



Worldwide Healthcare Trust

Mid-Year Update

12 October 2023

Portfolio Managers: Sven Borho & Trevor Polischuk

Sven Borho, CFA

Managing Partner



Sven H. Borho, CFA, is a founding Partner of OrbiMed. Mr. Borho heads the public equity team and he is the portfolio manager for OrbiMed's public equity and hedge funds.

Mr. Borho has played an integral role in the growth of OrbiMed's asset management activities. Mr. Borho started his career in 1991 when he joined OrbiMed's predecessor firm as a Senior Analyst covering European pharmaceutical firms and biotechnology companies worldwide. He has been a portfolio manager since 1993.

Mr. Borho studied business administration at Bayreuth University in Germany and received a M.Sc. (Econs.), Accounting and Finance, from The London School of Economics.

Trevor Polischuk, PhD

Partner



Trevor M. Polischuk, Ph.D., is a Partner on the public equity team, focused on the global pharmaceutical industry.

Previously, Dr. Polischuk worked at Lehman Brothers as a Senior Research Analyst covering the U.S. pharmaceutical industry. Dr. Polischuk began his career at Warner Lambert as a member of the Pharmaceutical Global Marketing Planning team, focused on commercial forecasts for the global pipeline.

Dr. Polischuk holds a Doctorate in Neuropharmacology & Gross Human Anatomy from Queen's University and an M.B.A. from Queen's University in Kingston, Ontario, Canada.



WORLDWIDE
HEALTHCARE
TRUST

Agenda

- 1 Performance
- 2 2023 Investment Themes Recap
- 3 Emerging Themes for 2024+
- 4 Portfolio and Positioning
- 5 Playbook
- 6 Q&A

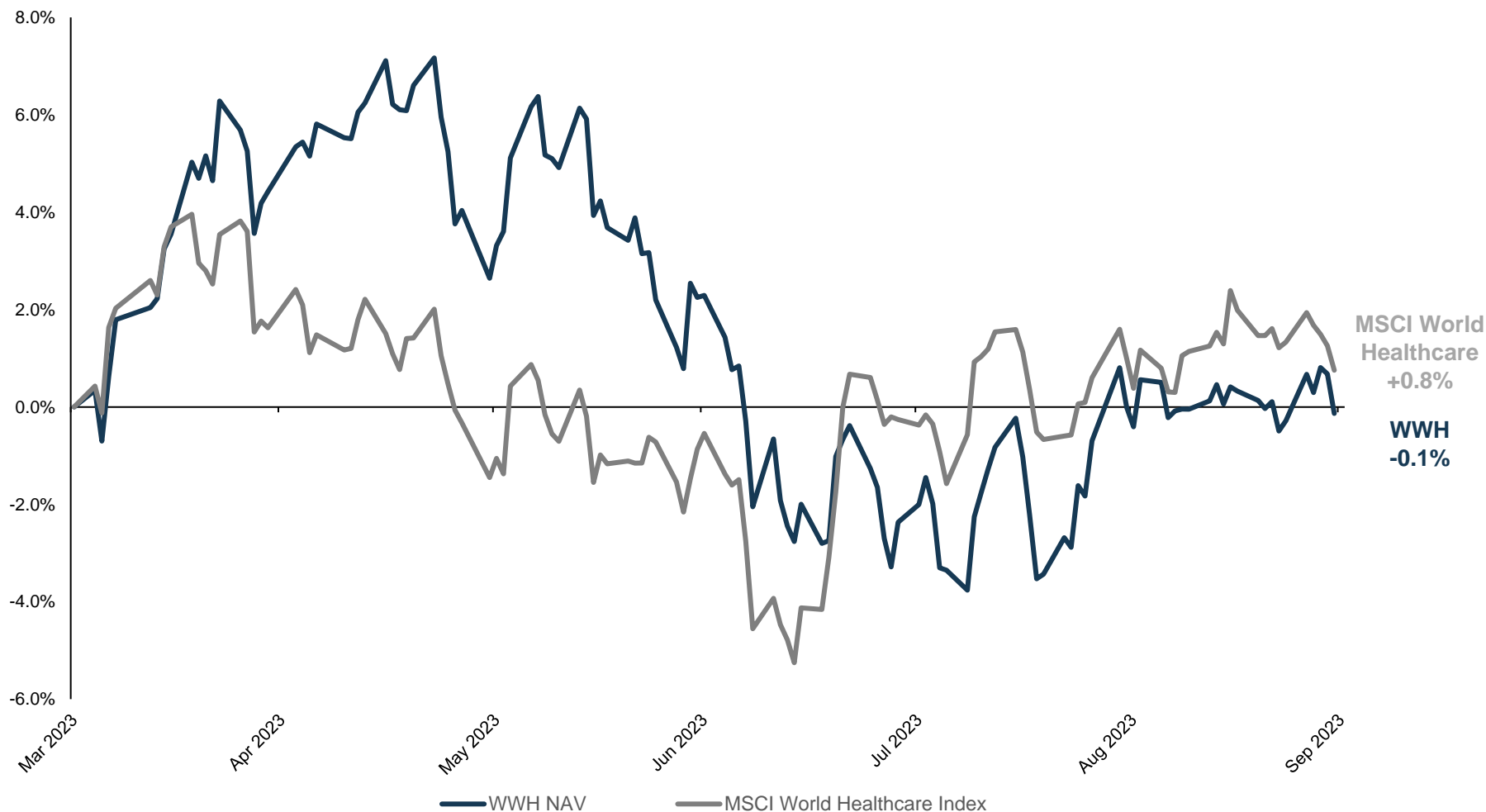


WORLDWIDE HEALTHCARE TRUST

Performance

FYTD Performance

6 months (to 29 September 2023)



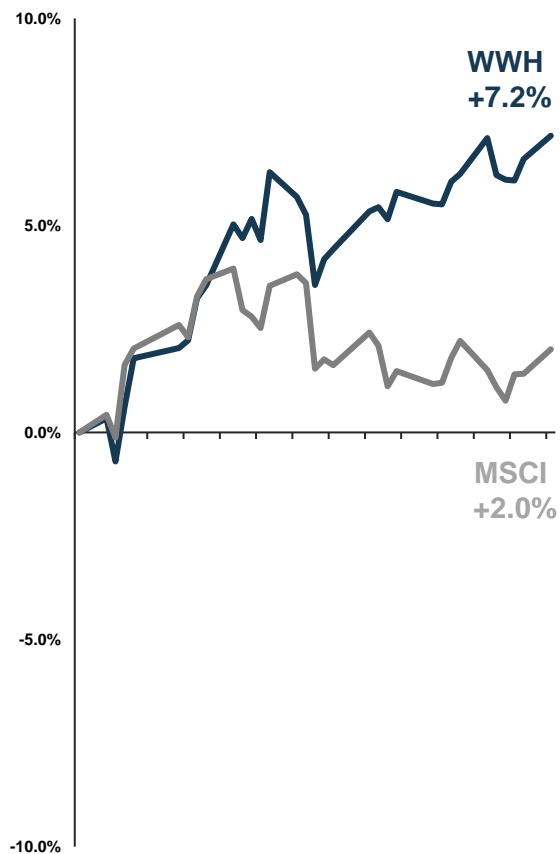
Source: Bloomberg, OrbiMed; Data updated through 29 September 2023

Note: WWH performance figures are net of fees

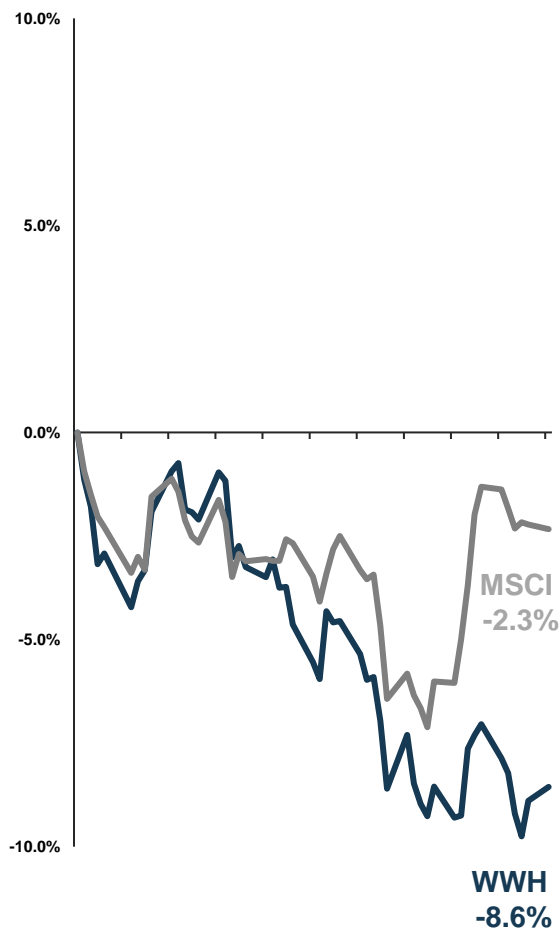
FYTD Performance

6 months (to 29 September 2023)

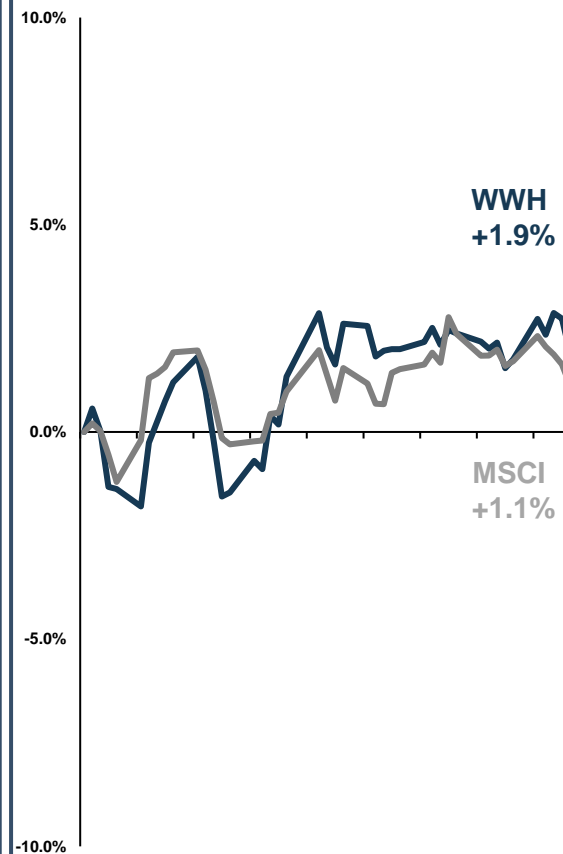
1 April 2023 – 22 May 2023



23 May 2023 – 31 July 2023

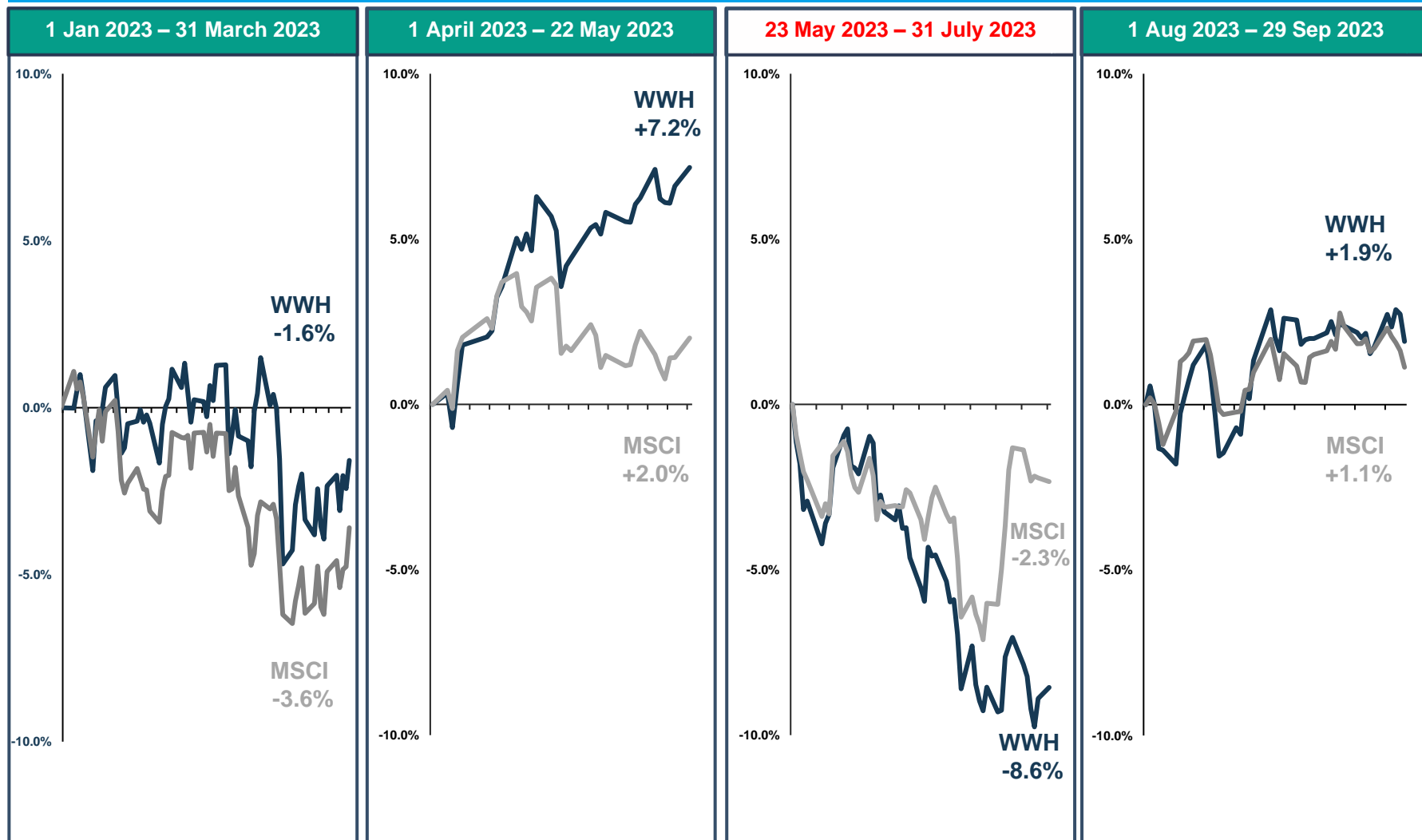


1 Aug 2023 – 29 Sep 2023



CYTD Performance

9 months (to 29 September 2023)

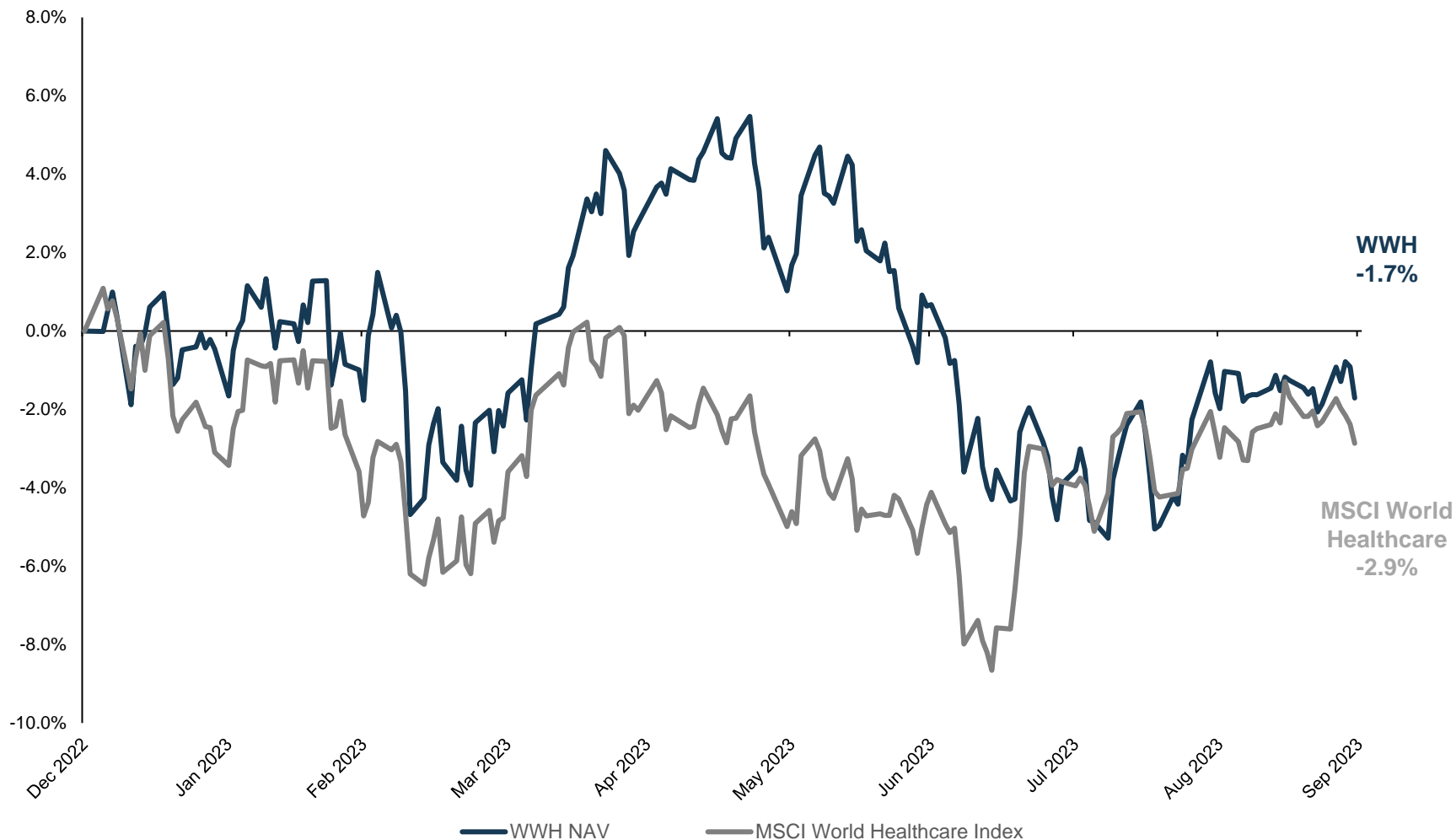


Source: Bloomberg, Orbimed; Data updated through 29 September 2023

Note: WWH performance figures are net of fees

CYTD Performance

9 months (to 29 September 2023)

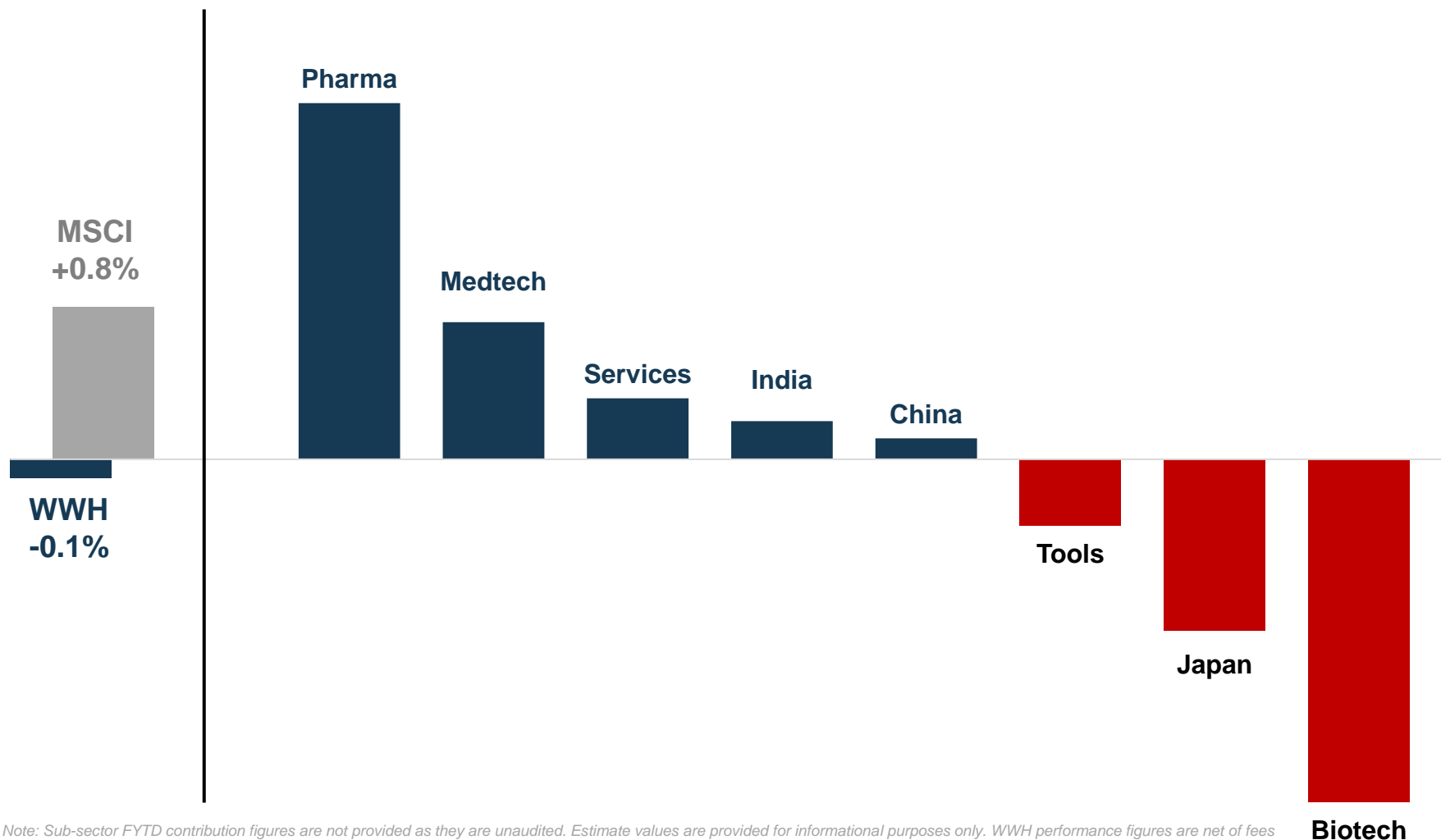


Source: Bloomberg, OrbiMed; Data updated through 29 September 2023

Note: WWH performance figures are net of fees

Attribution (Absolute)

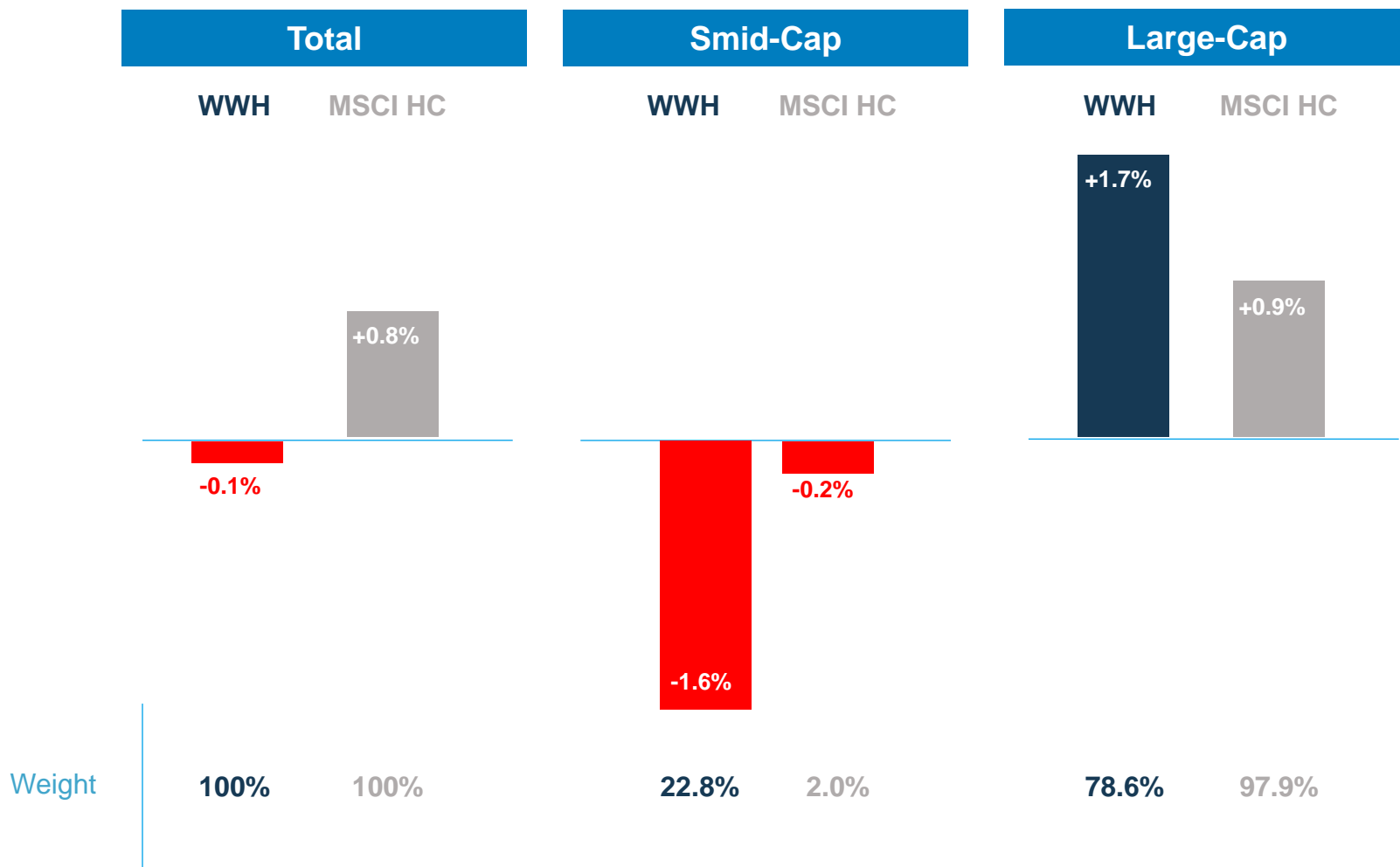
6 months (to 29 September 2023)



Note: Sub-sector FYTD contribution figures are not provided as they are unaudited. Estimate values are provided for informational purposes only. WWH performance figures are net of fees
Source: Bloomberg, OrbiMed

FYTD Attribution (by Market Cap)

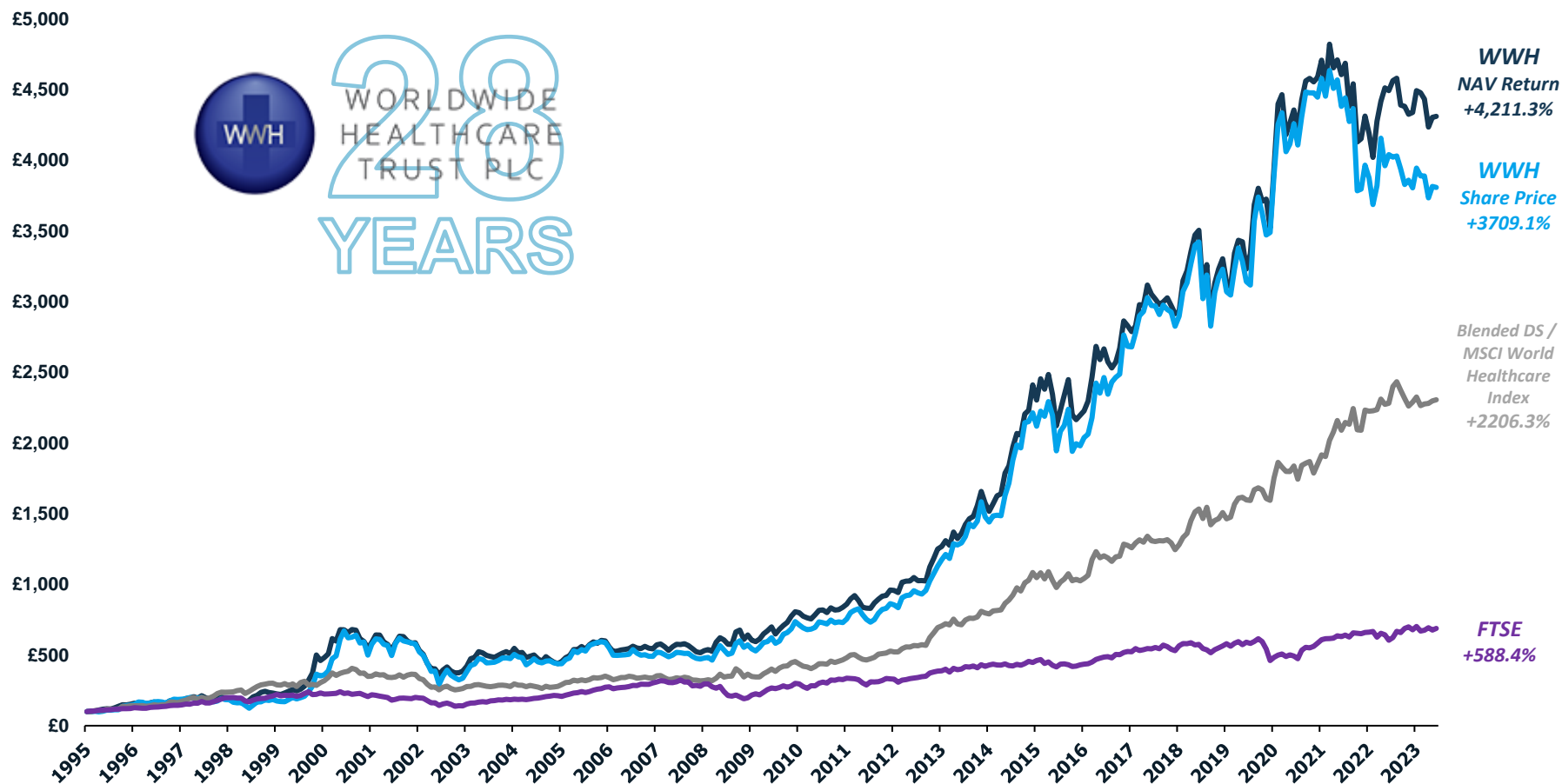
6 months (to 29 September 2023)



Source: Bloomberg, OrbiMed

Performance Since Inception

Multiple: **42x** 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 29 September 2023.



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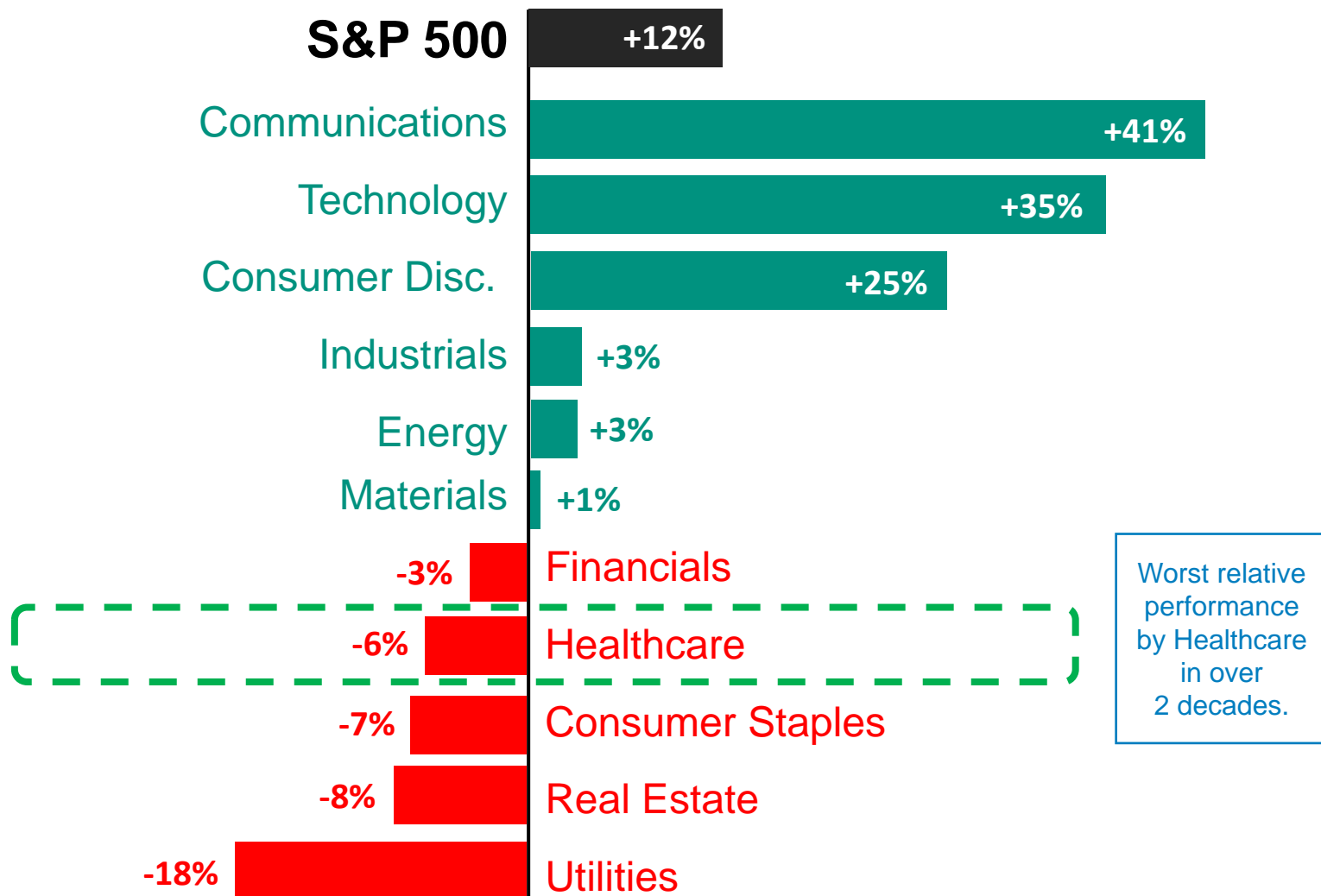
2023 Investment Themes Recap

2023 Investment Themes Recap



S&P 500 Performance CYTD

S&P Constituents by Industry (29 September 2023)



Source: Bloomberg

Note: Chart begins on Jan 1, 2023 and is updated through Sept 29, 2023

Dreadful Biotech Bear Market Continues to Underperform

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



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

Source: Bloomberg, OrbiMed

Note: Chart begins on 8 February 2021 and is updated through 29 September 2023

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 for patients
- 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.**

A Conversation with Dave Ricks – CEO, Eli Lilly & Co.

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



Lilly



Drug Price Inflation Cap

*“It is not a major issue...it's really kind of a non-event...it's kind of a **nothing burger** from our perspective.”*

Medicare Part D Redesign

*“There are (many) changes to part D design, that we saw as **positive** on a net basis.”*

Medicare Price Negotiations

*“Honestly, it was pretty **disappointing**...”*


















Source: JP Morgan June 2023

The Pharma industry has commenced legal proceedings against HHS

IRA Advances – First 10 Drugs Named

The “List of 10”		Area
1	  Bristol Myers Squibb  Pfizer	CV
2	 	Diabetes
3	 	CV
4	 	Diabetes
5	 	Diabetes
6	 	CV
7	 	RA
8	 	Oncology
9	 	RA
10	 	Diabetes

Source: CMS; IQVIA

Best Selling Drugs	
>\$30bn	COVID  COMIRNATY [®] (COVID-19 Vaccine, mRNA) 
	GENERIC  HUMIRA adalimumab 
	 KEYTRUDA [®] (pembrolizumab) injection 100 mg 
>\$20bn	COVID  SPIKEVAX [™] COVID-19 Vaccine, mRNA 
	COVID  PAXLOVID [™] (nirmatrelvir 150 mg tablets ritonavir 100 mg tablets) 
	LISTED  Eliquis [®] (apixaban) tablets 200 mg 
>\$10bn	GENERIC  Revlimid [®] (lenalidomide) capsules 
	LISTED  imbruvica [®] (ibrutinib) 
	LISTED  Stelara [®] (ustekinumab) 

Net financial impact expected to be modest...

IRA Advances – The Industry Responds

Lawsuits		Arguments	
1	 Pfizer RESEARCH • PROGRESS • HOPE	1	Compelled Speech (1 st Amendment)
2	 U.S. Chamber of Commerce	2	Takings Clause (5 th Amendment)
3	 Bristol Myers Squibb	3	Excessive Fines (8 th Amendment)
4	 Johnson & Johnson	4	Standing Clause
5	 MERCK	5	Due Process
6	 AstraZeneca	6	Orphan Drug Act
7	 NOVARTIS	7	Non-Delegation
8	 Boehringer Ingelheim	8	Separation of Powers
9	 astellas	9	Unconstitutional Condition

The industry is taking a
“shots on goal” approach.

Any judge from any district from
any court could rule in favor of
the industry on any argument.

Even a SINGLE ruling against
the government could halt the
drug price negotiations portion
of the IRA.

Ultimately the Supreme Court
will have the final say.

Optionality to quash price negotiations remains anytime ahead of the 2026 enactment

M&A Activity Surging

2022			
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	Sumitomo	50%
10/18/22	AVEO	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	mirobio	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	GSK	39%

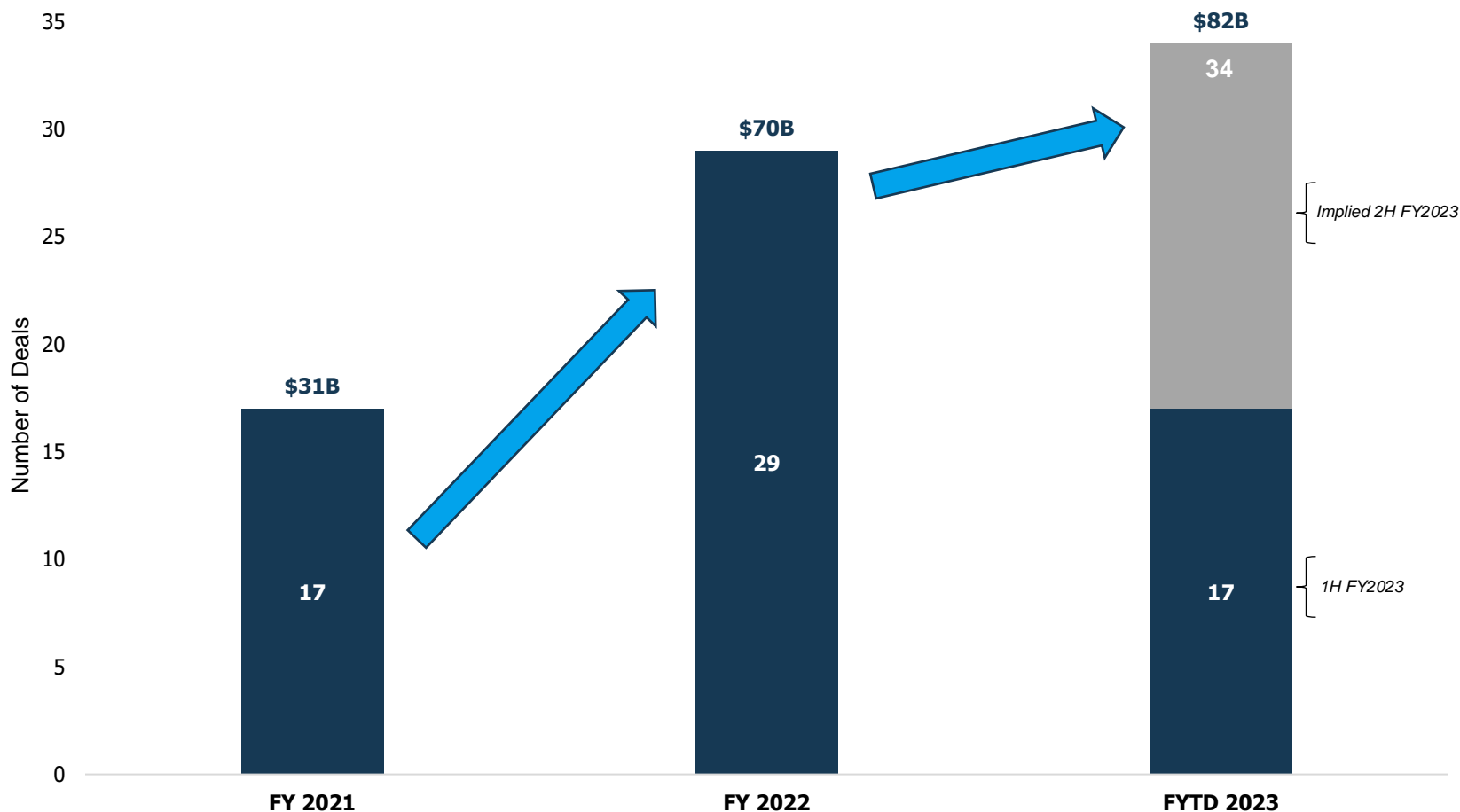
2023			
Date	Target	Acquirer	% Premium
09/26/23	Intercept	ALFASIGMA	82%
08/30/23	EMBARKBIOTECH	novo nordisk	\$519 (private)*
08/14/23	Zynherba	H3 HARMONY BIOSCIENCES	226%
08/10/23	inversago	novo nordisk	\$1,075 (private)
08/09/23	Decibel	REGENERON	169%*
07/28/23	REATA	Biogen	59%
07/17/23	DTX PHARMA	NOVARTIS	\$1,000 (private)*
07/14/23	Versanis	Lilly	\$1,925 (private)
06/29/23	sigilon	Lilly	~380%
06/20/23	DICE	Lilly	~40%
06/12/23	CHINOOK	NOVARTIS	83%
05/22/23	VectivBio	Ironwood	80%
05/10/23	CTI	sobi	89%
04/30/23	IVERIC	astellas	23%
04/25/23	SPECTRUM	ASSERTIO	~94%*
04/18/23	Bellus	GSK	>100%
04/16/23	Prometheus	MERCK	75%
03/27/23	Jounce	Concentra Biosciences	75%
03/13/23	Seagen	Pfizer	42%
03/13/23	proventionbio	sanofi	278%
01/19/23	CoNCERT	SUN PHARMA	~67%*
01/09/23	CINCOR	AstraZeneca	>200%*
01/09/23	Albireo	IPSEN	>100%
01/08/23	AMRYT	Chiesi	>100% (100% CVR)

Source: FactSet, Company Websites as of September 29, 2023

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

M&A Activity Remains Elevated

M&A Activity by Fiscal Year*



M&A activity remains robust in FY23; expected to continue in 2H and beyond

Source: FactSet, data as of September 29, 2023

*Excludes deals with a transaction value over \$40B

Innovation: The Next Big Thing?

Oncology



POSITIVE

ADCs



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

POSITIVE

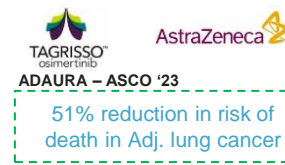
IO



Awaiting the final analysis in
lung cancer, expected 2024

POSITIVE

Targeted Therapy



51% reduction in risk of
death in Adj. lung cancer

FLAURA2 – WCLC '23
38% reduction in PFS or
death in 1L lung cancer

Obesity



POSITIVE

tirzepatide



Filed

POSITIVE

semaglutide



Approved

SELECT CVOT

-20% RRR on MACE

POSITIVE

orals



Positive data across multiple
oral tx's at ADA 2023

Alzheimer's



FAIL

gantenerumab

**GRADUATE 1/2
CLINICAL TRIALS**



Patients on drug improved;
but outcome was not SS

POSITIVE

lecanemab



Met all endpoints & reduced
cognitive decline by -27%

POSITIVE

donanemab



Met all endpoints & reduced
cognitive decline by -36%

Note: Examples may not be representative of portfolio holdings.

2023 “Catalysts to Watch”: Large Cap Pharmaceuticals



There are many highly anticipated catalysts in pharma.



ONCE-WEEKLY
wegovyTM
semaglutide injection **2.4 mg**

SELECT
Cardiovascular
Outcomes Trial

- Showed **-20% RRR** in MACE in obese patients



Dato-DXd

Dato-DXd
TROPION-Lung01
Monotherapy

- Met primary endpoint of PFS...OS immature
- Awaiting final readout



tiragolumab

Phase III
SKYSCRAPER-01

- Leaked interim data showed **+20% benefit**
- Awaiting final readout



DUPIXENT[®]
(dupilumab)

Dupixent^{®A}
COPD

- Showed **-30% RRR** in lowering exacerbations
- Awaiting 2nd trial readout



donanemab

TRAILBLAZER
ALZ-3

- Showed **36% slowing** in cognitive decline

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

Examples may not be representative of portfolio holdings

2023 “Catalysts to Watch”: Medical Technology

UPDATED

Significant improvements in current technologies can materially impact sales.

DELAYED

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.

Whilst the new robot was initially delayed due to regulatory concerns, the company has consistently hinted to an imminent debut of the next generation surgical robot.

POSITIVE

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 clinical trial in paroxysmal Afib showed non-inferior and superior trend vs. SOC

These catalysts can drive end market demand in two “hot” technology areas.

2023 “Catalysts to Watch”: Landmark Catalysts in Biotech

Selected first-in-class approvals and important clinical trial results



First gene therapies approved for hemophilia A and B

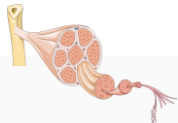
BIOMARIN uniQure



First FDA approval of an oral microbiome therapy for *C. difficile* infection



First topical gene therapy approved for rare genetic skin disease



First gene therapy approved for Duchenne muscular dystrophy



First therapy approved for Friedrich's ataxia



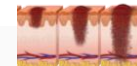
Positive Phase 3 results of RNAi drug in amyloidosis with cardiomyopathy



Positive Phase 3 results of anti-amyloid antibody for Alzheimer's



Positive Phase 3 results of drug for liver fibrosis



Positive Phase 2 results of mRNA cancer vaccine in melanoma



Examples may not be representative of portfolio holdings



WORLDWIDE HEALTHCARE TRUST

Emerging Themes for 2024+

Emerging Themes for 2024+

Obesity



- Supply?
- Lilly's formal launch
 - Global roll outs
- Additional indications
 - Reimbursement
- Next generation injectables
 - Novel orals
 - New targets



Vaccines



- RSV
- Cancer
- COVID?
- Combinations
 - Flu (new)
- Pneumococcal (new)



Oncology



- Rise of IO+IO Combos
 - TIGIT
 - LAG3
 - CTLA4
 - Bi-Specifics
 - ADCs (cont.)
- Targeted Tx (cont.)
- Radiopharmaceuticals



Alzheimer's



- Leqembi launch
- LLY approval/launch
- Earlier intervention
- Next gen products
- New formulations
 - New targets
 - New entrants



Immunology



- "Hot Space" (M&A)
- Psoriasis / HS / AD
 - IBD / UC / CD
 - COPD
- New targets



Cardiovascular



- "Back in Vogue"
 - Factor Xla
 - PAH
 - TTR
 - Lp(a)
- Oral PCSK-9



Examples may not be representative of portfolio holdings



WORLDWIDE HEALTHCARE TRUST

Portfolio and Positioning

WWH vs. MSCI World Health Care Index

As of 29 September 2023

WWH as of 29 September 2023

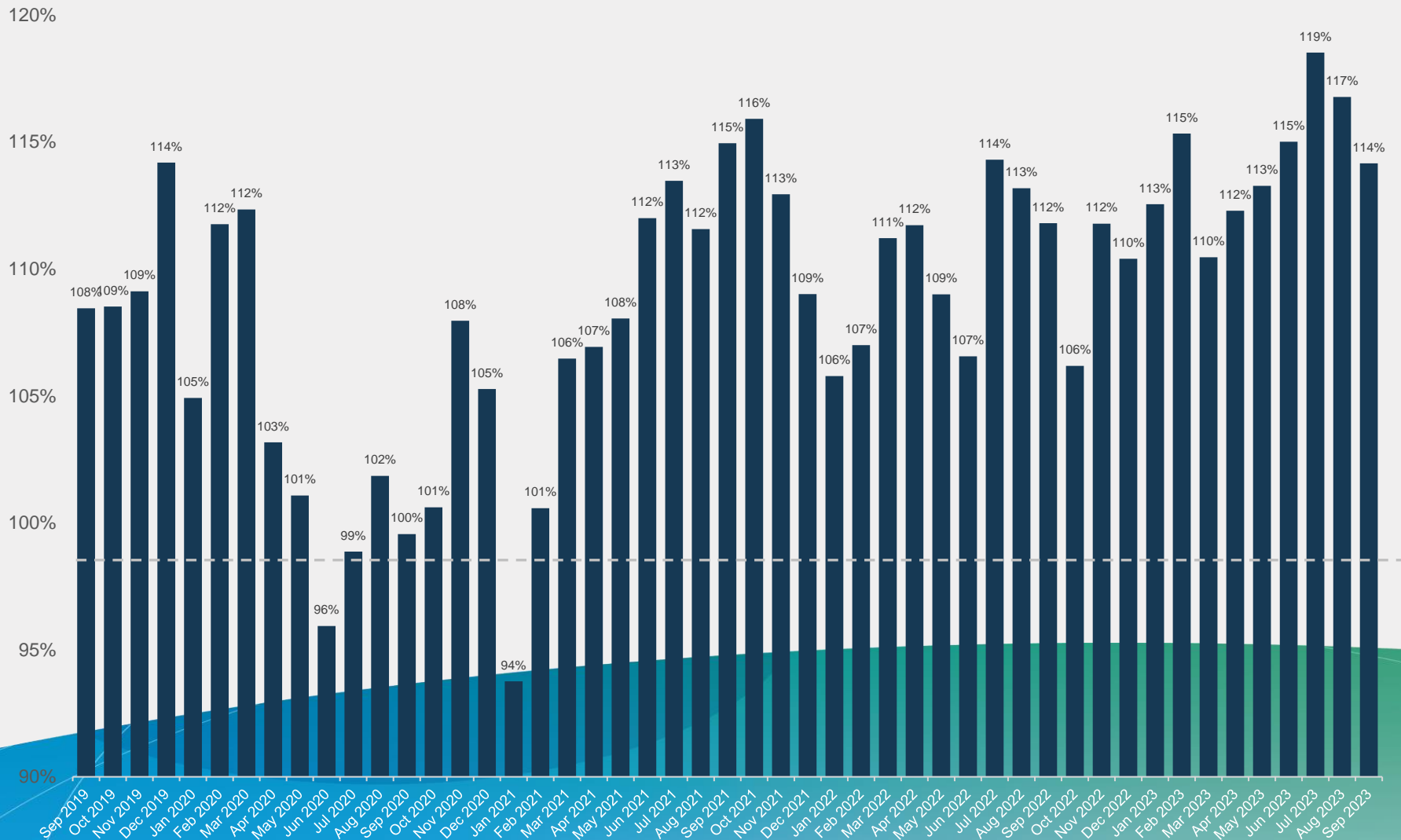
WWH as of 31 March 2023

Subsector	WWH %NAV	MSCI HC	Delta	WWH %NAV	MSCI HC	Delta
Pharmaceuticals	29.9	44.5	(14.5)	26.7	43.1	(16.4)
Big Pharma	29.5	41.3	(11.7)	26.4	39.7	(13.3)
Spec Pharma	0.4	3.0	(2.6)	0.2	3.2	(3.0)
Generics	0.0	0.2	(0.2)	0.0	0.1	(0.1)
Biotechnology	28.2	9.4	18.9	23.9	9.4	14.6
Big Biotech	3.2	5.2	(2.0)	2.7	5.1	(2.4)
Emerging Biotech	25.1	4.2	20.9	21.3	4.3	17.0
Life Science Tools	4.6	11.0	(6.4)	3.8	12.3	(8.4)
Medtech/Devices	16.6	15.5	1.1	19.3	16.2	3.2
Healthcare Services	15.0	15.6	(0.6)	15.4	14.9	0.5
Japan	6.5	4.0	2.5	6.3	4.2	2.1
Emerging Markets	5.9	0.0	5.9	8.0	0.0	8.0
Structured Finance & ETFs	0.0	0.0	0.0	0.0	0.0	0.0
Privates	7.4	0.0	7.4	6.8	0.0	6.8
Total	114.2	100.0	14.2	110.2	100.0	10.2

*Excludes Options. Basket positions have their constituents allocated to their respective subsectors. Future weightings may differ.

WWH Leverage over Time

(29 September 2023)



Source: Orbimed, Bloomberg PORT



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Playbook

Playbook for 2024 and Beyond

- | | | |
|---|---|--|
| 1 | Continue to Invest in Innovation |  |
| 2 | IRA is Manageable (does it even stick?) |  |
| 3 | Continued High Expectations for M&A |  |
| 4 | Remain Patient with Biotech |  |
| 5 | Healthcare Underperformance Unsustainable |  |
| 6 | Valuations Undemanding |  |
| 7 | Overall Bullish Outlook into 2024 |  |



WORLDWIDE HEALTHCARE TRUST

Q&A

Endnotes

General Notes

1. The information presented herein relates to Worldwide Healthcare Trust PLC (the "Fund"). 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 Fund's 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 Fund, 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.
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No guarantee or representation is made that the 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 Shares could lose all or a substantial amount of their value. 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 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 programs.

7. 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 Shares.
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Endnotes (continued)

Indices

Information about indices is provided to allow for comparison of the performance of the Shares to the Fund's benchmark and certain other recognized indices. Investors cannot invest directly in an index, which also does not take into account trading commissions and costs. The indices shown 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 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.