

ALPS Medical Breakthroughs ETF

Monthly Insights | August 2021

Key Takeaways

- The ALPS Medical Breakthroughs ETF returned 6.37% during the month of August 2021 while the broader US equity market rose by roughly 3.00%.
- SBIO's Rare & Orphan Disease segment was the best performer in August 2021, with thirty of its forty companies posting positive performance during the month.
- **Company Spotlight:** Arcturus Therapeutics Holdings Inc. (**ARCT**; **0.84% weight***) rose 75.06% in August after gaining approval to begin trials of their mRNA COVID vaccine from Vietnam and Singapore.

Performance Notes

- SBIO returned 6.37% in August 2021 while the broader US equity market rose roughly 3.0%. Renewed positive sentiment around biotech M&A (mergers & acquisitions) and encouraging drug trial data drove SBIO in August.
- SMID-cap biotech (SBIO) outperformed large-cap biotech in August, as represented by the ICE Biotechnology Index. SBIO's mid and small cap names are prime targets for acquisition and this month SBIO's immunotherapy-focused portfolio witnessed one constituent acquisition, among a few other immunotherapy-focused acquisitions that took place.

	Aug-21	Year to Date	1 Year
ALPS Medical Breakthroughs ETF (SBIO)	6.37%	-8.47%	13.36%
S&P Biotechnology Select Industry Index	7.71%	-5.46%	19.26%
ICE Biotechnology Index	4.08%	18.91%	32.90%

Performance as of 8/31/2021.

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

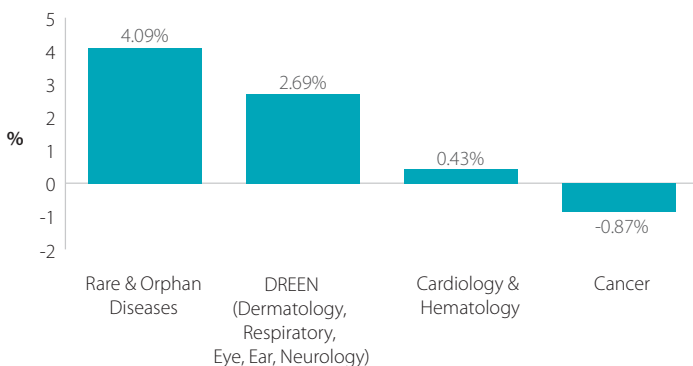
- SBIO screens for small- to mid-cap biotech companies with at least one drug or therapy in Phase II or Phase III (late-stage) clinical trials
 - Late stage drug trials can potentially capture greater odds of success as they are further along the Food & Drug Administration (FDA) drug trial process.
- 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 Rare & Orphan Diseases segment, the leader last month, was once again the best performer in August 2021. Arcturus Therapeutics Holdings Inc. (**ARCT**; **0.84% weight***) was the top security this month (+75.06%) and is highlighted below in the company spotlight. Cortexyme Inc. (**CRTX**; **1.68% weight***) followed closely behind, +70.41%, after demonstrating key biomarkers for its antibody immunotherapy to treat Alzheimer's disease.
- Infinity Pharmaceuticals Inc. (**INFI**; **0.18% weight***), a company within SBIO's Cancer segment, rose nearly 70% and was the second best performer in the fund in the month of August. The Massachusetts based company soared after JP Morgan updated their price target after recent data for their cancer drug, Eganalisib, to treat urothelial cancer showed positive but underappreciated results in trials.
- Within the DREEN (Dermatology, Respiratory, Eye, Ear, Neurology) segment, Altimmune Inc. (**ALT**; **0.34% weight***), an immunotherapy company developing therapies for respiratory and viral infections, skyrocketed 65.27% this month after several price target raises from analysts.

SBIO Company Focus Contribution To Return



Source: Bloomberg L.P., as of 8/31/2021.

Past performance is not indicative of future results.

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Valuation Update

- The S-Network Medical Breakthroughs Index (PMBI) has a weighted average cash-burn of just over 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 \$2.57 billion, with 56.17% classified as mid-caps, and 43.83% classified as small-caps.

Index Characteristics	S-Network Medical Breakthroughs Index	S&P Biotechnology Select Industry Index	ICE Biotechnology Index
Number of Constituents	126	195	266
Weighted Average Market Cap (\$ million)	\$2,571	\$9,309	\$50,389
Price/Sales	10.17x	9.37x	8.57x
Cash burn (months)	37.15	29.53	31.89

Source: Bloomberg L.P., as of 8/31/2021.

Past performance is not indicative of future results.

August 2021 Company Spotlight

Company: Arcturus Therapeutics Holdings Inc. (ARCT)

Weight: 0.84%

Focus Group: Rare & Orphan Diseases

- Arcturus Therapeutics is a California based company that focuses on RNA therapeutics for the treatment of diseases.
- Arcturus had an excellent month, +75.06% after gaining approval to begin trials of their mRNA COVID vaccine from the Vietnam Ministry of Health as well as the Singapore Health Sciences Authority at the beginning of the month. Both countries approved the ARCT-154 vaccine study, with Singapore also giving the greenlight for ARCT-165 (both mRNA vaccines). The study, which involves both vaccines as well as for a booster to existing mRNA vaccines will start in the next few weeks.

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SBIO Performance as of 8/31/21

Total Returns	Cumulative as of 8/31/2021				Annualized as of 6/30/2021			
	1 Mo.	3 Mo.	YTD	S.I.	1 Yr.	3 Yr.	5 Yr.	S.I. ¹
ALPS Medical Breakthroughs ETF (Net Asset Value)	6.37%	0.56%	-8.47%	99.36%	17.12%	10.67%	17.70%	11.94%
ALPS Medical Breakthroughs ETF (Market Price) ²	6.40%	0.51%	-8.56%	99.19%	17.08%	10.76%	17.69%	11.92%
NASDAQ Biotechnology Total Return Index	4.16%	12.35%	12.85%	73.55%	20.52%	14.90%	14.44%	8.21%
S-Network Medical Breakthroughs Total Return Index (Benchmark)	6.42%	0.69%	-8.22%	103.78%	17.57%	10.94%	18.01%	12.30%

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 1.866.675.2639 or visit www.alpsfunds.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 12/30/14.

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.

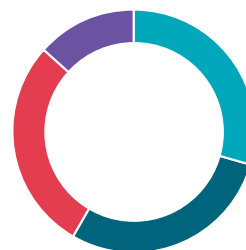
Gross Expense Ratio: **0.50%**

Top 10 Holdings (%)[^]

VIR BIOTECHNOLOGY INC	3.94
APELLIS PHARMACEUTICALS INC	3.12
LEGEND BIOTECH CORP-ADR	3.05
ALKERMES PLC	2.95
KODIAK SCIENCES INC	2.84
CEREVEL THERAPEUTICS HOLDING	2.37
TG THERAPEUTICS INC	2.26
SPRINGWORKS THERAPEUTICS INC	2.16
IOVANCE BIOTHERAPEUTICS INC	2.16
KARUNA THERAPEUTICS INC	2.06

[^] Source: ALPS Inc. as of 8/31/21.

Holdings subject to change.

Treatment Focus Breakdown[^]

Rare & Orphan Diseases	29.62%
DREEN (Dermatology, Respiratory, Eye, Ear, Neurology)	28.79%
Cancer	28.28%
Cardiology & Hematology	13.32%

[^] Source: S-Network Global Indexes, as of 8/31/21.

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 and the owners of shares may purchase or redeem shares from a fund in creation units (blocks of 50,000 shares) only.

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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