

ALPS Medical Breakthroughs ETF

Monthly Insights | December 2021

Key Takeaways

- The ALPS Medical Breakthroughs ETF fell 1.56% during the month of December 2021 while the broader US equity market gained.
- SBIO's Cardiology & Hematology segment was the best performer in December 2021, with four companies gaining over 10%.
- Company Spotlight:** Arena Pharmaceuticals Inc. (**ARNA**; **3.74% weight****) rose 68.47% in December after announcing it will be acquired by Pfizer Inc. (**PFE**; **not in SBIO**).

Performance Notes

- SBIO fell 1.56% in December 2021 while the broader US equity market gained 4.47%. SBIO underperformed the broad market in the final month of the year as markets rallied into 2022 on a strong value rotation away from growth.
- SMID-cap biotech (SBIO) underperformed large-cap biotech in December, 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 high beta and lack of revenue/earnings in some cases. Additionally, the Omicron variant put some large cap biotech stocks back in the spotlight for their vaccines and treatments.

	Dec-21	YTD	1 Yr.
ALPS Medical Breakthroughs ETF (SBIO)	-1.56%	-17.54%	-17.54%
S&P Biotechnology Select Industry Index	-3.74%	-20.38%	-20.38%
ICE Biotechnology Index	-0.95%	5.40%	5.40%

Performance as of 12/31/2021

Performance data quoted represents past performance, which is not a guarantee of future results. Current performance may be lower or higher than the performance quoted. You can obtain performance data current to the most recent month end by calling 1-866-759-5679 or visit www.alpsfunds.com.

For standardized performance, please see Page 3.

Strategy Breakdown

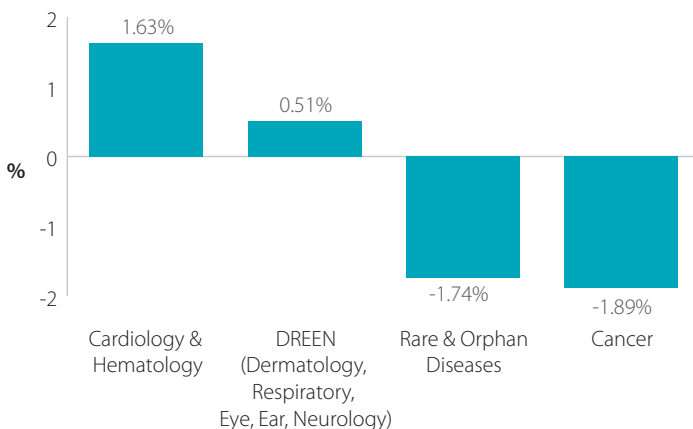
- SBIO screens for small- to mid-cap biotech companies with at least one drug or therapy in Phase II or Phase III (late-stage) clinical trials.
 - Late stage drug trials can potentially capture greater odds of success as they are further along the Food & Drug Administration (FDA) drug trial process.
- 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.



Contribution to Return by Treatment Focus

- SBIO's Cardiology & Hematology segment was the best performer in December 2021. Arena Pharmaceuticals Inc. (**ARNA**; **3.74% weight****) was the top security within the segment, +68.47% and is the highlight in the company spotlight below. Protagonist Therapeutics (**PTGX**; **1.03% weight***) was the next best performer in the segment after announcing new mid-stage trials for its inflammatory bowel disease drug.
- Within the DREEN (Dermatology, Respiratory, Eye, Ear, Neurology) segment, Prometheus Biosciences Inc. (**RXDX**; **0.97% weight***) was the top performer, +32.64% after several price target upgrades and positive early trial news for its immune-mediated disease product.
- Within the Rare & Orphan Disease segment, Syndax Pharmaceuticals Inc. (**SNDX**; **0.70% weight***) was a top performer, +37.07% after the company jumped this month after releasing promising drug trial data for its leukemia treatment.

SBIO Company Focus Contribution To Return



Source: Bloomberg L.P., as of 12/31/2021

Past performance is not indicative of future results.

ALPS Medical Breakthroughs ETF

Valuation Update

- The S-Network Medical Breakthroughs Index (PMBI) has a weighted average cash-burn of 43 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 \$2.163 billion, with 48.15% classified as mid-caps, and 51.85% classified as small-caps.

Index Characteristics	S-Network Medical Breakthroughs Index	S&P Biotechnology Select Industry Index	ICE Biotechnology Index
Number of Constituents	130	188	372
Weighted Average Market Cap (\$ million)	\$2,165	\$9,271	\$41,566
Price/Sales	7.00x	7.99x	6.92x
Cash burn (months)	43.12	30.40	32.33

Source: Bloomberg L.P., as of 12/31/2021

Past performance is not indicative of future results.

December 2021 Company Spotlight

Company: [Arena Pharmaceuticals Inc. \(ARNA\)](#)

Weight: 3.74% weight**

Focus Group: Cardiology & Hematology

- Arena Pharmaceuticals is a California based biotech company that focuses on treatments for ulcerative colitis and Crohn's disease, among others.
- Although dropped from SBIO in a rebalance on December 17, 2021, Arena Pharmaceuticals gained 68.47% in the final month of the year, adding 1.53% of positive contribution to the fund after announcing it will be acquired by Pfizer Inc. (**PFE; not in SBIO**) on December 13th. The \$6.7 billion deal highlights the attractiveness of mid and small cap companies in the biotech space for M&A activity.

ALPS Medical Breakthroughs ETF

SBIO Performance as of 12/31/21

Total Returns	Cumulative as of 12/31/2021				Annualized as of 12/31/2021			
	1 Mo.	3 Mo.	YTD	S.I.	1 Yr.	3 Yr.	5 Yr.	S.I. ¹
ALPS Medical Breakthroughs ETF (Net Asset Value)	-1.56%	-7.22%	-17.54%	79.61%	-17.54%	14.42%	14.02%	8.72%
ALPS Medical Breakthroughs ETF (Market Price) ²	-1.45%	-7.22%	-17.55%	79.61%	-17.55%	14.63%	14.01%	8.72%
S-Network Medical Breakthroughs Total Return Index (Benchmark)	-1.52%	-7.24%	-17.31%	83.61%	-17.31%	14.73%	14.31%	9.06%

Performance data quoted represents past performance. Past performance does not guarantee future results. Current performance may be higher or lower than actual data quoted. Call 1-866-759-5679 or visit www.alpfunds.com for current month end performance. The investment return and principal value of an investment will fluctuate so that an investor's shares, when redeemed, may be worth more or less than their original cost.

¹ Fund inception date of 12/31/14

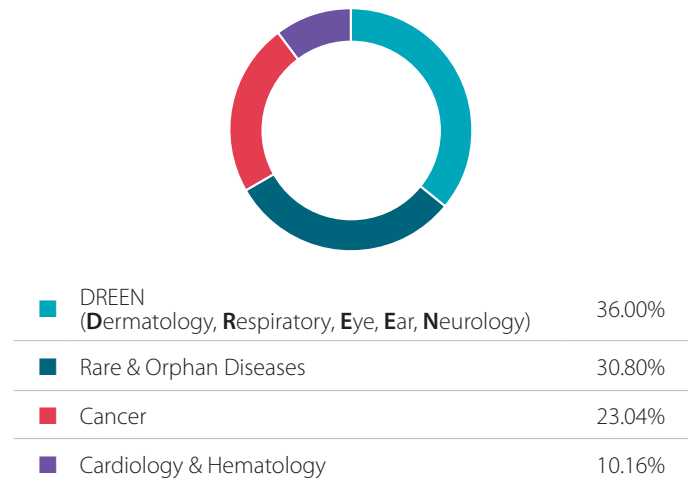
² Market Price is based on the midpoint of the bid/ask spread at 4 p.m. ET and does not represent the returns an investor would receive if shares were traded at other times..

Gross Expense Ratio: **0.50%**

Top 10 Holdings (%)[^]

CEREVEL THERAPEUTICS HOLDING	3.02
KODIAK SCIENCES INC	2.77
IONIS PHARMACEUTICALS INC	2.72
KARUNA THERAPEUTICS INC	2.45
CYTOKINETICS INC	2.42
ALKERMES PLC	2.38
ACADIA PHARMACEUTICALS INC	2.37
GALAPAGOS NV-SPON ADR	2.30
OPKO HEALTH INC	2.07
INSMED INC	2.04

[^] Source: ALPS Inc. as of 12/31/21
Holdings subject to change.

Treatment Focus Breakdown[^]

[^] Source: S-Network Global Indexes, as of 12/31/21
Holdings subject to change.

ALPS Medical Breakthroughs ETF

Important Disclosures & Definitions

An investor should consider the investment objectives, risks, charges and expenses carefully before investing. To obtain a prospectus which contains 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.

This fund may not be suitable for all investors. There are risks involved with investing in ETFs including the loss of money. The Fund is considered non-diversified and as a result may experience great volatility than a diversified fund. 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 S-Network Medical Breakthroughs Index (PMBI) is designed to capture research and development opportunities in the biotechnology industry. PMBI consists of small- to mid-cap biotechnology stocks listed on US exchanges that have one or more drugs in either Phase II or Phase III US FDA clinical trials. The total return includes the reinvestment of cash dividends.

The NASDAQ Biotechnology Total Return Index is a modified market capitalization-weighted index designed to measure the performance of all NASDAQ stocks in the biotechnology sector. The index was developed with a base value of 200 as of November 1, 1993. The total return includes the reinvestment of cash dividends.

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

The S&P Biotechnology Select Industry Total Return Index is comprised of stocks in the S&P total market index that are classified in the GICS Biotechnology sub-industry. The total return includes the reinvestment of cash dividends.

One may not invest directly in an index.

ALPS Portfolio Solutions Distributor, Inc. is the distributor for the ALPS Medical Breakthroughs ETF.

SMB000416 1/31/2023