

# Nasdaq Leading the Way in Biotech

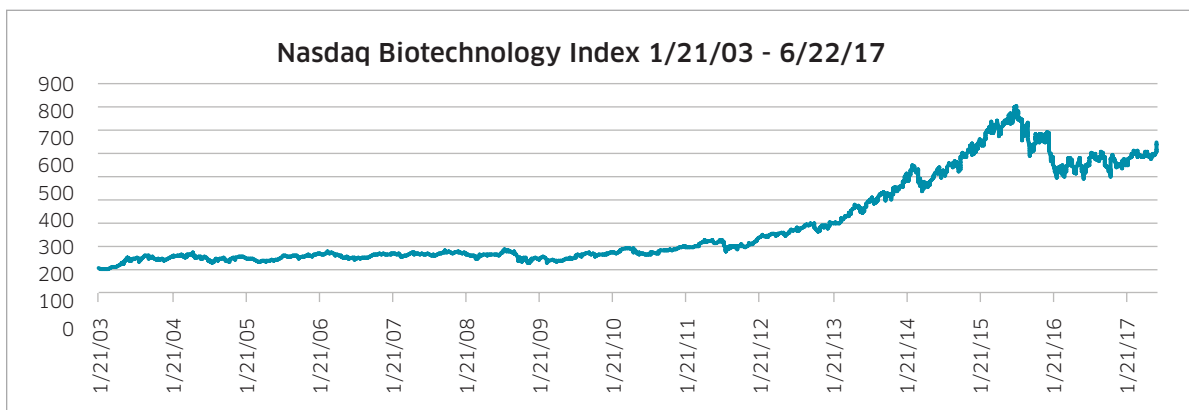
BY: CHRIS MOYER & EFRAM SLEN, NASDAQ GLOBAL INFORMATION SERVICES

LUKE BROWN, NASDAQ CORPORATE SOLUTIONS

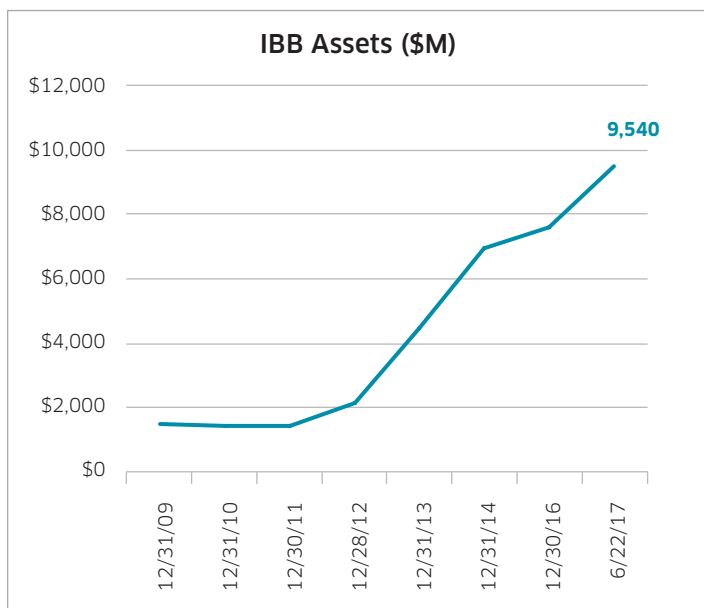
Over the past five years, Biotech stocks have been fueled by a more favorable regulatory environment, new cutting-edge technology, and a fresh infusion of IPOs and venture capital. The Nasdaq Biotechnology Index has experienced impressive performance since its inception.

Below is a graphic which encompasses performance over the time frame between 1/21/03 - 6/22/17 in which the index had a cumulative return of 550%, an annualized return of 14%, and annualized volatility of 25%. The spike in performance which began in 2012 can largely be attributed to the factors we listed above. Although the index did top out in late summer of 2015, the correction has appeared to stabilize over the past few years and just recently has seen a rather sharp move higher.

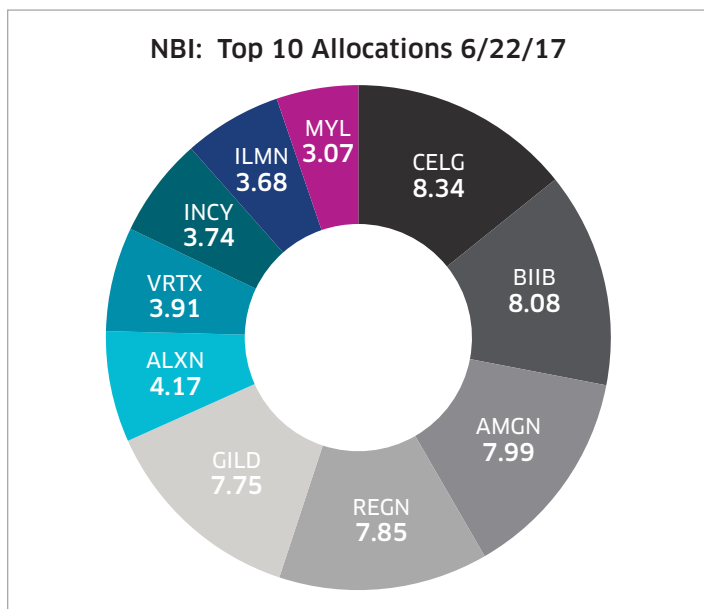
1/21/2003 - 6/22/17	CUMULATIVE RETURN	ANNUALIZED RETURN	ANNUALIZED VOLATILITY
NBI	550%	14%	25%



Along with this impressive performance came a nice boost in AUM for IBB (which is the largest corresponding ETF that tracks the Nasdaq Biotechnology Index globally). In fact, the AUM as of 12/31/09 was roughly \$1.5B and by the end of 6/22/2017 had jumped all the way to \$9.54B. The largest YoY increase came between 12/31/13 and 12/31/14 which saw a jump of \$2.5B.



The most heavily weighted allocations within NBI as of 6/22/17 were led by Celgene, Gilead, Biogen, and Amgen. The largest allocation within these names was Celgene at 8.34%, followed by Biogen at 8.08%. Within the rest of the top 10 holdings, the rest of the allocations spanned from 7.99% (Amgen) to the smallest at MYL (3.07%).



## Index Methodology

- The security’s U.S. listing must be exclusively on the Nasdaq Global Select Market or the Nasdaq Global Market (unless the security was dually listed on another U.S. market prior to January 1, 2004 and has continuously maintained such listing);
- The issuer of the security must be classified according to the Industry Classification Benchmark (ICB) as either biotechnology or pharmaceutical;
- Have a market capitalization of at least \$200 million;
- Have an average daily trading volume of at least 100,000 shares;
- Index eligibility is limited to specific security types only. The security types eligible for the Index include common stocks, ordinary shares, ADRs, and shares of beneficial interest or limited partnership interests.
- The Index Securities are evaluated annually in December. The eligibility criteria is applied using market data through the end of October and is updated for total shares outstanding submitted in a publicly filed SEC document via EDGAR through the end of November. Securities meeting the criteria are included in the Index.
- The index is modified market cap weighted with a maximum weight of any security at 8% and no more than 5 securities can have a weight in excess of 4%.

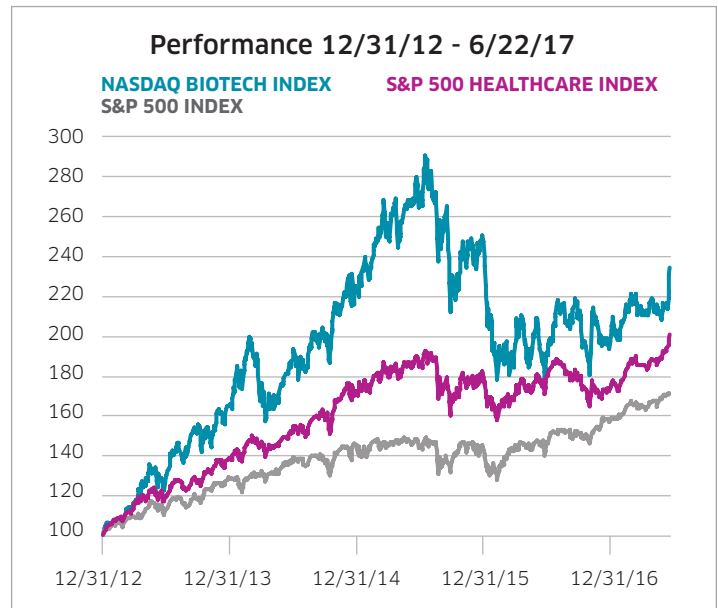
## Aging Population

The size and scope of the Baby Boomer generation has opened an abundance of opportunities for both companies and investors alike. The first of America’s Baby Boomers, born during the period 1946 to 1964, just hit their 70th year during 2016. As this generation of Americans grows older, the implications on the country’s healthcare infrastructure will be vast. The large portion of the population that the Boomer generation represents will soon have to contend with a higher incidence of health issues that often come with age, including serious diseases such as Alzheimer’s and Parkinson’s. Fortunately, these Boomers are living in an unprecedented age of scientific discovery when it comes to the use of pharmaceuticals and other therapies to treat conditions ranging from arthritis to cancer. One recently announced planned study, focusing on a commonly used diabetes drug, even hopes to find ways of slowing the aging process itself. While this generation of retirees will require a constant ebb and flow of treatments, biotech companies are stepping up their research efforts with the goal of capitalizing on this huge market.

## Drivers of Growth

A tremendous amount of innovation continues to occur in biotech, such as immunotherapy, which involves using the body’s own immune system to treat serious diseases, have helped to fuel a boom in the biotechnology sector. As new discoveries draw investors to the sector, other factors are adding fuel to the fire behind the sector’s strong performance. The regulatory environment was very accommodating to pharma and biotech companies during 2014 and 2015. In fact, according to a Reuter’s article, over this two year period a 19 year high was reached in regards to new medicine approval. More specifically, in 2015 alone the number of new drugs approved by the FDA in 2015 was 45. This trend appeared to stabilize a bit during 2016 when new drug approvals fell to six-year low in 2016 at just 22. “Most industry executives remain upbeat about the hunt for new medicines, given recent advances in fighting cancer and an improved understanding of the genetic basis of other diseases, which has resulted in full development pipelines at many firms.”<sup>1</sup>

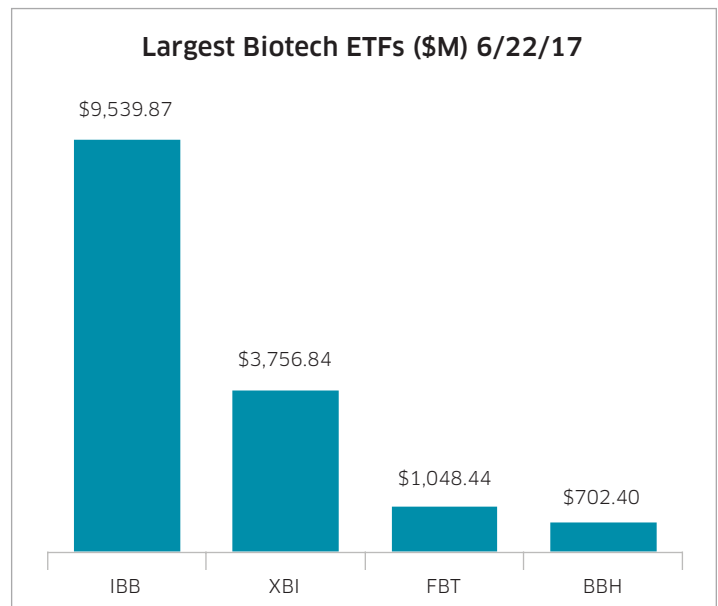
Although the biotech sector in general experienced a rather volatile 2016, sharp inflows towards IBB continue to be seen thus far into 2017. The Nasdaq Biotechnology Index, which tracks a number of bellwether companies in the space, was down -22% in 2016, which compared to the S&P 500 Index (+10%) and the S&P 500 Healthcare Index (-4%). However, on a longer term time frame, the chart below confirms the Nasdaq Biotech Index has outperformed.



Strong biotech performance over the longer term has helped send investors flocking to biotech-related ETPs in record numbers. Collectively, the top four largest biotech ETFs as of 6/22/17 held roughly \$15.04 billion. Having just over \$9.5 billion in assets as of 6/22/17, the iShares Biotech ETF is the largest product tracking the Nasdaq Biotechnology Index. The next largest fund is the SPDR Biotech ETF (XBI), which stands at roughly \$3.7 billion in assets.

Performance: 12/31/12 - 6/22/17

	Nasdaq Biotechnology Index	S&P 500 Index	S&P 500 Healthcare Index
Cumulative Return	134%	71%	101%
Annualized Return	21%	13%	17%
Annualized Volatility	26%	12%	15%



In addition to the iShares Nasdaq Biotechnology ETF, there are a number of other ETFs listed globally tied to the Nasdaq Biotechnology Index including those in London (Source NASDAQ Biotech UCITS ETF - SBIO), Korea (Mirae Asset TIGER Nasdaq BIO ETF - 203780), Taiwan (Capital NASDAQ Biotechnology Index Exchange Traded Fund - 00678) and Israel (Tachlit NASDAQ Biotechnology ILS - TCBI105). Along with these products, in the US ProShares offers geared ETFs: +3x (UBIO), +2x (BIB), -2x (BIS), and -3x (ZBIO).

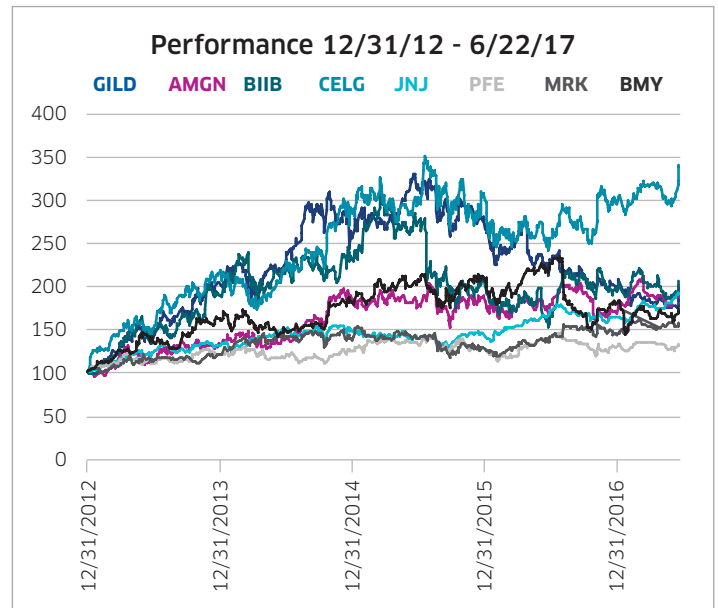
**Valuations: As of 6/22/17**

Biotech is becoming a mature industry with a growing number of profitable and cash-generating companies. Examining the Price-to-Earnings ratio of a few of the largest constituents of the Nasdaq Biotechnology Index, they have valuations aligned with those of traditional mature pharmaceutical companies. Although valuation metrics are similar to those of “Big Pharma,” performance statistics over the time frame we studied (12/30/12 - 6/22/17) show quite a bit of dispersion. Gilead, Biogen, and Celgene have outperformed by a wide margin during this time frame. In addition, these current multiples seem rather reasonable considering biotech names tend to exhibit greater future growth prospects when compared to more mature healthcare names. The lowest P/E Ratio in Biotech was GILD at 6.9, while the highest was Celgene at 27.9. In regards to Big Pharma stocks, ranging from 18.5 to 20.1. Although Celgene did have a higher P/E ratio, the performance it has exhibited (which we display below) was very impressive.

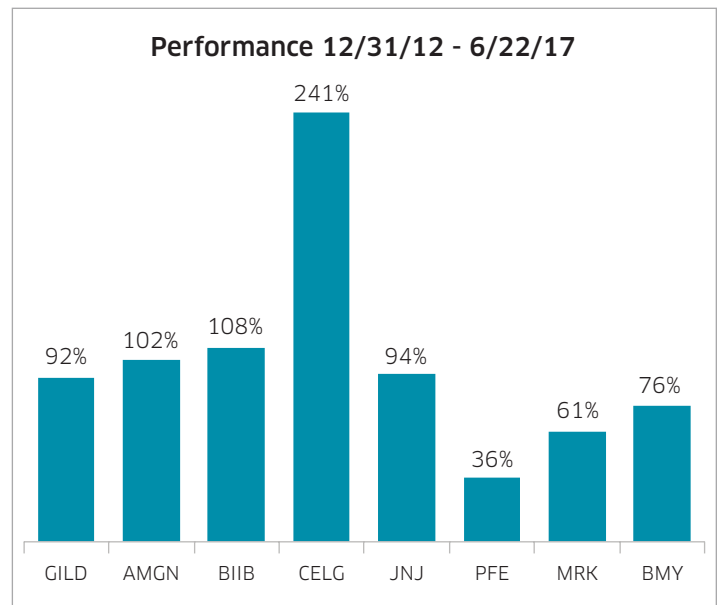
**Biotech vs. Big Pharma P/E Ratio**

GILD	7.1	JNJ	21.5
AMGN	15.5	PFE	18.6
BIIB	15.6	MRK	21.3
CELG	30.1	BMJ	19.4

Performance comparison below of the individual holdings within our P/E Ratio comparison gives us a good idea for some of the volatility these stocks experienced during the time frame we are studying. The price appreciation of biotech stocks has for the most part outpaced the broader market in recent years (with the exception of 2016).



To get a better idea of how these numbers actually stack up when comparing Biotech vs. Big Pharma on a longer term basis, the below graphic displays the actual performance figures for each of these 8 securities between 12/30/12 - 6/22/17. Celgene clearly led the pack at 241%, while Amgen (+102%), and Biogen (+108%) also had triple digit gains. The rest of the performance figures for the securities in this study are listed in chart below.



## Biotech IPOs from 2016

In 2016 there were 33 IPOs in the Biotech & Pharmaceuticals space. Thirty listed on Nasdaq. This statistic clearly demonstrates Nasdaq's leadership when it comes to company listings within these industry groups. Below is the full list of those companies along with the first trade date, the IPO price, and the performance for each from launch date to 12/30/16. In terms of performance during 2016, a number of these IPOs posted triple digit gains including NOVN (+145.64%), AVXS (+138.65%), and MRUS (+111.10%). There were also a number of names that lagged including PZRZ (-69.00%), MBRX (-62.00%), and AGLE (-56.50%). All 2016 performance figures for the 33 IPOs can be found in the below table.

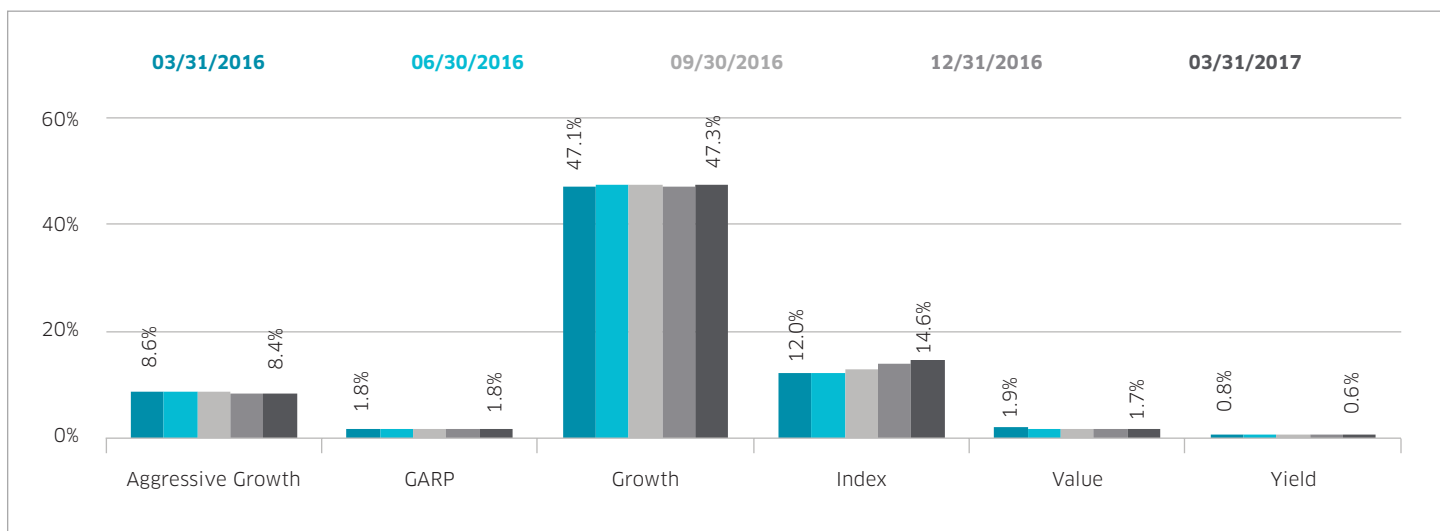
Ticker	Name	First Trade Date	Exchange	IPO Price	12/30/16 Price	Performance
MTFB	MOTIF BIO PLC-SPON ADR	11/18/2016	Nasdaq	6.98	6.19	-11.31%
MYOV	MYOVANT SCIENCES LTD	10/27/2016	NYSE	15.00	12.44	-17.07%
RARX	RA PHARMACEUTICALS INC	10/26/2016	Nasdaq	13.00	15.19	16.85%
CRSP	CRISPR THERAPEUTICS AG	10/19/2016	Nasdaq	14.00	20.26	44.71%
AZRX	AZURRX BIOPHARMA INC	10/11/2016	Nasdaq	5.50	4.74	-13.82%
OBLN	OBALON THERAPEUTICS INC	10/6/2016	Nasdaq	15.00	8.85	-41.00%
FLGT	FULGENT GENETICS INC	9/29/2016	Nasdaq	9.00	11.57	28.56%
ACIU	AC IMMUNE SA	9/23/2016	Nasdaq	11.00	12.98	18.00%
NOVN	NOVAN INC	9/21/2016	Nasdaq	11.00	27.02	145.64%
MEDP	MEDPACE HOLDINGS INC	8/11/2016	Nasdaq	23.00	36.07	56.83%
PTGX	PROTAGONIST THERAPEUTICS INC	8/11/2016	Nasdaq	12.00	21.99	83.25%
GEMP	GEMPHIRE THERAPEUTICS INC	8/5/2016	Nasdaq	10.00	7.84	-21.60%
APOP	CELLECT BIOTECHNOLOGY LT-ADR	7/29/2016	Nasdaq	6.50	3.09	-52.46%
KDMN	KADMON HOLDINGS INC	7/27/2016	NYSE	11.55	5.35	-53.68%
PTHN	PATHEON NV	7/21/2016	NYSE	21.00	28.71	36.71%
BOLD	AUDENTES THERAPEUTICS INC	7/20/2016	Nasdaq	15.00	18.27	21.80%
SYRS	SYROS PHARMACEUTICALS INC	6/30/2016	Nasdaq	12.50	12.16	-2.72%
SELB	SELECTA BIOSCIENCES INC	6/22/2016	Nasdaq	14.00	17.15	22.50%
CLSD	CLEARSIDE BIOMEDICAL INC	6/2/2016	Nasdaq	7.00	8.94	27.71%
MBRX	MOLECULIN BIOTECH INC	6/2/2016	Nasdaq	6.00	2.28	-62.00%
NH	NANTHEALTH INC	6/2/2016	Nasdaq	14.00	9.94	-29.00%
RETA	REATA PHARMACEUTICALS INC-A	5/26/2016	Nasdaq	11.00	21.83	98.45%
MRUS	MERUS NV	5/19/2016	Nasdaq	10.00	21.11	111.10%
PLSE	PULSE BIOSCIENCES INC	5/18/2016	Nasdaq	4.00	6.50	62.50%
PZRZ	PHASERX INC	5/18/2016	Nasdaq	5.00	1.55	-69.00%
SBPH	SPRING BANK PHARMACEUTICALS	5/6/2016	Nasdaq	12.00	7.99	-33.42%
NTLA	INTELLIA THERAPEUTICS INC	5/6/2016	Nasdaq	18.00	13.11	-27.17%
AGLE	AEGLEA BIOTHERAPEUTICS INC	4/7/2016	Nasdaq	10.00	4.35	-56.50%
CRVS	CORVUS PHARMACEUTICALS INC	3/23/2016	Nasdaq	15.00	14.30	-4.67%
HCM	HUTCHISON CHINA MEDITECH-ADR	3/17/2016	Nasdaq	13.50	13.57	0.52%
SNDX	SYNDAX PHARMACEUTICALS INC	3/3/2016	Nasdaq	12.00	7.17	-40.25%
PTI	PROTEOSTASIS THERAPEUTICS IN	2/11/2016	Nasdaq	8.00	12.26	53.25%
AVXS	AVEXIS INC	2/11/2016	Nasdaq	20.00	47.73	138.65%
BGNE	BEIGENE LTD-ADR	2/3/2016	Nasdaq	24.00	30.36	26.50%
EDIT	EDITAS MEDICINE INC	2/3/2016	Nasdaq	16.00	16.23	1.44%

## Share Ownership

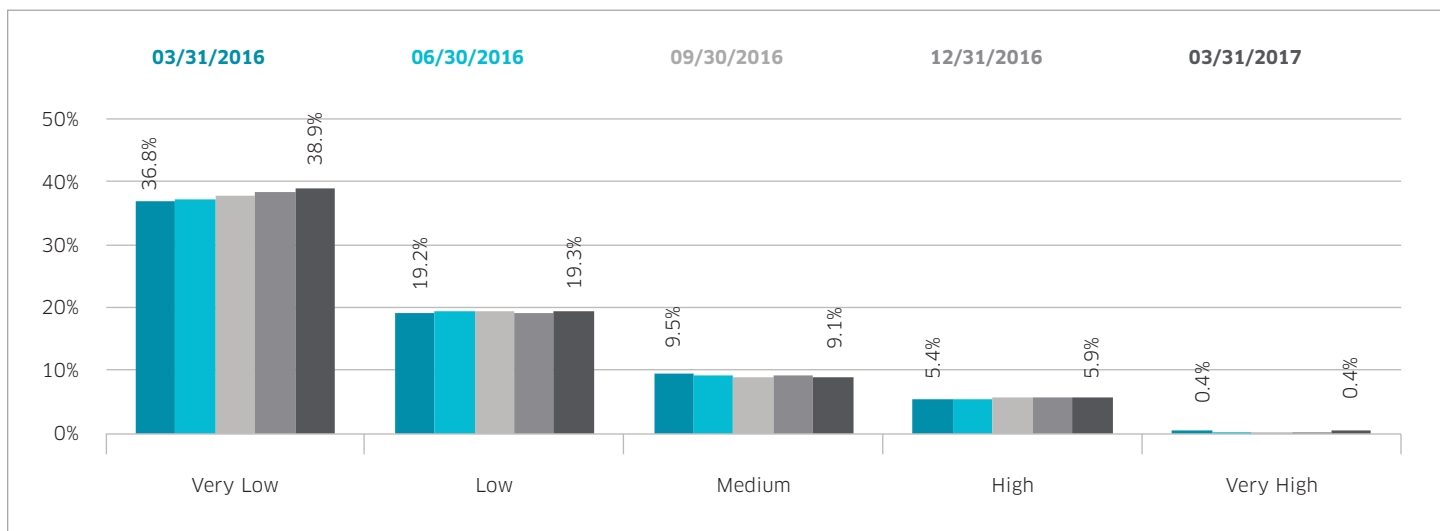
While valuations of biotech stocks tend to be highly volatile due to the release of binary data points, the overall ownership picture of the industry is more stable than one would think when examining the constituency of the Nasdaq Biotechnology Index (162 companies) between 1Q16 and 1Q17. From style, turnover, investor type and institutional ownership percentage standpoints, the industry is steady and appears to be gaining footing.

[Plain] Vanilla growth names compose just north of 47% of Nasdaq Biotechnology Index names and slowly inching toward half of all ownership of the index. In looking at the style evolution chart, can see that the only bucket to see a meaningful shift over the course of the year was index, gaining 2.6% pushing the ownership figure up to 14.6% [probably ETF growth]. Value and aggressive growth names declined very modestly during the period. From a turnover perspective, investors that tend to churn their portfolio at a very low clip increased from 36.8% to 38.9%. There were no meaningful changes among low, medium, high and very high turnover shops year over year. Generalists and hedge funds compose the overwhelming bulk of investors in biotech, representing a combined 61.5% of the investment population. Both buckets have been largely stable, increasing from 42.2% to 44.4% and 16.9% and 17.1%, respectively. Lastly, overall institutional ownership (sans retail and registered shareholders) represents 74.7% of the investment portfolio, an increase of 2.1% from 1Q16 to 1Q17. Of note, activists represent a tiny portion of biotech ownership. Investors considered to be high or very high activist threats compose 2.4% of the investment base and are holding steady.

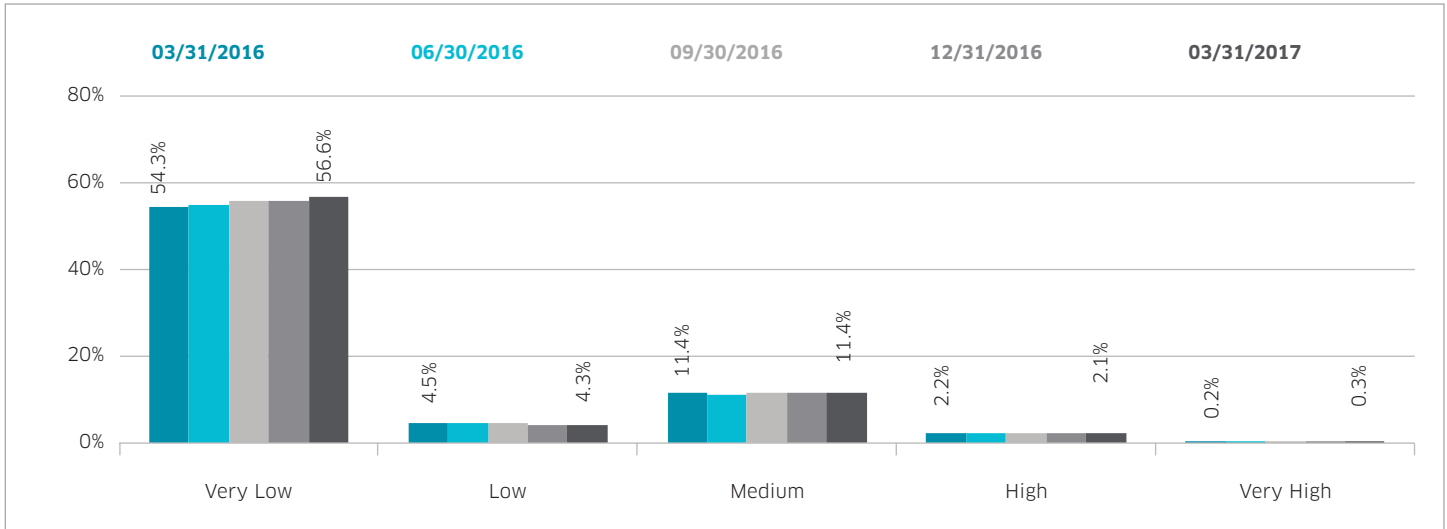
### Style Evolution



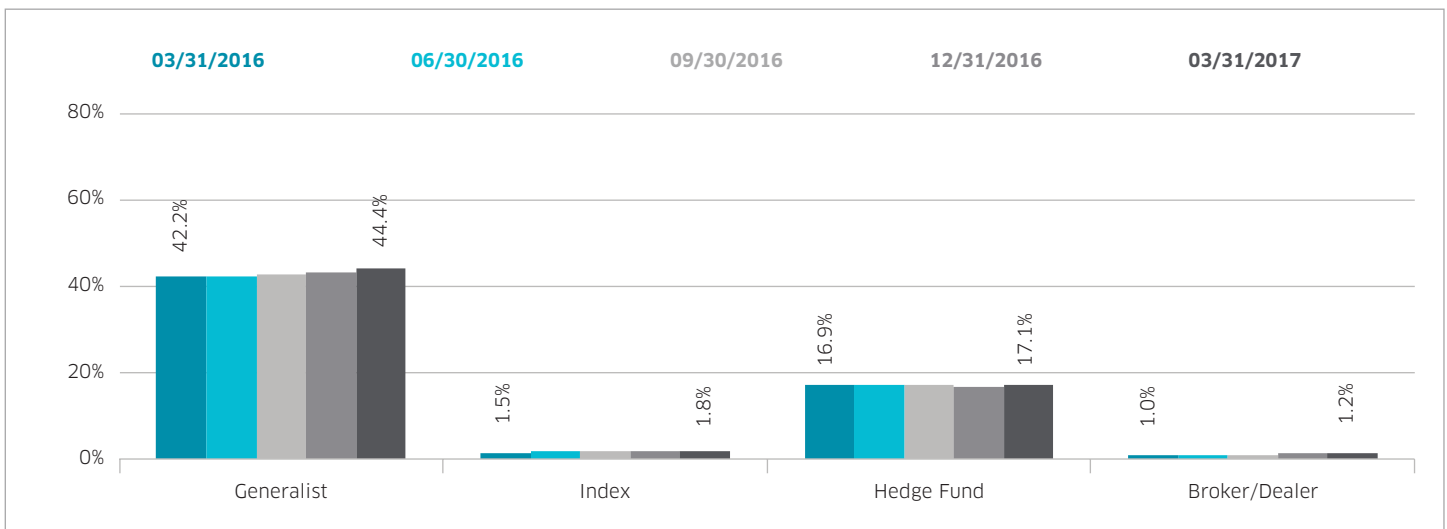
### Turnover Evolution



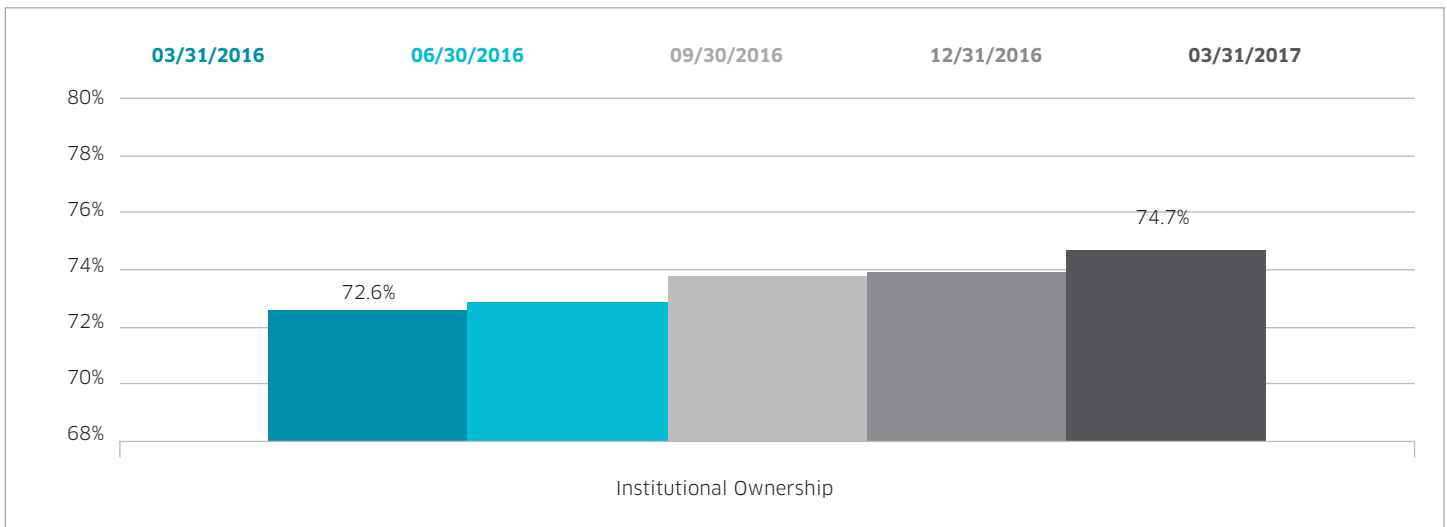
### Activist Threat



### Investor Type



### Institutional Ownership



## Conclusion

Since its inception, the Nasdaq Biotechnology Index has shown impressive performance over the years. A more favorable regulatory environment as well as an aging population have become just a few of the factors which have helped continue to increase demand for biotechnology related company products, particularly in more recent years. We presented a number of statistics which go into further detail regarding some of the holdings which have helped drive this performance over the past five years, as well as break down of the top allocations as of 5/31/17. From a share ownership perspective, perhaps the most interesting is the steady increase in institutional. Nasdaq, as an exchange, remains a leader in terms of IPO listings within the Biotechnology and Big Pharma spaces, accounting for 30 of the 33 listings which occurred in 2016. In addition, Nasdaq accounts for over 90% of all Biotechnology and Big Pharma company listings with approximately 250 of the nearly 350 eligible for the Nasdaq Biotech Index from a listing perspective (listed on Nasdaq GM or Nasdaq GS). Market participants can gain access to the Nasdaq Biotechnology index through a number of ETFs, the largest being IBB.

## FOOTNOTES

1 <http://www.reuters.com/article/us-pharmaceuticals-approvals-idUSKBN14M08R>

Sources: Nasdaq Global Index Research, FactSet, Bloomberg.

<https://www.census.gov/prod/2014pubs/p25-1141.pdf>

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<http://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/DrugInnovation/UCM430299.pdf>

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<http://www.nasdaq.com/markets/ipo/activity.aspx?tab=pricings&month=2015-01>

<http://www.nasdaq.com/markets/ipo/activity.aspx?tab=pricings&month=2015-02>

<http://www.nasdaq.com/markets/ipo/activity.aspx?tab=pricings&month=2015-0>

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