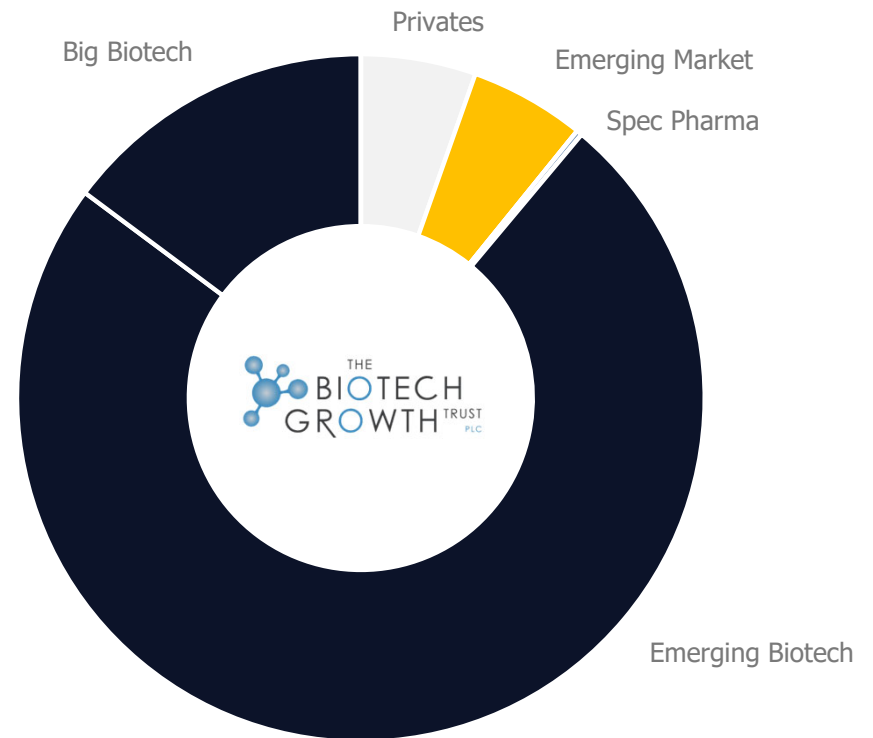
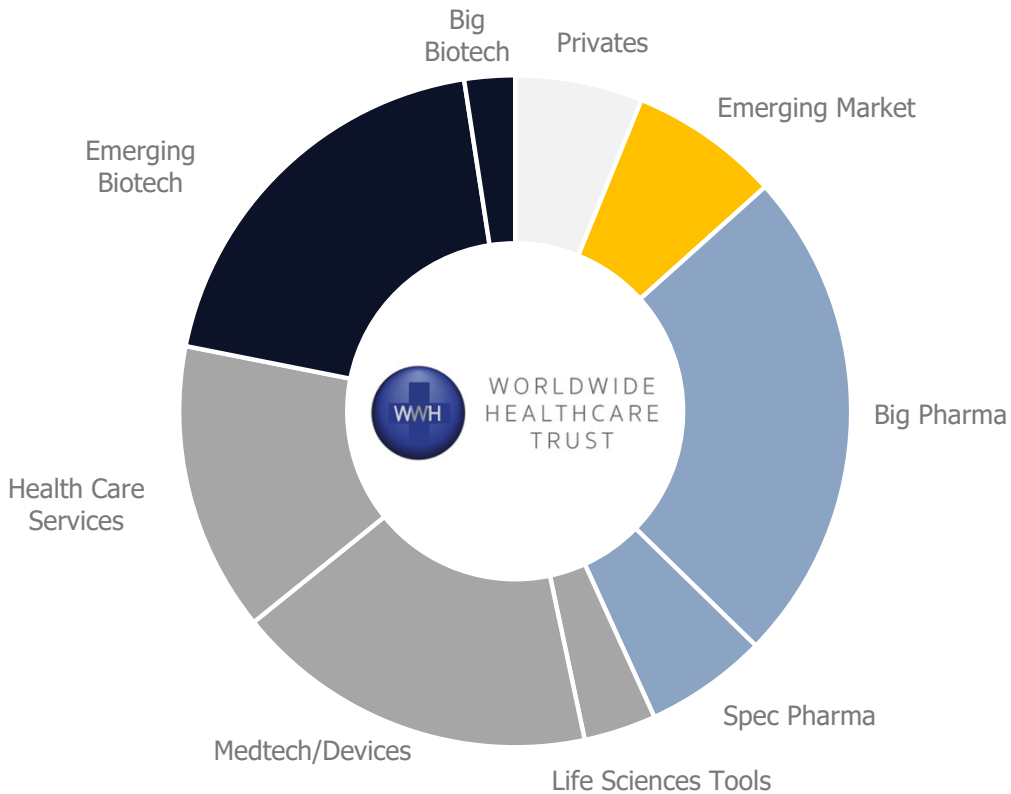
# OrbiMed Corporate Update

**Total AUM: \$17.1 billion**



Source: OrbiMed; Data updated as of 31 March 2023

# WWH/BIOG – Subsector Allocation Comparison



	Biotechnology	24.2%
	Pharmaceuticals	33.0%
	Non-Therapeutics	38.6%
	Emerging Markets	8.0%
	Privates	6.8%

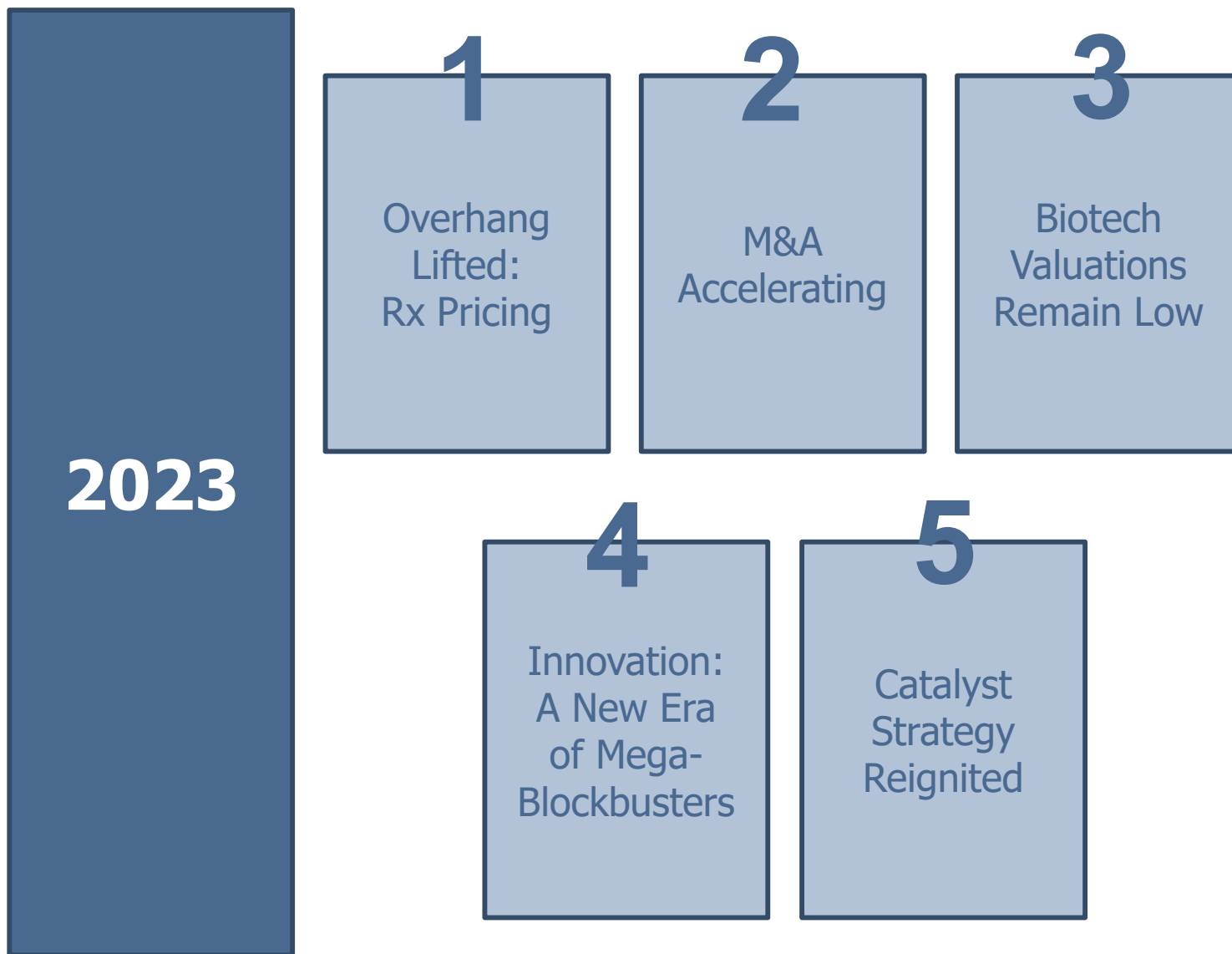
	Biotechnology	97.2%
	Pharmaceuticals	0.3%
	Non-Therapeutics	0.0%
	Emerging Markets	5.9%
	Privates	5.9%

Note: As of 31 March 2023. Percentages may not sum to 100% due to cash and/or leverage. Portfolio composition is estimated and as of the date hereof, and may differ in the future.



## 2023 Investment Themes

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# U.S. Drug Price Reform: Overhang Lifted

## Three Main Components to the IRA 2022 re: Drug Price Reform



### Drug Price Inflation Cap

Requires drug co.s to pay rebates to Medicare if they increase drug prices faster than inflation

#### NEUTRAL

- Price is no longer a revenue driver for pharma
- LIST prices do rise today, but < levels of inflation
- NET prices are cut even further due to rebating
- Curbs bad actors = positive for industry image

### Medicare Part D Redesign

Removes the "donut hole" and replaces it with an "out-of-pocket cap" of \$2,000 per patient

#### POSITIVE

- Lowers out of pocket expenses
- Increases affordability of medicines
- Increases adherence / treatment duration of times
- Increases patient access
- Should result in increased volumes

### Medicare Price Negotiations

Enables Health & Human Services to set the prices of certain costly drugs within the Medicare program

#### NEGATIVE but MANAGEABLE

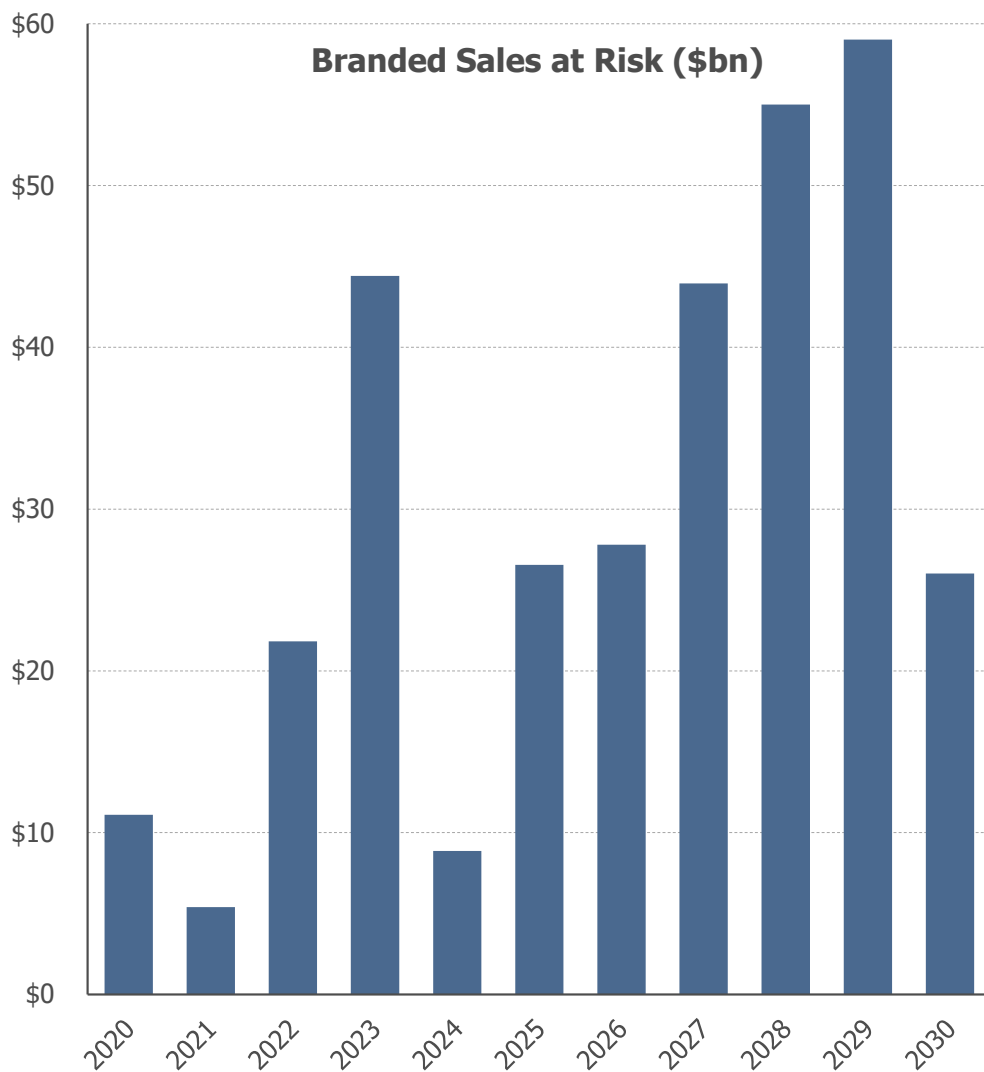
- Not in effect until 2026
- Only 10 drugs per year are negotiated
- Targets medicines that are near the end of their life cycles but do not yet have generic competition (9 yrs – small molecules / 13 yrs – biologics)
- Only a potential \$40 billion incremental hit to U.S. Rx revenues to 2032 (out of \$660 billion)

**The IRA will have an impact but the net of it is manageable.  
Perhaps the biggest benefit is that the headline risk is now behind us.**



# Large Cap Pharma: Patent Cliff Approaching

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



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

Co.	Drug	US Loss of Exclusivity (Projected)	'22 Global Sales* (\$bn)
abbvie	<b>HUMIRA</b> adalimumab	2023	\$21.2
MERCK	<b>KEYTRUDA</b> (pembrolizumab) Injection 100 mg	2028	\$20.9
Bristol Myers Squibb™ Pfizer	<b>Eliquis</b> (apixaban) tablets 5mg, 2.5mg	2026	\$18.2
abbvie Johnson & Johnson	<b>imbruvica</b> ™	2027	\$9.8*
Johnson & Johnson	<b>Stelara</b> (ustekinumab)	2023	\$9.7
Bristol Myers Squibb™	<b>OPDIVO</b> (nivolumab)	2028	\$8.3
Pfizer	<b>IBRANCE</b> palbociclib	2027	\$5.4*
MERCK	<b>Januvia</b>	2023	\$5.3*

Source: S&P Global report, data as of February 17, 2022; Company Reports

\*2021 sales

# M&A Activity Surging

2022 Acquisitions			
Date	Target	Acquirer	% Premium
11/29/22	HORIZON	AMGEN	48%
11/29/22	neo:gene	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	AKOUOS	Lilly	121%
10/03/22	LogicBio	AstraZeneca	667%
09/01/22	forma	novo nordisk	49%
08/08/22	GBT	Pfizer	102%
08/04/22	CHEMOCENTRYX	AMGEN	116%
08/04/22	mirëbio	GILEAD	\$405m (private)
07/11/22	VIACYTE	VERTEX	\$320m (private)
07/11/22	La Jolla	INNOVIVA	84%
07/05/22	TeneoTwo	AstraZeneca	\$1,270 (private)
06/17/22	Seagen	MERCK	Rumored
06/03/22	Turning Point	Bristol Myers Squibb	122%
05/31/22	Affinivax	GSK	\$2,650 (private)
05/10/22	biohaven	Pfizer	79%
04/13/22	SIERRA ONCOLOGY	GSK	39%

Source: FactSet, Company Websites  
 Note: Public companies shown here are not necessarily representative of portfolio holdings

2023 Acquisitions			
Date	Target	Acquirer	% Premium
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	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	>100%
01/08/23	AMRYT	Chiesi	>100%

\* With CVR

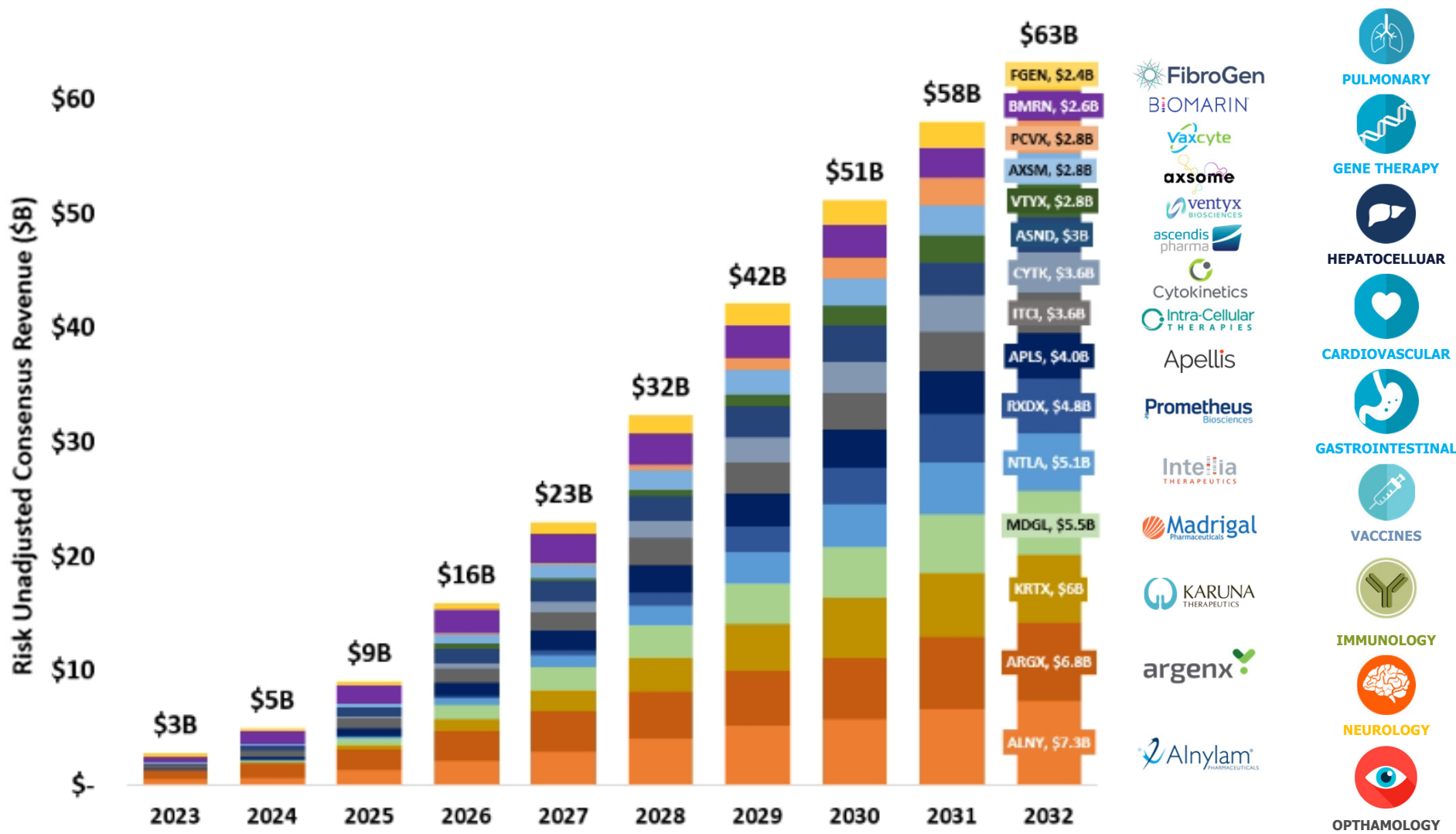
## M&A: Material Inflection YOY

	# of Deals	\$ Value of Deals
FY 2021	17	\$31 billion
FY 2022	30	\$113 billion
YOY	+76%	+265%

\*Represent announced transactions where the target was a publicly traded company.  
 Source: FactSet, data as of April 30, 2023

# M&A: "Filling the Gap"

## 15 Novel Biotech-Sourced Launches with >\$60 billion in Cumulative Revenues



Stretching the list to 25 products could fill an additional >\$20 billion in revenues.

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

# Biotech Rebounding From Lows

## S&P Biotechnology ETF (XBI)

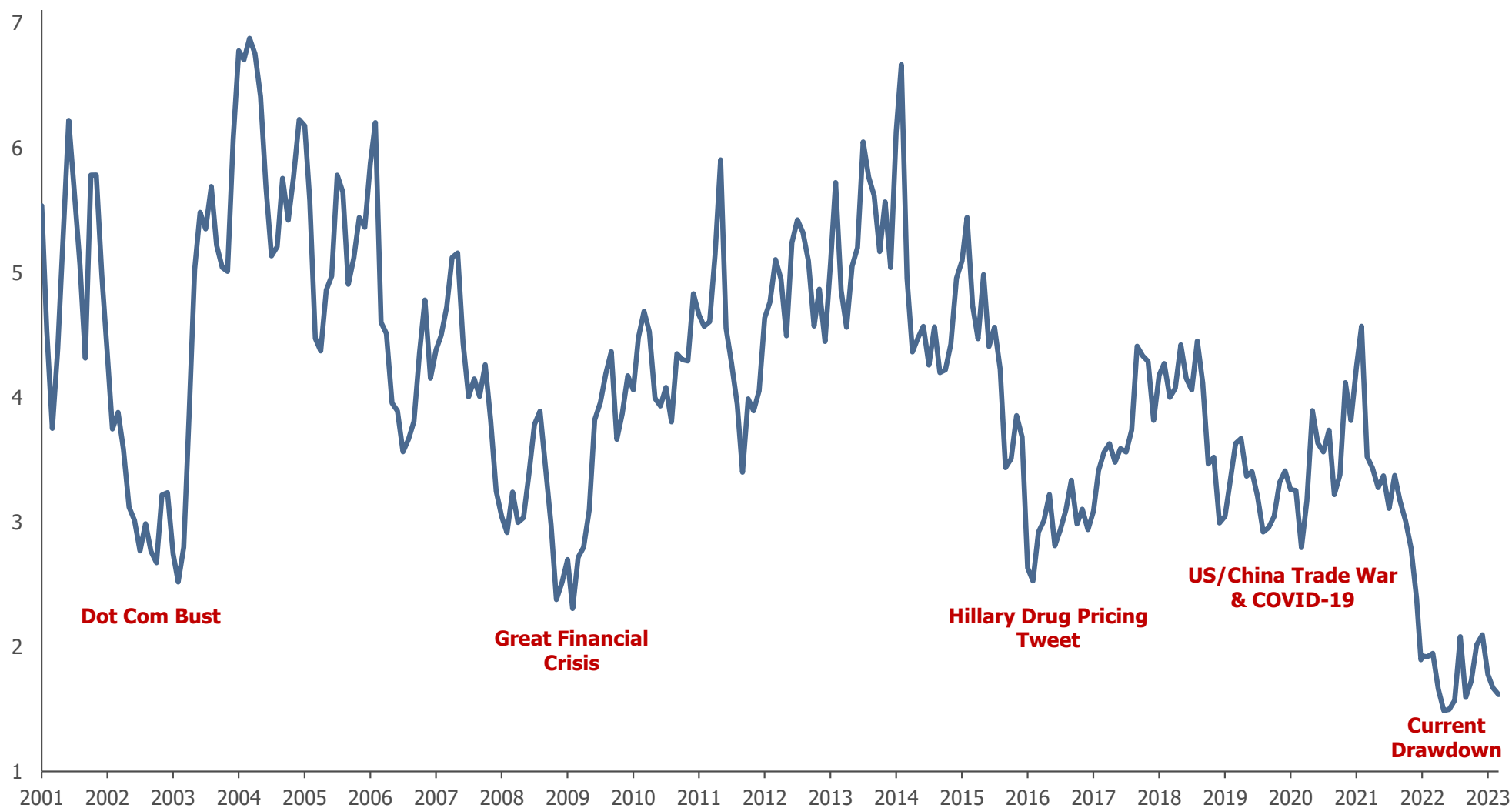


**XBI moved as much as +50% off the lows, but is still >100% away from all-time highs**

Source: Bloomberg  
Note: Chart begins on February 8, 2021 and is updated through March 31, 2023  
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# Biotech Valuations at 20-Year Lows

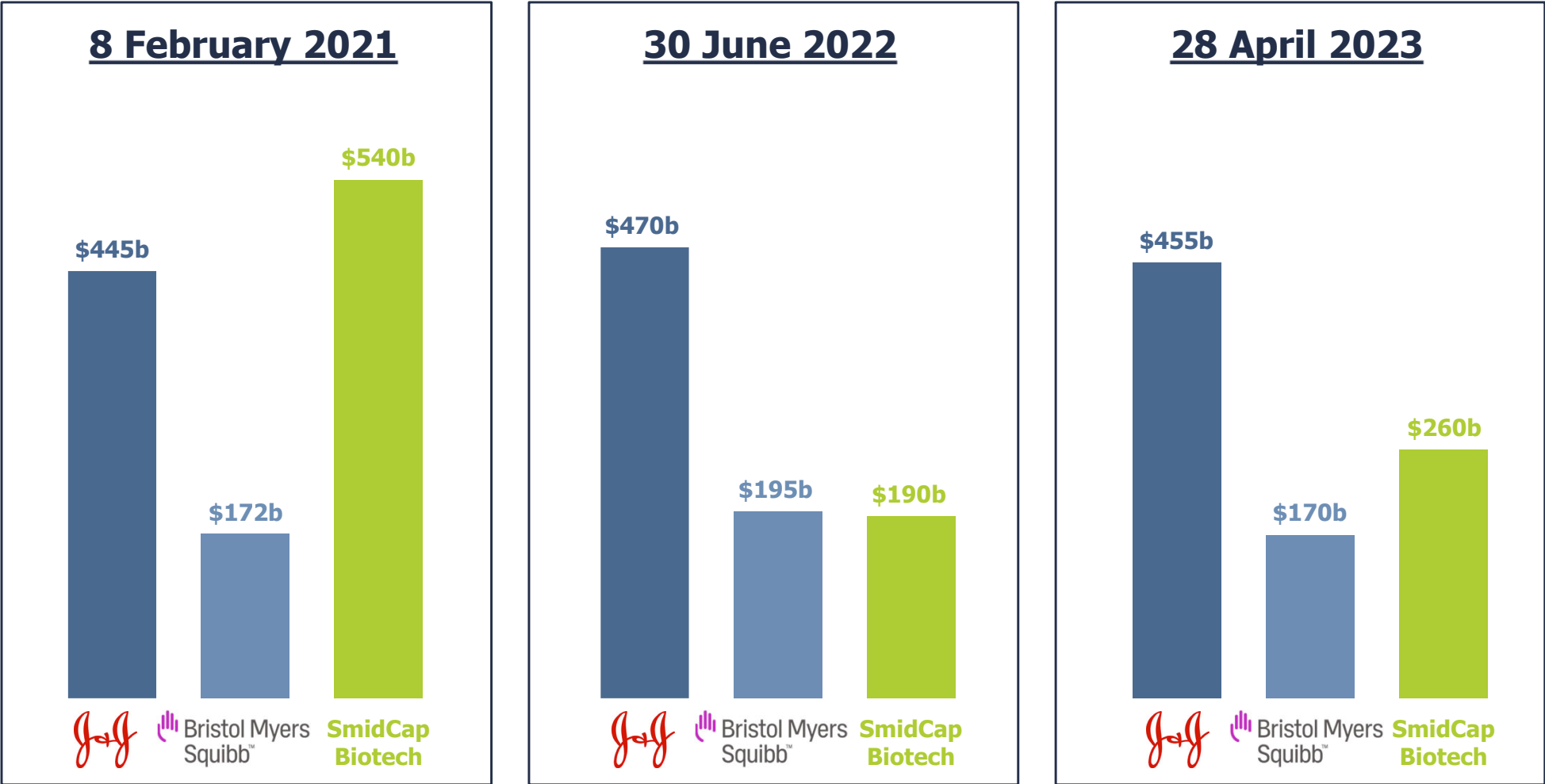
## Ratio of Market Cap to Net Cash on Balance Sheet (Median)



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 March 2023.

# Dislocated Biotech Valuations

## Enterprise Value



**Biotech valuations have been crushed compared to their Pharma counterpart**

Source: Bloomberg, SMID Cap Biotech defined by GICS biotechnology stocks with market caps less than \$5bn (Includes >1,000 companies).

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

Drawdowns in spread followed by historically strong recoveries

## XBI - SPX spread since XBI inception

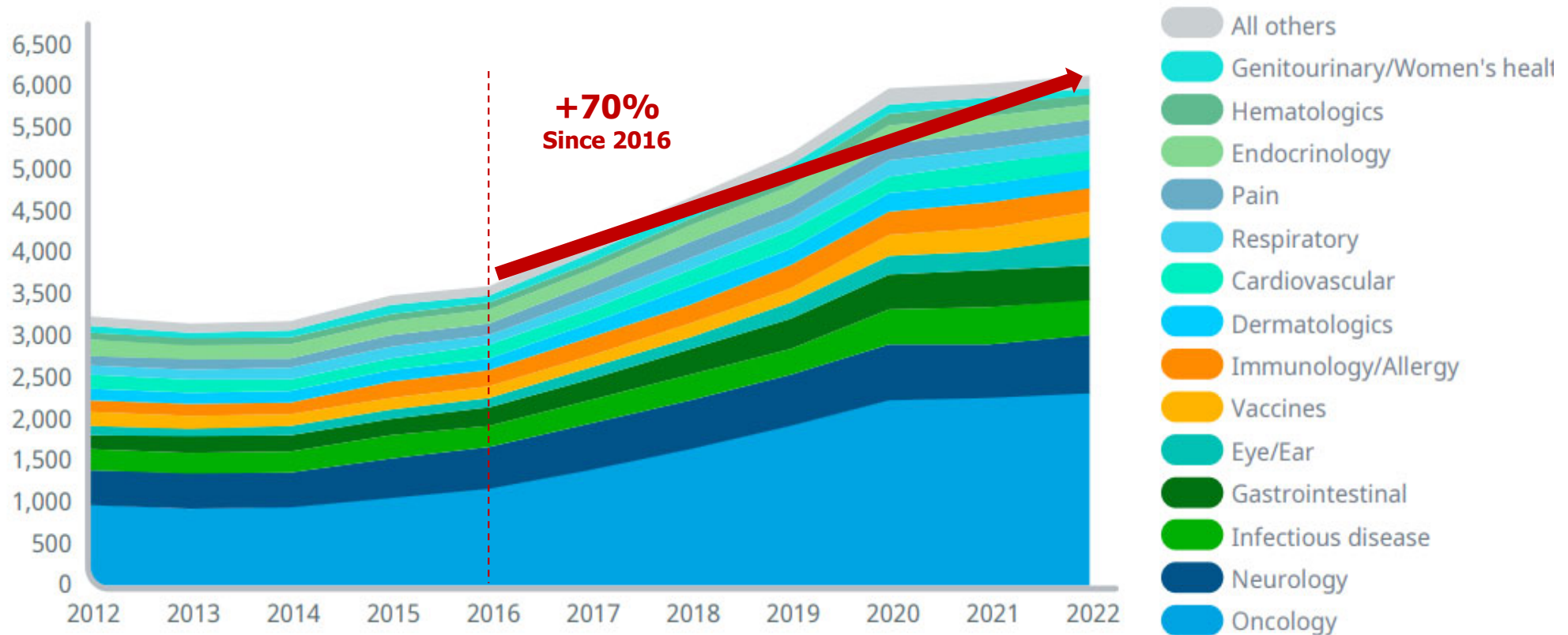


Note: Drawdowns are calculated using daily closing prices, while chart is shown using monthly periodicity for smoothing purposes. Updated as of 31 March 2023.  
Source: JPM [Drawdowns and Recoveries] | OrbiMed (XBI - SPX Spread Chart since XBI Inception).



# Innovation: Pipelines are Full

## Record Number of Molecules Under Development



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

## Pipeline Products: (Phase I → Filing / Therapeutic Class / 2012-2022)

# Innovation: The Next Big Thing?

## Oncology



**POSITIVE**

### ADCs

**ENHERTU<sup>®</sup>**  
fam-trastuzumab deruxtecan-nxki  
20 mg/ml INJECTION FOR INTRAVENOUS USE

AstraZeneca  Daiichi-Sankyo 

New Standard of Care in HER2+ "low" metastatic BC

### IO

**APPROVED** **Opdivalag<sup>™</sup>**  
(nivolumab and relatlimab-mbwi)  
Injection for intravenous use | 480 mg/168 mg

Bristol Myers Squibb 

**FAIL** **TIGIT** 

TIGIT missed PFS endpoint at interim analysis

**POSITIVE**

### Targeted Therapy

**TAGRISSO<sup>™</sup>** AstraZeneca   
osimertinib 

Disease Free Survival surpasses 5 years in EGFR+ lung cancer

## Obesity



### tirzepatide

**NOW APPROVED** **mounjaro<sup>™</sup>**   
once weekly (tirzepatide) injection 0.5 mL  
2.5 mg | 5 mg | 7.5 mg | 10 mg | 12.5 mg | 15 mg

**NEXT GENERATION**  
• GGG

Tirzepatide for chronic weight management (SURMOUNT-2)  
Tirzepatide for chronic weight management (SURMOUNT-3)  
Tirzepatide for chronic weight management (SURMOUNT-4)

### semaglutide

**ONCE-WEEKLY** **wegovy<sup>®</sup>**   
semaglutide injection 2.4 mg novo nordisk<sup>®</sup>

**SELECT** **NEXT GENERATION**  
Cardiovascular Outcomes Trial • cagri-sema

### orals

**Pfizer**  **SOSEI**   
**HEPTARES**

**CHUGAI**  **Lilly**   
novo nordisk<sup>®</sup> 

## Alzheimer's



**FAIL**

### gantenerumab

**GRADUATE 1/2**  
CLINICAL TRIALS

Patients on drug improved; but outcome was not SS

**POSITIVE**

### lecanemab

  
Clarity AD

Met all endpoints & reduced cognitive decline by -27%

### donanemab

**TRAILBLAZER**  
**ALZ-3**

**Lilly** 

Note: Examples may not be representative of portfolio holdings.

# New Era of Mega-Blockbuster Drugs

Peak Sales		
Revenue	Drug	Company
>\$30bn	 COMIRNATY <sup>™</sup> (COVID-19 Vaccine, mRNA)	
	 HUMIRA adalimumab	
	 KEYTRUDA <sup>®</sup> (pembrolizumab) injection 100 mg	
>\$20bn	 spikevax <sup>™</sup> COVID-19 Vaccine, mRNA	
	 PAXLOVID <sup>™</sup> (nirmatrelvir 150 mg tablets   ritonavir 100 mg tablets)	
	 Eliquis. (apixaban) tablets 5mg / 2.5mg	
	 Revlimid <sup>®</sup> (lenalidomide) capsules	
>\$10bn	 imbruvica <sup>®</sup> (ibrutinib)	
	 Stelara <sup>®</sup> (ustekinumab)	

2030 (OrbiMed Estimates)	
Drug	Company
 ONCE WEEKLY wegovy <sup>™</sup> semaglutide injection 2.4 mg	
 NOW APPROVED once weekly mounjaro <sup>™</sup> (tirzepatide) injection	
 ENHERTU <sup>®</sup> fam-trastuzumab deruxtecan-nxki 20 mg/mL INJECTION FOR INTRAVENOUS USE	  AstraZeneca
<b>Dato-DXd</b>	  AstraZeneca
<b>milvexian</b>	 Bristol Myers Squibb
 DUPIXENT <sup>™</sup> (dupilumab)	
 Skyrizi <sup>®</sup> risankizumab-rzaa	
 LEQEMBI <sup>™</sup> (lecanemab-irmb) 100 mg/mL	  Biogen.
<b>donanemab</b>	

Source: Fierce Pharma. The top 20 pharma companies by 2021 revenue. 4/12/22; OrbiMed estimates

# Catalyst Driven Strategy Rebounds in 2H22 and into 2023

The market had grown overly negative about clinical catalysts...



*Cardiomyopathy*



*Alzheimer's*



*ALS*



*Liver Fibrosis*



*Cancer Vaccine*



*Pneumococcal Vaccine*



...but 2H22 saw many of these catalysts deliver positive outcomes.

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

# 2023 “Catalysts to Watch”: Gene Therapy

After years of promise, 2023 could mark inflection point for gene therapies

uniQure

 HEMGENIX®  
etranacogene dezaparvovec-drlb

The first and only  
FDA-approved gene  
therapy for hemophilia B

B:OMARIN®

 ROCTAVIAN

- For hemophilia A
- Approved in the EU
- US approval expected  
June 2023

 SAREPTA  
THERAPEUTICS 

delandistrogene  
moxeparvovec

- For DMD
- US approval expected  
May 2023
- EU filing expected '23



















**These newer therapies will impact thousands of patients' lives.**

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



# 2023 "Catalysts to Watch": Biotech Catalyst Basket

## Imminent catalyst basket provides exposure to highly anticipated 2023 events

 <p>revumenib              axatilimab</p> <ul style="list-style-type: none"> <li>For leukemia</li> <li>Pivotal Data 3Q23</li> <li>For GVHD</li> <li>Pivotal Data mid-'23</li> </ul>	   <ul style="list-style-type: none"> <li>For ALS</li> <li>Commercial launch ongoing</li> </ul>
 <p>upifitamab</p>  <ul style="list-style-type: none"> <li>ADC</li> <li>For Ovarian Cancer</li> <li>Pivotal Data 3Q23</li> </ul>	 <p>Paltusotine</p> <ul style="list-style-type: none"> <li>For acromegaly</li> <li>Multiple pivotal data readouts '23</li> </ul>
  <p>(idecabtagene vicleuce)              Bristol Myers Squibb</p> <ul style="list-style-type: none"> <li>anti-BCMA CART cell therapy</li> <li>For Multiple Myeloma</li> <li>Blockbuster Potential</li> <li>Pivotal Data '23</li> </ul>	 <p>VTX958</p> <ul style="list-style-type: none"> <li>For psoriasis</li> <li>Pivotal data '23</li> </ul> <p>VTX002</p> <ul style="list-style-type: none"> <li>For ulcerative colitis</li> <li>Pivotal data 2H23</li> </ul>
 <p>sparsentan</p> <ul style="list-style-type: none"> <li>For IgA Neuropathy</li> <li>Approved Feb 2023</li> <li>Phase III FSGS</li> <li>Data expected 2Q23</li> </ul>	 <p>BLU-5937</p>  <ul style="list-style-type: none"> <li>For chronic cough</li> <li>Data expected 2H23</li> <li>Completed PDUFA expected 4Q23</li> </ul>
 <p>zetomipzomib</p> <ul style="list-style-type: none"> <li>For Lupus Nephritis</li> <li>POC Data Expected '23</li> </ul>	 <p>KarXT</p> <ul style="list-style-type: none"> <li>For Schizophrenia</li> <li>NDA submission mid-23</li> <li>Potential approval and launch 2H24</li> </ul>
 <p>AT-GAA</p> <ul style="list-style-type: none"> <li>For Pompe Disease</li> <li>Inspection scheduled 2Q23</li> <li>Approval expected 3Q23</li> </ul>	

**Positive outcomes would inflect the valuations of these companies.**

# 2023 "Catalysts to Watch": Large Cap Pharmaceuticals

There are many highly anticipated catalysts in pharma.



ONCE-WEEKLY  
**wegovy**<sup>™</sup>  
semaglutide injection 2.4 mg

**SELECT**  
Cardiovascular  
Outcomes Trial

- For Obesity
- Pivotal Data 1H23



**Dato-DXd**

**Dato-DXd**  
TROPION-Lung01  
Monotherapy

- ADC
- For 2L Lung Cancer
- Pivotal Data 2Q23



**tiragolumab**

**Phase III**  
**SKYSCRAPER-01**

- Novel IO Agent
- For 1L Lung Cancer
- Pivotal Data mid-23



**DUPIXENT**<sup>®</sup>  
(dupilumab)

**Dupixent**<sup>®A</sup>  
COPD

- Additional Indication
- Pivotal Data 1H23



**donanemab**

**TRAILBLAZER**

- For Alzheimer's
- Pivotal Data 1H23

Positive clinical trial readouts will inflect the valuations of these companies.

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



# 2023 "Catalysts to Watch": Medical Technology

**Significant improvements in current technologies can materially impact sales.**

INTUITIVE  
SURGICAL®



**DaVinci Xi**  
Surgical Robot

Investors are eagerly awaiting the best kept secret in medical technology: the unveiling of the latest version of the DaVinci surgical robot.



SAGES March 2024?

Boston  
Scientific



**FARAPULSE**  
Pulsed Field Ablation (PFA)

The atrial fibrillation market is the fastest growing market in medical technology.

Boston Scientific's latest electrophysiology offering is perhaps "best in class".

The ADVENT IDE clinical trial in paroxysmal Afib is expected to read out in 2H23E.

**These catalysts can drive end market demand in two "hot" technology areas.**

# Playbook for 2023

<b>1</b>	Continue to Invest in Innovation	
<b>2</b>	Key Overhangs Lifted	
<b>3</b>	Continued High Expectations for M&A	
<b>4</b>	Re-ignite our Catalyst Strategy	
<b>5</b>	Great Entry Point for Biotech	
<b>6</b>	Valuations Undemanding	
<b>7</b>	Overall Bullish Outlook	



Q&A

# Endnotes

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1. The information presented herein relates to The Biotech Growth Trust PLC and Worldwide Healthcare Trust PLC (collectively, the "Funds"). OrbiMed Capital LLC ("OrbiMed") is an investment adviser registered with the U.S. Securities and Exchange Commission (the "SEC") that specializes in the investment of clients' assets, including the Funds' assets, in healthcare and life sciences companies, including the biotechnology and pharmaceutical sectors, across a number of products and strategies. This presentation includes information specifically relating to the Funds, and potential OrbiMed clients or fund investors should be aware that such information may not be applicable to other OrbiMed funds, products or strategies. The information contained in this presentation is not intended to supplement or replace the disclosures made in Part 2 of OrbiMed's Form ADV filed with the SEC or in the prospectus or other offering document for any investment fund sponsored and/or managed by OrbiMed or its affiliates. SEC Registration does not imply a certain level of skill or training. This document is confidential and may not be reproduced, in whole or in part, and may not be disclosed or distributed to any person other than the person to whom it was originally delivered and to such person's advisers without the prior written consent of OrbiMed.
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# Endnotes (continued)

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The MSCI World Health Care Index is a market-value weighted index of health care sector equities within the MSCI World Index, a free float-adjusted market capitalization weighted index that is designed to measure the equity market performance of developed markets. Index data for the MSCI World Health Care Index is available since December 30, 1994. For the period from the Fund's inception through December 30, 1994, returns of the MSCI World Health and Personal Care Index are used as a proxy for the MSCI World Health Care Index. Return numbers for these indices include reinvestment of dividends net of withholding taxes, as calculated by the index provider.

The MSCI World Index is a free float-adjusted market capitalization weighted index that is designed to measure the equity market performance of developed markets. The NASDAQ Biotechnology Index 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 SPDR S&P Biotech ETF seeks to provide investment results that, before fees and expenses, correspond generally to the total return performance of the S&P Biotechnology Select Industry. The FTSE All-Share Index is a market-capitalization weighted index representing the performance of all eligible companies listed on the London Stock Exchange's main market, which pass screening for size and liquidity. The Russell 2000 Index measures the performance of the small-cap segment of the U.S. equity universe. It includes approximately 2000 of the smallest securities based on a combination of their market cap and current index membership.