

ALPS Medical Breakthroughs ETF

Quarterly Insights | Q1 2025

Key Takeaways

- The ALPS Medical Breakthroughs ETF (SBIO) fell -14% during the first quarter of 2025 as biotechnology stocks continue to slump on uncertainty around Federal Reserve (Fed) rate cuts and new administrative policy as it relates to the sector.
- SBIO's Cardiology & Hematology treatment segment was the best performer among the four biotech segments in the fund during Q1 of 2025.
- **Company Spotlight:** Akero Therapeutics Inc. (AKRO, 2.71% weight*) gained 45.51% in Q1 after announcing positive data for its liver drug to treat metabolic dysfunction-associated steatohepatitis (MASH).

Performance Notes

- SBIO's small-to-mid (SMid) cap biotech portfolio fell -14% in the first quarter of 2025, underperforming the S&P Biotech Select Industry Index (-9.96%) and large-cap biotech, as measured by the NASDAQ Biotechnology Index (-1.31%). SBIO's names have a smaller average market cap than major biotech indices, with SBIO being comprised of a portfolio of biotech companies with late-stage (Phase II and Phase III) clinical trials. Larger cap biotech names have outperformed in 2025 amid market uncertainty surrounding the new administration as well as uncertainty around potential Federal Reserve (Fed) rate cuts.
- Merger & acquisition (M&A) activity has been quiet so far in 2025 after seven underlying holdings in SBIO were acquired/announced acquisitions with an average deal premium of 55.39% at the time of announcement in 2024.

Performance Summary

	Q1 2025	YTD	1 Y
SBIO (NAV)	-14.00%	-14.00%	-17.71%
S-Network Medical Breakthroughs Index - TR	-14.05%	-14.05%	-17.67%
NASDAQ Biotechnology Index - TR	-1.31%	-1.31%	-3.39%
S&P Biotechnology Select Industry Index	-9.96%	-9.96%	-14.43%

As of 3/31/2025

Performance data quoted represents past performance. Past performance is no guarantee of future results so that shares, when redeemed, may be worth more or less than their original cost. The investment return and principal value will fluctuate. Current performance may be higher or lower than the performance quoted. For current month-end performance call 1-866-759-5679 or visit www.alpsfunds.com. Performance includes reinvested distributions and capital gains.

For standardized performance please see page 3.

Strategy

- SBIO screens for small- to mid-cap biotech companies with at least one drug or therapy in Phase II or Phase III (late-stage) clinical trials.
 - Late stage drug trials can potentially capture greater odds of success as they are further along the Food and Drug Administration (FDA) drug trial process.
- SBIO constituents must have at least 24 months of cash burn on hand.
 - This quality screen helps to protect against the equity dilution that comes with raising capital to support drug trials.



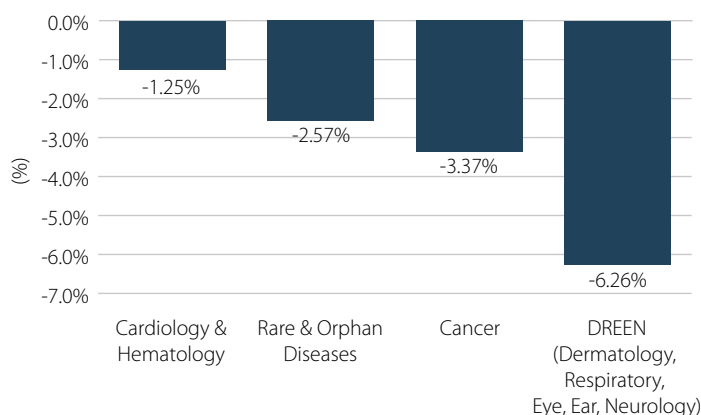
Contribution to Return by Treatment Focus

- SBIO's Cardiology & Hematology treatment segment, although still negative for the quarter, was the top-performing category in Q1. Within the segment, Protagonist Therapeutics Inc. (**PTGX, 2.57% weight***) was a top performer, 25.28%, after reporting positive top line results for its active ulcerative colitis (a bowel disease) drug in Phase 2b trials.
- SBIO Rare & Orphan Disease treatment name, Akero Therapeutics Inc. (**AKRO, 2.71% weight***) rose 45.51% in Q1 and is highlighted below in the Company Spotlight while Verona Pharma PLC (**VRNA, 4.39% weight***) also had a strong quarter, +36.71%. The London-based biopharma company gained on several price target raises from analysts, citing a strong outlook for Ohtuvayre, its lung disease treatment for chronic obstructive pulmonary disease (COPD).
- In Q1, SBIO's Cancer treatment segment was led by Zai Lab Limited (**ZLAB, 3.17% weight***), which soared 37.99% in a quarter in which its Schizophrenia drug, KarXT, had its application accepted by Chinese regulators and the US Food and Drug Administration (FDA) granted an orphan drug designation for its treatment for small cell lung cancer.

Valuation Update

- The S-Network Medical Breakthroughs Index (PMBI) has a weighted average cash-burn of 44.09 months that continues to exceed peer biotechnology indices and is a distinguishing defensive characteristic for the fund.
- PMBI's holdings have an average market value of \$2.50 billion, with 54.65% classified as mid-caps, and 45.35% classified as small-caps.

SBIO Company Focus Contribution To Return



Source: Bloomberg L.P., as of 3/31/2025

Past performance is no guarantee of future results.

Index Characteristics

	S-Network Medical Breakthroughs Index	S&P Biotechnology Select Industry Index	ICE Biotechnology Index
Number of Constituents	98	123	255
Weighted Average Market Cap (\$M)	\$2,497	\$28,663	\$51,431
Price/Sales	7.33x	6.05x	5.34x
Cash burn (months)	44.09	34.15	41.42

Source: Bloomberg L.P., as of 3/31/2025

Past performance is no guarantee of future results.

Q1 2025 Company Spotlight

Company: Akero Therapeutics Inc. (**AKRO, 2.71% weight***)

Treatment Segment: Rare & Orphan Disease

- San Francisco-based Akero Therapeutics, which focuses on treatments for metabolic diseases, gained 45.51% this quarter and was the top performing name in SBIO.
- Akero Therapeutics soared this month after reporting blockbuster positive data for its liver drug, efruxifermin ("EFX"), in patients with metabolic dysfunction- associated steatohepatitis (MASH), a form of fatty liver disease. "We believe today's first-ever public report of reversal of cirrhosis due to MASH... sets EFX apart from other approved or investigational treatments in the MASH landscape as a compound with transformational potential," said Akero's CEO, Dr. Andrew Cheng.

* Weight in SBIO as of 3/31/2025

ALPS Medical Breakthroughs ETF (SBIO) Performance as of 3/31/2025

Total Returns	Cumulative				Annualized				
	1 M	3 M	YTD	SI ¹	1 Y	3 Y	5 Y	10 Y	SI ¹
NAV (Net Asset Value)	-9.09%	-14.00%	-14.00%	25.54%	-17.71%	-4.29%	-1.50%	0.36%	2.24%
Market Price	-9.12%	-14.05%	-14.05%	25.50%	-17.67%	-4.26%	-1.48%	0.34%	2.24%
S-Network Medical Breakthroughs Index - TR	-9.08%	-14.03%	-14.03%	30.27%	-17.49%	-3.85%	-1.09%	0.72%	2.61%
NASDAQ Biotechnology Index - TR	-5.98%	-1.31%	-1.31%	41.90%	-3.39%	1.46%	5.39%	2.30%	3.47%

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Market Price is based on the midpoint of the bid/ask spread at 4 p.m. ET and does not represent the returns an investor would receive if shares were traded at other times.

¹ Fund inception date: 12/30/2014

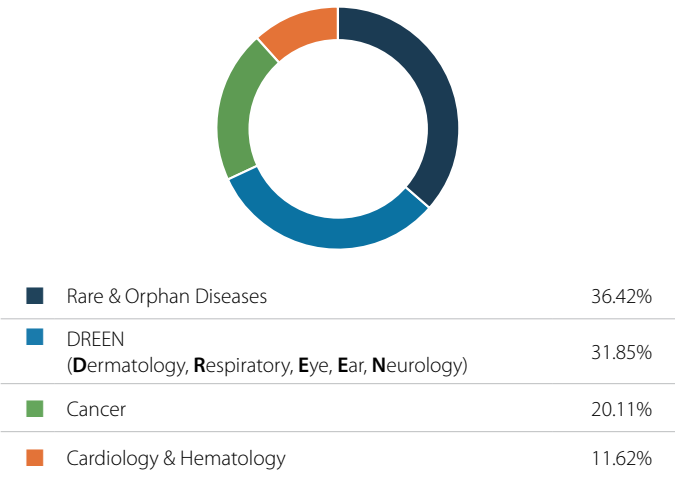
Total Operating Expenses: **0.50%**

Top 10 Holdings

Alkermes Plc	4.86%
Axsome Therapeutics Inc	4.66%
Verona Pharma Plc	4.55%
Zai Lab Ltd	3.67%
Ptc Therapeutics Inc	3.45%
Avidity Biosciences Inc	3.01%
Rhythm Pharmaceuticals Inc	2.98%
Akero Therapeutics Inc	2.91%
Protagonist Therapeutics Inc	2.79%
Crinetics Pharmaceuticals Inc	2.66%

Source: SS&C ALPS Advisors, as of 3/31/2025, subject to change
Daily holdings are available at www.alpsfunds.com.

Treatment Focus Breakdown



Source: S-Network Global Indexes, as of 3/31/2025, holdings subject to change

Important Disclosures & Definitions

An investor should consider the investment objectives, risks, charges and expenses carefully before investing. To obtain a prospectus containing this and other information, call 1-866-759-5679 or visit www.alpsfunds.com. Read the prospectus carefully before investing.

Shares of ETFs are bought and sold at market price (not NAV) and are not individually redeemable.

Performance data quoted represents past performance. Past performance is no guarantee of future results; current performance may be higher or lower than performance quoted.

All investments are subject to risks, including the loss of money and the possible loss of the entire principal amount invested. Additional information regarding the risks of this investment is available in the prospectus.

The Fund's investments are concentrated in the pharmaceuticals and biotechnology industries, and underperformance in these areas will result in underperformance in the Fund. Investments in small and micro capitalization companies are more volatile than companies with larger market capitalizations. Companies in the pharmaceuticals and biotechnology industry may be subject to extensive litigation based on product liability and similar claims. Legislation introduced or considered by certain governments on such industries or on the healthcare sector cannot be predicted.

Companies in the pharmaceuticals industry are subject to competitive forces that may make it difficult to raise prices and, in fact, may result in price discounting. The profitability of some companies in the pharmaceuticals industry may be dependent on a relatively limited number of products. In addition, their products can become obsolete due to industry innovation, changes in technologies or other market developments. Many new products in the pharmaceuticals industry are subject to government approvals, regulation and reimbursement rates. The process of obtaining government approvals may be long and costly. Many companies in the pharmaceuticals industry are heavily dependent on patents and intellectual property rights. The loss or impairment of these rights may adversely affect the profitability of these companies.

The development of new drugs generally has a high failure rate, and such failures may negatively impact the stock price of the company developing the failed drug. Biotechnology companies may have persistent losses during a new product's transition from development to production. In order to fund operations, biotechnology companies may require financing from the capital markets, which may not always be available on satisfactory terms or at all.

The Fund is considered nondiversified and as a result may experience greater volatility than a diversified fund.

The Fund employs a "passive management" - or indexing - investment approach and seeks investment results that correspond (before fees and expenses) generally to the performance of its underlying index. Unlike many investment companies, the Fund is not "actively" managed. Therefore, it would not necessarily sell or buy a security unless that security is removed from or added to the underlying index, respectively.

ICE Biotechnology Index: a rules-based, modified float-adjusted market capitalization-weighted index that tracks the performance of qualifying US listed biotechnology companies.

NASDAQ Biotechnology Index: designed to track the performance of a set of securities listed on The NASDAQ Stock Market (NASDAQ) that are classified as either biotechnology or pharmaceutical companies, and is a modified market capitalization weighted index.

Price/Sales (P/S) Ratio: represents the weighted average of the price/sales ratios of the stocks in a portfolio. Price/sales represent the amount an investor is willing to pay for a dollar generated from a particular company's operations.

S-Network Medical Breakthroughs Index: comprised of small and mid-cap stocks of biotechnology companies that have one or more drugs in either Phase II or Phase III of the US Food and Drug Administration ("FDA") clinical trials.

S&P Biotechnology Select Industry Index: comprises stocks in the S&P Total Market Index that are classified in the GICS biotechnology sub-industry.

One may not invest directly in an index.

ALPS Advisors, Inc., registered investment adviser with the SEC, is the investment adviser to the Fund. ALPS Advisors, Inc. is affiliated with ALPS Portfolio Solutions Distributor, Inc.

ALPS Portfolio Solutions Distributor, Inc. is the distributor for the Fund.

Not FDIC Insured • No Bank Guarantee • May Lose Value

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