



**OrbiMed**  
Healthcare Fund Management

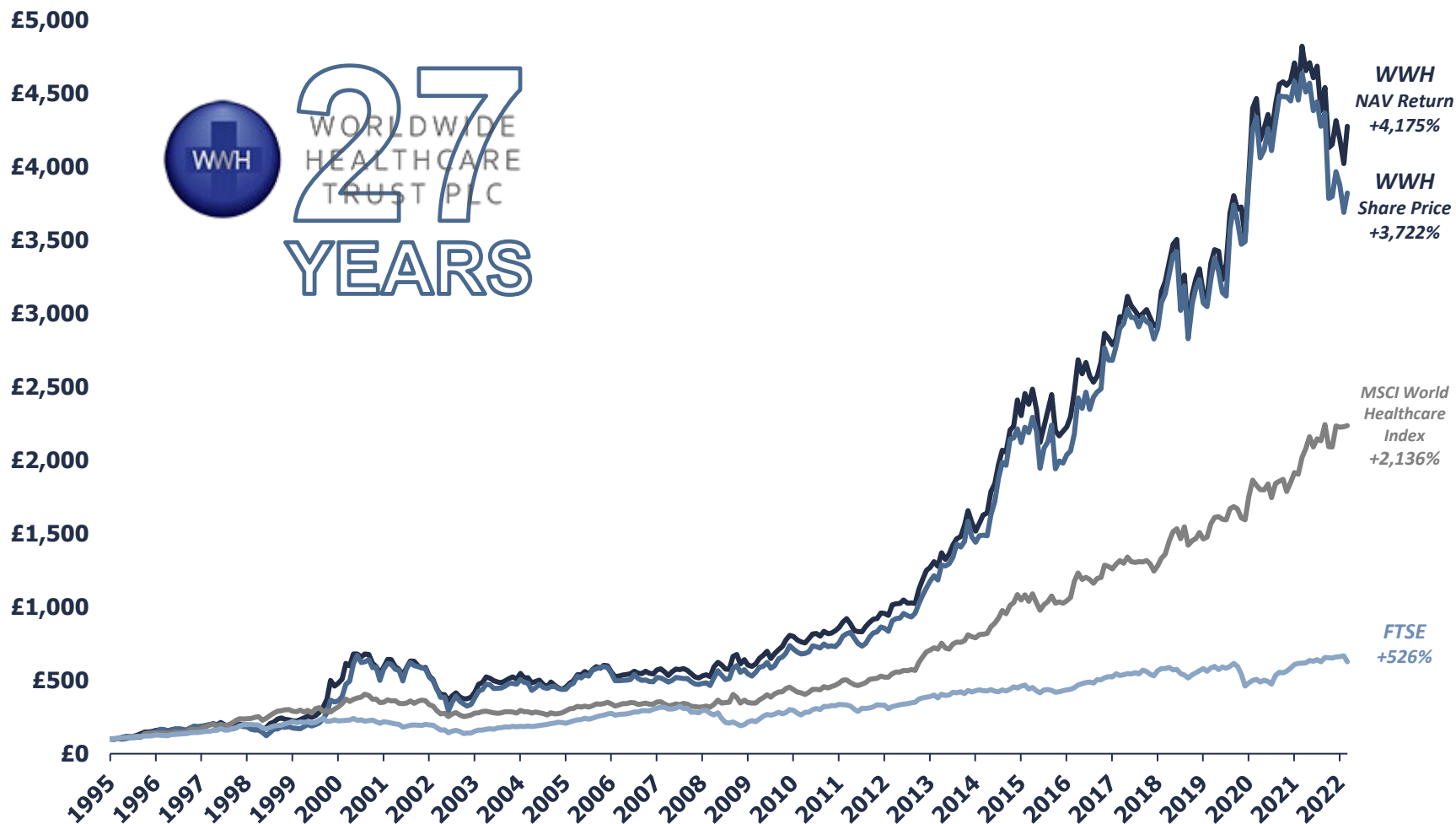
# Worldwide Healthcare Trust PLC

Annual General Meeting  
6 July 2022

*This document does not constitute an offer to sell, or the solicitation of an offer to purchase, any security or fund. Any such offer may only be made by means of a confidential private placement memorandum, which is available to prospective investors upon request. This presentation is as of the date noted above and may be changed without notice, and nothing herein shall, under any circumstances, create any implication that there has been no change in the affairs of any fund referenced in this document since the date hereof.*

# Performance Since Inception

Multiple: **41x** since inception



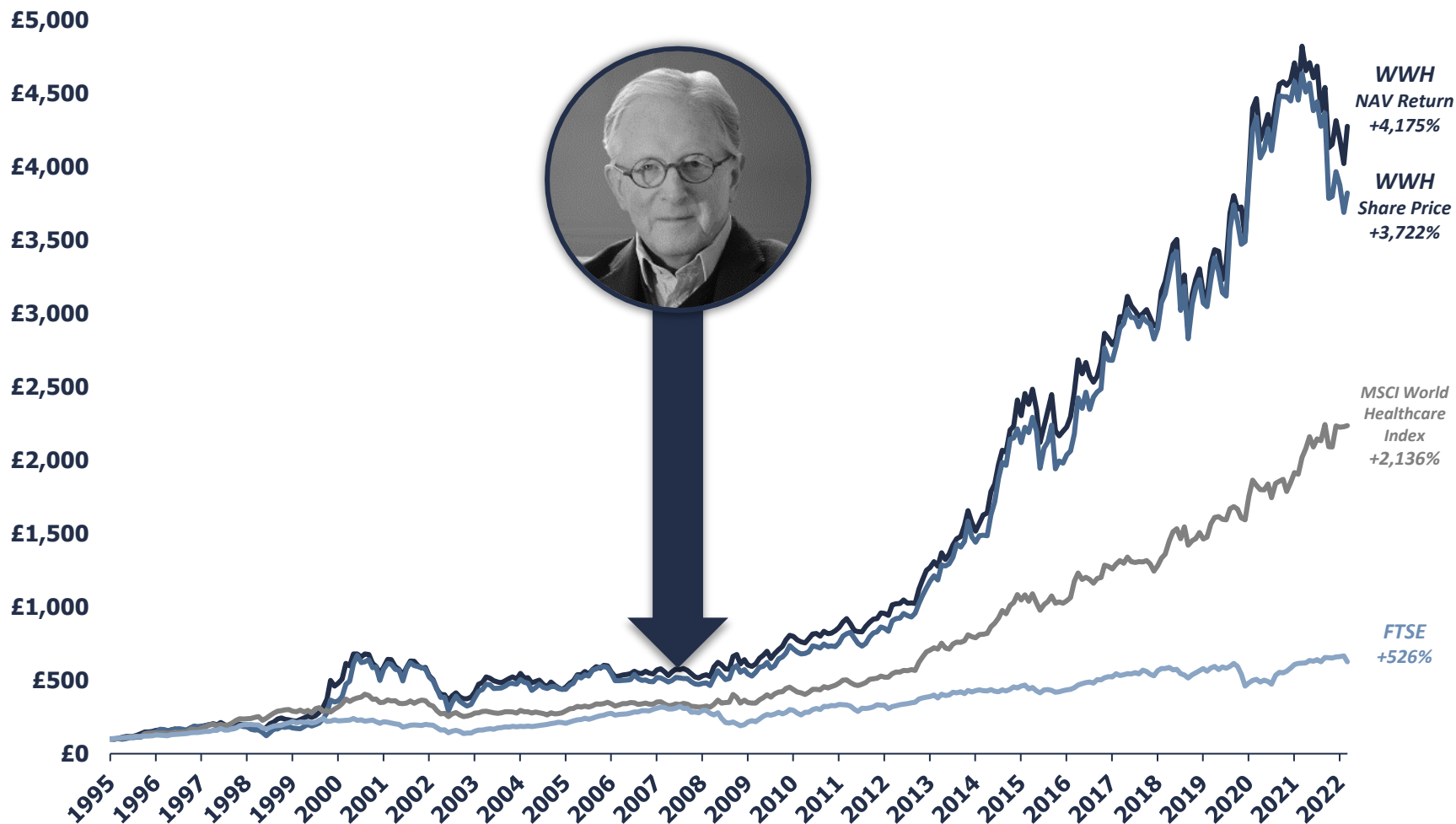
\*The "Blended DS/MSCI Benchmark" uses the Datastream World Pharma/Biotech TR Index from inception to September 30, 2010, the MSCI World Health Care Gross Index from September 30, 2010 to December 31, 2011, and the MSCI World Health Care Net Index from December 31, 2011. Past performance is no guarantee of future results. See Endnotes for additional information regarding the performance presented in this slide and those that follow. Updated through 30 June 2022 using estimated NAVs sourced from Frostrow as of 7.1.22.

Source: Frostrow, Bloomberg

© 2022 OrbiMed Advisors LLC. All Rights Reserved. CONFIDENTIAL

# The Reign of Sir Martin Smith: 8 November 2007

## Sir Martin Smith Joins the WWH Board



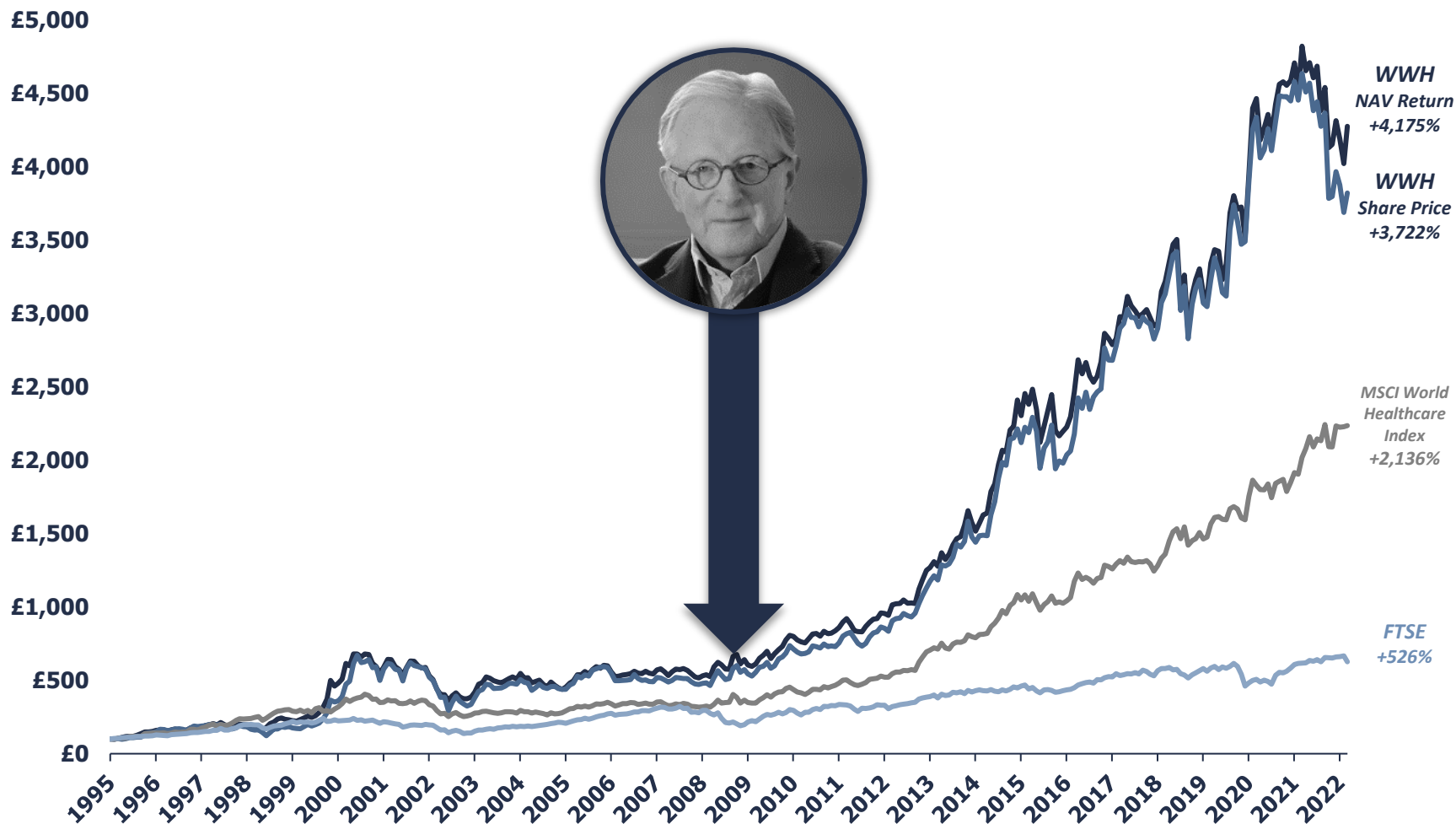
\*The "Blended DS/MSCI Benchmark" uses the Datastream World Pharma/Biotech TR Index from inception to September 30, 2010, the MSCI World Health Care Gross Index from September 30, 2010 to December 31, 2011, and the MSCI World Health Care Net Index from December 31, 2011. Past performance is no guarantee of future results. See Endnotes for additional information regarding the performance presented in this slide and those that follow. Updated through 30 June 2022 using estimated NAVs sourced from Frostrow as of 7.1.22.

Source: Frostrow, Bloomberg

© 2022 OrbiMed Advisors LLC. All Rights Reserved. CONFIDENTIAL

# The Reign of Sir Martin Smith: November 2008

**Sir Martin Smith: "This must be the investment opportunity of a lifetime"**



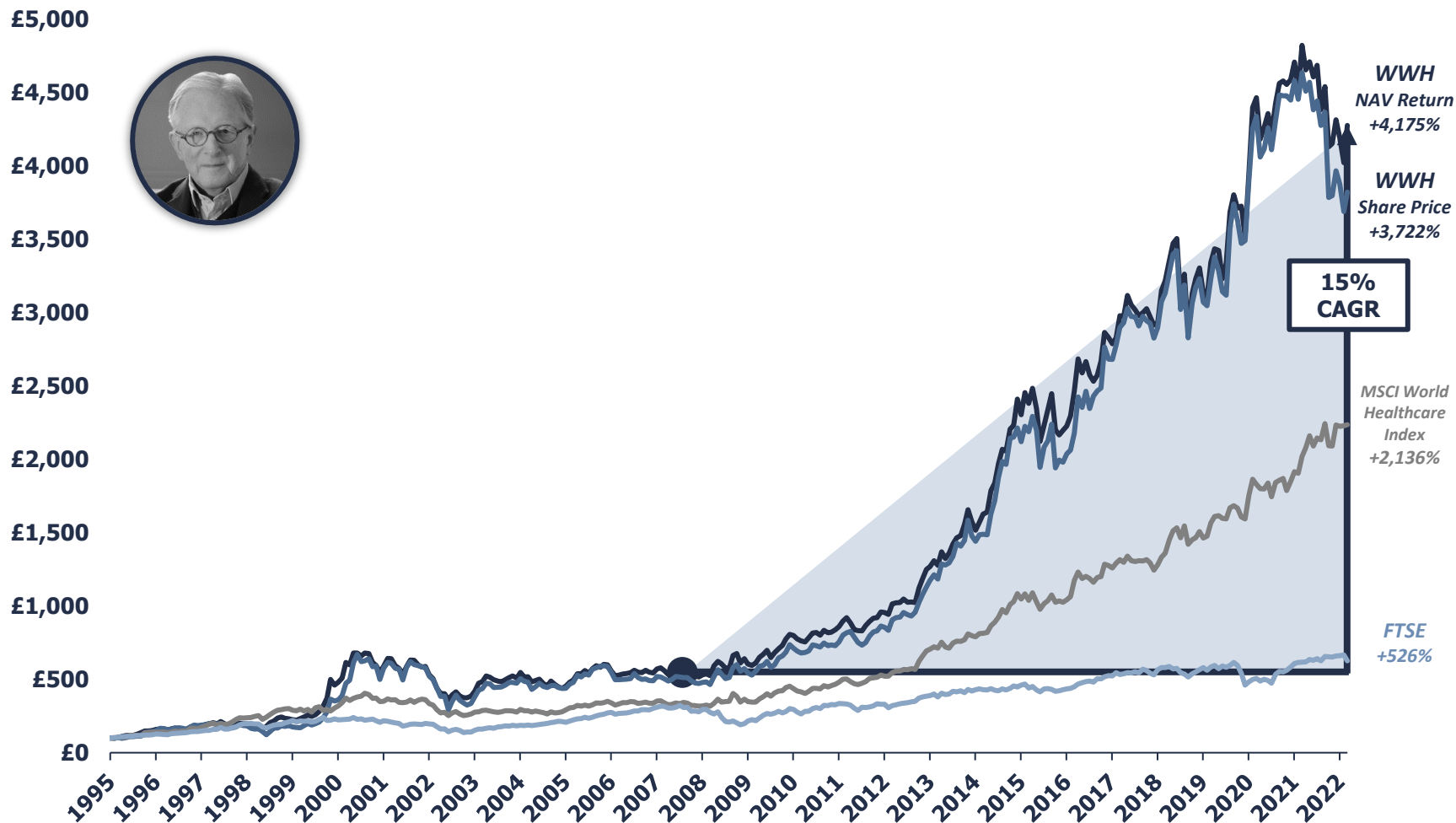
\*The "Blended DS/MSCI Benchmark" uses the Datastream World Pharma/Biotech TR Index from inception to September 30, 2010, the MSCI World Health Care Gross Index from September 30, 2010 to December 31, 2011, and the MSCI World Health Care Net Index from December 31, 2011. Past performance is no guarantee of future results. See Endnotes for additional information regarding the performance presented in this slide and those that follow. Updated through 30 June 2022 using estimated NAVs sourced from Frostrow as of 7.1.22.

Source: Frostrow, Bloomberg

© 2022 OrbiMed Advisors LLC. All Rights Reserved. CONFIDENTIAL

# The Legacy of Sir Martin Smith

## 15 Years of 15% Returns



\*The "Blended DS/MSCI Benchmark" uses the Datastream World Pharma/Biotech TR Index from inception to September 30, 2010, the MSCI World Health Care Gross Index from September 30, 2010 to December 31, 2011, and the MSCI World Health Care Net Index from December 31, 2011. Past performance is no guarantee of future results. See Endnotes for additional information regarding the performance presented in this slide and those that follow. Updated through 30 June 2022 using estimated NAVs sourced from Frostrow as of 7.1.22.

Source: Frostrow, Bloomberg

© 2022 OrbiMed Advisors LLC. All Rights Reserved. CONFIDENTIAL

# OrbiMed Public Equity

## A deep team of investment and industry expertise



Sven H. Borho, CFA  
*Partner*



Trevor M. Polischuk, PhD  
*Partner*

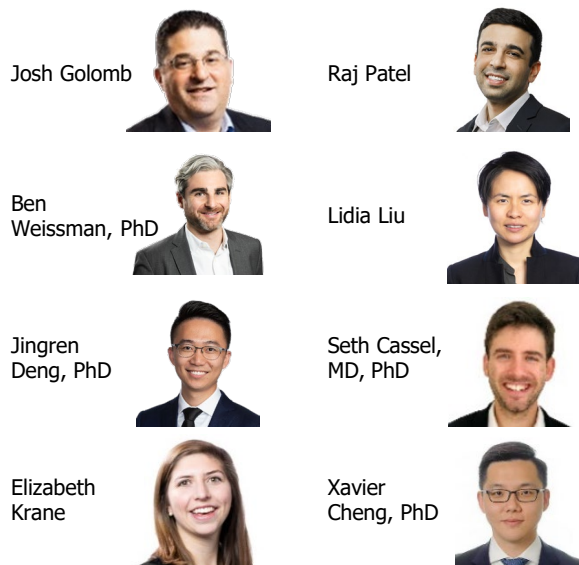


Geoffrey C. Hsu, CFA  
*Partner*

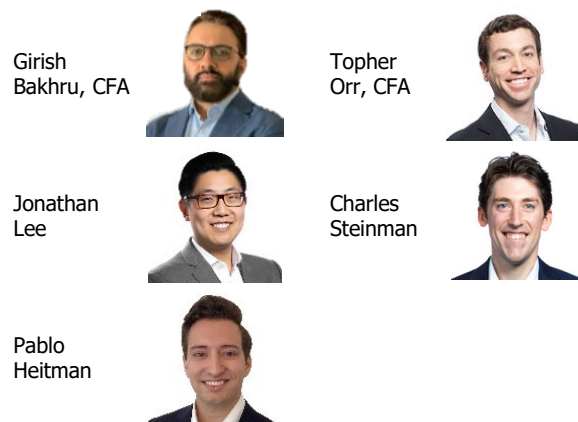


C. Scotland Stevens  
*Partner*

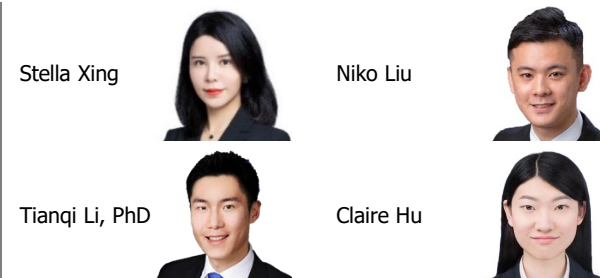
### Therapeutics



### Non-Therapeutics



### Emerging Markets



### ESG



### Risk, Trading, Analytics & Operations

Andrew  
Kanarek, CFA, CIPM,  
*Chief Risk Officer*

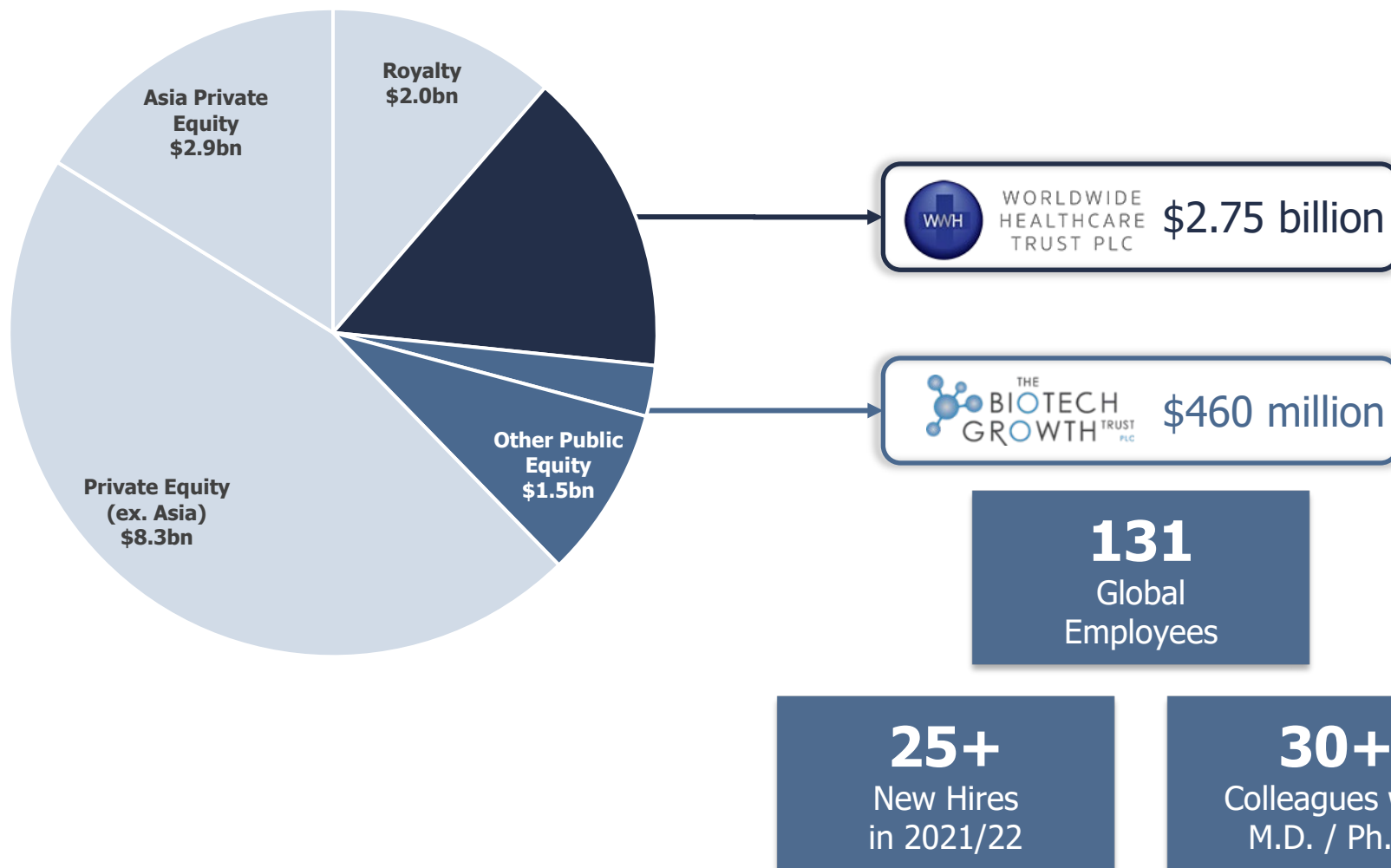


Jason Kahn, CMT, *Senior Trader*  
Jason Glover, CFA, *Derivatives Trading*  
Joseph Kleeman, *Senior Trader*  
Kevin Olsen, *Director of Trading Operations*  
Eric Magleby, *Senior Operations Associate*

Kevin Chappell, *Operations Associate*  
Cason Kim, CFA, *Quantitative Analyst*  
Corey Schrader, *Vice President, Data Engineer*  
Stanley Patela, *Senior Data Engineer*

# OrbiMed Corporate Update

**Total AUM: \$18 billion**



Source: OrbiMed, AUM as of 30 April 2022, employee data as of 31 March 2022



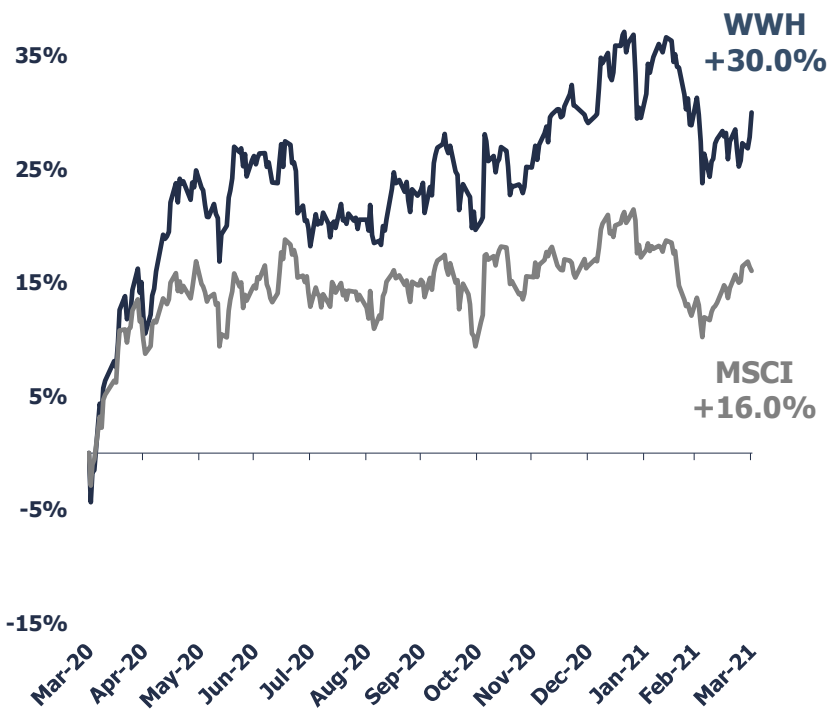
**Fiscal Year March 31, 2022**



# Fiscal Year Performance

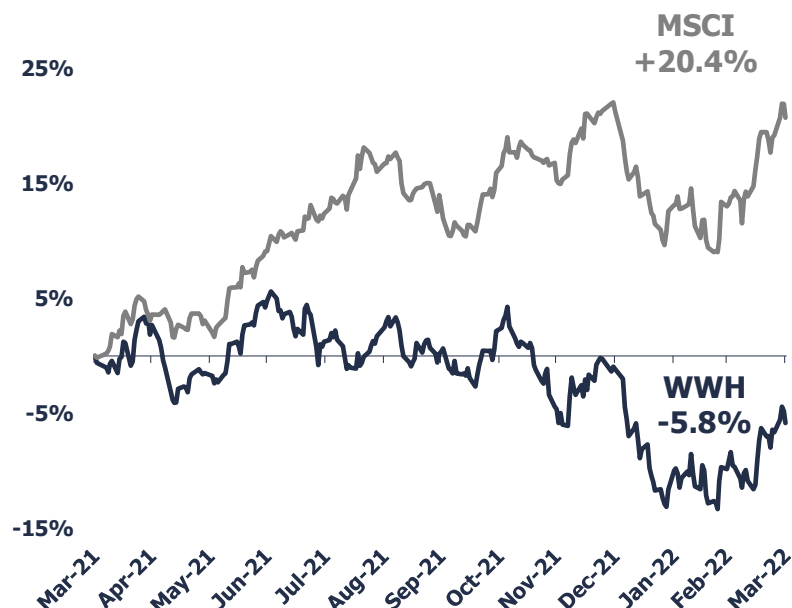
## FY2021 (ending March 31, 2021)

- FY2021 was one of the best years for the performance of WWH
- Despite the pandemic volatility, Healthcare traded mostly on fundamentals
- Our strategy of investing in innovation was successfully rewarded



## FY2022 (ending March 31, 2022)

- FY2022 has been a challenging year
- Large portions of Healthcare have traded almost exclusively on macro factors
- Our investment strategy was a mis-match for this environment



# Performance Drivers

**Drivers of performance in 2021 have been practically the inverse of 2020**

## CY2020

- Fundamental factors moved stocks
- Biotech “bull” market
- China healthcare outperformance
- IPO market strong
- Drug pricing “backburner”
- Small cap outperformance
- Value to growth rotation
- COVID tailwinds for healthcare
- Catalysts rewarded
- No war
- Fed status quo
- No inflation



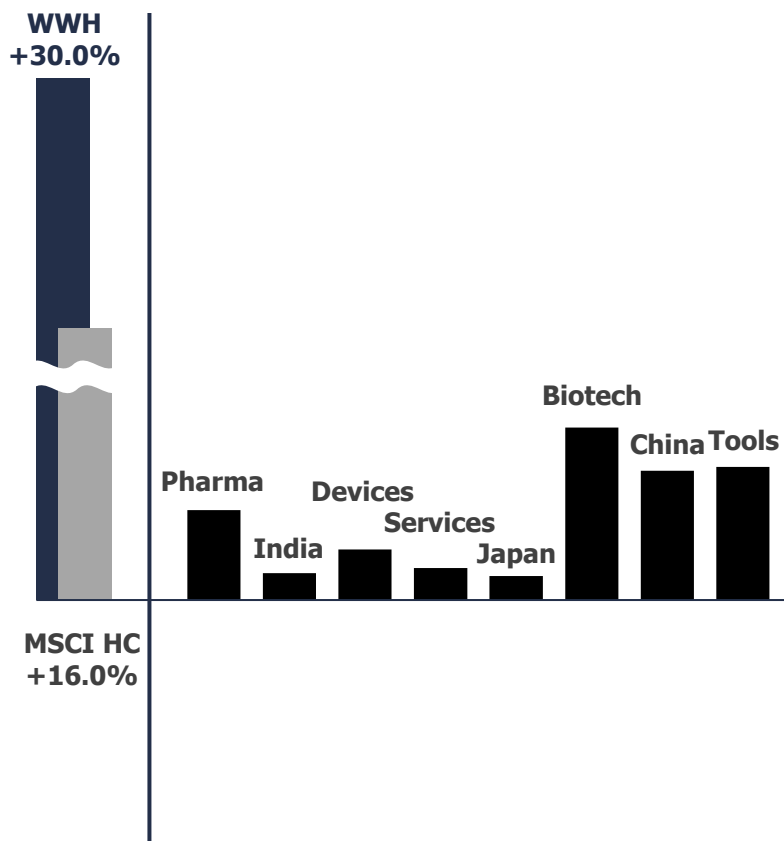
## CY2021

- Macro factors moved stocks
- Biotech “bear” market
- China healthcare sell-off
- IPO market fades
- Drug pricing overhang
- Small cap underperformance
- Growth to value rotation
- COVID headwinds for healthcare
- Catalysts punished
- Russia invades Ukraine
- Fed tightening
- Rapid inflation

**Despite our optimism that the turn of the calendar year would see a reversion, the first half of CY22 has seen a worsening of the trends of 2021.**

# Sources of Absolute Contribution – FY2022 (March 31, 2022)

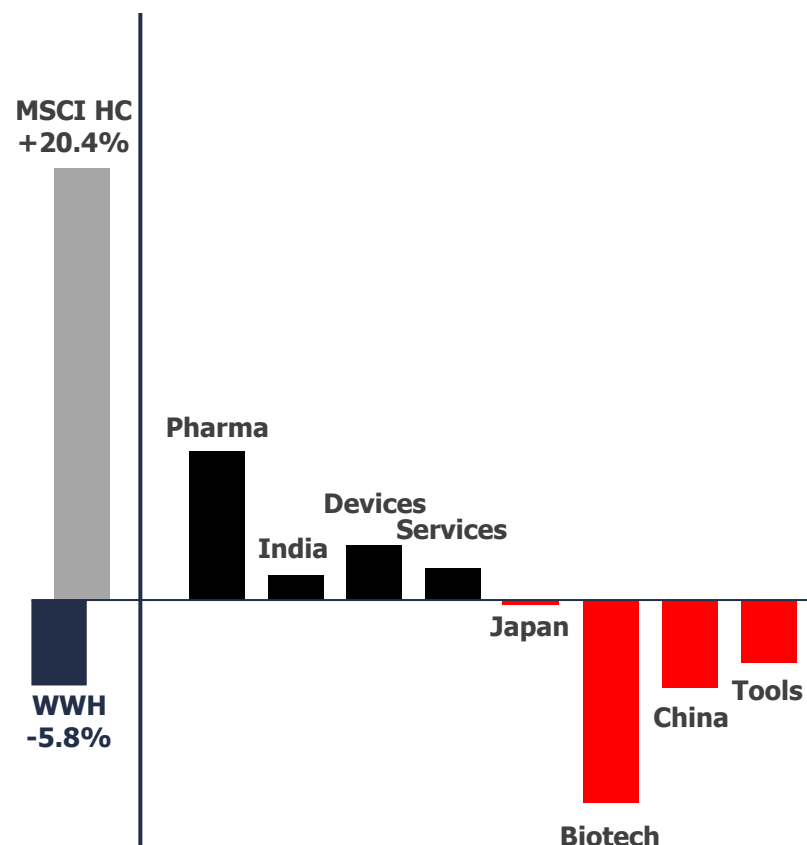
## FY2021: Positive fundamentals and “COVID-halo” drive healthcare stocks higher



**Our two KEY strategic overweights → the largest source of OUT-performance.**

Source: Bloomberg PORT

## FY2022: Macro factor drive large caps higher → sole driver of benchmark returns



**Our two KEY strategic overweights → the largest source of UNDER-performance.**

Source: Bloomberg PORT

# FY2022: Top 5 Contributors / Detractors

## Top 5 Contributors

	Country	Sector	Contribution £'000	Contribution per share* £
Abbvie	USA	Pharmaceuticals	43,658	0.7
AstraZeneca	UK	Pharmaceuticals	39,516	0.6
UnitedHealth Group	USA	Healthcare Providers & Services	29,254	0.4
Shanghai Bio-Heart Biological Technology	China	Healthcare Equipment & Supplies	24,934	0.4
Bristol-Myers Squibb	USA	Pharmaceuticals	24,633	0.4

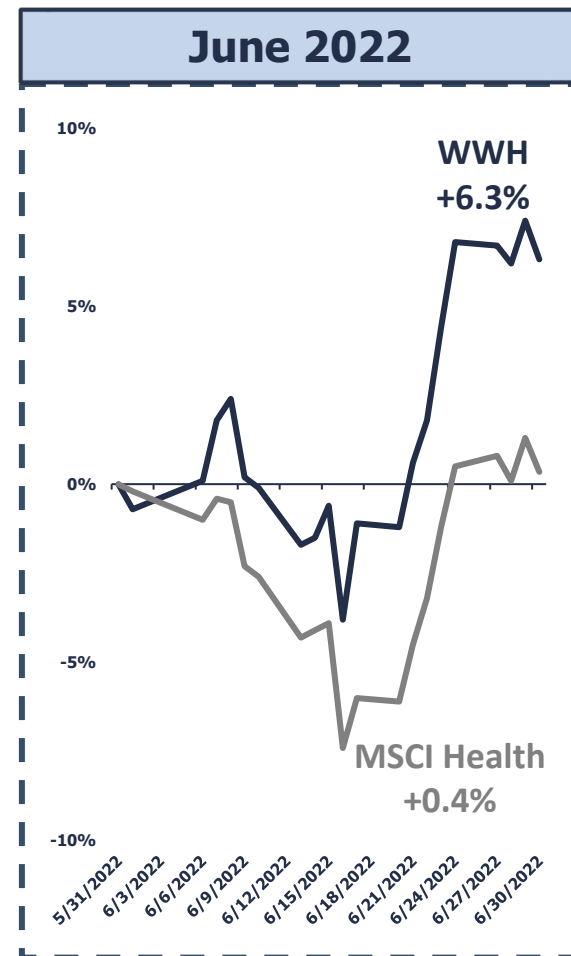
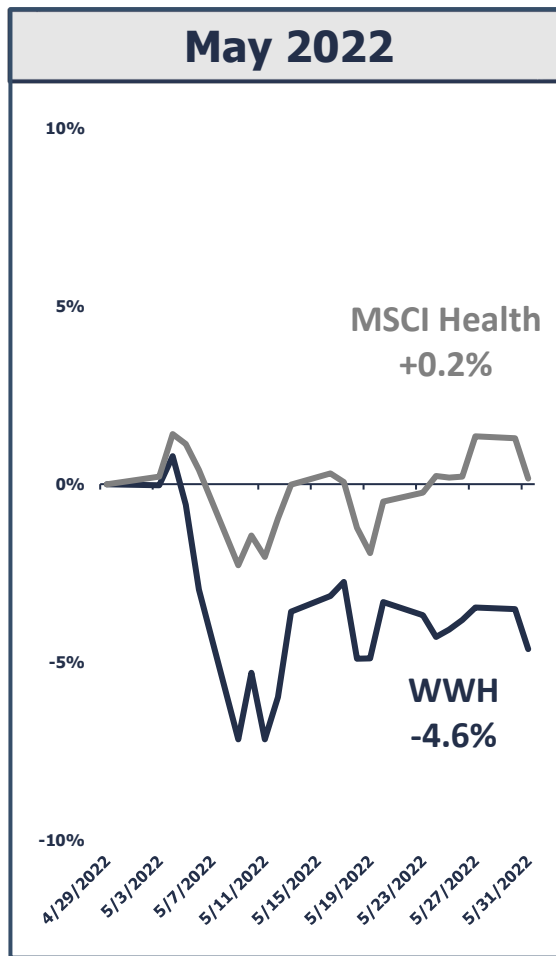
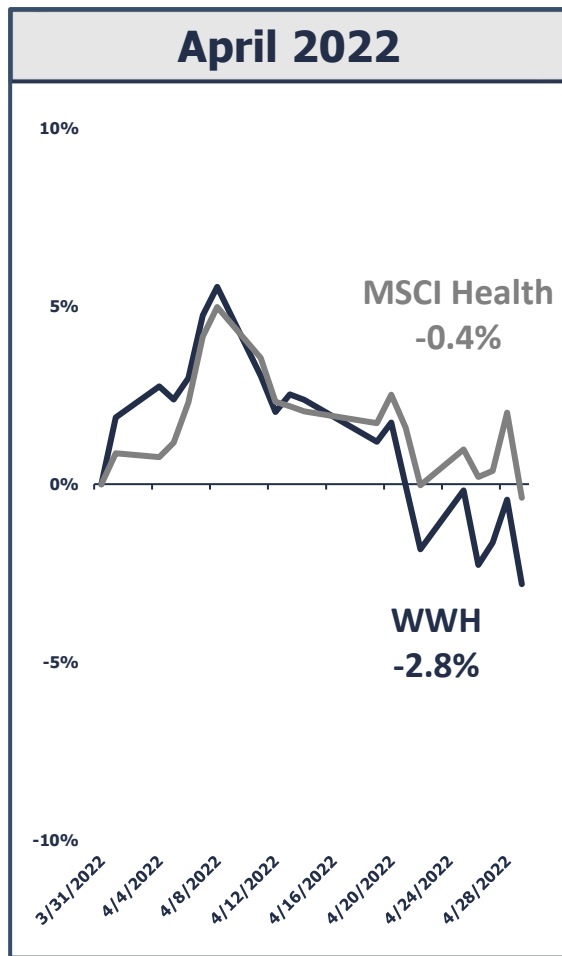
## Top 5 Detractors

SPDR S&P Biotech ETF **	USA	Biotechnology	(26,637)	(0.4)
Deciphera Pharmaceuticals **	USA	Biotechnology	(32,923)	(0.5)
Guardant Health	USA	Life Sciences Tools & Services	(34,062)	(0.5)
Natera	USA	Life Sciences Tools & Services	(35,122)	(0.5)
Mirati Therapeutics	USA	Biotechnology	(45,742)	(0.7)

Past performance is no guarantee of future results. See Endnotes for more information. Excludes the effect of Structured Finance and Options and represents fund performance before fees and costs. Total return numbers are estimated and based on an unaudited holdings-based attribution model that excludes trading costs, fees, and expenses.

# Performance FY1Q22 – are we at the turn?

## Macro-driven performance continued in April and May 2022...



...but June 2022 performance may be signaling a turn.



## Investment Themes

# Performance Drivers for FY2023

## **Overhangs Lifting:**

**U.S. FDA  
U.S. Drug Pricing  
Reform  
Biopharma  
M&A**

## **Rebound in Emerging Biotechnology**

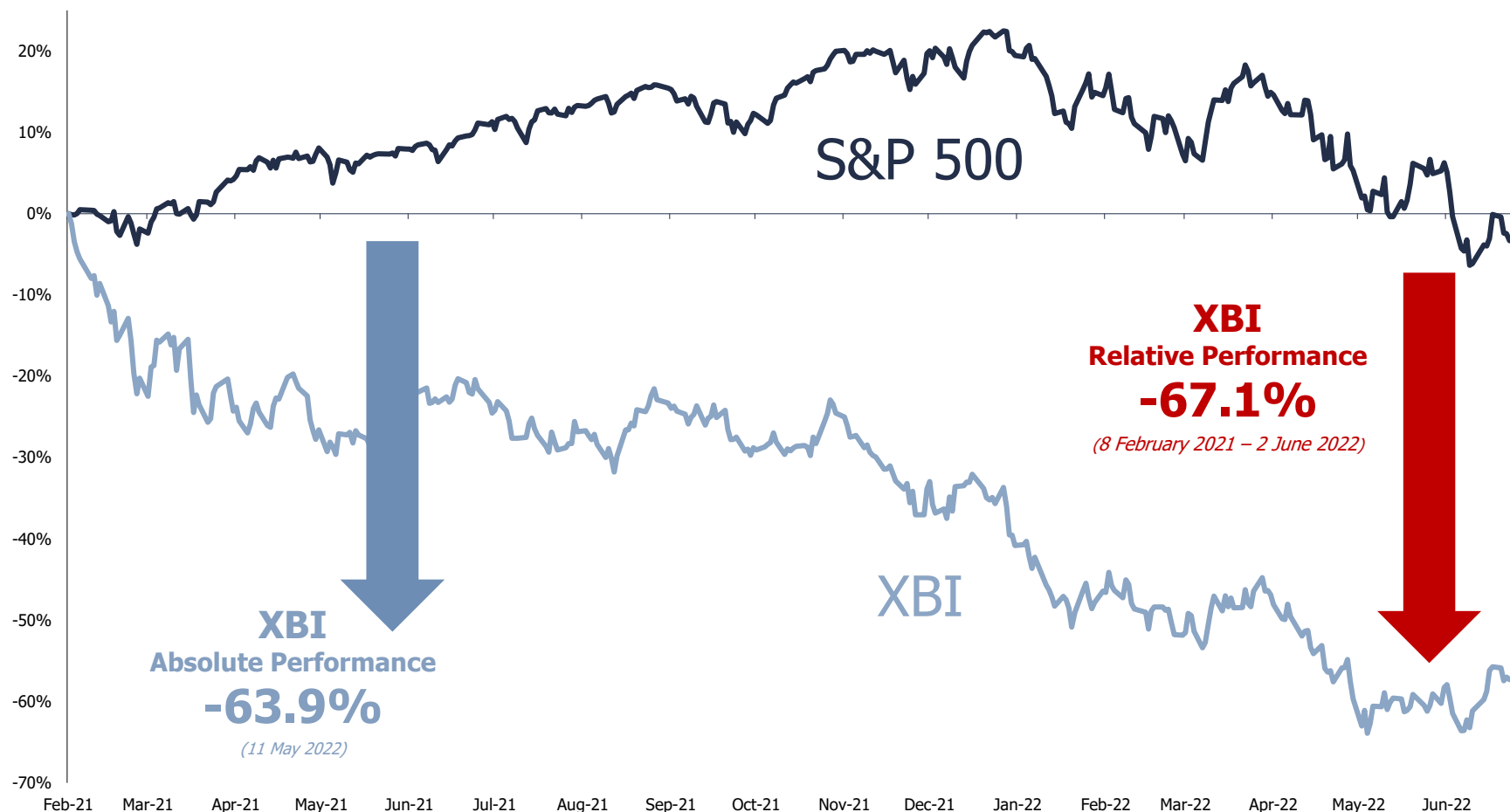
## **Strong Performance from Innovative, High-growth Companies**

## **Innovation**

## **Positioning**

# When Will the Dreadful Biotech Bear Market End?

## S&P Biotechnology Index (XBI) vs. S&P 500 Index



Record Setting: (1) Longest, (2) Largest Absolute, (3) Largest Relative

Source: Bloomberg, OrbiMed

Note: Chart begins on 8 February 2021 and is updated through 30 June 2022. Drawdown as of 30 June 2022 was -54.0%

© 2022 OrbiMed Advisors LLC. All Rights Reserved. CONFIDENTIAL

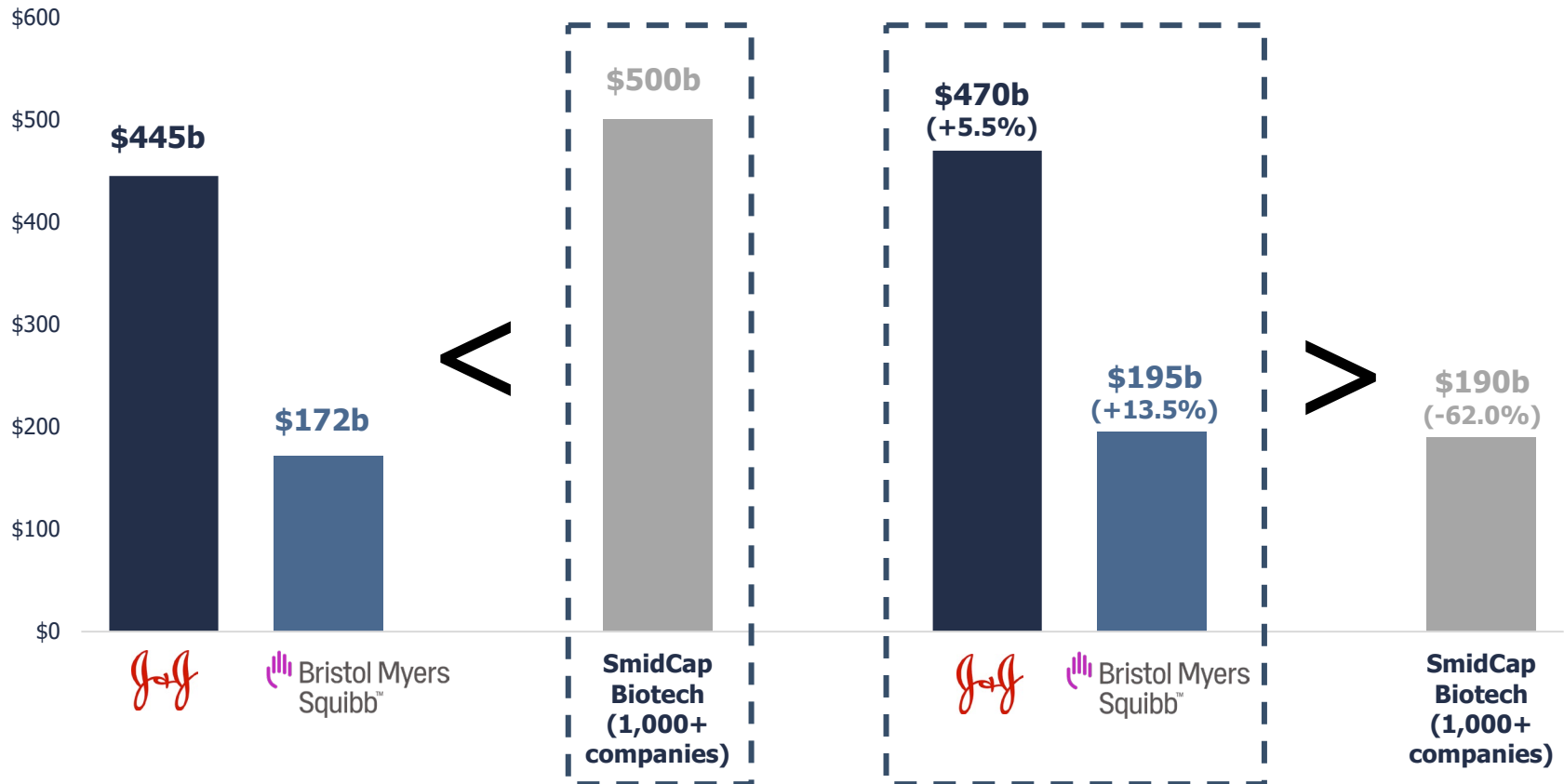


# Biotech Valuations – how low can they go?

## Enterprise Value

**8 February 2021**

**30 June 2022**



Source: Bloomberg

© 2022 OrbiMed Advisors LLC. All Rights Reserved. CONFIDENTIAL

# Biotech Valuations at 20-Year Lows

## Biotech stocks trading below cash:

**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 30 June 2022*

# Healthcare Overhangs Lifting...

1

## U.S. Food & Drug Administration

- Agency operating "near normal" despite COVID pressures
- Record # of new drug approvals the past 5 years (256)
- The vacant Commissioner's seat was finally filled



Dr. Robert Califf

- World renowned cardiologist
- Duke University
- Previous Commissioner 2015-17
- Appointed by President Obama
- Viewed as "Industry Friendly"

We believe Dr. Califf's appointment will be viewed as a net positive for the biopharma industry.

2

## U.S. Drug Price Reform

- Investor "wall of worry" over Biden Administration's drug price reforms has been building since January 2021
- This issue was partially responsible for significant compression of healthcare multiples
- However, broad Democratic support failed in the fall 2021
- Now, Russia's invasion of Ukraine and other economic concerns have completely altered Biden's focus



We now expect the "BBB" bill (and US drug price reform) to totally fade away --- especially as we approach midterm elections later this year.

3

## M&A Acceleration Expected



*"Business development remains our top priority to further renew and diversify our portfolio"*  
- Giovanni Carforio, Q1 2022

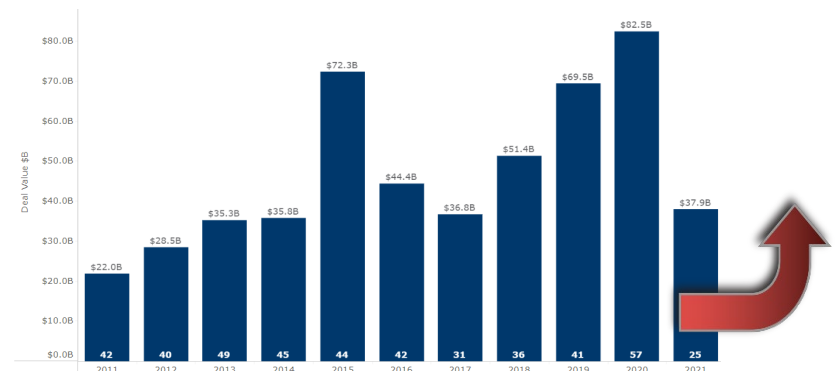


*"While we have a strong track record of business development, we know we need to do more."*  
- Rob Davis, Q1 2022



*"On M&A, we have said repeatedly that we are most interested in compounds that have potential to be real breakthroughs"*  
- Albert Bourla, Q1 2022

### Number of M&A Transactions + Total Deal Value



Source: BIO

# Innovation: The Next Big Thing?

## Oncology



### ADCs



### IO



### Targeted Therapy



## Obesity



### tirzepatide



### semaglutide



### danuglipron



## Alzheimer's



### gantenerumab

### GRADUATE 1/2 CLINICAL TRIALS



### lecanemab



### donanemab



Note: The above does not represent current portfolio holdings.

# Enhertu: Key Growth Driver for Two Portfolio Positions

## ADC: 3<sup>rd</sup> Generation Antibody Drug Candidate

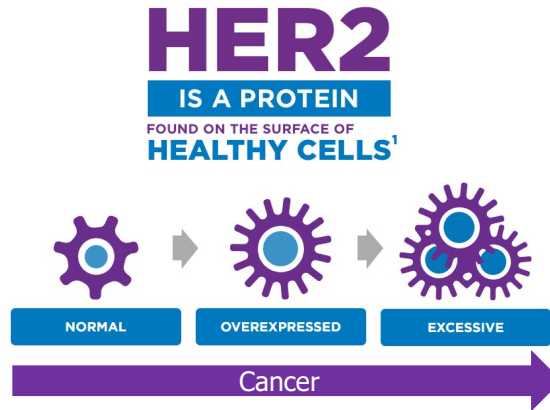
Discovered by:



Co-marketed &  
Co-Developed by:



Overexpression of HER2  
leads to cancer



Enhertu  
First FDA Approval: Dec '19



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

**UNPRECEDENTED**  
**EFFICACY**

Metastatic Breast Cancer

**HIGH HER2+ EXPRESSION**  
**EFFICACY SUPERIOR TO KADCYLA**

↓ Risk of Death by 72%

**LOW HER2+ EXPRESSION**  
**ESTABLISHED NEW STANDARD OF CARE**

↓ Risk of Death by 50%

Additional Indications

- Gastric
- Colon
- Lung
- Earlier lines of therapy

Mega-Blockbuster with peak sales potential in excess of

**\$15 billion**

Source: Various broker research reports, company reports and analysis by OrbiMed. Overall Market Potentials are estimates of aggregate potential peak sales for all drugs launched or expected to be launched in the relevant category. Such estimates are based on various assumptions and are subject to the occurrence of future events.

© 2022 OrbiMed Advisors LLC. All Rights Reserved. CONFIDENTIAL



## Portfolio & Positioning

# WWH vs. MSCI World Health Care Index

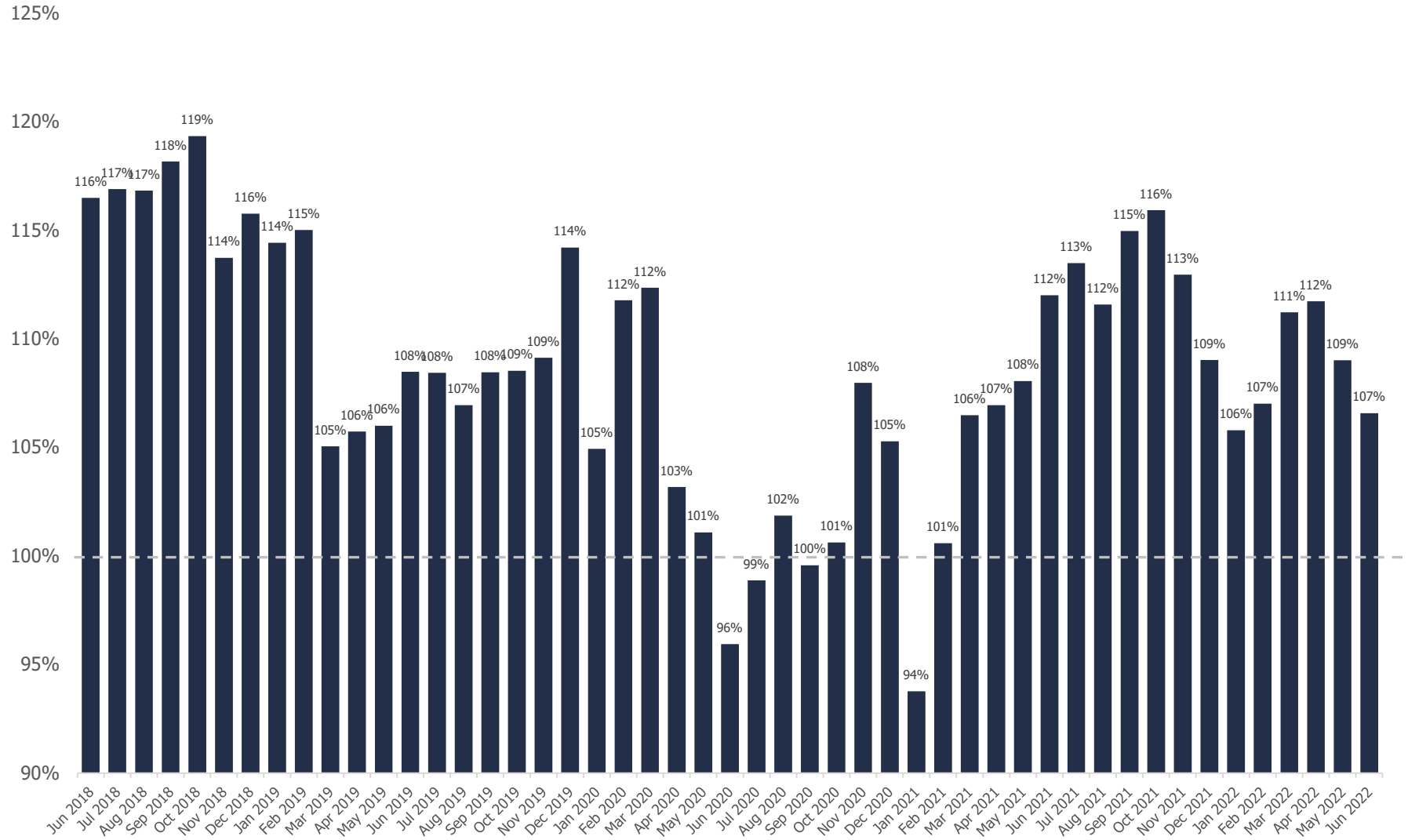
As of June 30, 2022

Subsector	WWH %NAV	MSCI World HC	Delta
<b>Pharmaceuticals</b>	<b>32.0</b>	<b>45.1</b>	<b>(13.1)</b>
Big Pharma	28.2	41.4	<b>(13.2)</b>
Spec Pharma/Generics	3.8	3.7	<b>0.1</b>
<b>Biotechnology</b>	<b>24.2</b>	<b>8.3</b>	<b>15.9</b>
Big Biotech	0.0	4.4	<b>(4.4)</b>
Emerging Biotech	24.2	3.9	<b>20.3</b>
<b>Life Science Tools</b>	<b>4.2</b>	<b>11.0</b>	<b>(6.9)</b>
<b>Medtech/Devices</b>	<b>13.8</b>	<b>15.2</b>	<b>(1.4)</b>
<b>Healthcare Services</b>	<b>11.5</b>	<b>16.2</b>	<b>(4.7)</b>
<b>Japan</b>	<b>2.5</b>	<b>4.2</b>	<b>(1.6)</b>
<b>Emerging Markets</b>	<b>10.1</b>	<b>0.0</b>	<b>10.1</b>
<b>Structured Finance</b>	<b>0.6</b>	<b>0.0</b>	<b>0.6</b>
<b>Privates</b>	<b>7.7</b>	<b>0.0</b>	<b>7.7</b>
<i>Total</i>	<b>106.6</b>	<b>100.0</b>	<b>6.6</b>

*\*Excludes Options. Future weightings may differ.*

# WWH Leverage over Time

## As of June 30, 2022



Source: OrbiMed, Bloomberg PORT



# Worldwide Healthcare Trust Holdings

## As of June 30, 2022

	Market Price \$ Millions	Pct. Value		Market Price \$ Millions	Pct. Value		Market Price \$ Millions	Pct. Value
<b>Biotechnology</b>			<b>Healthcare Services / Distributors</b>			<b>Medtech</b>		
Achilles Therapeutics PLC	3.5	0.1	Evolut Health Inc	39.2	1.4	Boston Scientific Corp	110.8	4.0
Arcutis Biotherapeutics Inc	17.7	0.6	Humana Inc	124.6	4.5	Edwards Lifesciences Corp	76.4	2.7
Argenx SE	42.9	1.5	Progyny Inc	13.8	0.5	Intuitive Surgical Inc	80.5	2.9
BioMarin Pharmaceutical Inc	87.6	3.2	Tenet Healthcare Corp	27.4	1.0	RxSight Inc	15.0	0.5
Celldex Therapeutics Inc	2.7	0.1	UnitedHealth Group Inc	115.2	4.1	SI-BONE Inc	25.0	0.9
Erasca Inc	9.3	0.3		<b>320.1</b>	<b>11.5</b>	Stryker Corp	76.1	2.7
Global Blood Therapeutics Inc	36.4	1.3	<b>Emerging Markets</b>				<b>383.8</b>	<b>13.8</b>
Harpoon Therapeutics Inc	2.8	0.1	Abbisko Cayman Ltd	4.2	0.2	<b>Privates</b>		
Ikena Oncology Inc	7.2	0.3	Aier Eye Hospital Group Co Ltd	15.5	0.6	API Holdings	28.1	1.0
Ionis Pharmaceuticals Inc	7.3	0.3	Alphamab Oncology	12.9	0.5	Caris	45.0	1.6
Iovance Biotherapeutics Inc	6.5	0.2	Apollo Hospitals Enterprise Lt	45.1	1.6	Caris Series D	5.1	0.2
MeiraGTx Holdings plc	8.5	0.3	Arrail Group Ltd	22.2	0.8	Crossover	21.4	0.8
MERGER BASKET	121.0	4.4	Burning Rock Biotech Ltd	2.2	0.1	DingDang	16.4	0.6
Mirati Therapeutics Inc	47.6	1.7	China Medical System Holdings	2.5	0.1	Edda	20.6	0.7
Neurocrine Biosciences Inc	53.5	1.9	Clover Biopharmaceuticals Ltd	3.8	0.1	MabPlex	7.4	0.3
Passage Bio Inc	4.9	0.2	Joynn Laboratories China Co Lt	26.4	1.0	Peloton	0.6	0.0
Seagen Inc	65.6	2.4	MicroTech Medical Hangzhou Co	1.0	0.0	RIMAG	15.4	0.6
Turning Point Therapeutics Inc	34.9	1.3	New Horizon Health Ltd	10.6	0.4	Ruipeng Pet Group	17.0	0.6
uniQure NV	15.4	0.6	Shanghai Bio-heart Biological	58.3	2.1	Visen	17.2	0.6
Vertex Pharmaceuticals Inc	82.7	3.0	Shanghai Bio-heart Biological	23.8	0.9	Yuanxin Tech	18.5	0.7
Vor BioPharma Inc	4.1	0.1	Shanghai Fosun Pharmaceutical	14.8	0.5		<b>212.9</b>	<b>7.7</b>
Xenon Pharmaceuticals Inc	10.9	0.4	Shanghai Kindly Medical Instru	21.3	0.8	<b>Structured Finance &amp; Privates</b>		
	<b>673.2</b>	<b>24.2</b>	Shenzhen Hepalink Pharmaceutical	10.7	0.4		<b>228.4</b>	<b>8.2</b>
<b>Pharmaceuticals</b>			Simcere Pharmaceutical Group L	2.2	0.1	<b>Cash</b>		
AbbVie Inc	118.2	4.3	United Laboratories Internatio	4.0	0.1		<b>-182.6</b>	<b>-6.6</b>
AstraZeneca PLC	175.6	6.3		<b>281.5</b>	<b>10.1</b>	<b>Total Portfolio</b>		
Bristol-Myers Squibb Co	156.1	5.6	<b>Life Science Tools &amp; Services</b>				<b>2778.5</b>	<b>100.0</b>
Chugai Pharmaceutical Co Ltd	21.4	0.8	Guardant Health Inc	30.1	1.1			
Daiichi Sankyo Co Ltd	27.7	1.0	Natera Inc	38.2	1.4			
Eisai Co Ltd	21.2	0.8	Thermo Fisher Scientific Inc	47.0	1.7			
Horizon Therapeutics Plc	105.3	3.8		<b>115.3</b>	<b>4.2</b>			
Pfizer Inc	103.2	3.7						
Roche Holding AG	125.8	4.5						
Sanofi	104.4	3.8						
	<b>958.8</b>	<b>34.5</b>						

	WWH %NAV	WWH Active Share%
Top 10	45.2	67.4%
Top 15	60.7	
Top 20	71.6	WWH % Equity Book [Companies with Positive Net Income]
Top 30	85.5	
		74%

# Playbook for 2022 and Beyond

1	Continue to Invest in Innovation – Non-Therapeutics (Medical Technology, Diagnostics, Life Science Tools)	
2	Continue to Invest in Innovation – Therapeutics (Smid-Cap Biotechnology, Select Pharmaceuticals)	
3	Reposition the Portfolio for Dislocated Sectors (Emerging Biotechnology & China)	
4	Key Overhangs Lifting (FDA & US Drug Price Reform )	
5	Increased Expectations for BioPharma M&A	
6	Re-ignite our Catalyst Strategy	
7	Continue to use Gearing in a Tactical Fashion	
8	Overall Bullish Outlook (high innovation, low valuations, reversion to the mean, receding political risks)	

# Endnotes

## General Notes

1. The information presented herein relates to Worldwide Healthcare Trust PLC and the Biotech Growth Trust PLC (together, 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.
2. 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.
3. Opinions and estimates may be changed without notice. This presentation is as of the date hereof and may be changed without notice, and nothing herein shall, under any circumstances, create any implication that there has been no change in the affairs of the Funds since the date hereof. OrbiMed does not warrant or guarantee the accuracy or completeness of the information presented herein.
4. This document has been prepared solely for prequalification and discussion purposes and should not be relied upon in evaluating the merits of investing in any securities. It does not purport to be all inclusive or to contain all the information that a prospective investor may desire in investigating a potential investment in the Funds. Prospective investors are cautioned not to rely on the prior returns or other information set forth herein in deciding whether to purchase any Interests and must conduct and rely on their own evaluation of the Funds and the terms on which Interests may be offered, including the merits and risks involved, in making an investment decision with respect to the Interests.
5. **An investment in the Funds is speculative and involves a high degree of risk.** In considering an investment in the Funds, prospective investors should be aware of certain 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 a 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 Funds; and tax-related risks arising from the status and operation of the Funds. See the Fund Documents for more detail on those and other risks related to investing in the Funds.
6. No guarantee or representation is made that the Funds will achieve their investment objective or that the Funds' risk management strategies will be successful. The Funds' performance may be volatile, and investors in the Funds could lose all or a substantial amount of their investment. In addition, the fees and expenses charged in connection with an investment in the Funds may be higher than those charged in connection with other investments, and in some market conditions may offset trading profits. Accordingly, Interests are suitable only for sophisticated investors for whom an investment in the Funds does not constitute a complete investment program and who fully understand and are willing to assume the risks involved in the Funds' investment program.
7. An investment in the Funds is also suitable only for investors who have no need for immediate liquidity in their investment because Interests are not freely transferable and may be withdrawn or redeemed only under the limited circumstances set forth in the Fund Documents. There is no public or secondary market for Interests and it is not expected that a public or secondary market will develop.
8. Prospective investors are not to construe the contents of this presentation as legal, business or tax advice. Each investor should consult such advisers as it deems appropriate concerning a potential investment in the Funds.
9. No securities commission or regulatory authority in the United States or in any other country has in any way passed upon the merits of an investment in the Funds or the accuracy or adequacy of this information booklet or the material contained herein.

# Endnotes (continued)

## Indices

Information about indices is provided to allow for comparison of the performance of the Funds to that of certain recognized healthcare industry indices. Investors cannot invest directly in an index, which also does not take into account trading commissions and costs. The volatility of indices may be materially different from the performance of the Funds. In addition, the Funds' portfolio holdings may differ significantly from the securities that comprise the indices.

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.