

ALPS Medical Breakthroughs ETF

Monthly Insights | March 2022



Key Takeaways

- The ALPS Medical Breakthroughs ETF (SBIO) gained 0.27% during the month of March 2022 while the broader US equity markets rebounded after a rocky start to the year.
- SBIO's Rare & Orphan Diseases segment was the best performer among the four biotech segments in SBIO in March 2022.
- **Company Spotlight:** Longeveron Inc. (**LGVN; 0.21% weight***) rose 104.14% in March after its Alzheimer's treatment met its primary endpoint in Phase 1 trials.

Performance Notes

- SBIO gained 0.27% in March 2022 while the broader US equity market gained 3.71%. SBIO underperformed the broad market, as markets rebounded following a rocky start to the year amid Russia/Ukraine tensions and Fed uncertainty.
- SMID-cap biotech (SBIO) underperformed large-cap biotech in March, as represented by the ICE Biotechnology Index. SBIO's mid and small cap names can oftentimes be more volatile amid times of uncertainty compared to large cap biotech names due to their longer duration of expected earnings. Large cap biotech came back into focus in March as new COVID strains have emerged, causing mass lockdowns in China.

Performance Summary

	Mar-22	YTD	1 Y
SBIO (NAV)	0.27%	-20.27%	-32.88%
S-Network Medical Breakthroughs Index - TR	0.06%	-19.55%	-33.54%
ICE Biotechnology Index	3.30%	-14.53%	-9.93%

As of 3/31/2022

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 & 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.



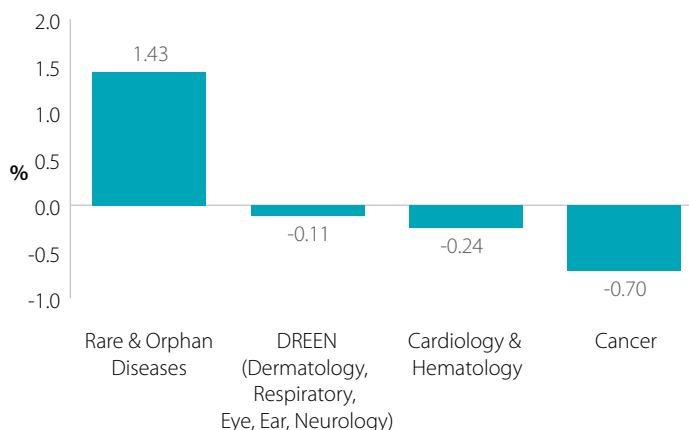
* Weight in SBIO as of 3/31/2022

ALPS Medical Breakthroughs ETF

Contribution to Return by Treatment Focus

- SBIO's Rare & Orphan Diseases segment was the best performer in March 2022. Within the segment, Longeveron Inc. (**LGVN; 0.21% weight***), highlighted below, was the top performer, +104.14%, and Clene Inc. (**CLNN; 0.19% weight***) was the second best, +27.51%. Clene gained after its ALS treatment showed promising results.
- Within the Cardiology & Hematology segment, REGENXBIO Inc. (**RGNX; 1.12% weight***) gained 26.63% after unveiling an ambitious plan to advance five of its gene therapies to advanced stages by 2025.
- Within the DREEN (Dermatology, Respiratory, Eye, Ear, Neurology) segment, MannKind Corp. (**MNKD; 0.73% weight***) had a healthy month, +40.46%, after insider buying signaled managements faith in the company moving forward.

SBIO Company Focus Contribution To Return



Source: Bloomberg L.P., as of 3/31/2022

Past performance is no guarantee of future results.

Valuation Update

- The S-Network Medical Breakthroughs Index (PMBI) has a weighted average cash-burn of 38 months that continues to exceed peer biotechnology indexes, and is a distinguishing defensive characteristic for the fund.
- PMBI's holdings have an average market value of \$2.054 billion, with 39.01% classified as mid-caps, and 60.99% classified as small-caps.

Index Characteristics

	S-Network Medical Breakthroughs Index	S&P Biotechnology Select Industry Index	ICE Biotechnology Index
Number of Constituents	130	156	371
Weighted Average Market Cap (in Mil, \$)	\$2,054	\$10,020	\$38,943
Price/Sales Ratio	6.14x	6.83x	5.48x
Cash Burn (months)	38.03	28.11	30.25

Source: Bloomberg L.P., as of 3/31/2022

Past performance is no guarantee of future results.

March 2022 Company Spotlight

Company: Longeveron Inc. (**LGVN; 0.21% weight***)

Focus Group: Rare & Orphan Diseases

- Longeveron, based in Florida, focuses on therapies for aging and life threatening conditions.
- Longeveron gained over 100% in March after the company said its Phase 1 trial for its cell therapy to treat Alzheimer's disease treatment met its primary endpoint, in an announcement late in the month. The results support further trials, with Phase 2 underway in an effort to treat a disease that is estimated to impact 50 million people worldwide.

* Weight in SBIO as of 3/31/2022

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ALPS Medical Breakthroughs ETF (SBIO) Performance

Total Returns	Cumulative as of 3/31/2022				Annualized as of 3/31/2022			
	1 M	3 M	YTD	SI ¹	1 Y	3 Y	5 Y	SI ¹
NAV (Net Asset Value)	0.27%	-20.27%	-20.27%	43.19%	-32.88%	-2.32%	6.46%	5.08%
Market Price	0.30%	-20.37%	-20.37%	43.02%	-32.97%	-2.34%	6.43%	5.06%
S-Network Medical Breakthroughs Index - TR	0.32%	-20.18%	-20.18%	46.55%	-32.68%	-2.04%	6.74%	5.41%
NASDAQ Biotechnology Index - TR	4.35%	-11.67%	-11.67%	35.88%	-11.16%	6.54%	6.93%	4.32%

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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%**

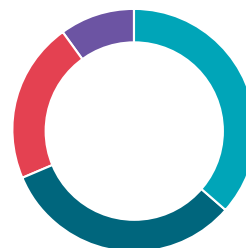
Top 10 Holdings

Ionis Pharmaceuticals Inc	4.12%
Cerevel Therapeutics Holding	4.07%
Alkermes PLC	3.35%
Galapagos NV-Spon ADR	3.18%
Acadia Pharmaceuticals Inc	3.07%
Karuna Therapeutics Inc	2.97%
Cytokinetics Inc	2.42%
Insmed Inc	2.19%
Springworks Therapeutics Inc	2.19%
PTC Therapeutics Inc	2.09%

Source: SS&C ALPS Advisors, as of 3/31/2022, subject to change

Daily holdings are available at www.alpsfunds.com.

Treatment Focus Breakdown



DREEN (Dermatology, Respiratory, Eye, Ear, Neurology)	36.62%
Rare & Orphan Diseases	32.16%
Cancer	21.47%
Cardiology & Hematology	9.75%

Source: S-Network Global Indexes, as of 3/31/2022,

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 are not individually redeemable. Investors buy and sell shares on a secondary market. Only market makers or "authorized participants" may trade directly with the Fund, typically in blocks of 5,000, 25,000 or 50,000 shares.

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.

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.

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.

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

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.

One may not invest directly in an index.

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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