



Invest in Biotech Stocks, Risk, Reward, and A Lot of Fun

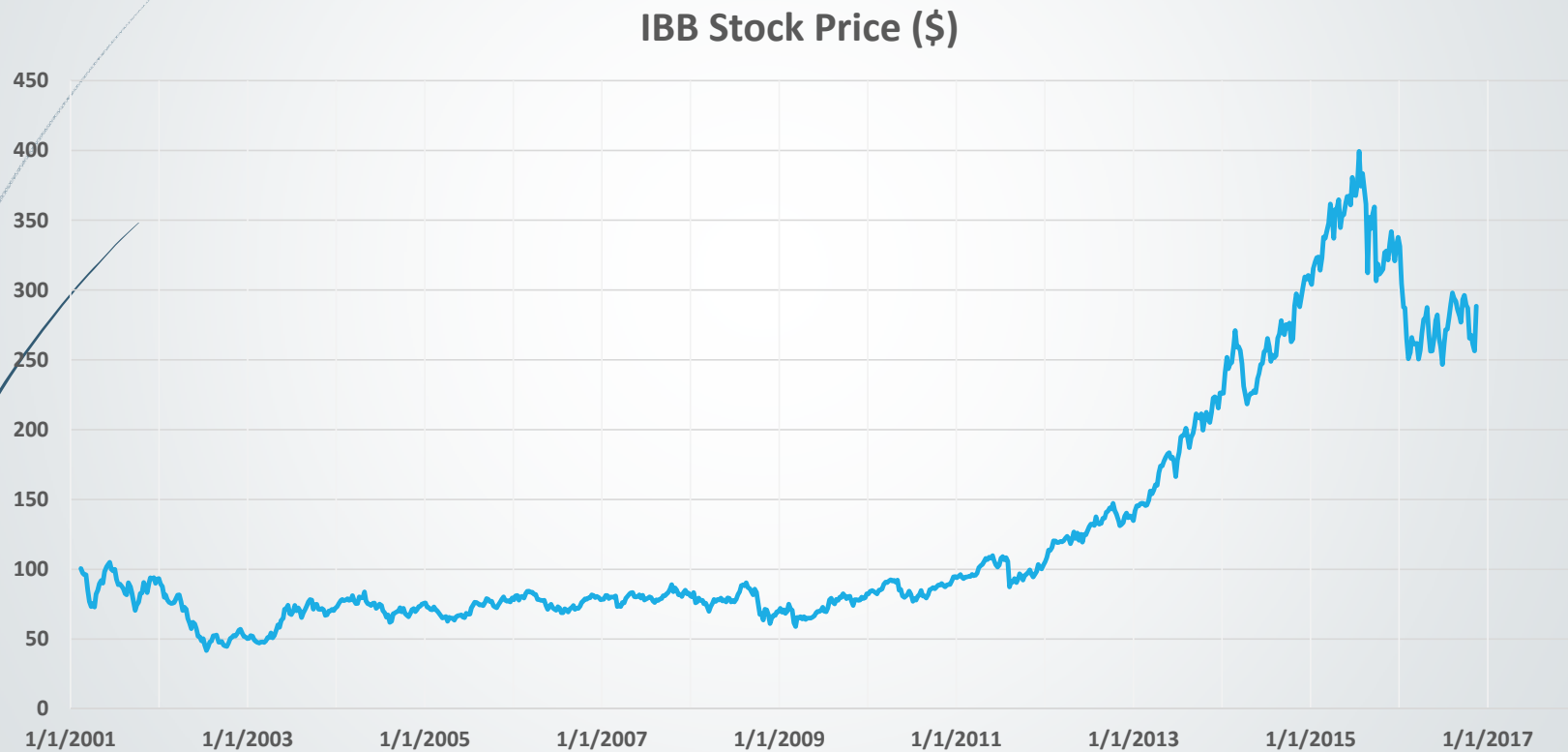
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CCAA 2016 annual Meeting

INTRODUCTION: THE BIOTECH STOCKS

- ▶ ^BTK in NASDAQ
- ▶ Defined by Merriam-Webster: Biotech is the manipulation of living organisms or their components to produce useful usually commercial products.
- ▶ According to Wikipedia, there are 189 stocks as of June 2016 in NASDAQ stock exchange qualified to be on the NASDAQ Biotech Index.
- ▶ Black Rock provides the largest Exchange-Traded Fund (ETF) for Biotech Stocks, traded with the symbol IBB. There are many mutual funds dedicated to Biotech Stocks in US.

INTRODUCTION: THE BIOTECH STOCKS





Major Advances of Biotechnologies in the Last Three Decades

- ➔ Recombinant DNA
- ➔ Mono-Clonal Antibodies (MAbs)
- ➔ Fast DNA Sequencing
- ➔ Immunotherapy
- ➔ Antibody-Drug Conjugates (ADCs)


Risks of Biotech Stocks



Warning: Buy/sell single stocks is gambling, only risk what you can lose



Risks!



Big Risks - Example: DVAX

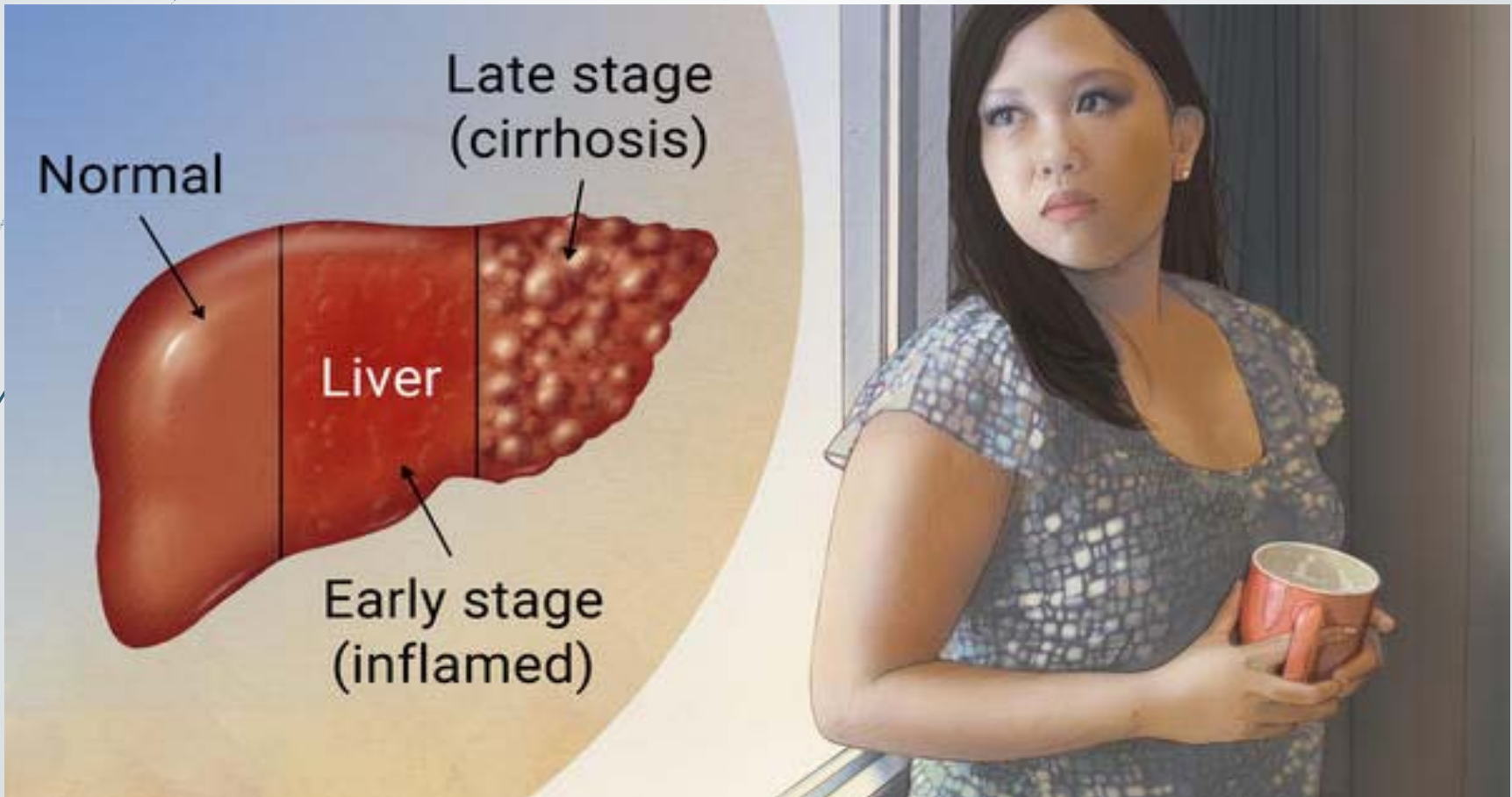
Dynavax Technologies Corporation



Case for DVAX

- ❖ Innovation in immunotherapy – adjuvant for vaccines and cancer drugs
- ❖ Leading drug Heplisav (Hepatitis B vaccine) addresses potentially 2 billion HB patients and carriers in the world.
- ❖ Current vaccines 3 shots & ~70% effective with \$200M/yr
- ❖ Phase III of Heplisav results very impressive, 2 shots & >90% effective.
- ❖ This might be the way to eliminate HB for the world.
- ❖ DVAX has other adjuvants to assist cancer immunotherapy.

DVAX Continued Hepatitis B



DVAX Continued

Case against the DVAX investment

- ❖ Adjuvant vaccine is based on stimulating our own immune system; there might be an autoimmune concern
- ❖ Since there is an existing vaccine, the hurdle of approval is much higher if there is a safety concern
- ❖ HB minor issue for US (~20,000 new cases/yr)
- ❖ Post 2013 rejection, FDA asked for 8,000+ person trial to verify safety.
- ❖ Small biotech companies has much harder drug approval records.
- ❖ The costs of doing large trials are very expensive, \$800+M is average for each successful drug to market.
- ❖ Small biotech companies such as DVAX have low cash reserve to sustain long FDA review delays.

DVAX Continued

➤ My DVAX investment

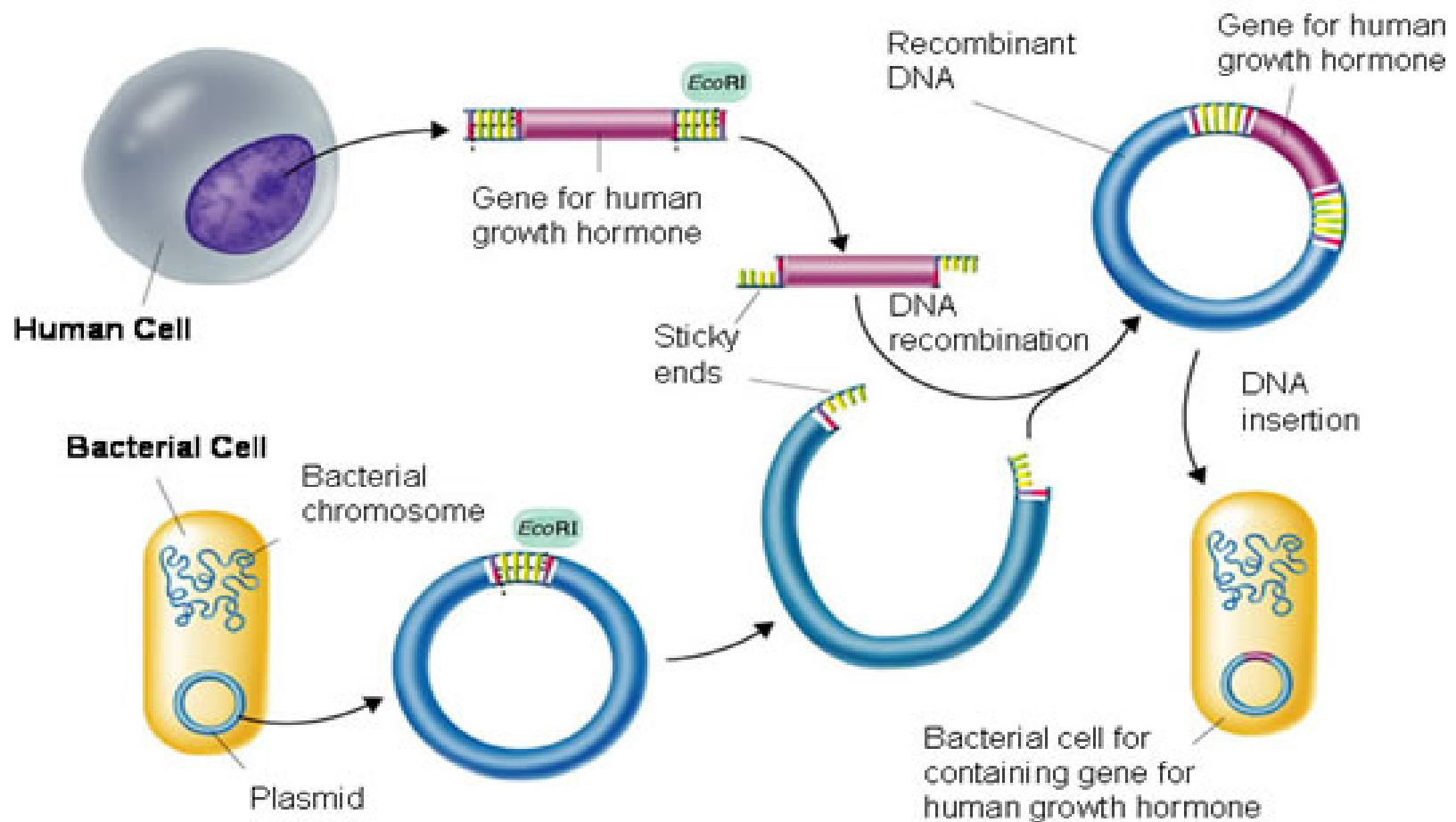
- ❖ Stock price looked attractive in 2013 with FDA rejection of New Drug Application (NDA) due to “bogus” vaccine safety concerns. Started to buy around \$11/share
- ❖ New expanded Phase III data continue to be good.
- ❖ Share price went up above \$31/share in September 2015 after completion of new Phase III trial.
- ❖ Average entry price around \$19/share
- ❖ New NDA filed in March 2016. Stock price at \$18/share.
- ❖ Three consecutive FDA delays caused the stock price to plummet to between \$3 to \$5 in the past weeks.
- ❖ My largest lost in 30-some years.

Big Rewards - Example 1: AMGN (Amgen Inc.)

Case for AMGN

- ❖ Innovation in recombinant DNA – Epogen or Epoetin Alfa (EPO, $C_{815}H_{1317}N_{233}O_{241}S_5$, the red blood cell growth factor) is the first commercially successful biologic drug
- ❖ Inventor 林福坤 (Lin Fu-Kuen, 1941 台湾基隆) in 1983.
- ❖ EPO addresses needs of red blood growth such as kidney dialysis, after chemo, anemia, etc. about \$12 billion/yr worldwide sales market. Amgen has about half.
- ❖ Currently AMGN has 15 approved drugs and dozens in pipeline.

AMGN – Recombinant DNA



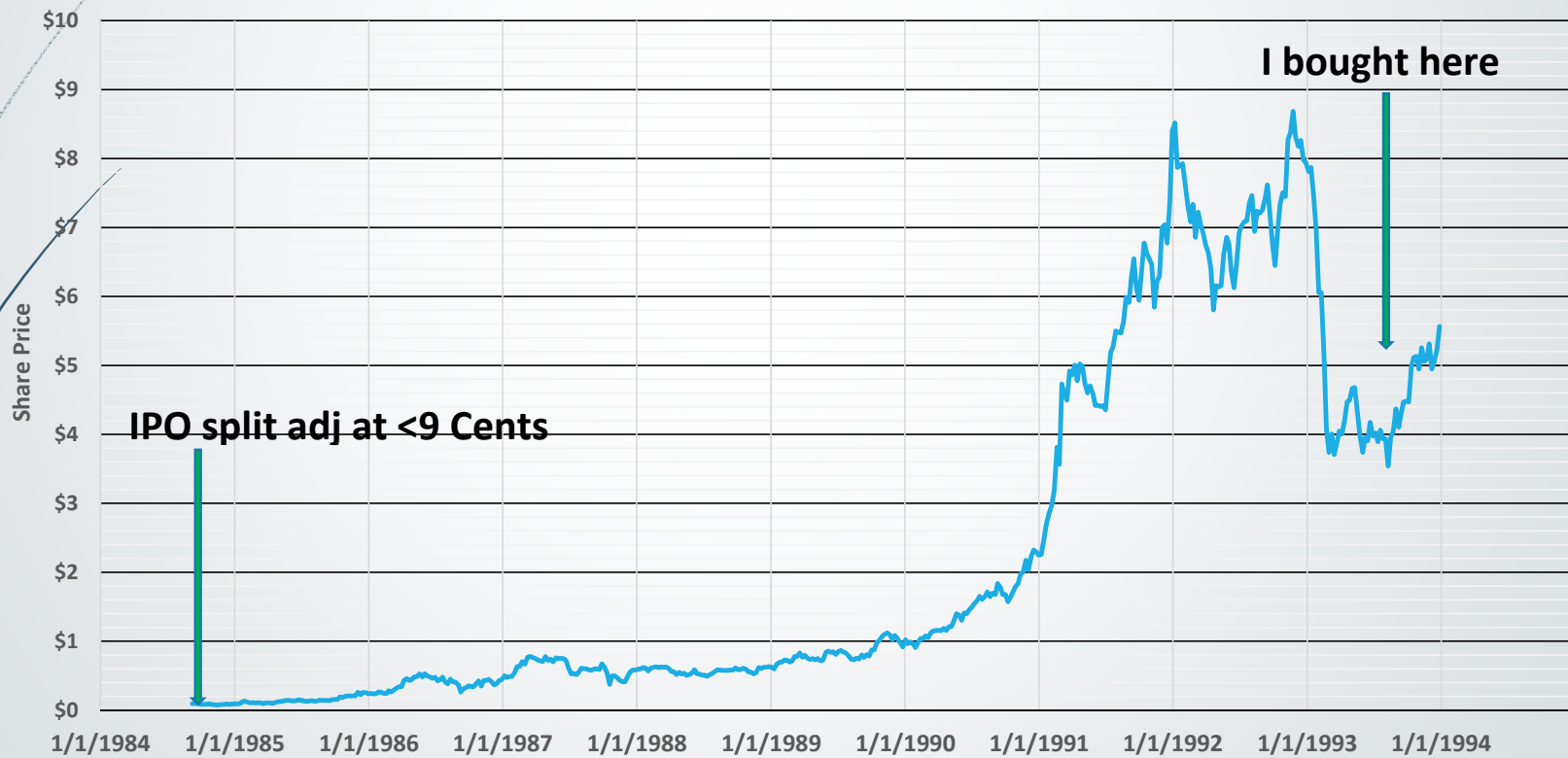
AMGN Continued My Investment in AMGN

AMGN Share Price



AMGN Continued, I could have done better

AMGN (1984-1994)



Big Rewards - Example 2:

AMLN (Amylin Pharmaceuticals)

▶ Trivia of Amylin

- ❖ Amylin is a hormone, a 37 amino acid peptide.
- ❖ Amylin is secreted by pancreas with insulin at the ratio of 100:1. For a long time nobody knows why.
- ❖ We now know that Amylin is a partner of insulin in glycemic control. Amylin slows down digestion so that we don't have to have extremely high insulin needs for short period of time.
- ❖ Many of the Alzheimer patients have a polymerized form of Amylin in their brain called beta-amyloids.

AMLN Continued

▶ Case for AMLN

- ❖ Worldwide patients of diabetes has grown from 108 million (1980) to 422 million (2014).
- ❖ US diabetes by CDC in 2012: 29 million (9.3% of total population). About 200,000 Type I, and rest are Type II. Total cost to US ~\$245Billion with ~\$176Billion in medical/health care cost.
- ❖ A fraction of that money for drugs to drastically reduce the overall cost can make us a lot of money.
- ❖ AMLN produced three FDA approved drugs, Symlin (March 2005), Byetta (April 2005) and Bydureon (January 2012).

AMLN Continued

▶ Stories of AMLN (Symlin)

- ❖ Terrific love story: Allen Andersson and his daughter Rachel who has Type I diabetes
- ❖ Andersson wrote a \$6 Million check to Joe Cook in Bethesda 1999 to save AMLN so that Rachel can have her diabetic drug developed



AMLN Continued

► Stories of AMLN (Byetta)

- ❖ **Terrific biochemistry:** In 1992, Dr. John Eng, VA Medical Center at Bronx, NYC discovered a hormone from the saliva of Gila Monsters that treats Type II diabetes better than any other medicine.



AMLN Continued

▶ Case against AMLN

- ❖ Long FDA approval delays
- ❖ Hard to sell injectable drugs; all AMLN's drugs are injectables; none have even close to \$1 billion/year sales
- ❖ Competitions, especially from oral pills.
- ❖ Top competition: Merck's Januvia/Janumet, early marketing unofficial slogan: "Byetta in a pill" with ~\$5 billion/year sales.

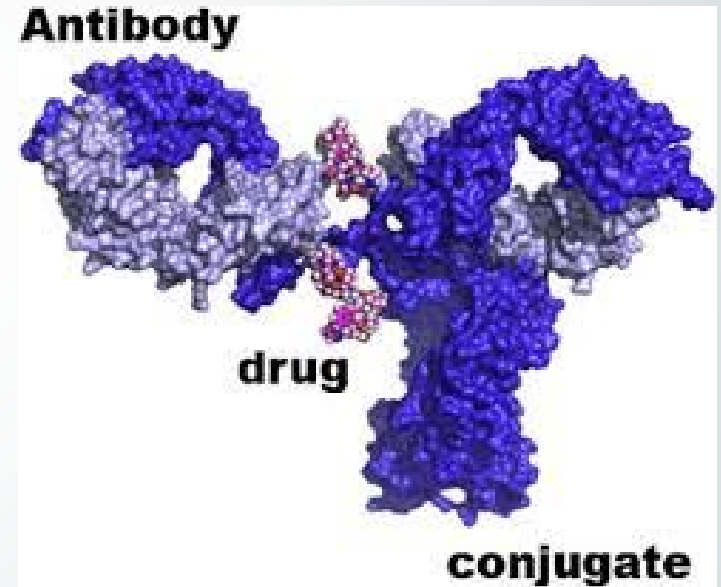
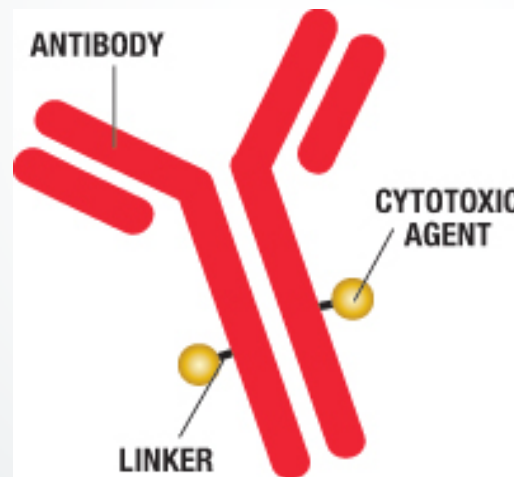
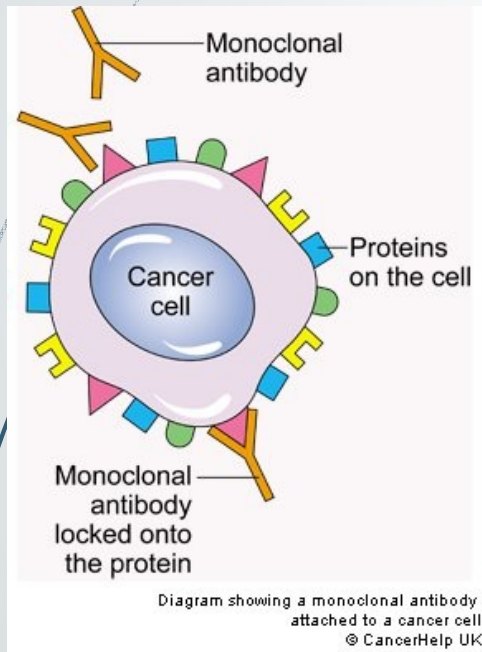
AMLN Continued

➤ My AMLN investment

- ❖ My classmate told me about that J&J had pulled out of AMLN in early 1999 after he invested in it.
- ❖ I looked in the history/chemistry and bought in at \$1.25/share in January 1999. Through many years, average cost was ~\$8/share.
- ❖ First recommended in IWY at \$3.75/share in August 1999.
- ❖ Elevated it to “IWY Investment of Life Time” in 2000
- ❖ Went to all time high >\$52/share in January 2006 after Byetta approval in April 2005
- ❖ Many FDA approval delays on long-term acting Byetta dropped AMLN to \$8/share in March 2009
- ❖ Price eventually recovered after Bydureon is approved in 2012.
- ❖ AMLN acquired by Bristol Myers @ \$5.3 Billions (~\$30/share) in 2014.
- ❖ My biggest winner in 30-some years of investment

A Tale of Two ADC Stocks: SGEN and IMGN

- ▶ Monoclonal Antibodies (Mabs) and Antibody Drug Conjugates (ADCs)



IMGN & SGEN Continued



IMGN & SGEN Continued

- **My IMGN/SGEN investments**
 - ❖ **IWY named IMGN and SGEN stock picks of the quarter in October 2010 and January 2011 respectively.**
 - ❖ **I started buying at ~\$10/share for IMGN and ~\$15/share for SGEN.**
 - ❖ **Silly me bought more of the cheaper stock (IMGN) than the more expensive one (SGEN)**
 - ❖ **Both have had FDA approved ADC drugs to treat cancer very successfully. In fact, IMGN's Kadcyra (for breast cancer) has much larger sales than SGEN's Adcetris (for Hodgkin Lymphoma and other Lymphomas).**
 - ❖ **The difference is in the royalty fee in contract (IMGN with Roche for ~3%) vs. SGEN owns its drug (100%).**
 - ❖ **SGEN is my third overall most profitable stock investment and I have lost small amount with IMGN.**

Trump Effects?

- Clinton was going to regulate drug prices. With Trump's surprise win, Biotech stocks had a significant bounce up.
- Recently Trump tweeted that drug prices are too high; Biotech stocks dropped.
- Trump and the Republican Senate/House will likely reduce corporate tax from 35% to 15% in 2017; increasing the largesse of the big pharmaceuticals to acquire good Biotech companies.
- Trump might also create tax holidays to allow off-shore profits coming home to US. The largest of these are held by big pharmaceuticals; creating more M&A price hikes.



Conclusions

- **Like it or not, we are in the BIOTECH Century**
- **There are serious risks and rewards involved with investing in biotech stocks**
- **Individual biotech stocks are fun to study; along with it, you learn new medical discoveries that may benefit your own health.**

Recommendations

- **If you want to have excellent potential investment returns, you should consider biotech stocks**
- **Diversification**
- **If individual stocks are too hard to pick, you can look into mutual funds or ETF such as IBB, Fidelity, TR Price, Franklin, & Janus.**