

ALPS Medical Breakthroughs ETF

Quarterly Insights | Q4 2023

Key Takeaways

- The ALPS Medical Breakthroughs ETF (SBIO) returned 20.94% during the fourth quarter of 2023 as biotechnology companies bounced back on possible signs of lower inflation and interest rates in the future.
- SBIO's Cancer treatment segment was the best performer among the four biotech segments in the fund during Q4 of 2023, rallying over 37%.
- **Company Spotlight:** RayzeBio Inc. (**RYZB, 2.55% weight***) skyrocketed 135.58% in Q4 after announcing it will be acquired by Bristol-Myers Squibb (**BMJ, not in SBIO**).

Performance Notes

- SBIO's small-to-mid (SMid) cap biotech portfolio returned 20.94% in the fourth quarter of 2023, slightly underperforming the S&P Biotech Select Industry Index (+22.18%) for the same period but outperforming large-cap biotech, measured by the ICE Biotechnology Index (+11.13%). Signals of possible rate cuts and slowing inflation benefitted the fund in the final quarter of the year as well as tailwinds in the form of rising merger & acquisition (M&A) activity and positive drug trial data in the fund in 2023.
- The fourth quarter 2023 saw four more SBIO names announce that they will be acquired: Point Biopharma Global Inc. (**PNT, acquired**), Cerevel Therapeutics Holdings Inc. (**CERE, 4.09% weight***), Icosavax Inc. (**ICVX, 0.55% weight***) and RayzeBio Inc. (**RYZB, 2.55% weight***). Thirteen underlying holdings in SBIO were acquired / announced acquisitions in 2023 with an average deal premium of 80.27% at the time of announcement.

Performance Summary

	Q4 2023	YTD	1 Y
SBIO (NAV)	20.94%	8.17%	8.17%
S-Network Medical Breakthroughs Index - TR	21.08%	8.39%	8.39%
NASDAQ Biotechnology Index - TR	10.75%	4.59%	4.59%
S&P Biotechnology Select Industry Index	22.18%	7.50%	7.50%

As of 12/31/2023

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.



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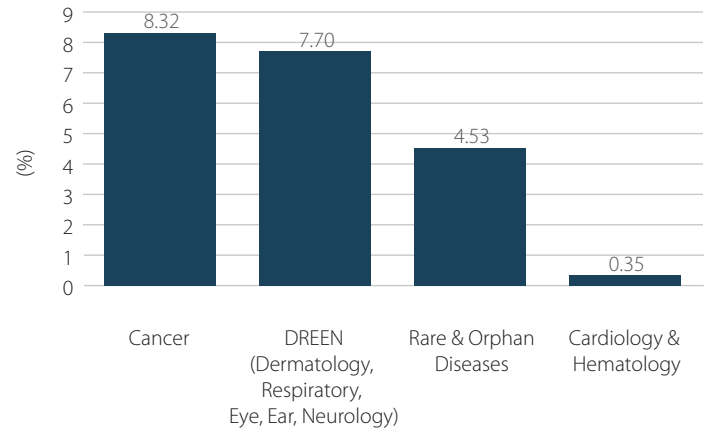
Contribution to Return by Treatment Focus

- SBIO's Cancer treatment segment was the top performer in Q4. Within the segment, ALX Oncology Holdings Inc. (**ALXO, drop in December rebalance**) was the top performer, +182.29%. ALX Oncology gained on positive news from its Phase II trial for its HER2-positive gastric/gastroesophageal junction cancer treatment.
- Within SBIO's DREEN (Dermatology, Respiratory, Eye, Ear, Neurology) segment last quarter, Altimune Inc. (**ALT, drop in December rebalance**) surged 195% and was the top performing name in the segment. Altimune rallied on positive topline results for its obesity drug, pemvidutide, in a mid-stage trial. In a 48-week trial, patients lost up to 16% of their bodyweight, which would put Altimune's drug on par with some competitors.
- Within the Rare & Orphan Diseases treatment segment, Scholar Rock Holding Corp. (**SRRK, drop in December rebalance**) was the leader, +167.32%, after receiving a price target upgrade from an analyst at Jefferies, citing positive odds on the success of a Phase III study for a Spinal Muscular Atrophy treatment and a new obesity drug as the potential catalysts.
- SBIO's Cardiology & Hematology segment was led this month by Aerovate Therapeutics Inc. (**AVTE, 0.42% weight***), which gained 66.76% in the final quarter of the year. Aerovate climbed in part due to reporting cash runway on hand to last into 2026, as well as positive analyst commentary on the success of its pulmonary arterial hypertension treatment.

Valuation Update

- The S-Network Medical Breakthroughs Index (PMBI) has a weighted average cash-burn of 38.94 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 \$2.682 billion, with 54.52% classified as mid-caps, and 45.48% classified as small-caps.

SBIO Company Focus Contribution To Return



Source: Bloomberg L.P., as of 12/31/2023

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	93	121	221
Weighted Average Market Cap (in Mil, \$)	\$2,682	\$14,105	\$44,910
Price/Sales Ratio	9.47x	7.12x	6.25x
Cash Burn (months)	38.94	22.63	28.14

Source: Bloomberg L.P., as of 12/31/2023

Past performance is no guarantee of future results.

Q4 2023 Company Spotlight

Company: RayzeBio Inc. (RYZB, 2.55% weight*)

Focus Group: Cancer

- RayzeBio is a cancer treatment company based out of San Diego that specializes in radiopharmaceutical therapeutics ("RPT"), which is the use of radioactive isotopes in pharmaceutical drugs. The company focuses on treatments for solid tumors and small cell lung cancer, among others.
- RayzeBio was one of the top performers in SBIO this quarter, climbing +135.58% after announcing it will be acquired by Bristol-Myers Squibb (**BMY, not in SBIO**) in an all-cash deal. The deal will help bolster Bristol-Myers oncology portfolio but also highlighted the attractiveness of SBIO's SMid-cap biotech companies as M&A targets. "Radiopharmaceutical therapeutics are already transforming cancer care, and RayzeBio is at the forefront of pioneering the application of this novel modality. We look forward to supporting and accelerating RayzeBio's preclinical and clinical programs and advancing its highly innovative radiopharmaceutical platform."¹ – Bristol-Myers CEO Christopher Boerner.
- The deal is expected to close in the summer of 2024 and represented a 144% premium at the time of announcement.

* Weight in SBIO as of 12/31/2023

¹ Bristol Myers Squibb Adds Premier Radiopharmaceutical Platform with Acquisition of RayzeBio, December 26, 2023.

ALPS Medical Breakthroughs ETF (SBIO) Performance as of 12/31/2023

Total Returns	Cumulative				Annualized			
	1 M	3 M	YTD	SI ¹	1 Y	3 Y	5 Y	SI ¹
NAV (Net Asset Value)	25.11%	20.94%	8.17%	40.13%	8.17%	-13.67%	3.17%	3.82%
Market Price	25.17%	20.95%	8.24%	40.09%	8.24%	-13.69%	3.28%	3.82%
S-Network Medical Breakthroughs Index - TR	25.20%	21.08%	8.39%	44.95%	8.39%	-13.25%	3.58%	4.21%
NASDAQ Biotechnology Index - TR	12.91%	10.75%	4.59%	44.61%	4.59%	-2.03%	8.26%	4.18%

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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

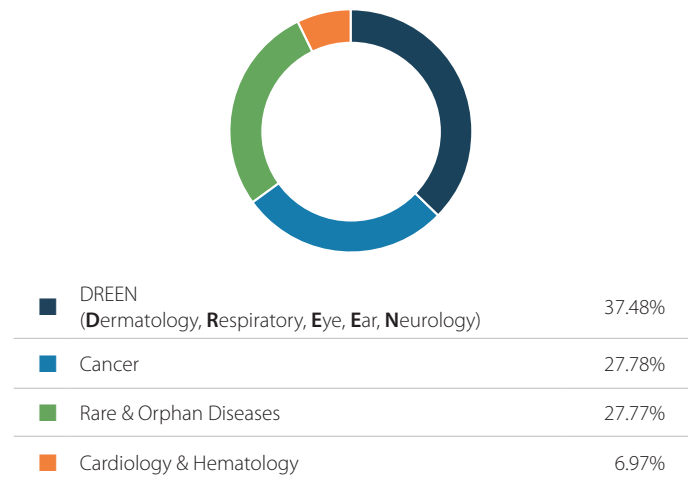
Total Operating Expenses: **0.50%**

Top 10 Holdings

CEREVEL THERAPEUTICS HOLDING	4.09%
VAXCYTE INC	4.05%
ACADIA PHARMACEUTICALS INC	3.46%
ALKERMES PLC	3.20%
REVOLUTION MEDICINES INC	3.15%
AXSOME THERAPEUTICS INC	2.55%
RAYZEBIO INC	2.55%
CORCEPT THERAPEUTICS INC	2.32%
MOONLAKE IMMUNOTHERAPEUTICS	2.32%
XENON PHARMACEUTICALS INC	2.31%

Source: SS&C ALPS Advisors, as of 12/31/2023, subject to change
Daily holdings are available at www.alpsfunds.com.

Treatment Focus Breakdown



Source: S-Network Global Indexes, as of 12/31/2023, holdings subject to change

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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

SMB000457 5/31/2024