Will Trump Make Biotechnology Great Again?
Housekeeping

- Ask Questions

- Polls

- Survey & Giveaway
  - Complete survey for a chance to win $50 Starbucks gift card
Today’s Presenters

Moderator
Tom Lydon
Editor & Publisher
ETF Trends

Panelist
Paul Yook
Founder of LifeSci Index Partners, LLC
Co-Portfolio Manager of BioShares funds

Panelist
Andrew McDonald, Ph.D.
CEO of LifeSci Advisors, LLC
Co-Portfolio Manager of the BioShares funds
November 8th, 2016
A Sea Change for Biotech

• The outlook for the biotech sector changed dramatically with the results of the November 8th 2016 Presidential Election
  › Donald Trump surprised most of the world by beating Hillary Clinton
  › Republicans keep the Senate (upset) and the House
  › California referendum Proposition 61 relating to lower drug prices shockingly failed to pass
  › Prospect of multiple Trump-nominated Supreme Court justices

• Selected sellside equity research analyst comments:
  › RBC’s Michael Yee: “Best case election scenarios playing out…” (11/9/2016)
  › Morgan Stanley’s Matthew Harrison: “as fears around drug price eroded … We see cash repatriation, pipeline innovation and competition as the key new themes for investor focus” (11/10/2016)
  › Stifel’s Stephen Wiley: “Repeal and replace of ACA now likely becomes centerpiece of HC reform discussion” (11/9/2016)
  › Jefferies’ Brian Abrahams: “GOP Sweep, Prop 61. Failure Take Near Term Edge Off Drug Pricing Worries” (11/10/2016)
Hillary was an Overhang on Biotech

- Hillary Clinton’s infamous tweet on 9/21/2015 “Price gouging like this in the specialty drug market is outrageous…” led to $132 billion of biotech investor losses by 9/29/2015 (source: MarketWatch (a))

- Hillary proposed changes to healthcare which would have hurt the profitability of the drug and biotechnology companies (b)
  - Restrictions on direct-to-consumer advertising by the drug industry
  - Mandating minimum R&D spending
  - Allowing drug “reimportation” into the US
  - Capping out-of-pocket spending by individuals
  - Reducing patent protection for certain drug categories

- Tweets and TV ads targeting Specialty Pharmaceutical companies (Turing Pharmaceuticals, Valeant Pharmaceuticals, Mylan) hit the biotech sector hard
  - “EpiPens can be the difference between life and death. There’s no justification for these price hikes” (Hillary Clinton tweet 8/24/2016)

(b) https://www.hillaryclinton.com/briefing/factsheets/2015/09/21/hillary-clinton-plan-for-lowering-prescription-drug-costs/
Will Trump “Make Biotech Great Again?”

• On the campaign trail, Donald Trump discussed repealing the ACA/Obamacare and allowing drug reimportation

• Update on Trump’s policy website the weekend following the election dropped mentions of reining in high drug prices or drug reimportation (a)
  > Trump has recently indicated the intent to keep certain elements of Obamacare including pre-existing conditions; and does not expect to suddenly drop coverage for the 20mm covered lives but instead have a transition plan in place

• In interview with 60 Minutes, Trump relieved certain fears of a sudden end to ACA, and instead discussed simultaneously replacing with an improved plan (affecting ~20mm covered lives)

• Key facet of Trump healthcare reform may involve the potential for insurance plans to compete across state lines

• In another surprise, California’s Proposition 61 referendum failed in a 54% to 46% vote
  > This bill would have allowed Medicaid in California to pay the lower drug prices that the Veteran’s Administration has contracted at the cost of a more limited menu of drugs

(a) http://www.greatagain.gov/policy/healthcare.html
Biotechnology – Where are we now?

• After a strong run fueled by strong fundamentals, biotechnology stocks are experiencing their largest retrenchment in the past 10+ years.

The S&P 500 Index is a free float market capitalization-weighted index of 500 of the largest U.S. companies. The NASDAQ Biotechnology Index contains securities of NASDAQ-listed companies classified according to the Industry Classification Benchmark as either Biotechnology or Pharmaceuticals which also meet other eligibility criteria. The NASDAQ Biotechnology Index is calculated under a modified capitalization-weighted methodology.

Index returns are for illustrative purposes only and do not represent fund performance. The indexes are calculated on a total return basis with dividends reinvested. The indexes are unmanaged, its returns do not reflect any fees, expenses, or sales charges, and are not available for direct investment. Data as of 11/11/2016.

Performance data quoted represents past results. Past performance is no guarantee of future results and current performance may be higher or lower than the performance shown. Investment return and principal value will fluctuate so your shares, when redeemed, may be worth more or less than their original cost.”
Biotechnology – Where are we now?

• Mature Biotechs are near 10-year low P/E of 12x; vs 18x for the S&P 500

Comparing Bloomberg Mature Biotech Index (consisting of GILD, CELG, AMGN, and BIIB, and GENZ prior to acquisition) with the S&P 500 Index. The Bloomberg Mature Biotech Index is compiled and calculated by Bloomberg to track the performance of the largest biotechnology companies in the U.S. markets. P/E ratios are Bloomberg forward P/E ratios. Data as of 11/11/2016.

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Why Are Investors Interested in the Biotechnology Industry?

• Biotechnology is the fastest growing segment in the healthcare sector
  › Sector formed in the early 1980s, now >20% of the market value of all publicly traded healthcare companies \(^{(a)}\)

• Breakthrough drug discoveries and blockbuster drugs across many disease categories
  › Hepatitis C, HIV, breast cancer, lysosomal storage disorders
  › Increased life expectancy and quality of life for pediatric and adult diseases

• Today’s companies have increased access to funding and ability to attract top scientific talent
  › Startups are backed by blue chip VC firms, large pharma companies, universities and even major corporations (Google, Samsung)

• New innovative approaches could lead to next generation of life-saving medicines

• Public policy concerns on how to pay for expensive new therapies

\(^{(a)}\) Source: Bloomberg data as of 11/11/2016
Healthcare Continues to Outpace GDP

- US healthcare costs grew 7.2% annually between 1990 and 2008 (a)

- Since then, costs have been curbed somewhat and are expected to grow 5.7% annually between 2013 and 2023, according to CMS (b)

- As a % of GDP, US healthcare spending still leads the world at 17.1% in 2013
Is Drug Spend Rising Again?

Prescription Drug Costs

% of Healthcare Spend - 2014

<table>
<thead>
<tr>
<th>Category</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospital Care</td>
<td>32.1</td>
</tr>
<tr>
<td>Professional Services</td>
<td>26.4</td>
</tr>
<tr>
<td>Prescription Drugs</td>
<td>9.8</td>
</tr>
<tr>
<td>Net Insurance Cost</td>
<td>6.4</td>
</tr>
<tr>
<td>Nursing Care</td>
<td>5.1</td>
</tr>
<tr>
<td>Research/Investment</td>
<td>5.1</td>
</tr>
<tr>
<td>Medical Products</td>
<td>3.4</td>
</tr>
<tr>
<td>Home Health</td>
<td>2.7</td>
</tr>
<tr>
<td>Government Public Health</td>
<td>2.6</td>
</tr>
<tr>
<td>Government Admin &amp; Other</td>
<td>6.3</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>100.0</strong></td>
</tr>
</tbody>
</table>

Source: CMS, Office of the Actuary, National Health Statistics Group

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Key Players in the Biotech Sector

- Predominantly U.S. companies (some in Europe, Australia and nascent in Asia)

- The largest segment is made up of Biotechnology Drug companies, but other sub-sectors include: Tools (e.g. Illumina), AgBio (e.g. Monsanto) and Specialty Pharma

- Many types of entities contribute to biotechnology research:
  - Stand-alone biotechnology company
  - Subsidiary of pharmaceutical giant (Roche/Genentech, Pfizer, Sanofi-Genzyme)
  - University labs and institutes
  - Government-funded entities (National Cancer Institute, National Institutes of Health)
A Brief History of Biotech

• Legacy drug discovery approach (early 1900s to 1970s) was largely trial and error

• Major scientific discoveries pave the way (Watson & Crick 1953; Herb Boyer and Stanley Cohen 1972 DNA cloning)

• First biotech-specific companies formed late 1970s/early 1980s (Genentech 1976, Biogen 1978, Amgen 1980)

• Cetus IPO in 1981 raises a record $108 million; Kary Mullis invents PCR in 1983

• First products were proteins and enzyme-replacements (1982 Genentech’s insulin, 1991 Genzyme’s Ceredase for Gaucher’s)


• Genomics boom (and bust?) ~2000 in combination with Human Genome Project

• 2013/2014 record biotech drug launches – Biogen’s Tecfidera, Gilead’s Sovaldi

• In 2014 FDA approves a record 41 biotech drugs
The Drug Approval Process

Pre-Clinical Stage

Lead Development
Animal Testing
3-6 Years

Clinical Trial Stage

Phase 1
Phase 2
Phase 3
6-7 Years

Products Stage

FDA Approval
1/2 - 2 Years

Only 1 in 30 “Leads” eventually become FDA approved at average cost of ~$1 billion and 13 years

Source: Pharmaceutical Research and Manufacturers of America
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Robust Rate of Drug Approvals

• 2013/2014 had several biotech blockbuster launches (Sovaldi/Harvoni, Tecfidera, Imbruvica, Eyelea), but 2015 was relatively quiet (Praluent, Repatha)

• Streamlined FDA approval pathways in 2015 (31% Fast Track, 22% Breakthrough, 53% Priority Review, 13% Accelerated Approval)

• Orphan Drugs were 47% of all approvals in 2015; First-in-Class drugs were 36%
Top Drugs by Global Sales

2014 Sales in Billions

- **Humira**: $12.5
- **Sovaldi**: $10.3
- **Remicade**: $9.2
- **Rituxan**: $8.7
- **Enbrel**: $8.5
- **Lantus**: $7.3
- **Avastin**: $7.0
- **Herceptin**: $6.8
- **Advair**: $6.4
- **Crestor**: $5.9

Source: Genetic Engineering & Biotechnology News
Commercial Stage Companies

• Commercialization Options
  › Go-it-alone strategy
  › Joint Venture / Partnership with Large Pharma
  › Outlicense to Large Pharma and receive royalty

• During commercial phase, companies require additional expertise
  › Manufacturing, Sales/Marketing
  › Managing Wall Street expectations on quarterly results and future guidance
  › Managed Care relationships on pricing

• Focus on pipeline and future growth
Current Topics in Biotechnology

- Immuno-oncology technologies
  - Harnessing the power of one’s immune system to naturally kill their own cancer

- Gene Therapy and Gene Editing
  - Early successes in narrow indications but failures in heart failure and back-of-eye diseases

- Companion Diagnostics
  - Tailored medicines based on a patient’s specific genetic profile or disease subtype

- M&A
  - Continued buyer’s appetite among large pharmaceutical players with patent expirations and slow growth to acquire higher growth biotechnology products

- Pricing Pressure
  - Pharmacy benefit manufacturers, physician groups, politicians and media have been proactive on Hepatitis C, cancer, multiple sclerosis and specialty drugs

- Valuations and Financing Environment
  - What is fair value for biotech stocks and is the financing window “open”?
Approaches to Biotechnology Investing

- Individual Stocks
- Mutual Funds (actively managed)
- ETFs (passively managed, indexed)
- Hedge Funds
- Venture Capital Funds
- Startup Companies
BioShares Biotechnology ETFs

BioShares ETFs are the only biotechnology funds to separate Clinical Trials companies and Products companies into **two distinct funds**

<table>
<thead>
<tr>
<th>BioShares Clinical Trials -BBC</th>
<th>BioShares Products -BBP</th>
</tr>
</thead>
<tbody>
<tr>
<td>• 75 biotech stocks; average market cap $1 billion(^{(a)})</td>
<td>• 34 biotech stocks; average market cap $17 billion(^{(a)})</td>
</tr>
<tr>
<td>• No product sales; focused on success of clinical trials</td>
<td>• Focused on driving sales ramp</td>
</tr>
<tr>
<td>• Major binary event risk -trial results, FDA</td>
<td>• Less significant binary event risk</td>
</tr>
<tr>
<td>• Managing cash burn rate and equity financing strategy</td>
<td>• Cash flow positive, or expected in near term</td>
</tr>
<tr>
<td>• Typically smaller market cap companies</td>
<td>• Typically larger market cap companies</td>
</tr>
<tr>
<td>• Higher volatility stocks</td>
<td>• Lower volatility stocks</td>
</tr>
</tbody>
</table>

\(^{(a)}\) Data as of 11/11/2016.

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BioShares Biotechnology ETFs

Only BioShares BBP and BBC target 100% pure biotechnology with no Specialty Pharma exposure

- Investors are now beginning to distinguish between the innovative Biotechnology sector from the opportunistic Specialty Pharma sector
  - Biotech spends more on R&D as % of Sales
    - Big Biotech 25.6% average in 2014 (GILD/AMGN/BIIB/CELG/REGN)
    - Large Pharma 19.6% (PFE/JNJ/MRK/BMY/LLY)
    - Spec Pharma 5.4% (VRX/MNK/AKRX/HZNP)
  - Most “biotech” ETFs contain significant exposure to Specialty Pharma

- In an election year, Specialty Pharma will continue to be under scrutiny
- Most “biotech” ETFs contain significant exposure to Specialty Pharma
  - Top Spec Pharma holdings: AKRX, MYL, CTLT, HZNP, IPXL, PCRX, ENDP, EBS, AAAP, JAZZ, SHPG
  - BBP and BBC have no Specialty Pharma exposure
BioShares Index Methodology

- The BioShares funds passively track the LifeSci Biotechnology Indexes, administered and calculated by LifeSci Index Partners, LLC and Indxx, LLC, respectively
- Products Index – companies with lead drug on market or with FDA approval
- Clinical Trials Index – companies with lead drug in Phase 1, 2 or 3 trial
- Index construction
  - First step is ICB sector code screen (code 4570: pharma/biotech) for US listed stocks
  - Liquidity and size filter: Minimum market cap of $250 million and Average Daily Turnover of $1 million average over last 30 days and $2 million average over last 6 months
  - 3 month waiting period for IPOs
  - Exclude companies which are not pure biotech, such as large pharma, specialty pharma, medical devices, life science tools, diagnostics, healthcare services, agriculture, animal health and diversified healthcare
- Equally weighted
- Semi-Annual reconstitution/rebalancing (June 15th and December 15th)
- Index Committee reviews upon specified corporate actions such as merger, acquisitions, bankruptcies and spinoffs

Note: For detailed methodology of the LifeSci Biotechnology Indexes, please visit www.lifesciindex.com
Please refer to the Prospectus for more information regarding management of the Funds.

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Questions?

Please submit your questions using the Q&A box.
Performance Summary

**BioShares™ Biotechnology Clinical Trials ETF (Nasdaq: BBC)**

**BioShares™ Biotechnology Products ETF (Nasdaq: BBP)**

As of 9/30/16

<table>
<thead>
<tr>
<th>BBC Performance as of 9/30/16</th>
<th>1 Month - Sep-16</th>
<th>Q3 2016</th>
<th>1 Year</th>
<th>Since Inception</th>
<th>BBP Performance as of 9/30/16</th>
<th>1 Month - Sep-16</th>
<th>Q3 2016</th>
<th>1 Year</th>
<th>Since Inception</th>
</tr>
</thead>
<tbody>
<tr>
<td>NAV</td>
<td>12.87 %</td>
<td>25.24 %</td>
<td>-14.06 %</td>
<td>-5.13 %</td>
<td>NAV</td>
<td>9.98 %</td>
<td>23.07 %</td>
<td>22.10 %</td>
<td>18.22 %</td>
</tr>
<tr>
<td>Market Price</td>
<td>12.97 %</td>
<td>25.49 %</td>
<td>-14.00 %</td>
<td>-5.11 %</td>
<td>Market Price</td>
<td>10.12 %</td>
<td>23.23 %</td>
<td>22.32 %</td>
<td>18.29 %</td>
</tr>
<tr>
<td>Index Performance</td>
<td>12.94 %</td>
<td>25.46 %</td>
<td>-13.38 %</td>
<td>-4.67 %</td>
<td>Index Performance</td>
<td>10.12 %</td>
<td>23.33 %</td>
<td>23.22 %</td>
<td>19.19 %</td>
</tr>
</tbody>
</table>

**Total Annual Fund Operating Expenses:** 0.85% (BBC & BBP)

Performance data quoted represents past performance and is inclusive of capital gains and dividend distributions. Past performance is not a guarantee of future results; current performance may be higher or lower than performance quoted. Investment returns and principal value will fluctuate and Shares, when redeemed, may be worth more or less than their original cost. See www.bioshares.com for more information including monthly performance data.

**Inception Date of the Funds:** 12/16/2014.

**Index: LifeSci Biotechnology Products Index.** The LifeSci Biotechnology Products Index is designed to track the performance of U.S. listed biotechnology stocks with at least one drug therapy approved by the U.S. Food and Drug Administration for marketing. The index is unmanaged, its returns do not reflect any fees, expenses, or sales charges, and is not available for direct investment.

**LifeSci Biotechnology Clinical Trials Index.** The LifeSci Biotechnology Clinical Trials Index is designed to track the performance of U.S. listed biotechnology stocks with a lead drug in the clinical trial stage of development, typically a Phase 1, Phase 2 or Phase 3 trial, but prior to receiving marketing approval. The index is unmanaged, its returns do not reflect any fees, expenses, or sales charges, and is not available for direct investment.
Disclosures

**Fund Risks:**

**Exchange Traded Funds:** The value of an ETF may be more volatile than the underlying portfolio of securities the ETF is designed to track. The costs of owning the ETF may exceed the cost of investing directly in the underlying securities.

**Industry/Sector Concentration:** A fund that focuses its investments in a particular industry or sector will be more sensitive to conditions that affect that industry or sector than a non-concentrated fund.

**Market Price/NAV:** At the time of purchase and/or sale, an investor’s shares may have a market price that is above or below the fund’s NAV, which may increase the investor’s risk of loss.

**Correlation to Index:** The performance of the fund and its index may vary somewhat due to factors such as fund flows, transaction costs, and timing differences associated with additions to and deletions from its index.

**Non-Diversified:** The fund is non-diversified and may be more susceptible to factors negatively impacting its holdings to the extent that each security represents a larger portion of the fund's assets.

**No Guarantee:** There is no guarantee that the portfolio will meet its objective.

**Prospectus:** For additional information on risks, please see the fund's prospectus.

The Fund is an actively managed exchange-traded fund (“ETF”) and does not seek to replicate the performance of a specified index. The Fund may have a higher portfolio turnover than funds that seek to replicate the performance of an index.

The “net asset value” (NAV) of the Fund is determined at the close of each business day, and represents the dollar value of one share of the Fund; it is calculated by taking the total assets of the Fund, subtracting total liabilities, and dividing by the total number of shares outstanding. The NAV of the Fund is not necessarily the same as its intraday trading value. Fund investors should not expect to buy or sell shares at NAV because shares of ETFs such as the Fund are bought and sold at market price (not NAV) and are not individually redeemed from the Fund. Thus, shares may trade at a premium or discount to their NAV in the secondary market. Brokerage commissions will reduce returns.

**Performance data quoted represents past performance and is no guarantee of future results. Current performance may be lower or higher than the performance data quoted. Investment return and principal value will fluctuate so that an investor’s shares, when redeemed, may be worth more or less than original cost. NAV returns are calculated using the Fund’s daily 4:00 p.m. NAV, and include the reinvestment of all dividends and other distributions -reinvested at the Fund’s NAV on distribution ex-date . Market price returns are calculated using the 4:00 pm midpoint between the bid and offer, and include the reinvestment of all dividends and other distributions -reinvested at the 4:00pm bid/offer midpoint on distribution ex-date . Market price returns do not represent the return you would receive if you traded at other times.**

**Please consider the investment objectives, risks, charges and expenses of the Fund carefully before investing. The prospectus contains this and other information about the Fund. Contact us at 888-383-0553 or visit [www.bioshares.com](http://www.bioshares.com) for a copy of the Fund’s prospectus. Read the prospectus carefully before you invest or send money.**

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