

ALPS Medical Breakthroughs ETF

Monthly Insights | October 2021



Key Takeaways

- The ALPS Medical Breakthroughs ETF gained 1.14% during the month of October 2021 while the broader US equity market gained 5.74%.
- SBIO's DREEN segment was the best performer in October 2021, with six companies gaining over 20%.
- **Company Spotlight:** Xenon Pharmaceuticals Inc. (**XENE; 0.75% weight***) rose 103.86% in October after announcing positive results for its Epilepsy Treatment.

Performance Notes

- SBIO gained 1.14% in October 2021 while the broader US equity market gained 5.74%. SBIO underperformed the broad market in a healthy month that saw the broad markets rebound on better than expected earnings.
- SMID-cap biotech (SBIO) once again outperformed large-cap biotech in October, as represented by the ICE Biotechnology Index. SBIO's mid and small cap names reported some excellent drug trial data this month again as SBIO only selects companies with drugs in Phase II or III of clinical trials, leading to greater odds of success.

	Oct-21	Year to Date	1 Year
ALPS Medical Breakthroughs ETF (SBIO)	1.14%	-10.11%	5.57%
S&P Biotechnology Select Industry Index	-0.01%	-11.27%	11.16%
ICE Biotechnology Index	-1.20%	10.30%	27.50%

Performance as of 10/31/2021.

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 (866)759-5679 or visit www.alpsfunds.com.

For standardized performance, please see Page 3.

Strategy Breakdown

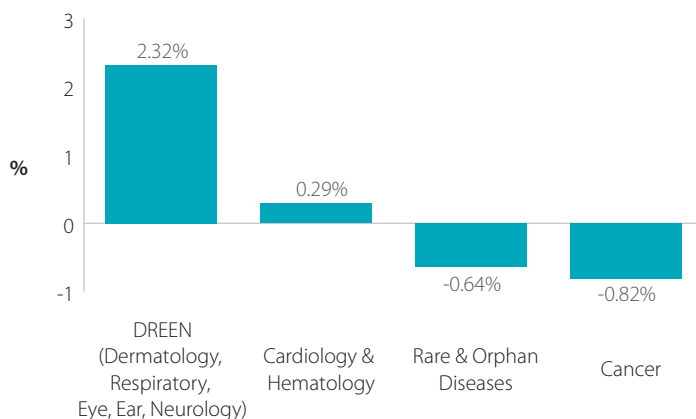
- SBIO screens for small- to mid-cap biotech companies with at least one drug or therapy in Phase II or Phase III (late-stage) clinical trials
 - Late stage drug trials can potentially capture greater odds of success as they are further along the Food & Drug Administration (FDA) drug trial process.
- 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 DREEN (Dermatology, Respiratory, Eye, Ear, Neurology) segment was the best performer in October 2021. Chemocentryx Inc. (**CCXI; 1.42% weight***) was the top security within the segment, +103.57%, after gaining FDA approval for their treatment for adult's with active anti-neutrophil cytoplasmic autoantibody-associated vasculitis.
- Within the Cardiology & Hematology segment, Global Blood Therapeutics Inc. (**GBT; 1.33% weight***) was the top performer after the company, which focuses on blood disorders, received a price target upgrade from Jefferies, citing potential sickle cell disease (SCD) market share size as a catalyst.
- Within the Cancer segment, although down for the month of October, four names did gain over 10%, including XBiotech Inc. (**XBIT; 0.26% weight***). XBiotech gained after announcing a plan to begin a clinical study for a treatment to help reduce brain damage after a stroke.

SBIO Company Focus Contribution To Return



Source: Bloomberg L.P., as of 10/31/2021.

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 37 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 \$2.696 billion, with 56.91% classified as mid-caps, and 43.09% classified as small-caps.

Index Characteristics	S-Network Medical Breakthroughs Index	S&P Biotechnology Select Industry Index	ICE Biotechnology Index
Number of Constituents	125	187	265
Weighted Average Market Cap (\$ million)	\$2,696	\$8,721	\$44,915
Price/Sales	10.26x	8.94x	7.80x
Cash burn (months)	37.17	29.49	33.97

Source: Bloomberg L.P., as of 10/31/2021.

Past performance is not indicative of future results.

October 2021 Company Spotlight

Company: Xenon Pharmaceuticals Inc. (XENE)

Weight: 0.75%

Focus Group: Rare & Orphan Diseases

- Xenon Pharmaceuticals develops therapeutics for neurological disorders. Based in Canada, the company was the top performing security in SBIO this month, +103.86%, after announcing positive results for its Epilepsy Treatment.
- Xenon surged over 100% to begin the month after results from its Phase 2 trial for focal epilepsy yielded statistically significant results that beat and surprised Wall Street. One analyst said this has potential to be a "blockbuster" drug with \$1 billion in sales per year. Several other price target raises followed the announcement leading to the impressive month for the SBIO holding.

ALPS Medical Breakthroughs ETF

SBIO Performance as of 10/31/21

Total Returns	Cumulative as of 10/31/2021				Annualized as of 9/30/2021			
	1 Mo.	3 Mo.	YTD	S.I.	1 Yr.	3 Yr.	5 Yr.	S.I. ¹
ALPS Medical Breakthroughs ETF (Net Asset Value)	1.14%	4.47%	-10.11%	95.79%	10.72%	6.02%	12.83%	10.28%
ALPS Medical Breakthroughs ETF (Market Price) ²	1.10%	4.54%	-10.16%	95.71%	10.82%	6.03%	12.84%	10.28%
NASDAQ Biotechnology Total Return Index	-1.89%	-2.75%	5.35%	62.02%	20.21%	10.51%	11.54%	7.71%
S-Network Medical Breakthroughs Total Return Index (Benchmark)	1.14%	4.56%	-9.83%	100.21%	11.17%	6.38%	13.13%	10.64%

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¹ Fund inception date of 12/30/14.

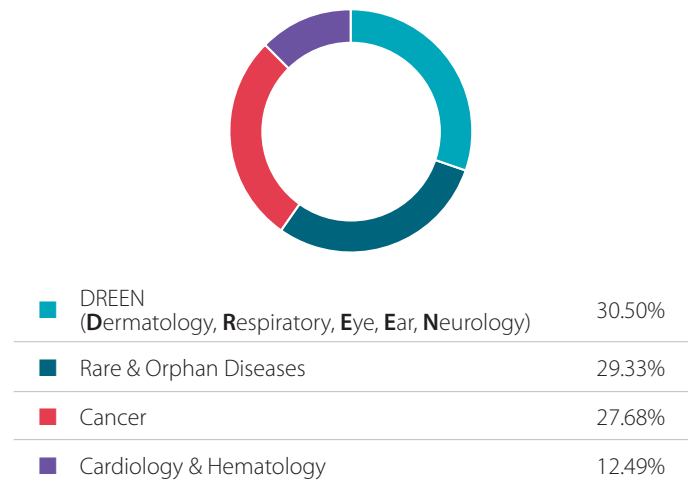
² Market Price is based on the midpoint of the bid/ask spread at 4 p.m. ET and does not represent the returns an investor would receive if shares were traded at other times.

Gross Expense Ratio: **0.50%**

Top 10 Holdings (%)[^]

LEGEND BIOTECH CORP-ADR	4.45
KODIAK SCIENCES INC	3.53
CEREVEL THERAPEUTICS HOLDING	3.45
VIR BIOTECHNOLOGY INC	2.89
ALKERMES PLC	2.87
TG THERAPEUTICS INC	2.61
AURINIA PHARMACEUTICALS INC	2.48
KARUNA THERAPEUTICS INC	2.43
IOVANCE BIOTHERAPEUTICS INC	2.21
ARENA PHARMACEUTICALS INC	2.05

[^] Source: ALPS Inc. as of 10/31/21.
Holdings subject to change.

Treatment Focus Breakdown[^]

[^] Source: S-Network Global Indexes, as of 10/31/21.
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 which contain this and other information call 844.234.5852 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

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