The politics, pricing pitfalls, risk — and potential reward in biotech stocks

Federated Hermes

Key takeaways

- Tailwinds are building for a biotech rebound, as innovation has accelerated, interest rates have likely peaked and big pharma appears ready to deploy record cash reserves
- Biotech is a stock picker's space with high volatility and significant return dispersion. Active management can add value
- Biotech themes to watch include autoimmune therapies, obesity medicines and genetic medicines

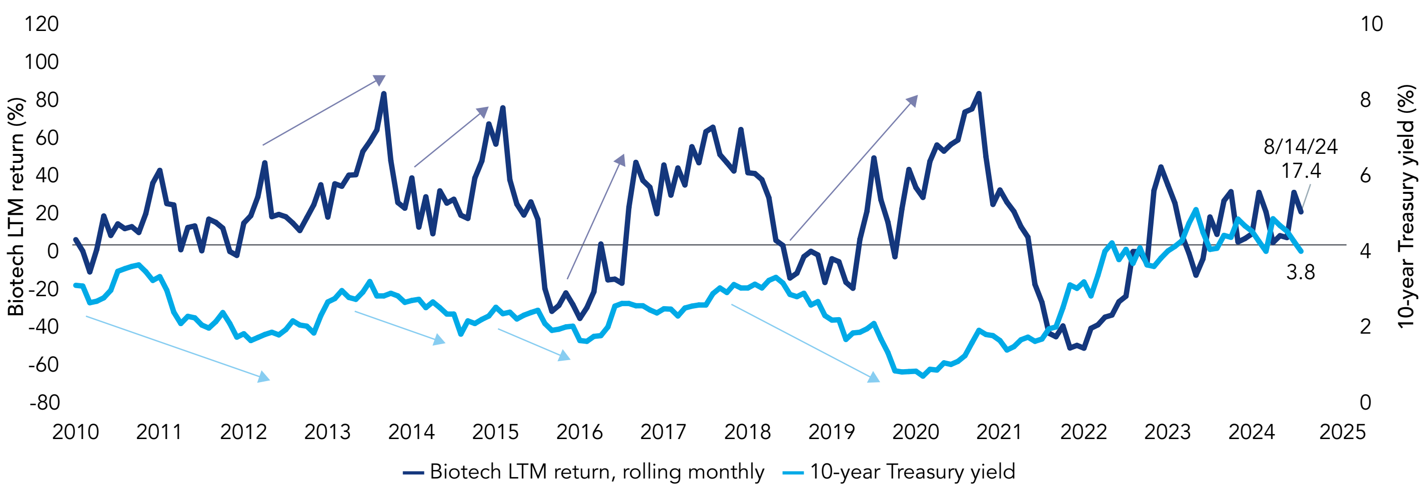
Biotech innovation can transcend traditional business cycles, offering the potential for attractive uncorrelated excess returns versus the broad stock market. Over the last few years, higher rates and politics have weighed on the industry, bankruptcies have hit a 10-year high[1] and despite a brief pickup in July, the Russell 2000® Growth Biotechnology Subsector Index is still down -52.5% since its peak 2/8/21 through 8/14/24 (the S&P 500® is up 47.1% over the same period). Is now a buying opportunity?

Tailwinds for a biotech rebound

- **Declining interest rates.** Small biotech companies are sensitive to rates and market risk appetite because most are still in the drug development process, during which they continually need to raise money to fund research and clinical trials. Higher rates means they are competing with high yields on cash. Also, a higher discount rate lowers their present value in stock valuation models, and vice versa. In the past, biotech stocks have rallied as the 10-year declined. [**Exhibit 1**]
- **Innovation.** The speed and significance of recent innovations is very promising. Within the last few years, the industry has commercialized new anti-obesity medications, made advances in diagnostics for disease detection and developed new genomic and regenerative medicine techniques. Mentions of innovation-related keywords on Health Care sector earnings calls have topped 1,000 several quarters since 2020, up from ~200 10 years ago, according to Goldman Sachs.

Exhibit 1: In the past, a peak in Treasuries has preceded a biotech rally

Biotech is still down -52.5% from its 2021 high.

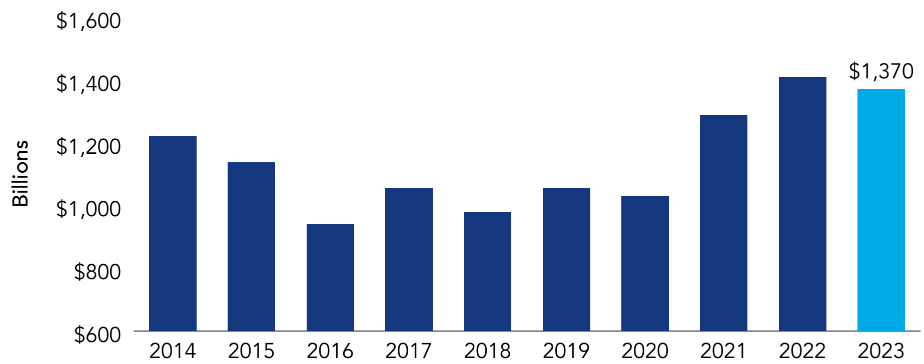


As of 8/14/24. Sources: FactSet, Russell 2000® Growth Biotechnology Subsector Index, Federated Hermes. Last twelve months is abbreviated LTM.
Past performance is not indicative of future results. This is for illustrative purposes only and is not indicative of any specific investment.

Tailwinds for a biotech rebound, continued

- **Large and growing market.** The global population is growing and getting older. The percentage of Americans 65+ is expected to increase 42% by 2050.[2] People tend to spend more on healthcare as they age.
- **Artificial intelligence (AI)** can digest and analyze the complex data generated by the healthcare industry, leading to increased productivity and accuracy, lower costs and other as-yet unimagined outcomes.
- **Record big pharma cash reserves.** Big pharma had $1.37 trillion in cash available as of December 12, 2023, the most cash on record (records going back to 2014), excluding 2022. [**Exhibit 2**]

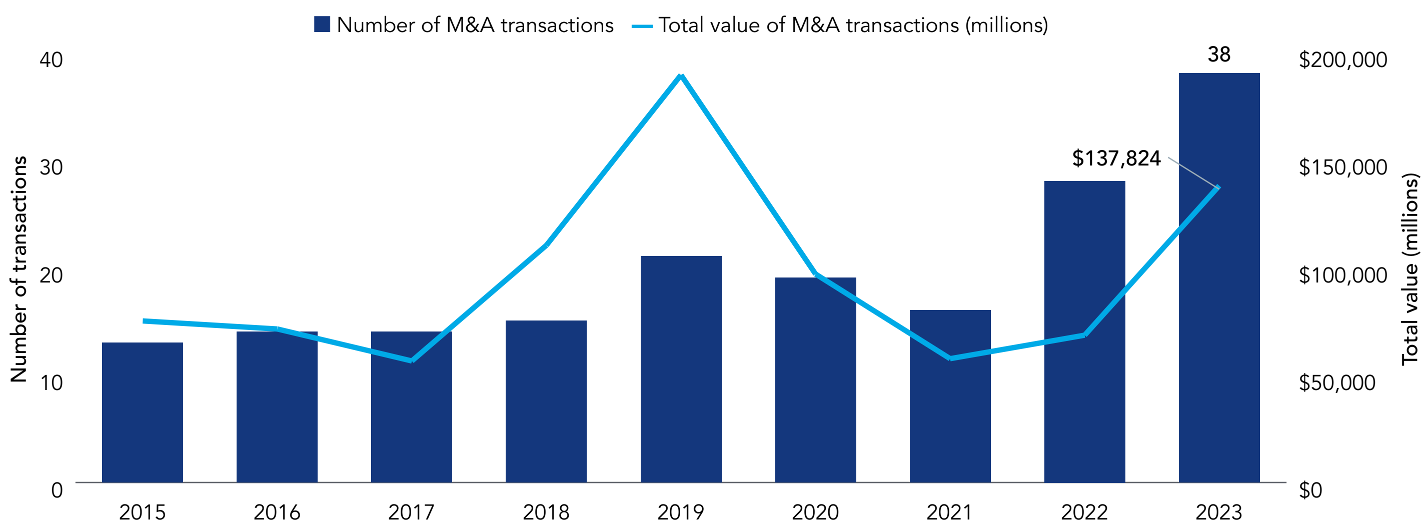
Exhibit 2: Big pharma has hundreds of drug patents expiring soon—and near-record firepower available for deals



As of 12/7/23. Sources: Ernst & Young, Capital IQ.

- **A steep, fast-approaching patent cliff.** The top 10 big pharma companies have 190 drugs that will lose or already lost patent exclusivity between 2022 and 2030, including 69 blockbuster drugs.[3] New drugs cost billions and take years to develop, so big pharma companies often acquire smaller biotech companies that already have clinical proof-of-concept (Phase III or later). With many promising biotechs trading at attractive valuations, big pharma may look to rebuild their pipelines. Merger and acquisition (M&A) and initial public offerings (IPOs) are two of the main ways that biotech investors get a return on their investment because biotechs primarily raise money by selling equity, not issuing debt. As such, increased deal activity [**Exhibit 3**] signals a potential period of attractive returns available in biotech and typically precedes it.

Exhibit 3: The number of biotech M&A transactions hit a high of 38 in 2023

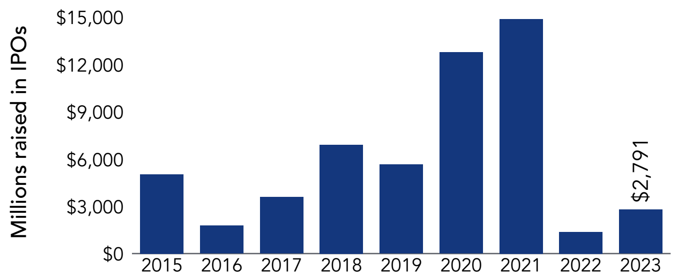


As of 12/31/23. Source: Evercore ISI.

Headwinds

- **Costs of capital.** Higher costs of capital challenge biotechs, which are reliant on external financing to fund their operations. Venture capital investments in biotech companies were approximately $24 billion in 2023, down from $54 billion in 2021.[4] If rates remain high, lack of funding may weigh on biotech.
- **Drug pricing.** Projecting the commercial success of products is challenging. The Inflation Reduction Act (IRA) recently added complexity, by empowering the government to negotiate select drug prices directly with biotech and pharma companies. Negotiated prices don't kick in until 13 years after approval for eligible biologics, but the effects on the industry are generally seen as negative.[5]

Exhibit 4: IPO activity is slowly recovering

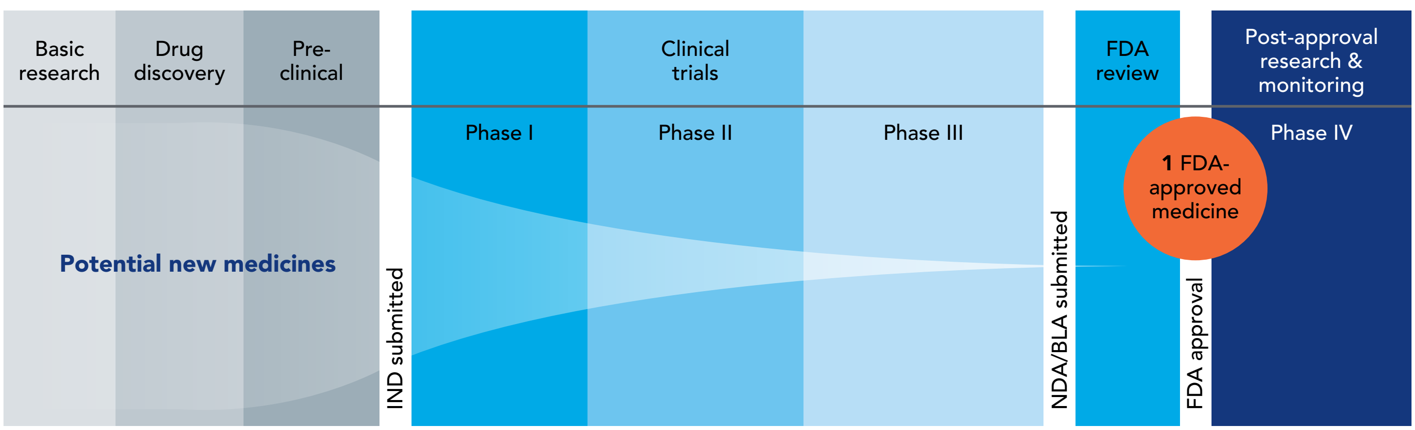


As of 12/31/23. Source: Evercore ISI.

- **Market sentiment.** New drug development requires substantial early and ongoing investment, and the path to potential profitability is years-long and complex [**Exhibit 5**]. Yet it is difficult to value biotech companies to determine if the risk is worth the potential reward. To compensate for upfront costs and high risks, investors seek high returns. Biotech investors tend to be highly discerning, requiring successful clinical trials or other hard data to push stocks higher.

Exhibit 5: The biopharmaceutical development process

It takes on average 10 years and $3.1 billion to bring a new drug to market. Only about 14% of drugs that reach Phase I of clinical trials achieve FDA approval.[6]



Key: IND = Investigational new drug application; NDA = New drug application; BLA = Biologics license application

Source: Suzanne S. Farid, Max Baron, Christos Stamatis, Wenhao Nie, Jon Coffman, *"Benchmarking biopharmaceutical process development and manufacturing cost contributions to R&D,"* May 2020. Accessed via National Library of Medicine on May 9, 2024.

- **Politics.** Both political parties favor policies that challenge the industry. Recently, expedited reviews have come under attack.
- **Regulations.** Regulatory headwinds could stall innovation progress and commercialization of new drugs. For example, gene editing will require a regulatory framework, and FDA approvals of new AI algorithms take time. However, if these innovations can improve patient outcomes, regulators should be keen to facilitate them.
- **Insurance coverage.** Costs of new biologics, such as GLP-1s, are considerably higher than small molecule chemical pharmaceuticals because of their complexity, making insurance coverage key to commercialization, but challenging to obtain.

Biotech themes to watch

While scientific breakthroughs are rare and difficult to identify in the early stages of development, they should eventually drive attractive returns no matter the market conditions. Each category below has drugs or technologies that could materially improve health and well-being outcomes in their focus areas, increasing their chances of success.

Autoimmune therapies

- Cell-therapy that can cure autoimmune diseases. For example, using CAR T-cell therapy, originally developed as a cancer treatment, to treat autoimmune disorders
- **Stock story: Argenx SE**** develops effective treatments for autoimmune diseases. The FDA approved Argenx's drug Vyvgart to treat myasthenia gravis, a muscle weakening illness, in 2021, and CIDP in 2024. Argenx is conducting trials to determine if Vyvgart treats a number of other autoimmune diseases. Argenx was first-to-market with Vygart, which might be a "pipeline in a product." Argenx also has exclusive access to a convenient drug delivery technology. The Federated Hermes Kaufmann Growth Equity Team participated in the company's IPO (ADR shares) in May 2017

Obesity medicines

- Addresses a huge unmet need; obesity affects over 40% of the US population
- Currently, market penetration of obesity drugs is relatively low – they are expensive, insurance coverage is limited, and the delivery mechanism (an injection) limits demand
- However, many obese individuals have comorbidities that could become eligible for insurance coverage pending upcoming clinical trials and regulatory approvals. For example, the anti-inflammatory effects of these drugs could provide treatments for neurodegenerative diseases
- Costs should decrease as more players come to market. Ease of use should also improve and drive demand
- **Stock story: Structure Therapeutics, Inc.**** is currently in Phase 2 of clinical trials testing a pill version of GLP-1, which is currently only available as an injection. The Federated Hermes Kaufmann Growth Equity Team participated in the company's IPO in February 2023

Genetic medicines

- Offers the potential for one-and-done treatment
- The FDA has been increasingly granting approvals for gene therapies. In December 2023, the FDA approved Casgevy, the first approved therapy to use CRISPR gene-editing technology. CRISPR is a breakthrough gene-editing technique that can be leveraged to create many new medicines
- Based on current estimates the gene therapy market could grow from $9 billion in 2024 to $45 billion by 2032[7]
- **Stock story: Alnylam Pharmaceuticals**** develops industry-leading therapeutics based on RNA interference (RNAi), a Nobel-prize winning discovery for the treatment of a wide range of severe and debilitating diseases. Alnylam has a deep pipeline of investigational medicines, including six product candidates that are in late-stage development. Alnylam's therapies use RNAi to silence disease-causing genes

Considerations for investors

US stock market investors may want to assess their exposure to biotech

The size of the industry, the regulatory oversight and the wide distribution of types of medical practices create inefficiencies that challenge passive investing [**Exhibit 8**], so investors should assess their allocations. The pharmaceutical biotechnology and life sciences industry is about 10% of the Russell 2000® Index. Investors who seek growth from their small cap allocation likely own more biotech; the industry is about 13% of the Russell 2000® Growth Index. This presents an opportunity to pursue uncorrelated excess returns in small-cap portfolios by engaging an active manager with the experience to navigate its challenges.

Active management can add value

Biotech results are binary [**Exhibit 7**]. Returns are driven by successful clinical trials, IPOs, M&A and commercialization, it takes years to achieve these milestones, and many fail along the way [**Exhibit 5**]. As a result, most biotech stocks have delivered very low returns. Only a few winners have provided 100%+ returns in the last three years [**Exhibit 7**]. Passive index funds can miss out on the full upside of these rare successes, as IPOs can take months to enter an index and biotech winners typically exit small-cap indexes through acquisition or by growing too large. The Federated Hermes Kaufmann Growth Equity Team views this as an opportunity to differentiate returns from other small-cap portfolios. The team actively participates in IPOs, secondary offerings and private investments in public equity (PIPE) deals, offering investors potentially better entry points and longer runways for potential outperformance.

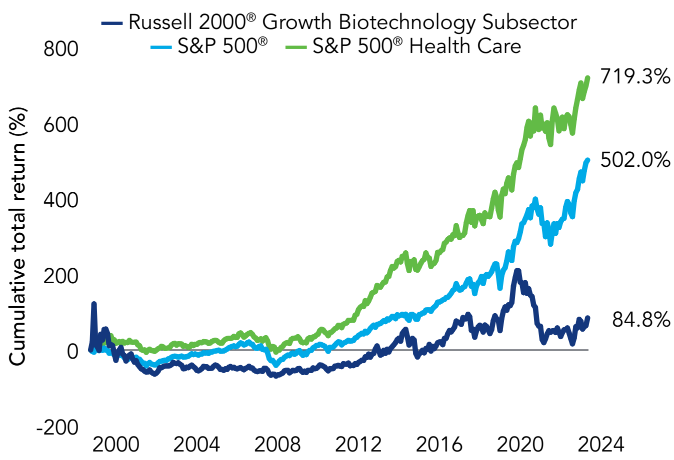
Exhibit 6: The biotech industry is volatile

Standard deviation	3-year	5-year	10-year
Russell 2000® Growth Biotechnology Subsector	32.6%	32.8%	32.1%
S&P 500®	17.8%	18.1%	15.3%
S&P 500® Health Care	14.8%	14.9%	14.1%

As of 7/31/24. Sources: FactSet, Federated Hermes analysis.
Past performance is not indicative of future results.

Exhibit 8: Biotech is a stock picker's space, challenging long-term passive investing

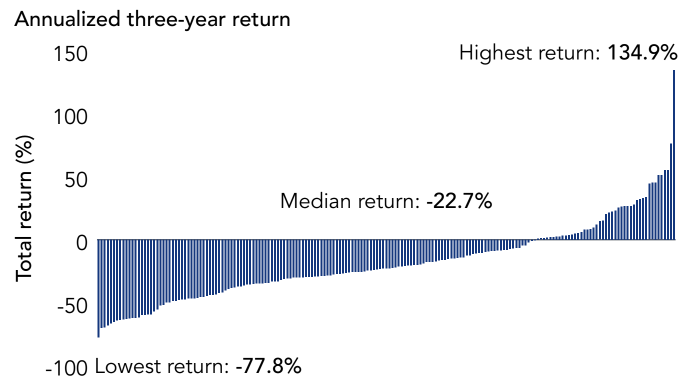
We believe active management is essential to unlock the return potential in the biotech space.

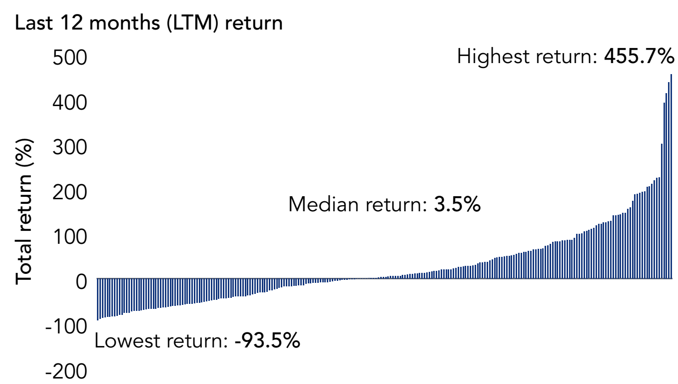


As of 7/31/24. Sources: FactSet, Federated Hermes analysis.
Past performance is not indicative of future results.

Exhibit 7: Biotech company returns tend to be binary

The high dispersion of individual company returns shown below reflects the industry's few winners and many losers.





As of 3/31/24. Based on Russell 2000® Growth Biotechnology Subsector Index holdings as of 3/31/24; 238 companies with LTM return history and 187 companies with three-year return history. Sources: Russell, Federated Hermes analysis. **Past performance is not indicative of future results.**

Access biotech opportunities selected by a team with decades of experience

We believe advanced biomedical knowledge is essential for identifying drug candidates with the greatest potential. In a space with tremendous dispersion where the bottom half of innovators will likely fail [**Exhibit 7**], Kaufmann Sector Portfolio Managers Tom Brakel, M.D. and Aditi Singhania, Ph.D. (Genetics) have an advantage in our view.

Exhibit 9: The Federated Hermes Kaufmann Small Cap Fund is overweight biotech

	Weight in biotech industry (%)
Federated Hermes Kaufmann Small Cap Fund	23.58
Russell 2000® Growth Index	10.96
Morningstar US Fund Small Growth Category Average	8.60

As of 6/30/24. Sources: Morningstar, Inc., Federated Hermes analysis.

Exhibit 10: Stock selection has driven biotech outperformance in the Federated Hermes Kaufmann Small Cap Fund

Annualized total returns (%), Pharmaceuticals, biotechnology & life sciences industry

	1-year	3-year	5-year
Federated Hermes Kaufmann Small Cap Fund	9.13	-5.69	7.52
Russell 2000® Growth Index	5.80	-14.93	0.07
Outperformance	3.33	9.24	7.45

As of 6/30/24. Sources: FactSet, Federated Hermes. **Past performance is not indicative of future results.**

Table shows the performance (gross of fees) of the fund's biotech holdings versus the index's. See the standard returns table below for more information.

The Federated Hermes Kaufmann Growth Equity Team understands the science and has deep experience investing in the sector and analyzing management teams, having covered biotech for decades. We believe both information advantages position the team to exploit inefficiencies in the biotech market and help generate above-benchmark returns over the long term on behalf of clients.

Average annual total returns (%) as of 6/30/24

Federated Hermes Kaufmann Small Cap Fund	Share class	1-year	3-year	5-year	10-year	Since inception 12/18/02	Expense ratio* Before waivers	Expense ratio* After waivers
FKALX	R6	7.43	-8.21	4.92	10.80	12.62	0.93	0.89
FKAIX	IS	7.42	-8.22	4.91	10.88	12.64	1.02	0.90
FKASX	A (NAV)	6.93	-8.64	4.43	10.45	12.45	1.51	1.36
FKASX	A (MOP)	1.05	-10.35	3.25	9.83	12.16	1.51	1.36
Russell 2000® Growth Index	–	9.14	-4.86	6.17	7.39	9.77	–	–

Performance quoted represents past performance, which is no guarantee of future results. Investment return and principal value will fluctuate so that an investor's shares, when redeemed, may be worth more or less than their original cost. Current performance may be lower or higher than what is stated. To view performance current to the most recent month-end, and for after-tax returns, contact us or visit FederatedHermes.com/us. Maximum offering price figures reflect the maximum sales charge of 5.5% for A Shares. See the prospectus for other fees and expenses that apply to a continued investment in the fund.

*** The fund's expense ratio is from the most recent prospectus. The expense ratio may reflect voluntary fee waivers and/or expense reimbursements determined by the fund's Advisor and its affiliates. The voluntary waivers and/or reimbursements, if applicable, are in effect up to but not including the later of 1/1/25 or the date of the fund's next effective prospectus.**

Learn more about Federated Hermes Kaufmann Growth Equities, including active small-, mid- and large-cap investment solutions. Call 1-888-400-7838 or talk to your Federated Hermes relationship manager.

Politics, pricing pitfalls, risk – and potentially big rewards in biotech stocks

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Views are as of August 26, 2024 and subject to change.

** As of 6/30/24, Argenx SE was 4.5%, and Structure Therapeutics was 1.2% and Alnylam was 0.0% of Federated Hermes Kaufmann Small Cap Fund.

The Fund is a managed portfolio and portfolio holdings are subject to change.

The holdings percentages are based on net assets at the close of business on 6/30/24 and may not necessarily reflect adjustments that are routinely made when presenting net assets for formal financial statement purposes.

1 Fierce Biotech, "Biotech bankruptcies hit 10-year peak in 2023." February 2024.

2 US Census Bureau. Projected Population by Age Group and Sex. July 2022.

3 Biospace, "Looming Patent Cliff will be Pharma's Moment of Truth." June 2022.

4 Larry Light, "Why Battered Biotech May Be Turning Around," January 2024, Chief Investment Officer. February 2024.

5 Daniel Gassull, Harry Bowen, Duane Schulthess. "IRA's impact on the US Biopharma Ecosystem." June 2023. Accessed via bio.org, August 2024.

6 Chi Heem Wong, Kien Wei Siah, Andrew W Lo."Estimation of clinical trial success rates and related parameters" January 2018. Accessed via American Council on Science and Health, May 2024.

7 Credence Research, "Gene Therapy Market Summary." May 2024.

Investors should carefully consider the fund's investment objectives, risks, charges and expenses before investing. To obtain a summary prospectus or a prospectus containing this and other information, contact us or visit FederatedHermes.com/us. Please carefully read the summary prospectus or the prospectus before investing.

The fund's R6 Shares commenced operations on September 1, 2017. For the period prior to the commencement of operations of the R6 Shares, the performance information shown is for the fund's A Shares adjusted to reflect the expenses of the fund's R6 Shares for each year for which the Fund's R6 Shares expenses would have exceeded the actual expenses paid by the fund's A Shares. The performance information has also been adjusted to reflect any applicable differences between the sales loads and charges imposed on the purchase and redemption of R6 Shares and A Shares, as well as the removal of any voluntary waivers/reimbursements of fund expenses that may have occurred during the periods prior to the commencement of operations of the R6 Shares.

The fund's Institutional Shares commenced operations on December 30, 2015. For the period prior to the commencement of operations for the Institutional Shares, the performance information shown is for the A Shares adjusted to reflect the expenses of the Institutional Shares for each year for which the expenses of the Institutional Shares would have exceeded the actual expenses paid by the fund's A Shares. The performance information has also been adjusted to reflect any applicable differences between the sales loads and charges imposed on the purchase and redemption of Institutional and A Shares, as well as the removal of any voluntary waivers/reimbursements of fund expenses that may have occurred during the periods prior to the commencement of operations of the Institutional Shares.

A word about risk

Mutual funds are subject to risks and fluctuate in value.

International investing involves special risks, including currency risk, increased volatility, political risks and differences in auditing and other financial standards.

In the event of any capacity constraints, the adviser may recommend (and has in the past recommended) that the fund be closed to certain new investors (a "soft-close"). In the event of a "soft-close," the fund may remain open to new investments by existing shareholders or new investments by certain new investors including employer-sponsored retirement plans and fully discretionary, home-office based advisory accounts if the fund is an established option as of the date of the "soft-close." Any determination to "soft-close" the fund or remain open to existing or new investors as described above will be subject to the recommendation of the adviser and determination of the Board that it is in the best interests of the fund and its shareholders at the time of any such potential future "soft-close."

The fund may invest in small capitalization (or "small-cap") companies. Small-cap companies may have less liquid stock, a more volatile share price, unproven track records, a limited product or service base and limited access to capital. The above factors could make small-cap companies more likely to fail than larger companies and increase the volatility of the fund's portfolio, performance and price. Suitable securities of small-cap companies also can have limited availability and cause capacity constraints on investment strategies for funds that invest in them.

Investing in IPOs involves special risks such as limited liquidity and increased volatility.

Investing in equities is speculative and involves substantial risks. The value of equity securities will rise and fall. These fluctuations could be a sustained trend or a drastic movement.

Biotech stocks are a risky healthcare investment due to the high research and development costs necessary to develop new drugs. Regulatory approval in the U.S. and abroad can be lengthy and challenging, and there is no guarantee that a new treatment will gain approval.

Index definitions

10-year Treasury yield is the yield received for investing in a US government issued treasury security that has a maturity of 10 years.

Russell 2000® Growth Index measures the performance of the small-cap growth segment of the U.S. equity universe. It includes those Russell 2000® Index companies with higher price-to-value ratios and higher forecasted growth values.

Russell 2000® Growth Index Biotechnology Subsector consists of companies in the Russell 2000® Growth Index that are engaged in research into and development of biological substances for the purposes of drug discovery and diagnostic development, and which derive the majority of their revenue from either the sale or licensing of these drugs and diagnostic tools. Indexes are unmanaged and cannot be invested in directly.

S&P 500® Index is an unmanaged capitalization-weighted index of 500 stocks designated to measure performance of the broad domestic economy through changes in the aggregate market value of 500 stocks representing all major industries.

S&P 500® Health Care comprises those companies included in the S&P 500® that are classified as members of the GICS® health care sector.

Indexes are unmanaged and cannot be invested in directly.

Morningstar Category identifies funds based on their actual investment styles as measured by their underlying portfolio holdings over the past three years. If the fund is less than three years old, the category is based on the life of the fund. ©2024 Morningstar, Inc. All Rights Reserved. The information contained herein: (1) is proprietary to Morningstar; (2) may not be copied or distributed; and (3) is not warranted to be accurate, complete or timely. Neither Morningstar nor its content providers are responsible for any damages or losses arising from any use of this information. Past performance is no guarantee of future results.

Performance dispersion measures the range of performance results of a portfolio or index.

Standard deviation is a statistical measurement of dispersion about an average which depicts how widely the returns varied over a certain period of time. The higher the standard deviation, the greater the volatility.

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