

ALPS Medical Breakthroughs ETF

Monthly Insights | September 2021

Key Takeaways

- The ALPS Medical Breakthroughs ETF fell -2.90% during the month of September 2021 while the broader US equity market fell by -4.65%.
- SBIO's Cancer segment was the best performer in September 2021, with five companies gaining over 10%.
- **Company Spotlight:** Kadmon Holdings Inc. (**KDMN; 0.89% weight***) rose 58.94% in September after announcing it will be acquired by Sanofi (SAN FP) in an all cash deal.

Performance Notes

- SBIO fell -2.90% in September 2021 while the broader US equity market fell -4.65%. SBIO outperformed the broad market in a turbulent month that saw the broad markets affected by debt ceiling talks and continued supply chain concerns.
- SMID-cap biotech (SBIO) once again outperformed large-cap biotech in September, as represented by the ICE Biotechnology Index. SBIO's mid and small cap names are prime targets for acquisition and we saw another acquisition announced this month highlighted in the company spotlight below. Positive news around drug trial data also contributed to outperformance over large cap names.

	Sep-21	Year to Date	1 Year
ALPS Medical Breakthroughs ETF (SBIO)	-2.90%	-11.12%	10.72%
S&P Biotechnology Select Industry Index	-5.43%	-10.59%	13.09%
ICE Biotechnology Index	-6.12%	11.64%	24.49%

Performance as of 9/30/2021.

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

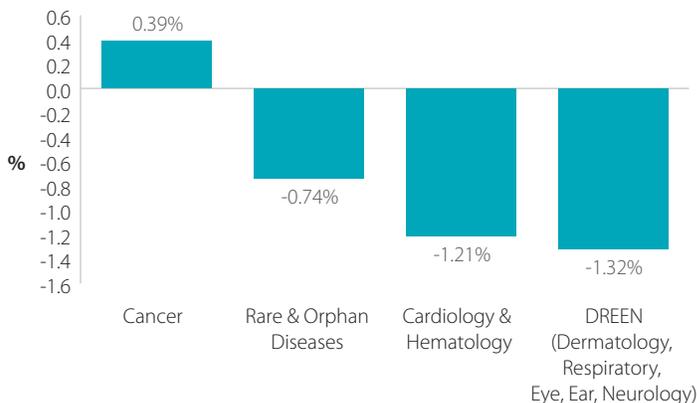
- SBIO screens for small- to mid-cap biotech companies with at least one drug or therapy in Phase II or Phase III (late-stage) clinical trials
 - Late stage drug trials can potentially capture greater odds of success as they are further along the Food & Drug Administration (FDA) drug trial process.
- 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 Cancer segment was the best performer in September 2021. Legend Biotech Corp (**LEGN; 4.33% weight***) was the top security within the segment, +32.04%. The New Jersey based company began phase 1 clinical trials for its T-Cell lymphoma immunotherapy this month.
- Within the Rare & Orphan Disease segment, Kadmon Holdings Inc. (**KDMN; 0.89% weight***) was the top performer and is mentioned below. Gossamer Bio Inc. (**GOSS; 0.56% weight***) was the second best performer after a competitor to its therapy for pulmonary arterial hypertension (PAH) announced it would be bought by Merck (MRK) at a 30% premium.
- Within the Cardiology & Hematology segment, REGENXBIO Inc. (**RGNX; 1.06% weight***), a virus gene therapy company, gained nearly 30% in September after announcing an eye care collaboration with AbbVie (ABBV; not in SBIO). REGENXBIO will be responsible for the trials of the treatment for wet age-related macular degeneration, diabetic retinopathy, and other retinal diseases, while AbbVie will handle commercialization later in the cycle.

SBIO Company Focus Contribution To Return



Source: Bloomberg L.P., as of 9/30/2021.

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 \$2.55 billion, with 52.57% classified as mid-caps, and 47.43% 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)	\$2,551	\$8,772	\$47,486
Price/Sales	9.98x	8.86x	7.89x
Cash burn (months)	37.18	28.84	31.78

Source: Bloomberg L.P., as of 9/30/2021.

Past performance is not indicative of future results.

September 2021 Company Spotlight

Company: Kadmon Holdings Inc. (KDMN)

Weight: 0.89%

Focus Group: Rare & Orphan Diseases

- Kadmon specializes in small molecule and biologics for unmet medical needs. The company's clinical pipeline includes treatments for immune and fibrotic diseases as well as immuno-oncology therapies
- Kadmon was the top performing security in SBIO this month after announcing it will be acquired by Sanofi (SAN FP) in an all cash deal, a 79% premium at the time of announcement. The nearly \$2 billion deal highlights the attractiveness of SMID companies that are ripe for acquisition by larger companies in the space.

ALPS Medical Breakthroughs ETF

SBIO Performance as of 9/30/21

Total Returns	Cumulative as of 9/30/2021				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)	-2.90%	-6.98%	-11.12%	93.58%	10.72%	6.02%	12.83%	10.28%
ALPS Medical Breakthroughs ETF (Market Price) ²	-2.82%	-6.91%	-11.14%	93.58%	10.82%	6.03%	12.84%	10.28%
NASDAQ Biotechnology Total Return Index	-4.84%	-1.08%	7.38%	65.15%	20.21%	10.51%	11.54%	7.71%
S-Network Medical Breakthroughs Total Return Index (Benchmark)	-2.86%	-6.88%	-10.85%	97.95%	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.

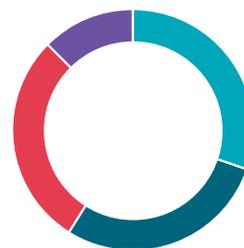
Gross Expense Ratio: **0.50%**

Top 10 Holdings (%)[^]

LEGEND BIOTECH CORP-ADR	4.33
VIR BIOTECHNOLOGY INC	3.36
ALKERMES PLC	2.95
KODIAK SCIENCES INC	2.92
TG THERAPEUTICS INC	2.81
CEREVEL THERAPEUTICS HOLDING	2.53
IOVANCE BIOTHERAPEUTICS INC	2.26
ARENA PHARMACEUTICALS INC	2.15
KARUNA THERAPEUTICS INC	2.14
PROTHENA CORP PLC	1.90

[^] Source: ALPS Inc. as of 9/30/21.

Holdings subject to change.

Treatment Focus Breakdown[^]

■ Rare & Orphan Diseases 30.31%

■ Cancer 28.81%

■ DREEN (Dermatology, Respiratory, Eye, Ear, Neurology) 28.53%

■ Cardiology & Hematology 12.35%

[^] Source: S-Network Global Indexes, as of 9/30/21.

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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