

ALPS Medical Breakthroughs ETF

Quarterly Insights | Q2 2025

Key Takeaways

- The ALPS Medical Breakthroughs ETF (SBIO) gained 5.51% during the second quarter of 2025 as biotechnology stocks rallied on an improving mergers and acquisitions (M&A) environment and potential interest rate cuts heading into the second half of 2025.
- SBIO's Cancer treatment segment was the best performer among the four biotech segments in the fund during Q2 of 2025.
- **Company Spotlight:** Upstream Bio, Inc. (UPB, 0.40% weight*) gained 79.41% in Q2 on positive trial development data within its drug pipeline, with its adult asthma treatment beginning Phase II trials.

Performance Notes

- SBIO's small-to-mid (SMid) cap biotech portfolio rallied 5.51% in the second quarter of 2025, outperforming the S&P Biotech Select Industry Index by 330 basis points (bps) and large-cap biotech, as measured by the NASDAQ Biotechnology Index, by 654 bps. SBIO's biotech holdings 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. While large-cap biotech names have outperformed thus far in 2025 due to a broad flight to quality amid market uncertainty, SBIO's portfolio of SMid-cap names rallied hard off the lows set in April as risk-on returned to the markets in the second quarter. SBIO's portfolio of companies, which are mainly focused on immunotherapies and gene therapies, will benefit from further artificial intelligence (AI) drug discovery methods and the looming patent cliff for large pharma, which should drive M&A opportunities and valuations for smaller-sized biotech names through 2030.
- 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

	Q2 2025	YTD	1 Y
SBIO (NAV)	5.51%	-9.26%	-7.39%
S-Network Medical Breakthroughs Index - TR	5.62%	-9.20%	-7.13%
NASDAQ Biotechnology Index - TR	-0.15%	-1.46%	-6.21%
S&P Biotechnology Select Industry Index	2.28%	-7.91%	-10.36%

As of 6/30/2025

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.



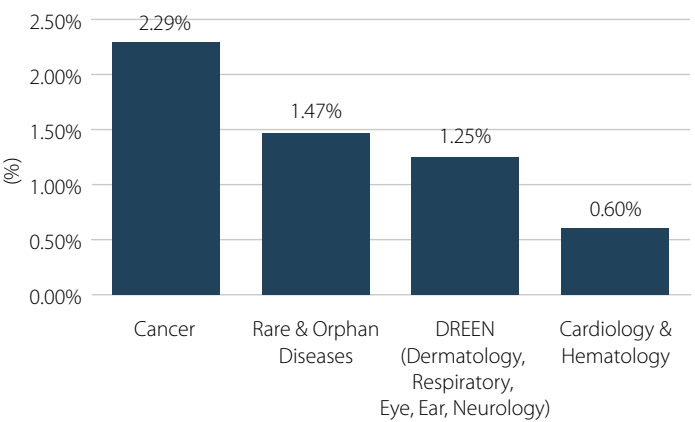
Contribution to Return by Treatment Focus

- SBIO's Cancer treatment segment was the top-performing category in Q2. Within the segment, iTeos Therapeutics, Inc. (ITOS, **0.26% weight***), led Cancer treatment names, rising 67% after management launched a strategic initiative to deliver near-term value to shareholders, including winding down its experimental lung cancer drug study with GSK (not in SBIO), preserving investment resources for other pipeline drugs. Also rising in SBIO's Cancer treatment segment in Q2 was Autolus Therapeutics plc (AUTL, **0.41% weight***), moving higher on positive commentary from analysts regarding progress across the company's acute lymphoblastic leukemia (ALL), lupus and other autoimmune disease treatments.
- SBIO DREEN (Dermatology, Respiratory, Eye, Ear, Neurology) treatment name, Stoke Therapeutics, Inc. (STOK, **0.42% weight***), rose over 70% in Q2 following comments from the FDA indicating efforts to reform and accelerate the drug development process for gene therapy drug-makers producing rare disease treatments, with analysts citing this a positive development that may lead to fewer conflicts of interest.
- In Q2 of 2025, SBIO's Rare & Orphan Disease segment was led by MBX Biosciences, Inc. (MBX, **0.26% weight***), soaring 54.61% on the back of a better-than-expected Q1 earnings report, with the endocrine and metabolic disorder treatment company displaying a cash and marketable securities runway for operations into mid-2027.

Valuation Update

- The S-Network Medical Breakthroughs Index (PMBI) has a weighted average cash-burn of 44 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 \$2.65 billion, with 61.04% classified as mid-caps, and 38.96% classified as small-caps.

SBIO Company Focus Contribution To Return



Source: Bloomberg L.P., as of 6/30/2025
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	102	124	251
Weighted Average Market Cap (\$M)	\$2,651	\$25,809	\$44,525
Price/Sales	6.26x	5.49x	5.07x
Cash burn (months)	44.00	30.00	37.00

Source: Bloomberg L.P., as of 6/30/2025
Past performance is no guarantee of future results.

Q2 2025 Company Spotlight

Company: **Upstream Bio, Inc. (UPB, 0.40% weight*)**
Treatment Segment: **DREEN (Dermatology, Respiratory, Eye, Ear, Neurology)**

- Upstream Bio, Inc. is a biotech company focusing on developing treatments for inflammatory diseases, with an emphasis on respiratory disorders.
- Upstream Bio soared nearly 80% in Q2, benefitting from its recent addition to the Russell 2000 Index as well as price target upgrades post Q1 2025 earnings results, where a recent Phase II launch of its asthma treatment and progress on immunotherapy drug, Verekitug, received praise from analysts as the guidance reflects strong execution and late-stage potential.

* Weight in SBIO as of 6/30/2025

ALPS Medical Breakthroughs ETF (SBIO) Performance as of 6/30/2025

	Cumulative				Annualized				
Total Returns	1 M	3 M	YTD	SI ¹	1 Y	3 Y	5 Y	10 Y	SI ¹
NAV (Net Asset Value)	3.72%	5.51%	-9.26%	32.46%	-7.39%	4.02%	-5.71%	-0.83%	2.71%
Market Price	3.79%	5.58%	-9.26%	32.50%	-7.33%	4.04%	-5.69%	-0.83%	2.72%
S-Network Medical Breakthroughs Index - TR	3.81%	5.62%	-9.20%	37.59%	-7.13%	4.39%	-5.32%	-0.48%	3.09%
NASDAQ Biotechnology Index - TR	3.70%	-0.15%	-1.46%	41.69%	-6.21%	4.94%	0.45%	1.55%	3.37%

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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

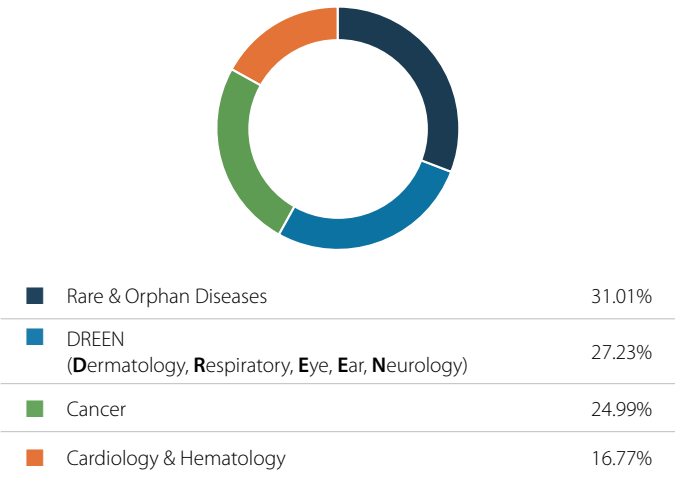
Total Operating Expenses: **0.50%**

Top 10 Holdings

Axsome Therapeutics Inc	3.47%
Nuvalent Inc	3.43%
Alkermes PLC	3.19%
Akero Therapeutics Inc	2.87%
Vaxcyte Inc	2.84%
Rhythm Pharmaceuticals Inc	2.71%
Krystal Biotech Inc	2.68%
Cytokinetics Inc	2.67%
Zai Lab Ltd	2.67%
Merus NV	2.65%

Source: SS&C ALPS Advisors, as of 6/30/2025, subject to change
Daily holdings are available at www.alpsfunds.com.

Treatment Focus Breakdown



Source: S-Network Global Indexes, as of 6/30/2025, 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.

Diversification does not eliminate the risk of experiencing investment losses.

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 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.

Basis Point (bps): a unit that is equal to 1/100th of 1% and is used to denote the change in a financial instrument.

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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