



The \$2.9 Million Biotech Trade Playbook

Learn How I Turned \$15,253 into over \$2,900,000
Trading Biotech Stocks



How to use the Playbook

This is your playbook to potentially generating what some call 'unrealistic' profits...

More specifically, it is a step-by-step walkthrough of how I select upcoming biotech catalyst events in the market to catch potentially explosive profit movements. In terms of raw profit potential, my strategies may be considered more valuable than spending countless years studying the markets...

There are 6 sections in this playbook. When you get to the last section, you'll find an invitation to one of my special online training sessions, but it's recommended that you first understand the material in this playbook since it serves as the foundation to additional training.

Inside, you will learn:

- ✓ How I was able to make a 18,000% ROI in just 4 years.
- ✓ 10 powerful reasons why biotech can be so lucrative
- ✓ How to zero-in on the most lucrative signals of a biotech stock
- ✓ What to do right after you've finished reading this playbook

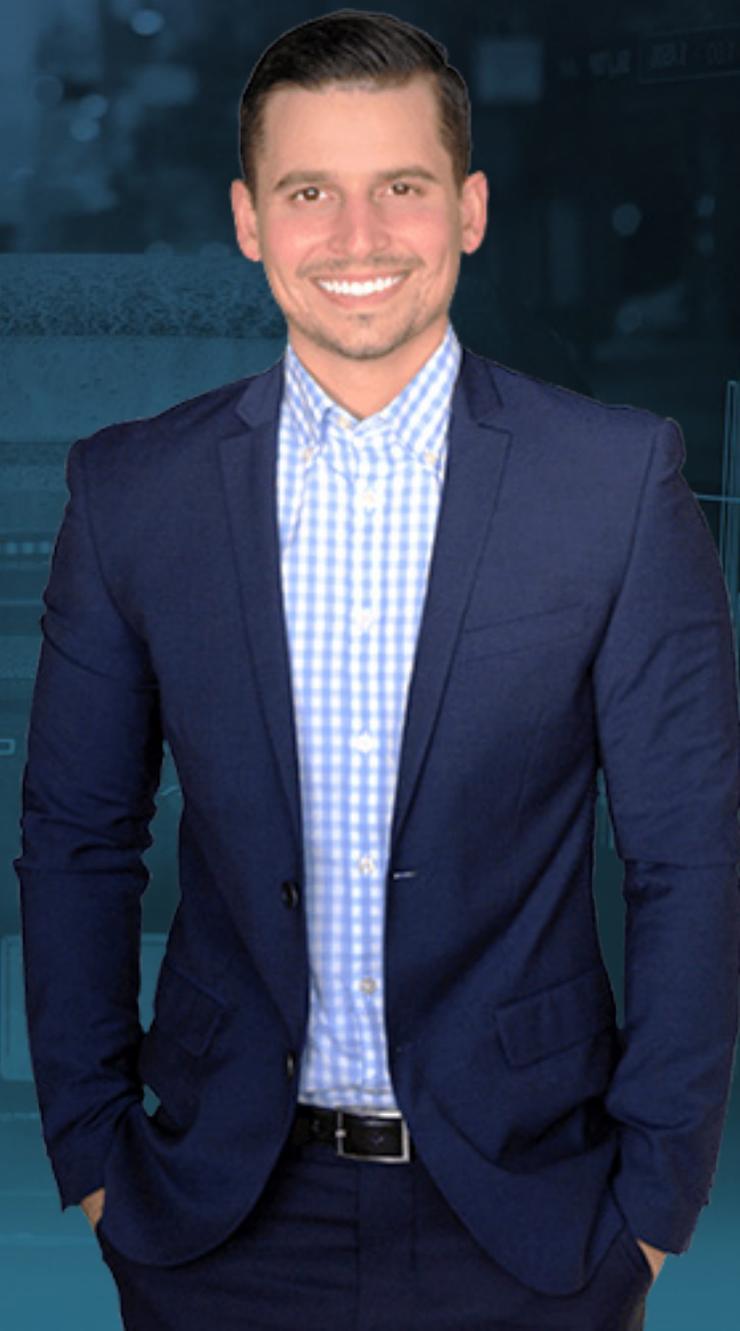
I'm only 26 years old, but as someone who's already earned millions trading stocks, I'm exponentially more qualified to teach you how to trade biotech stocks than anyone else.

I have a background in biotechnology, finance, and technical charting, which I've been able to use to my advantage in the markets. In the last few years I've been featured on Yahoo Finance, Market Watch, The Street, Seeking Alpha and the Money Show.

In my opinion, there is a toxic, wide-held belief regarding what profit opportunities are 'realistic'... DO NOT believe the masses. There ARE secrets to trading in niches that generate astounding returns while still managing risk carefully... I'm the master of the biotech niche... and I'm on year 5 of unrealistic profits.

My mission is to teach investors and stock traders like yourself how to discover, track and evaluate today's hottest Biotech companies on your own, so you can start trading their stocks for exceptional profits.

Kyle Dennis
Director & Co-Founder



I've earned \$2,900,000 in 4 years Trading Biotech Stocks

Here are EXACT copies of my tax forms and trade statements from the last three years.

The returns I've earned may sound unrealistic. No one on Wall Street will open up their statements like this... and that's why I'm sharing this with you to prove my success. As you can see, once I discovered my secret strategy, my gains exploded year over year!

2014

Form **1040** Department of the Treasury—Internal Revenue Service (99) **2014** OMB No. 1545-0074 IRS Use Only—Do not write or staple in this space.

For the year Jan. 1–Dec. 31, 2014, or other tax year beginning _____, 2014, ending _____, 20

See separate instructions.

Your first name and initial: **Kyle W** Last name: **Dennis** Your social security number: [REDACTED]

If a joint return, spouse's first name and initial: [REDACTED] Last name: [REDACTED] Spouse's social security number: [REDACTED]

Home address (number and street). If you have a P.O. box, see instructions. [REDACTED] Apt. no. [REDACTED]

City, town or post office, state, and ZIP code. If you have a foreign address, also complete spaces below (see instructions). [REDACTED]

Foreign country name: [REDACTED] Foreign province/state/county: [REDACTED] Foreign postal code: [REDACTED]

Filing Status

1 Single
 2 Married filing jointly (even if only one had income)
 3 Married filing separately. Enter spouse's SSN above and full name here. ▶
 4 Head of household (with qualifying person). (See instructions.) If the qualifying person is a child but not your dependent, enter this child's name here. ▶
 5 Qualifying widow(er) with dependent child

Check only one box.

Exemptions

6a Yourself. If someone can claim you as a dependent, do not check box 6a.
 b Spouse

Dependents:

(1) First name	Last name	(2) Dependent's social security number	(3) Dependent's relationship to you	(4) <input checked="" type="checkbox"/> If child under age 17 qualifying for child tax credit (see instructions)
				<input type="checkbox"/>

If more than four dependents, see instructions and check here

d Total number of exemptions claimed: **1**

Income

Line	Description	Amount
7	Wages, salaries, tips, etc. Attach Form(s) W-2	40,323.
8a	Taxable interest. Attach Schedule B if required	0.
8b	Tax-exempt interest. Do not include on line 8a	
9a	Ordinary dividends. Attach Schedule B if required	
9b	Qualified dividends	
10	Taxable refunds, credits, or offsets of state and local income taxes	
11	Alimony received	
12	Business income or (loss). Attach Schedule C or C-EZ	2,815.
13	Capital gain or (loss). Attach Schedule D if required. If not required, check here <input type="checkbox"/>	44,488.
14	Other gains or (losses). Attach Form 4797	
15a	IRA distributions	
15b	Taxable amount	
16a	Pensions and annuities	
16b	Taxable amount	
17	Rental real estate, royalties, partnerships, S corporations, trusts, etc. Attach Schedule E	
18	Farm income or (loss). Attach Schedule F	
19	Unemployment compensation	
20a	Social security benefits	
20b	Taxable amount	
21	Other income. List type and amount	
22	Total income	87,626.
23	Expenses	
24	Business expenses of reservists, performing artists, and government officials. Attach Form 2106 or 2106-EZ	
25	Employer's account deduction. Attach Form 8889	
26	Self-employment taxes. Attach Form 3903	
27	Part of self-employment tax. Attach Schedule SE	199.
28	Employer's SEP, SIMPLE, and qualified plans	
29	Employer's health insurance deduction	
30	Early withdrawal of savings	
31a	IRA distribution	
31b	Recipient's SSN	
32	Charitable contribution	
33	Charitable interest deduction	
34	Charitable fees. Attach Form 8917	
35	Production activities deduction. Attach Form 8903	
36	Other deductions (lines 23 through 35)	199.
37	Adjusted gross income	87,427.

Attach Form(s) W-2 here. Also attach Forms W-2G and 1099-R if tax was withheld.

If you did not get a W-2, see instructions.

For Disclosure, Privacy Act, and Paperwork Reduction Act Notice, see separate instructions. BAA REV 05/19/15 TTW Form **1040** (2014)

Kyle Trading Account	Net Account Value	Total Unrealized Gain
Positions	Performance & Value	Margin
Gains & Losses		
View	Tax Year	>Filters
Realized	2014	
Total Gain Realized \$48,591.24	Short-Term Gain Realized \$48,591.24	Long-Term Gain Realized \$0.00
		Total Commission & Fees \$10,972.50

For the year Jan. 1 - Dec. 31, 2015, or other tax year beginning , 2015, ending , 2015, See separate instructions.

Your first name and initial Last name Your social security number
 Kyle W. Dennis [REDACTED]

If a joint return, spouse's first name and initial Last name Spouse's social security number

Home address (number and street). If you have a P.O. box, see instructions. Apt. no.

City, town or post office, state, and ZIP code. If you have a foreign address, also complete spaces below (see instructions).

Foreign country name Foreign province/state/county Foreign postal code

Filing Status
 1 Single
 2 Married filing jointly (even if only one had income)
 3 Married filing separately. Enter spouse's SSN above & full name here. ▶
 4 Head of household (with dependents) (with instructions.) If the qualified but not your dependent, enter name here. ▶
 5 Qualifying widow(er) with dependent child

Exemptions
 6a Yourself. If someone can claim you as a dependent, do not check box 6a.
 b Spouse
 c **Dependents:**
 (1) First name Last name (2) Dependent's social security number (3) Dependent's relationship to you
 If more than four dependents, see instructions and check here...

d Total number of exemptions claimed		1
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Income	7 Wages, salaries, tips, etc. Attach Form(s) W-2	7	33,738.
	8a Taxable interest. Attach Schedule B if required	8a	24.
	b Tax-exempt interest. Do not include on line 8a	8b	
	9a Ordinary dividends. Attach Schedule B if required	9a	42.
	b Qualified dividends	9b	42.
	10 Taxable refunds, credits, or offsets of state and local income taxes	10	
	11 Alimony received	11	
	12 Business income or (loss). Attach Schedule C or C-EZ	12	-26,720.
	13 Capital gain or (loss). Attach Schedule D if required. If not required, check here <input type="checkbox"/>	13	838,353.
	14 Other gains or (losses). Attach Form 4797	14	-1,214.
	15a IRA distributions	15a	6,191.
	b Taxable amount	15b	691.
	16a Pensions and annuities	16a	
	b Taxable amount	16b	
	17 Rental real estate, royalties, partnerships, S corporations, trusts, etc. Attach Schedule E	17	1,214.
	18 Farm income or (loss). Attach Schedule F		
	19 Unemployment compensation		
	20a Social security benefits	20a	
	b Taxable amount		
	21 Other income. List type and amount		
	22 Combine the amounts in the far right column for lines 7 through 21. This is your total income		

Adjusted Gross Income	23 Educator expenses	23	
	24 Certain business expenses of reservists, performing artists, and fee-basis government officials. Attach Form 2106 or 2106-EZ	24	
	25 Health savings account deduction. Attach Form 8889	25	
	26 Moving expenses. Attach Form 3903	26	
	27 Deductible part of self-employment tax. Attach Schedule SE	27	
	28 Self-employed SEP, SIMPLE, and qualified plans	28	
	29 Self-employed health insurance deduction	29	
	30 Penalty on early withdrawal of savings	30	
	31a Alimony paid b Recipient's SSN	31a	
	32 IRA deduction	32	
	33 Student loan interest deduction	33	
	34 Tuition and fees. Attach Form 8917	34	
	35 Domestic production activities deduction. Attach Form 8903	35	
	36 Add lines 23 through 35	36	0.
	37 Subtract line 36 from line 22. This is your adjusted gross income	37	846,128.

2015

Kyle Trading Account ▼ Net Account Value Total Unrealized Gain

Positions	Performance & Value	Margin	Gains & Losses
View	Tax Year		
Realized ▼	2015 ▼	Filters	
Total Gain Realized [?]	Short-Term Gain Realized	Long-Term Gain Realized	Total Commission & Fees
\$829,718.59	\$829,718.59	\$0.00	\$53,438.19

2016

Kyle Trading Account ▼ Net Account Value Total Unrealized Gain

Positions	Performance & Value	Margin	Gains & Losses
View	Tax Year		
Realized ▼	2016 ▼	Filters	
Total Gain Realized [?]	Short-Term Gain Realized	Long-Term Gain Realized	Total Commission & Fees
\$1,108,344.56	\$1,108,344.56	\$0.00	\$127,201.19

Table of Contents

Introduction	7
10 Reasons Why I'm 100% Focused on Biotech Stocks	10
My Biotech Catalyst Trading Strategy	13
How to Find Upcoming Biotech Catalyst Events	18
Winning Your Biotech Company Analysis	23
What to do next...	35
Glossary of Biotech Catalysts	37



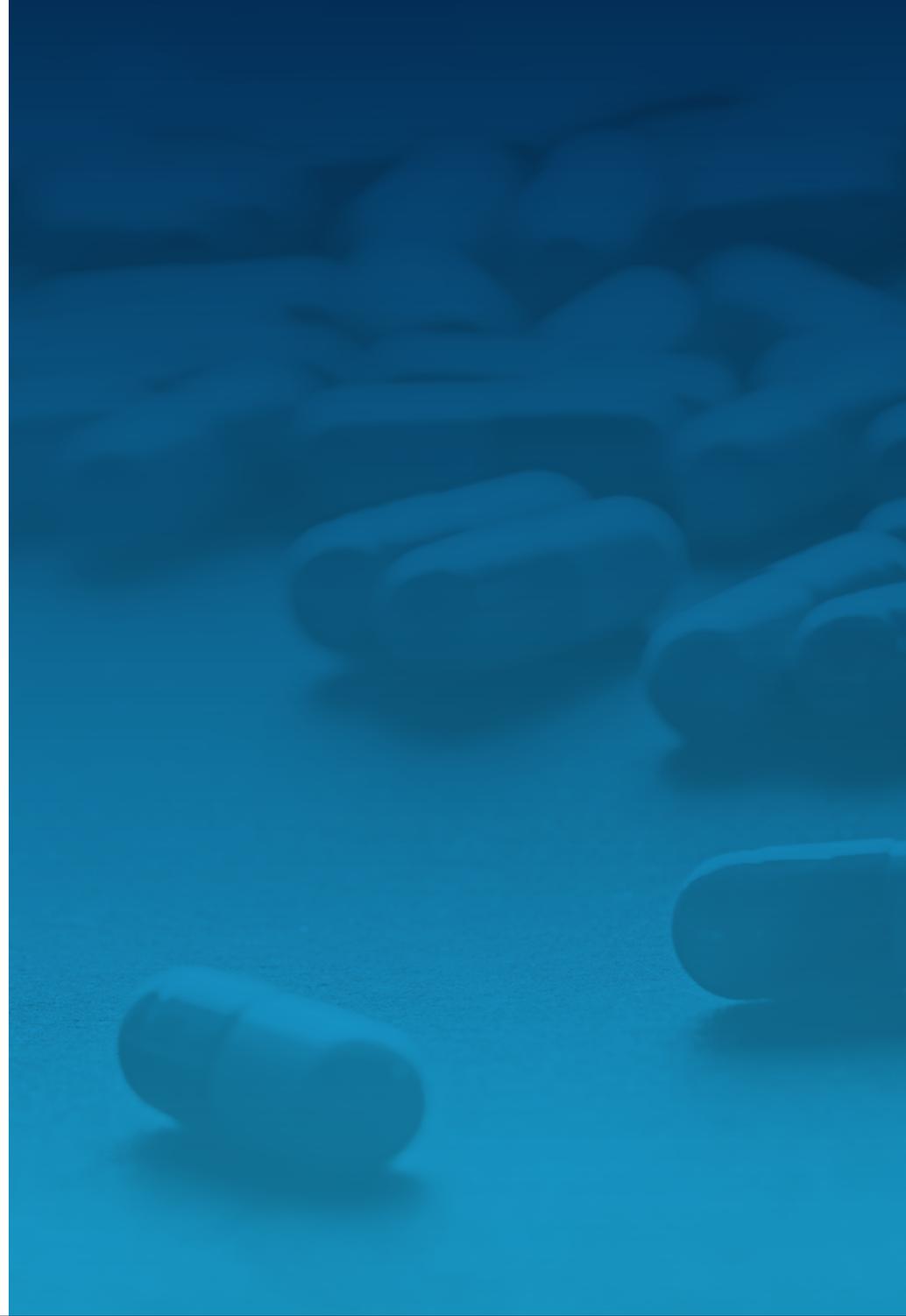
Introduction

What is Biotech Trading?

The biotech sector is an incredibly unique corner of the market. The companies in this market are all about creating drugs and solutions to help prevent or cure diseases and medical conditions.

As you can imagine, there are many hoops a biotech company must get through to fully come to fruition. These hoops are referred to as 'catalysts', which cause the price of a biotech stock to move in massive ways based on what it means for a biotech company's outlook.

By learning and mastering the 'catalysts' of the biotech sector, you can latch on to numerous massive upward trends in the market and potentially drive your profitability through the roof as I have proven to do continuously for the last 5 years now...



My Style of Trading

Before we get started, you'll need to know the difference between day trading, swing trading, and investing.

Let's start with day trading. If you're a day trader, that means you're buying and selling a stock within the same day to take advantage of price movements in a "short" time.

On the other hand, we have swing trading. This is a short-term trading strategy in which you hold your positions over one day, but the time you hold onto your position shouldn't last for more than a few weeks or so. This method is primarily used to identify a trend or catalyst in an attempt to potentially capture a larger price movement in the stock.

Moving on, investing is very different from both day and swing trading. With investing, your goal is to hold onto a position for an extended period of time. Your holding period is generally for multiple months or years. Investing primarily involves looking at the long-term changes in a stock, ranging from financial performance to catalysts that could drastically change the company.

Of the three styles I described above, I best fall into the category of swing trading... That's because I tend to focus on market events known as 'catalysts' which move the price of a stock up or down... We will get into trading catalysts in a moment, but first, let me explain

why all the catalysts I look for are specifically in the biotech sector.





10 Reasons Why I'm 100% Focused on Biotech Stocks

10 Reasons Why I'm Focused on Biotech Stocks

Most traders in the U.S. trade across the Nasdaq, Dow, S&P, and NYSE...

Great traders know how to get an advantage... they pick a sector and specialize... but even better traders pick the very BEST sector to specialize in...

For the next 20 years... **BIOTECH** is **THE** market to be in.

I've got 10 reasons that tell you exactly why biotech is the place to be:

1. Downright Outperformance - Over the last 5 years, biotech has drastically outperformed the S&P 500. The biotech index is up over 200%, while the S&P index is up about 90%.

2. Constant Acquisitions - Large cap Biotech companies continue to grow through acquisition of developmental Biotech companies. The large cap companies have a ton of cash that they've been putting to

work.

3. Data Releases - Biotech companies have binary events that can not only change lives, but make people fortunes. Since these biotech stocks can have such huge gains on a data release, they usually trend higher as the date approaches. As a trader, we can take advantage of this and capture large gains without taking the risk of holding through data.

4. An Information Arbitrage - Since many of these Biotech companies are so small, a lot of them are still flying below the radar. In other words, you'll rarely see them being talked about on CNBC and other major media outlets. This gives individual investors like you and me an edge when it comes to research. Additionally, many of these companies are too small for bigger institutions and hedge funds to invest in. This gives parttime and fulltime retail investors an added advantage.

5. The Small Cap Benefit - Most Biotech companies are valued at under \$1 billion, which means any positive catalysts or news about the company can be very important. Also, the share structures of these companies, and the relatively low number of outstanding shares, make it possible for traders to take advantage of extended moves and short squeezes.

6. Equity Protection via Partnerships - Big pharmaceutical companies have been partnering with smaller Biotech companies helping them to further develop their pipeline of drugs. Sometimes,

these small companies can develop a new drug without using much of their own money. This means a new drug could potentially go through clinical trials with little dilution to shareholders.

7. Profit Opportunity of Drug Exclusivity - When a new drug gets approved by the FDA, the company is protected for a period of time in which a generic cannot be produced or sold to the general public. That gives the drug exclusivity and if this happens to be a new treatment, the company can sell the drug without any competition. This makes developing a drug a very profitable venture, once it gets approved.

8. Continuous Demand of Breakthrough Technology - There is a continuous stream of new technology being developed by Biotech companies. Some of these new developments are giving us hope that will be able to better treat cancer, and even edit human genes.

9. Supportive Trend of the Sector - Everybody knows the U.S. population is aging. Baby boomers are by far the largest demographic in our country, and they'll continue to need quality medical care now, and in the years to come. It's easy to see how this constant influx of new older patients will be a positive catalyst for healthcare & biotechnology companies.

10. Increasing FDA Approval Rate - Over the last 10 years, the Food & Drug Administration has been quite lenient when approving new drugs. The last 5 years has seen record levels of drug approval, and this leniency has made these small cap biotech companies a lot more

valuable.

Quite frankly, the biotech market is a gold mine... and it can offer massive opportunities for the smart trader who is willing to do a little homework. Ok, let's get started!





My Biotech Catalyst Strategy

Catalyst Strategy

Now let's take a closer look at the term "catalyst." A catalyst is typically an event that moves the price of a stock up or down. This could range from an earnings release, company news, analyst comments, a lawsuit, FDA approval or the commencement of a Phase I, II or III trial. If you don't know what these terms mean, don't worry. You're probably wondering... what's a phase I,II, or III trial?

The clinical testing, or testing stage of a drug candidate on humans, is comprised of three trials.

You probably could figure out Phase I is the first stage.

A **Phase I trial** is typically a dose testing trial conducted in healthy volunteers. The end goal of this trial is to determine the maximum tolerable dose in healthy humans. If the company gets the okay to move onto a Phase II trial, a small patient population would be used to determine the safety, and sometimes the efficacy, of the drug.

The **Phase II trial** is divided into Phase IIa and IIb, sometimes. A Phase IIa trial is primarily conducted in order to test the dosing

requirements in patients. On the other hand, a Phase IIb done to test the initial efficacy.

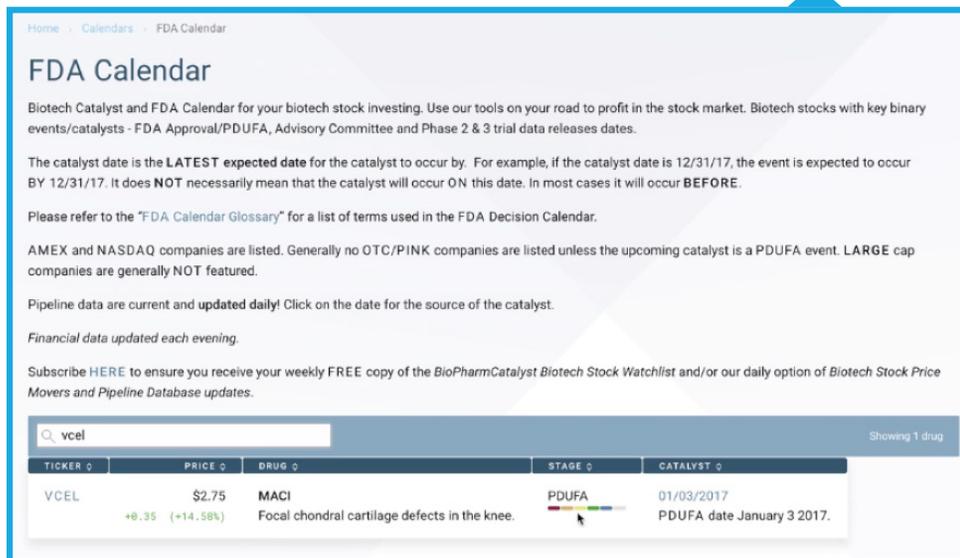
The **Phase III trial**, is a large scale, full-fledged, and often pivotal, trial to test the efficacy and safety, which standardly uses a drug arm and a control arm, ideally the current standard of care, or, barring that, a placebo. In short, the Phase III clinical trial is conducted to confirm the effectiveness, monitor the side effects, as well as compare the drug to other commonly used treatments. Consequently, data would be collected to determine whether the drug or treatment could be used safely.

As you can see, there is a fair amount of 'biotech catalyst event' terminology used in this form of trading. I've included a [complete glossary of biotech catalyst terms](#) to get familiar with at the end of this guide. When you come across a term you are not familiar with, it's likely a type of biotech catalyst event... so, please check the terminology section as needed.

Now, my strategy primarily involves following these kinds of events. I'll follow important events that may be coming, and I'll trade the stock in anticipation of the event. Generally, if a stock has a positive catalyst, it will go up, and vice versa.

Moving on, let's look at an example. Vericel Corp. (NASDAQ: VCEL) is one stock that I've traded, and I'd like to get into the reason behind the trade. For this stock, the company had a U.S. Food and Drug Administration (FDA) approval date on January

3, 2017, for its MACI drug, and I identified this event about a month before this event. To find this event I used a website, BioPharmCatalyst, as shown below:



The screenshot shows the 'FDA Calendar' page on the BioPharmCatalyst website. It includes a search bar with 'vcel' entered, a table of search results, and various informational text blocks. The table lists the ticker 'VCEL', price '\$2.75', drug 'MACI', stage 'PDUFA', and catalyst date '01/03/2017'. A mouse cursor is hovering over the 'PDUFA' stage.

Home . Calendars . FDA Calendar

FDA Calendar

Biotech Catalyst and FDA Calendar for your biotech stock investing. Use our tools on your road to profit in the stock market. Biotech stocks with key binary events/catalysts - FDA Approval/PDUFA, Advisory Committee and Phase 2 & 3 trial data releases dates.

The catalyst date is the **LATEST expected date** for the catalyst to occur by. For example, if the catalyst date is 12/31/17, the event is expected to occur **BY** 12/31/17. It does **NOT** necessarily mean that the catalyst will occur **ON** this date. In most cases it will occur **BEFORE**.

Please refer to the "FDA Calendar Glossary" for a list of terms used in the FDA Decision Calendar.

AMEX and NASDAQ companies are listed. Generally no OTC/PINK companies are listed unless the upcoming catalyst is a PDUFA event. **LARGE** cap companies are generally **NOT** featured.

Pipeline data are current and **updated daily!** Click on the date for the source of the catalyst.

Financial data updated each evening.

Subscribe [HERE](#) to ensure you receive your weekly **FREE** copy of the *BioPharmCatalyst Biotech Stock Watchlist* and/or our daily option of *Biotech Stock Price Movers and Pipeline Database updates*.

Showing 1 drug

TICKER	PRICE	DRUG	STAGE	CATALYST
VCEL	\$2.75 +0.35 (+14.58%)	MACI Focal chondral cartilage defects in the knee.	PDUFA	01/03/2017 PDUFA date January 3 2017.

Moving forward, I'll be using charts provided by TradingView, as it is a free service, and you could use it when you're first starting out.

Here's a look at VCEL ahead of the catalyst:



Now, I got long some shares at around \$2.25. Thereafter, the stock hit \$2.58 and it pulled back, and I thought, "This is a good time for me to add to my position." So I got into more shares and had an average price of around \$2.28 per share. Now, I rode this up to around \$2.60, and pulled back more. Thereafter, the stock moved higher in anticipation of the FDA approval and I sold out around \$2.66 per share.

Here's a look at where I got out:



Now, the company actually announced an early FDA approval and spiked up to around \$3.00. I swung this position around three to four weeks ahead of the FDA approval data, and it didn't really matter whether these results were good or bad. I took my profits, and I was rewarded for swinging this position. In my opinion, it makes sense to get into a position like this and exit on a pop ahead of the catalyst, as there is less risk than actually holding onto the position to see whether the stock has a positive or negative. Vericel ultimately got FDA approval, it would've been nice to have had the position when it got FDA approval in mid-December 2016, but this was really a tossup, and as swing traders, you'll need to follow a rules-based trading approach. If I held onto this position, in my opinion, this would have just been gambling, cause this event could have really went either way.

Let's move onto another example. Now Oncomed Pharmaceuticals Inc (NASDAQ: OMED) was selling off coming into the event. That in mind, traders may have gotten short, a few days ahead of the event, and bought back shares before its release, as shown in the chart below. However, keep in mind, having short positions is risky, and you generally not take short positions when you're first starting out.

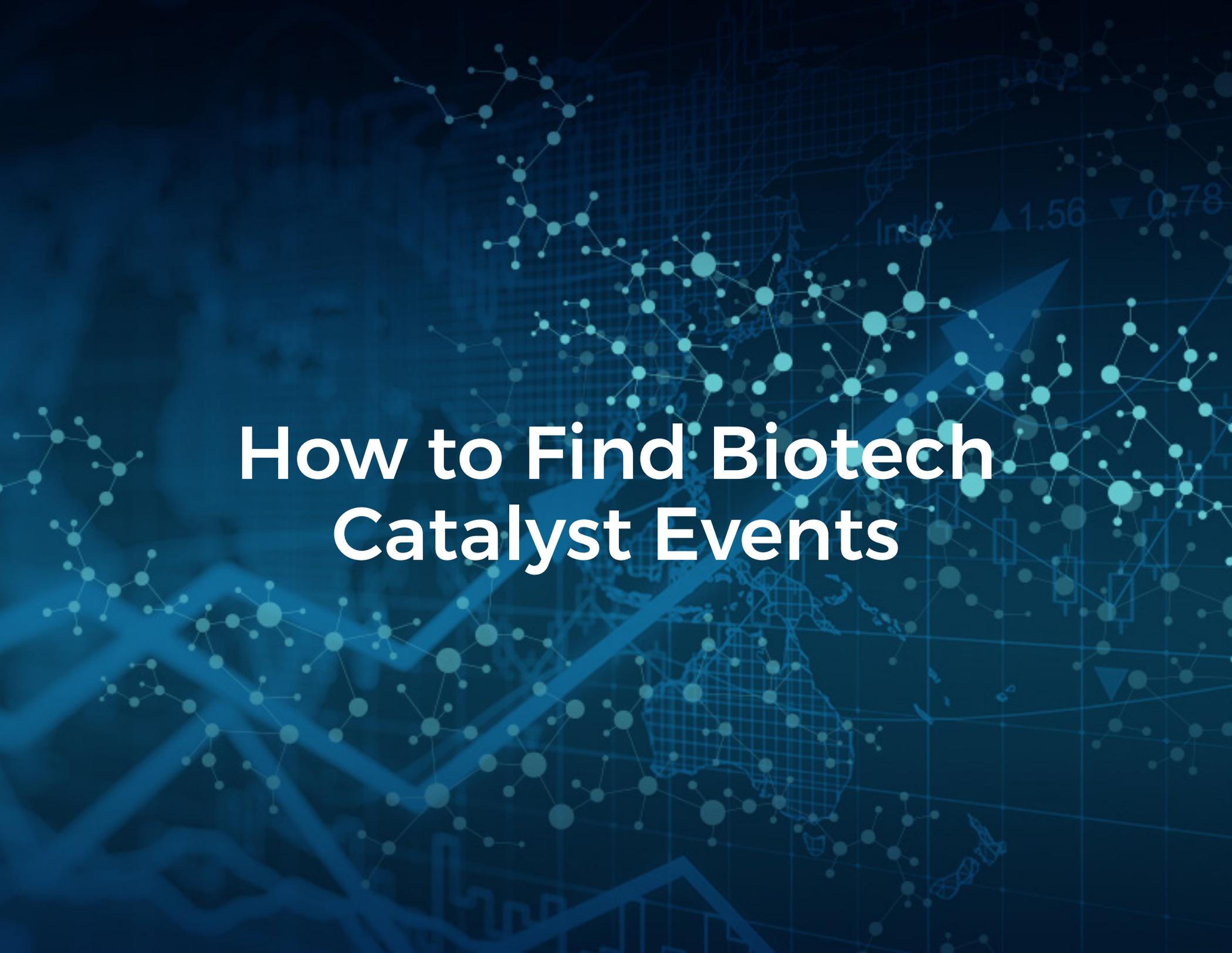


Let's look at a third example. Nektar Therapeutics (NASDAQ: NKTR) was expected to announce its Phase III data around March 20, 2017. Now, if you look at the chart below, the run up in the stock ahead of the catalyst, was quite similar to that of VCEL. Here's a look at the chart of NKTR with annotations.

The stock was expected to release data regarding its NKTR-181 treatment for lower back pain, and you could've gotten in around \$14.25 per share and got out when it popped before the release.



There's a plethora of information on BioPharmCatalyst, and you can get a heads up on the expected dates that companies may release data regarding their drugs, in addition to IPOs and PDUFA dates. Now, if you don't know what these terms mean, don't worry, as I mentioned earlier, just go use the [glossary of biotech catalyst terms](#) at the end as needed.



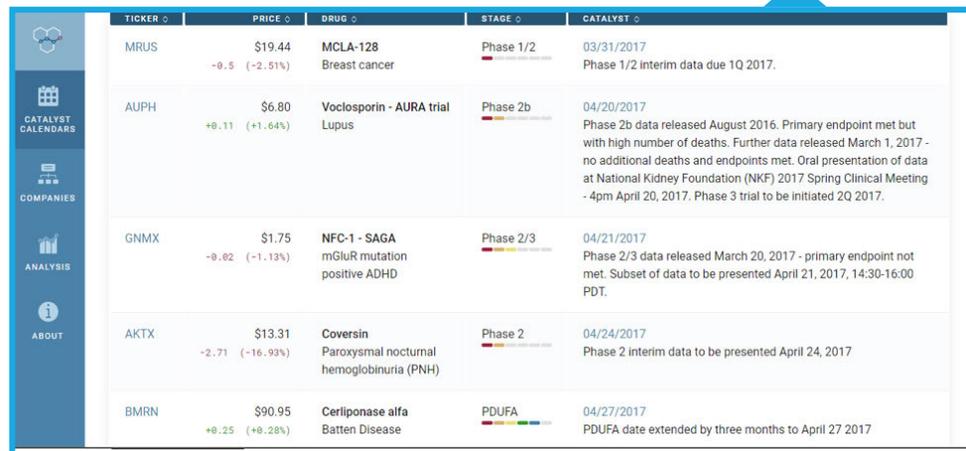
How to Find Biotech Catalyst Events

How to Find Biotech Catalyst Events

You should now have a good grasp on what type of trading we're focused on. In this chapter, we'll be going over how you could identify catalyst events in biotech and pharma names.

You can go to www.biopharmcatalyst.com to look at calendars of biotech events, such as Phase I, II and III data releases which are defined in the glossary at the end of this guide.

The site is free and categorizes upcoming events, for biotech and pharma companies. Here's a peek at where you'll need to look to find such events:

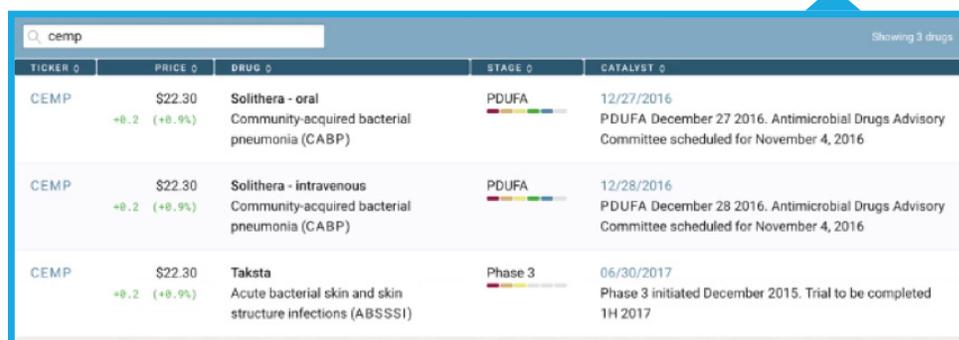


TICKER	PRICE	DRUG	STAGE	CATALYST
MRUS	\$19.44 -8.5 (-2.51%)	MCLA-128 Breast cancer	Phase 1/2	03/31/2017 Phase 1/2 Interim data due 1Q 2017.
AUPH	\$6.80 +9.11 (+1.64%)	Voclosporin - AURA trial Lupus	Phase 2b	04/20/2017 Phase 2b data released August 2016. Primary endpoint met but with high number of deaths. Further data released March 1, 2017 - no additional deaths and endpoints met. Oral presentation of data at National Kidney Foundation (NKF) 2017 Spring Clinical Meeting - 4pm April 20, 2017. Phase 3 trial to be initiated 2Q 2017.
GNMX	\$1.75 -8.02 (-1.13%)	NFC-1 - SAGA mGluR mutation positive ADHD	Phase 2/3	04/21/2017 Phase 2/3 data released March 20, 2017 - primary endpoint not met. Subset of data to be presented April 21, 2017, 14:30-16:00 PDT.
AKTX	\$13.31 -2.71 (-16.93%)	Coversin Paroxysmal nocturnal hemoglobinuria (PNH)	Phase 2	04/24/2017 Phase 2 interim data to be presented April 24, 2017
BMRN	\$90.95 +8.25 (+9.28%)	Cerliponase alfa Batten Disease	PDUFA	04/27/2017 PDUFA date extended by three months to April 27 2017

Source: [BioPharmCatalyst FDA Calendar](http://www.biopharmcatalyst.com)

If you refer to this link, this database will give you some, but not all, upcoming biotech catalyst events. There's a lot of events, so there could be a lot of opportunities. This will be one of your secret tools, when you're first starting out.

If you look from left to right, you'll notice the ticker, the price, the drug, the stage, and the expected date that the catalyst is being released. Let's pick one example and go over it together. For this, we'll look at Cempra Inc. (NASDAQ: CEMP). Just simply type in the ticker, and you should see something like this...



TICKER	PRICE	DRUG	STAGE	CATALYST
CEMP	\$22.30 +8.2 (+8.9%)	Solithera - oral Community-acquired bacterial pneumonia (CABP)	PDUFA	12/27/2016 PDUFA December 27 2016. Antimicrobial Drugs Advisory Committee scheduled for November 4, 2016
CEMP	\$22.30 +8.2 (+8.9%)	Solithera - intravenous Community-acquired bacterial pneumonia (CABP)	PDUFA	12/28/2016 PDUFA December 28 2016. Antimicrobial Drugs Advisory Committee scheduled for November 4, 2016
CEMP	\$22.30 +8.2 (+8.9%)	Taksta Acute bacterial skin and skin structure infections (ABSSSI)	Phase 3	06/30/2017 Phase 3 initiated December 2015. Trial to be completed 1H 2017

So with CEMP, you'll notice the drug, Solithera, which is taken orally, and used to treat community-acquired bacterial pneumonia (CABP), and the current stage it's in: PDUFA, which stands for Prescription Drug User Fee Act. This stage takes 10 months for standard designation, and 6 months for the accelerated designation, from the date of the new drug application (NDA) filing. PDUFA is an FDA approval date. Under the catalyst category, you'll notice the dates. For the indication of Solithera, PDUFA was expecting the approval date to be on, or around, December 27, 2016. Additionally, at the time, they were going to have an advisory committee meeting on

November 4, 2016.

Now, you look at its other drugs, you'll notice dates for the catalysts. However, keep in mind, these aren't exact dates, if you look at the catalyst for Taksta, you'll notice it says Phase III was initiated in December 2015, and the trial is expected to be completed during the first half of 2017. If you look at the date, it says June 30, 2017, note this is not an exact date, the data could come before that. When looking at these dates, make sure you read the description to know whether it's an exact date or not. If you click on the links (the dates are the links), you'll be directed to the press release.

Let's look at another example. Follow along, and type in the ticker NTRP. Neurotrope Inc (NASDAQ: NTRP). You should see the image below, depending on when you're doing your research:



TICKER	PRICE	DRUG	STAGE	CATALYST
NTRP	\$19.45 -0.39 (-1.97%)	Bryostatin Alzheimer's disease	Phase 2	04/30/2017 Phase 2 data due April 2017. Announced conclusion of dosing and patient monitoring February 28, 2017.

The drug is Bryostatin, which is used to treat Alzheimer's disease. Bryostatin is currently in the Phase II stage, and it's expected to report data for the Phase II clinical trial in April 2017. The company announced the conclusion of its dosing and patient monitoring on February 28, 2017. If you click on the link (the date under the catalyst category), you'll be directed to the [press release](#). The press release is issued by the company, so there's

no fake news here.

Here's what should come up, after you click the link:



If you follow the link above, you could get a detailed look at the press release on February 28, 2017. Keep in mind, again, this date here is not exact. The company expects to report data in April 2017, and it does not necessarily have to be on April 30, 2017. It's really important to keep in mind that these dates are exact, and we'll look at another example.

Let's take a look at Anthera Pharma (NASDAQ: ANTH).

EGLT	\$7.41 -0.1 (-1.33%)	Egalet-001 Abuse-Deterrent Morphine	PDUFA	10/14/2016 PDUFA October 14 2016. Advisory Committee Meeting August 4 2016 voted 18 to 1 to recommend approval
WINT	\$2.70 -0.16 (-5.59%)	Aerosurf Respiratory Distress Syndrome	Phase 2a	10/14/2016 Phase 2a data due in late September or early October 2016
MDVN	\$81.44 +0 (+0%)	XTANDI metastatic Castrate-resistant Prostate Cancer (CRPC)	PDUFA	10/22/2016 PDUFA for sNDA October 22, 2016
PRQR	\$6.89 -0.11 (-1.57%)	QR-010 Cystic Fibrosis	Phase 1b	10/27/2016 Phase 1b enrolment started June 2015. Preliminary data due at the North American Cystic Fibrosis Conference (NACFC) October 27 - 29, 2016
KERX	\$4.96 -0.46 (-8.49%)	Auryxia Iron deficiency anemia in non-dialysis dependent CKD patients	sNDA Filing	10/31/2016 Phase 3 top line data released late March 2016. sNDA to be filed early 4Q 2016
PTN	\$0.61 +0.01 (+1.67%)	Bremelanotide Female sexual dysfunction (FSD)	Phase 3	10/31/2016 Phase 3 initiated Dec 2014. Data due early 4Q 2016. October 31, 2016 listed as estimated last possible data for FDA Calendar date listing.
ANTH	\$3.01 -0.12 (-3.83%)	Blisibimod Lupus	Phase 3	10/31/2016 Missed primary endpoints in Phase 2b trial Jun 2012. Phase 3 final data due early 4Q 2016
INNL	\$5.98 -0.13 (-2.13%)	Cogenzia Diabetic foot ulcer infections	Phase 3	10/31/2016 Data due early 4Q 2016
INNL	\$5.98 -0.13 (-2.13%)	XaraColl Post-operative pain	NDA Filing	10/31/2016 NDA Filing due early 4Q 2016
TBPH	\$31.51 -5.93 (-15.84%)	Revefenacin COPD	Phase 3	10/31/2016 Phase 3 data due early 4Q 2016. October 31 estimate only for calendar purposes

If you look at where my pointer is hovering over, you'll notice Anthera, its drug Blisibimod, which is targeted to treat Lupus, as well as the catalyst. Notice the date here, it says October 31, 2016. However, if you look at the description, the company expected to release Phase III final data in early 4Q 2016. Now, this is open to interpretation. Early fourth quarter 2016 could mean October or November 2016. That in mind, you would not want to hold this stock in anticipation of the catalyst on October

31, 2016 because the date is not exact. You wouldn't want to hold this stock starting in mid-October 2016 in anticipation of the catalyst, and then the Phase III final data comes out early and the data is bad, and you weren't expecting it, which would cause the stock to drop.

Now, ultimately, ANTH released its Phase III results on November 10, 2016. Here's a look at a snippet of the press release:

Nov 10, 2016

← Previous Release | Next Release ▶

Anthera Announces that the Blisibimod CHABLIS-SC1 Phase 3 Study Did Not Achieve the Primary Endpoint in Patients with Active Systemic Lupus Erythematosus

- Assessing next steps for blisibimod for the treatment of Systemic Lupus Erythematosus
- Continuing to explore blisibimod as treatment for IgA nephropathy - Phase 2 data in December
- Sollipura™ SOLUTION phase 3 study in exocrine pancreatic insufficiency on track for topline data in December

HAYWARD, Calif., Nov. 10, 2016 (GLOBE NEWSWIRE) -- Anthera Pharmaceuticals, Inc. (NASDAQ:ANTH) today announced that the CHABLIS-SC1 clinical trial with blisibimod for the treatment of systemic lupus erythematosus (SLE) failed to meet its primary endpoint based upon the SLE Responder Index-6 (SRI-6) at 52 weeks. Although 47% of patients in the blisibimod arm versus 42% of patients in the placebo arm achieved this endpoint, the difference was not statistically significant. The SRI is a composite index comprised of SELENA-SLEDAI, BILAG and Physician Global Assessment criteria. A SRI-6 response requires a decrease of at least 6 points in SELENA-SLEDAI. The magnitude of blisibimod treatment effects for other SLE Response (SRI-4, and SRI-8) also did not achieve statistical significance.

Serum biological markers including B-cells, immunoglobulins, and complement demonstrated statistically significant treatment effects consistent with expectations and previous blisibimod clinical studies in lupus and IgA nephropathy. Adverse events between the blisibimod and placebo treatment arms were well balanced and blisibimod was generally well tolerated.

"We are disappointed that the results did not demonstrate a meaningful improvement in patients' disease activity as assessed by SRI endpoints," said William Shanahan, M.D., Anthera's Chief Medical Officer. "We would like to thank the patients, caregivers, investigators and key opinion leaders who made the CHABLIS-SC1 clinical study possible. It has yielded significant amounts of data which we look forward to sharing with the scientific community in the future which we believe will help to further inform the development of

If you're interested in looking at the results of this trial, you could read up on the [press release here](#).

Now, looking at more examples will help you reinforce this idea that these dates aren't exact. Once you get the hang of it, it should be easier for you to identify events.

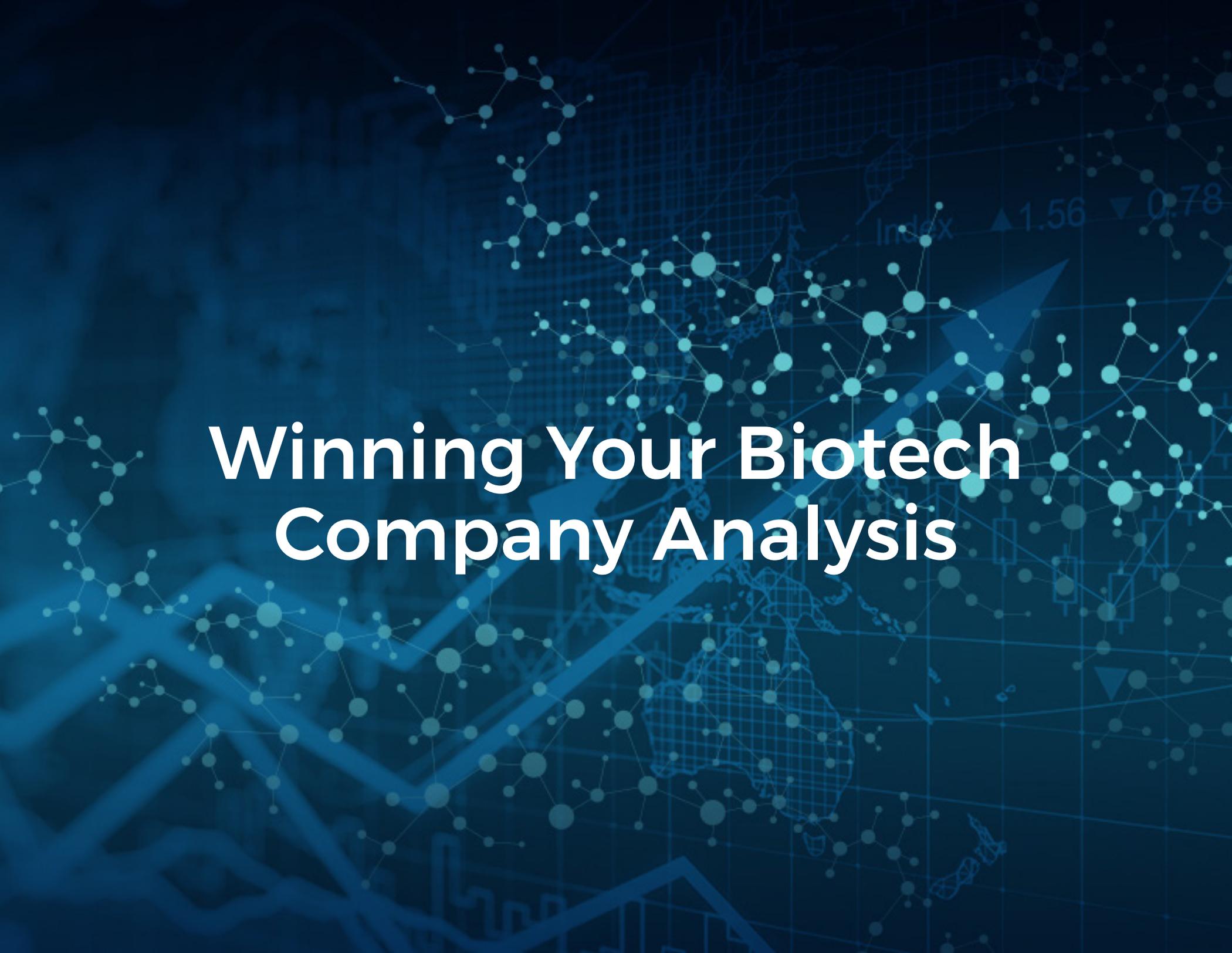
With that said, let's look at some other examples. Here, you'll notice Alder Biopharmaceuticals Inc (NASDAQ: ALDR). The drug is ALD403 - PROMISE 1, which is targeted for the treatment of frequent episodic migraine. The drug is in its Phase III stage. However, the date is unclear and not exact, it just simply says June 30, 2017.

ALDR	\$20.80	ALD403 - PROMISE 1	Phase 3	06/30/2017
	-0.3 (-1.42%)	Frequent episodic migraine		Phase 3 PROMISE 1 topline data due 1H 2017.

Notice how the description says Phase III PROMISE 1 topline data is due 1H 2017. That could mean anytime between January 2017 and June 30, 2017. Again, you wouldn't want to hold onto this anticipating a move around June 30, 2017.

This is just one part of the research process you'll need to do. Moving on, we'll look at some ways to analyze biotech companies.





Winning Your Biotech Company Analysis

Winning Your Biotech Company Analysis

Now, you'll learn how to find opportunities, trades and conduct more in-depth research.

First, we'll look at the general process of clinical trials, FDA approvals, and some of the best catalysts, in my opinion, to potentially profit off of. Moreover, we'll go over how to define risky situations, as well as timing entries and exits.

When a biotech company begins, or looks, to develop, there are multiple stages it'll need to pass before its treatment gets approval from the FDA. First off, a biotech company files an IND form, in other words, it's filing to commence the process of developing a new drug. Thereafter, the drug moves onto Phase I, Phase II and Phase III trials.

Generally, I find that Phase I trials are not that tradable since it's still early in the developmental stages. However, if the company provides Phase I data indicating the treatment is relatively safe to use with well-defined side effects and dosage ranges, then it would move onto the next developmental stage, which is Phase II. Thereafter, if it clears Phase II, the company would move onto a Phase III clinical trial.

Now, the Phase II and Phase III clinical trials are more tradable, in relation to the Phase I. The Phase II stage, the treatment is given to a larger group of people with a specified condition or disease. This stage involves gathering preliminary data regarding the efficacy, or effectiveness of the drug, as well as further assessing the treatment's safety and "best" dosage. After this stage, if the company has good data, it would move onto a Phase III clinical trial, which is conducted to confirm the effectiveness of the treatment. In addition, the company would monitor the side effects and compare the treatment to other commonly used treatments for the specified condition or illness. That in mind, when a company reaches the Phase II and Phase III stages, the company starts showing some potential value, proving the drug is safe and could be used as a treatment for the particular illness or condition.

Now, if it provides good data in the Phase III trial, then it gets sent of to an FDA approval. It could move right onto the approval, or the U.S. FDA could ask an advisory committee (adcom) to vote on whether the treatment would be approved. If we look at an example, Egalet Corporation (NASDAQ: EGLT) announced that the joint meeting of the FDA's Anesthetic and Analgesic Drug Products Advisory Committee and Drug Safety and Risk Management Advisory Committee voted 18 to 1, recommending the approval of its treatment ARYMO ER (morphine sulfate) for the treatment of daily severe pain.

Since traders were already expecting the company to gain FDA

approval for this stock, it's what traders would call a "priced-in event." This may explain one of the reasons why the stock was having a hard time running up. Here's a look at the daily chart of EGLT with annotations:



Source: [TradingView](#)

Notice how EGLT experienced some volatility during [the approval](#), and did not really break out, since the vote indicated that there was a high probability of the treatment becoming FDA approved.

Generally speaking, I find adcom votes, Phase II and III, and FDA approvals are better catalysts to trade off. However, don't get me wrong here. In some cases, Phase I data could be important, if it's for a disease or condition that currently doesn't have treatment.

In short, those are the developmental stages. Moving on,

in between the Phase III and the FDA adcom, the company sometimes will file what is known as an NDA, or New Drug Application, which you can learn more about in the glossary of terms. Then, the FDA will review the data and trials, before giving the company an approval or adcom meeting. Think of it as a college or job application, they'll review your application before they decide to accept you.

Let's take a look at some websites, tools and events that you could use to find catalysts, now you're not limited to only using these tools, these are just some websites that I find useful:

- As we've already stated earlier, [BioPharmCatalyst.com](#) is one tool that I find quite useful. Make sure you don't go to [BioPharmCatalyst](#) though, I've made that mistake a few times. You can find upcoming events on **BioPharmCatalyst.com**, they have most upcoming events, but not all.
- **FDATRacker.com** is another website, but it does cost around \$30 a month with some useful tools. However, if you're just starting out, you should try to limit your costs, and [BioPharmCatalyst.com](#) should be enough, until, if and when, you become profitable.
- Now, company websites and presentations could provide useful information. If you want to do some further analysis, after you've found a potential catalyst on [BioPharmCatalyst](#), you should refer to the company's websites to get a better idea of the treatment.
- [Seekingalpha.com](#) also provides earnings call transcripts,

which could also provide useful information.

- Biotech conferences, such as the ones conducted by JP Morgan, ASCO (typically a cancer conference) and ASH. The JP Morgan conference is usually at the beginning of the year, and some biotechs typically perform well during that time. Keep in mind, these aren't the only conferences out there, I just wanted to give you an idea that these could also be potential catalysts.

Now, the share price of the stock is quite important here. On April 21, 2017, BTX closed at just above \$3 per share. That in mind, you'll be able to hold more shares, while maintaining a 10% to 15% range of allocation in your portfolio. Therefore, you still have some leeway and won't use a bulk of your capital. A low stock price doesn't necessarily mean the company is worse than one with a higher price. Additionally, it's typically harder for a stock to double if it's say \$50 per share, because it would need to move 50 points. However, with a lower priced stock, such as one that's trading at \$3 per share only needs to 3 points to double.

Now, we've already gone over a little bit about how to use BioPharmCatalyst.com, but let's take a look at some more examples to reinforce what you should've already learned in the previous chapter. Take the case of BioTime, Inc. (NYSEMKT: BTX).

BTX	\$3.17	OpRegen	Phase 1/2	05/08/2017
	-0.01 (-0.31%)	Dry age-related macular degeneration (AMD)		Phase 2 second cohort underway. Data due May 8, 2017 at ARVO conference.

Source: [BioPharmCatalyst FDA Calendar](#)

The stock had a price of just over \$3 per share, as you could see next to the ticker. If you look right next to the price column, you'll notice the drug column. If you recall, this column shows the drug name, and the indication and what it would be used to treat. In this case, BTX's OpRegen targeted at Dry Age-Related Macular Degeneration (Dry-AMD). Generally, conditions and diseases that currently do not have any FDA-approved treatments, companies with treatments for these types of conditions could be more profitable. Getting back to the case of BTX.

Now, according to the [company's press release](#), it's expected to report data at the Association for Research in Vision and Ophthalmology. According to BioPharmCatalyst, you'll notice the development stage the company is in, next to the drug/indication column. Then, you'll notice the catalyst column, which shows that Phase II is underway, and data is expected to be released at ARVO conference on May 8, 2017.

Now, if you click on that link, it'll redirect you to [BioTime's press release](#). Dry-Age Macular Degeneration (Dry-AMD) currently affects approximately 10 million Americans. Dry-AMD is one of leading causes of blindness in people over the age of 60. That in mind, around 90% of these patients suffer from the dry form, and, at the time, there were no FDA-approved therapies.

Now, since there is currently no treatment for this drug, this stock could soar if it gets FDA approval.

Moving on, let's look at another example.

CLDX	\$4.39 +8.12 (+2.81%)	Glebatumumab vedotin Cancer - melanoma	Phase 2	10/08/2016 Phase 2 initiated December 2014. Data to be at the European Society for Medical Oncology (ESMO) Congress in October 2016
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Source: [BioPharmCatalyst](#)

Celldex Therapeutics (NASDAQ: CLDX) was set to report Phase II data for its melanoma cancer drug. This would be considered a better trader because the date was known, and the treatment is for cancer. Here's the press release that noted the data presentation date:

Program Updates:

Glebatumumab vedotin ("glemba"; CDX-011), an antibody-drug conjugate (ADC) targeting gpNMB in multiple cancers

- Enrollment continues in the Company's Phase 2b randomized study (METRIC) of glebatumumab vedotin in patients with metastatic triple negative breast cancers that overexpress gpNMB, a molecule associated with poor outcomes for triple negative breast cancer patients and the target of glebatumumab vedotin. Enrollment is open across the United States, Canada, and Australia and opened in the European Union in April, with close to 25 sites added in the EU in the second quarter. Additional sites continue to be added to support enrollment completion.
- Patient enrollment is complete, and the primary endpoint has been met in the Phase 2 single-agent study of glebatumumab vedotin in metastatic melanoma (post-progression on checkpoint therapy). The primary endpoint of the study, objective response rate, required a minimum of six responses in the first 52 patients to be deemed successful. [Celldex plans to present data from this study at the European Society for Medical Oncology \(ESMO\) Congress in October 2016](#). As previously announced, the Company has amended the protocol to add a second cohort of patients to a glebatumumab vedotin and varilumab combination arm to assess the potential clinical benefit of the combination and to explore varilumab's potential biologic and immunologic effect when combined with an ADC. This additional cohort is open to enrollment.
- Celldex is also evaluating glebatumumab vedotin in other cancers in which gpNMB is expressed.
 - Celldex has entered into a collaborative relationship with PRECOG, LLC, which represents a research network established by the Eastern Cooperative Oncology Group (ECOG), and PRECOG, LLC is conducting a Phase 1/2 study in squamous cell lung cancer. This study opened to enrollment in April 2016.
 - Celldex and the National Cancer Institute (NCI) have entered into a Cooperative Research and Development Agreement (CRADA) under which the NCI is sponsoring two studies of glebatumumab vedotin—one in uveal melanoma and one in pediatric osteosarcoma. Both studies are currently open to enrollment.

Source: [Celldex Therapeutics](#)

Celldex Therapeutics

www.celldex.com/

Celldex is developing targeted therapeutics to address devastating diseases for which available treatments are inadequate.

Pipeline

Celldex's pipeline is comprised of therapeutic antibodies, antibody ...

Press Releases

Investor Relations · Press Releases · Events ...

Glebatumumab vedotin

Glebatumumab vedotin is a fully-human monoclonal antibody ...

[More results from celldex.com »](#)

Current Opportunities

... Careers · Overview · Benefits · Current Opportunities ...

Varilumab

Varilumab is in development for hematologic malignancies and ...

Overview

Celldex's investigational medicines are being studied in ...

Now, if you go to the website, you could go under the about section to see what the company does, and what products it has.

Here's a look at Celldex's About Page:

The screenshot shows the Celldex Therapeutics website. The top navigation bar includes links for About, Pipeline, Science, Clinical Trials, Investors & Media, and Careers | Contact. The main content area features a large 3D logo for Celldex. Below the logo, there is a sidebar with a list of navigation options: Overview >, Management >, Board of Directors >, Scientific Advisory Board >, Business Development >, Careers >, and Locations >. The main content area displays the 'Overview' section, which states that Celldex Therapeutics (NASDAQ: CLDX) was founded based on a fundamental scientific belief that harnessing the power of the immune system would break significant barriers in drug development for a host of devastating diseases. The text describes the company's pipeline, which includes therapeutic antibodies, antibody-drug conjugates, immune system modulators, and other protein-based therapeutics. It also mentions that the company has created a leading pipeline in immunotherapy and targeted cancer therapies with six company-led clinical trials across five product candidates, including a registration study in triple negative breast cancer and five Phase 1 and Phase 2 clinical trials in a range of difficult-to-treat indications, and a robust preclinical engine.

Source: [Celldex](#)

You could also look at its Board of Directors, Management, and Scientific Advisory Board. If you click on the [Management link](#), you could get a more in-depth look at its management team. When researching a company, you'll want to see a management team with an experienced management team, which has worked at other biotech companies.

Next, you'll want to look into its drug pipeline. Here's a snapshot of Celldex's pipeline page:

Overview > **Celldex Therapeutics' Pipeline**

Glebatumumab vedotin >
 Varlilumab >
 CDX-0158 >
 CDX-3379 >
 CDX-1401 >
 CDX-301 >
 CDX-014 >

Celldex's pipeline is comprised of therapeutic antibodies, antibody drug conjugates, immune system modulators and other protein-based therapeutics that we believe have a higher probability of success because they are targeted to specific patient populations with high unmet medical need whose diseases express specific markers—including many underserved or completely un-served orphan indications. This has created a leading pipeline in immunotherapy and other targeted therapies with six company-led clinical trials across five product candidates, including a registration study in triple negative breast cancer and five Phase 1 and Phase 2 clinical trials in a range of difficult-to-treat indications, and a robust preclinical engine.

Celldex-Sponsored Studies

Drug Candidate and Indication	Target	Preclinical	Phase 1	Phase 2	Phase 3
Glebatumumab vedotin Triple negative breast cancer	gpNMB	METRIC (registrational study)			
Glebatumumab vedotin Metastatic melanoma	gpNMB	(3 arms: monotherapy complete; + varli & + checkpoint inhibitor ongoing)			
Varlilumab Head and neck, ovarian, colorectal and renal cell carcinomas, and GBM	CD27	+ nivolumab (BMS collaboration)			
CDX-0158 Gastrointestinal stromal tumors (GIST) and other KIT-positive tumors	KIT	monotherapy ongoing; combo planned			
CDX-3379 Multiple solid tumors	ErbB3	in combo regimens			

Source: [Celldex](#)

If you look at the company's drug pipeline page, you'll see the number of drugs in its pipeline, and the development stages it's in. Here's a look at the Celldex pipeline:

Celldex-Sponsored Studies

Drug Candidate and Indication	Target	Preclinical	Phase 1	Phase 2	Phase 3
Glebatumumab vedotin Triple negative breast cancer	gpNMB	METRIC (registrational study)			
Glebatumumab vedotin Metastatic melanoma	gpNMB	(3 arms: monotherapy complete; + varli & + checkpoint inhibitor ongoing)			
Varlilumab Head and neck, ovarian, colorectal and renal cell carcinomas, and GBM	CD27	+ nivolumab (BMS collaboration)			
CDX-0158 Gastrointestinal stromal tumors (GIST) and other KIT-positive tumors	KIT	monotherapy ongoing; combo planned			
CDX-3379 Multiple solid tumors	ErbB3	in combo regimens			
CDX-014 Renal cell carcinoma	TIM-1	monotherapy ongoing; combo planned			

You'll notice the Celldex is a cancer company, and you'll see it has 5 drugs in its pipeline.

Now, you would also want to look at a biotech company's Events & Presentations page. Celldex does not have any presentations, as of this recording. However, biotech companies typically have Presentations in the PDF format, as well as upcoming events.

You'll also want to go under the company's Investors & Media tab to see more information, such as SEC filings, financial results, press releases, and other information. Next, you'll need to know

the inner workings of the markets, this includes financials, how a company raises capital, and the initial public offering (IPO) process.

Knowing the inner workings of the stock market is critical to trading biotechs. We're always focused on trading and trying to pick the ones we think are poised to rise. However, that's all influenced by the inner workings of the markets, such as initial public offerings (IPOs), secondary offerings, warrants, and a lot of other things. At first glance, it might not seem like we need to learn about how the markets work, but they actually do affect what we're trading. That said, it's beneficial to learn these things, and if you do become an accredited investor one day, you might be able to participate in things like IPOs.

Let's say you have some hypothetical company, Company A, which is currently private. Let's say Company A is in the business of cybersecurity, and it has developed some technology and a lot of consumers and companies are using its technology to protect themselves against cyber attacks. Let's assume the company is generating some revenue, and there are just a few shareholders.

Now, the company wants to expand its reach, hire more coders to make its platform more efficient and salespeople. One way for Company A to raise capital is to take it public by conduct an initial public offering, also known as an IPO. There are multiple steps to issue an IPO. You've probably heard that word a bunch of times. But let's go over what that exactly means.

An IPO is one exit strategy that companies could take to raise capital. Now, an IPO is a process that allows a company to sell stock to the general public and be tradable on an exchange, such as the NYSE or NASDAQ. Now there's a long process for an IPO, which involves three periods: the pre-filing, waiting and post-effective.

In the pre-filing period, the company looking to conduct an IPO:

- First chooses an investment bank to lead the IPO. The investment bank leads the pricing and execution of the IPO, but there could be multiple underwriters selling shares to the public.
- Now, the company can't be sold to the general public until it registers with the SEC. The company would need to file an SEC Form S-1, which is an initial registration form for new securities, under the Securities Act of 1933.
- Typically, a prospectus is filed in conjunction with the Form S-1, and the company would have descriptions of the security being offered, business and management and risks faced by the business, as well as financial statements certified by independent accountants and any present or impending legal proceeds.

Thereafter, the company would move onto the waiting period, which is the period between the registration filing date and approval by the SEC. In this phase:

- Underwriters perform due diligence
- The company prepares for the road show, provides preliminary prospectus to market shares (also known as a red herring due to the red warnings that often indicate that the preliminary prospectus is not a solicitation for sale.) The red herring is generally the only source of information provided during the quiet period.
- In this stage, the underwriter(s) solicit offers. However, the offers may not be accepted during this period. The underwriter(s) also gather information regarding the potential market for the stock and the potential price range.
- The SEC also investigates the registration and may ask the company questions regarding the IPO and the registration statement.

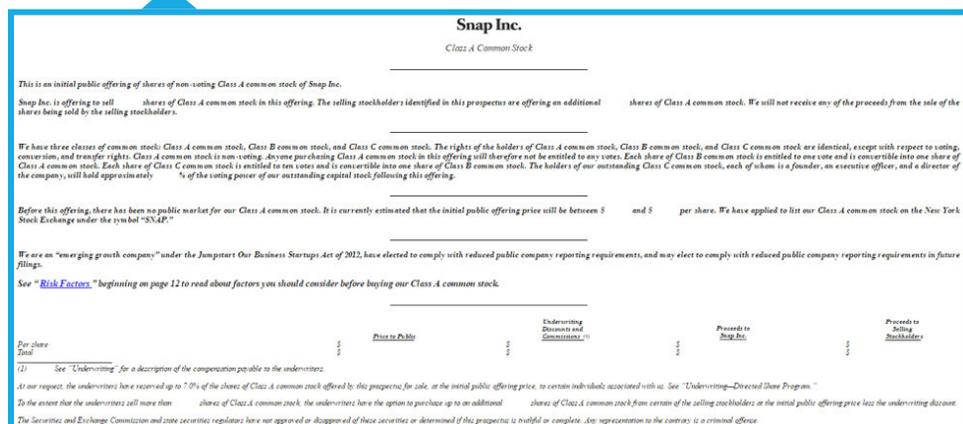
Next, the company moves onto the post-effective period. During this period:

- The company gains clearance from the SEC
- Initial offering price is set, that is the price at which the public could purchase shares at.
- The number of shares finalized for the IPO.
- Shares are offered to investors, and the company issues a press release.

- A final prospectus is provided, and the transaction closes.

Let's take a look at a company that was considering a popular IPO, at the time. Snap Inc. (NYSE: SNAP), whose products include Snapchat and Bitmoji, filed a Form S-1 with the SEC. Now, you could look at the [filings on Nasdaq's website here](#):

Here's a snippet of Snap's Form S-1:



Now, here are the underwriters:



To participate in the IPO and actually purchase shares of a company at the IPO price, you would need to be a client of the underwriters and have contact with a broker to potentially get shares.

Moving on, Snap Inc. filed an SEC Form 424B4, which is a

prospectus form. Now, in this form, companies indicate the risk factors, the IPO price, amount of shares being offered and net proceeds. Here's a look at a snippet of SNAP's Form 424B4 filing:

	Price to Public	Underwriting Discounts and Commissions to	Proceeds to Snap Inc.	Proceeds to Selling Stockholders
Per share	\$17.00	\$0.425	\$16.575	\$16.575
Total	\$3,400,000,000.00	\$55,000,000.00	\$2,403,375,000.00	\$911,625,000.00

(1) See "Underwriting" for a description of the compensation payable to the underwriters.

At our request, the underwriters have reserved up to 7.0% of the shares of Class A common stock offered by this prospectus for sale, at the initial public offering price, to certain institutions as well as individuals associated with us. See "Underwriting—Directed Share Program."

To the extent that the underwriters sell more than 200,000,000 shares of Class A common stock, the underwriters have the option to purchase up to an additional 30,000,000 shares of Class A common stock from us and certain of the selling stockholders at the initial public offering price less the underwriting discount.

The Securities and Exchange Commission and state securities regulators have not approved or disapproved of these securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

The underwriters expect to deliver the shares against payment in New York, New York on March 7, 2017.

Morgan Stanley
Barclays
Goldman, Sachs & Co.
Credit Suisse
J. P. Morgan
Allen & Company LLC
Deutsche Bank Securities

The company intended to sell 200M shares at \$17 per share, which would be gross proceeds of \$3.4B. Now, if the underwriters were able to sell over 200M shares, they would be granted the option to purchase an additional 30M shares of Snap's Class A common stock.

Take a look at SNAP's performance:



Now, Snap had an initial public offering price of \$17 per share, but it opened up at \$24. This was primarily due to the popularity of Snapchat and the demand for the stock.

Moving on, we've touched a little bit on secondary offerings earlier in the course, and now we'll go more in depth. A secondary offering is similar to an IPO, but since the company is already public it could issue this type of a secondary to raise capital. Now, the secondary offering process is quite similar to the IPO process. A company would need to contact investment banks, and it would price the offering at a discount to the regular market, typically.

Let's take a look at one company that issued a secondary offering. On Nasdaq's website, you could find a [list of companies that have recently had a secondary offering](#). Apricus Biosciences Inc. (APRI). Now, APRI filed a Form S-1, and here's a look at some pertinent information:

Approximate date of commencement of proposed sale to the public: As soon as practicable after the effective date of this registration statement.

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933 check the following box.

If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act please check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

If this Form is a post-effective amendment filed pursuant to Rule 463(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

If this Form is a post-effective amendment filed pursuant to Rule 463(d) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, or a smaller reporting company. See the definitions of "large accelerated filer," "accelerated filer" and "smaller reporting company" in Rule 12b-2 of the Exchange Act. (Check one)

Large accelerated filer Accelerated filer

Non-accelerated filer (Do not check if a smaller reporting company) Smaller reporting company

CALCULATION OF REGISTRATION FEE

Title of each class of securities to be registered	Proposed maximum aggregate offering price ⁽¹⁾	Amount of registration fee
Common Stock, \$0.001 per value per share	\$ 6,900,000	\$ 799.71

(1) Estimated solely for the purpose of calculating the amount of the registration fee in accordance with Rule 457(c) under the Securities Act. Includes the offering price of additional shares that the underwriter has the option to purchase.

The registrant hereby amends this registration statement on such date or dates as may be necessary to delay its effective date until the registrant shall file a further amendment which specifically states that this registration statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933 or until the registration statement shall become effective on such date as the Commission, acting pursuant to said Section 8(a), may determine.

The company is looking to raise capital through a secondary offering, and the proposed maximum aggregate offering price was \$6.9M. That in mind, the company wanted to raise up to \$6.9M, at the time. However, a few weeks later, Apricus filed an amendment to the Form S-1, and it looked to raise \$14.5M. The company added some securities to the proposed offering, and would now issue warrants as well. Take a look at the Form S-1/A:

CALCULATION OF REGISTRATION FEE			
Title of each class of securities to be registered ⁽¹⁾		Proposed maximum aggregate offering price ⁽²⁾	Amount of registration fee
Units consisting of:			
(1) Common Stock, \$0.001 par value per share ⁽³⁾	\$	—	—
(4) Warrants to purchase Common Stock ⁽⁴⁾	\$	—	—
Underwriter's warrants to purchase Common Stock ⁽³⁾	\$	—	—
Common stock issuable upon exercise of warrants to purchase Common Stock ⁽³⁾	\$	—	—
Total	\$	14,500,000	\$ 1,680.55 ⁽⁵⁾

(1) Estimated solely for the purpose of calculating the amount of the registration fee in accordance with Rule 457(c) under the Securities Act. Includes the offering price of additional units consisting of shares of Common Stock and warrants to purchase Common Stock that the underwriter has the option to purchase.

(2) Pursuant to Rule 416 under the Securities Act, the securities being registered hereunder include such indeterminate number of additional shares of common stock as may be issued after the date hereof as a result of stock splits, stock dividends or similar transactions.

(3) No additional registration fee is payable pursuant to Rule 457(g) under the Securities Act.

(4) Registrant previously paid \$1,442.96 of the registration fee.

This is pretty different from the original form. Most secondary offerings do not include warrants, and from what I've noticed when doing research, companies that issue warrants in a secondary offering are typically companies that are not performing well, or those in sectors that are out of favor.

Now, a warrant is simply just like an option. The owner of a warrant has the right, but not the obligation, to buy or sell a stock at a certain price before expiration. The price at which the underlying security can be bought or sold is typically referred to as the exercise price. The main difference is that warrants are generally issued by the company itself, and investors can't write warrants.

If you scroll down in a company's Form S-1/A, you could get the details of the offering. Let's look back to APRI's Form S-1/A, you'll generally find the information shown below later on in the filing:

5,000,000 Units Consisting of One Share of Common Stock and A Warrant to Purchase 0.75 of a Share of Common Stock		
We are offering 5,000,000 units, consisting of one share of our common stock and a warrant to purchase 0.75 of a share of our common stock at an exercise price per share of common stock equal to \$. The shares of our common stock and the warrants that form part of the unit are immediately separable and will be issued separately in this offering.		
We do not currently have a sufficient number of authorized shares of common stock to cover the shares issuable upon exercise of the warrants being offered by this prospectus. As a result, before any warrants can become exercisable, we need to receive stockholder approval of an amendment to our Amended and Restated Articles of Incorporation to increase the number of authorized shares of common stock to a total of 30,000,000 shares (the "Charter Amendment") at our next annual meeting of stockholders on May 17, 2017. While our board of directors has unanimously recommended that stockholders approve the Charter Amendment and all current directors and executive officers are supportive of the Charter Amendment, we cannot assure you that we will be able to obtain requisite stockholder approval of the Charter Amendment. The warrants will be exercisable on any day on or after the date that we publicly announce through the filing of a Current Report on Form 8-K that the Charter Amendment has been approved by our stockholders and has become effective. The warrants will expire five years from the date the warrants are first exercisable. In the event our stockholders do not approve the Charter Amendment, the warrants will not be exercisable and may not have any value.		
Our common stock is listed on The NASDAQ Capital Market under the symbol "APRI." On April 18, 2017, the last reported sale price for our common stock on The NASDAQ Capital Market was \$ 1.60 per share. There is no established public trading market for the warrants, and we do not expect a market to develop. In addition, we do not intend to apply for a listing of the warrants on any national securities exchange. The public offering price per unit will be determined between us and the underwriter at the time of pricing, and may be at a discount to the current market price of our common stock.		
Investing in our securities involves a high degree of risk. Please read "Risk Factors" beginning on page 4 of this prospectus and in the documents incorporated by reference into this prospectus for a discussion of factors you should consider before buying our securities.		
Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.		
	Per Unit	Total
Public offering price per unit	\$	\$
Underwriting discounts and commissions ⁽¹⁾	\$	\$
Proceeds, before expenses, to us	\$	\$

The company stated, "We are offering 5,000,000 units, consisting of one share of our common stock and a warrant to purchase 0.75 of a share of our common stock at an exercise price per share of common stock equal to \$. The shares of our common stock and the warrants that form part of the unit are immediately separable and will be issued separately in this offering."

Take note that Apricus did not disclose the exercise price of the warrants in the filing.

Thereafter, APRI filed a Form 424B4:

5,030,000 Units Consisting of One Share of Common Stock and A Warrant to Purchase 0.75 of a Share of Common Stock		
<p>We are offering 5,030,000 units, consisting of one share of our common stock and a warrant to purchase 0.75 of a share of our common stock at an exercise price per share of common stock equal to \$1.55. The shares of our common stock and the warrants that form part of the unit are immediately separable and will be issued separately in this offering.</p> <p>We do not currently have a sufficient number of authorized shares of common stock to cover the shares issuable upon exercise of the warrants being offered by this prospectus. As a result, before any warrants can become exercisable, we need to receive stockholder approval of an amendment to our Amended and Restated Articles of Incorporation to increase the number of authorized shares of common stock to a total of 30,000,000 shares (the "Charter Amendment") at our next annual meeting of stockholders on May 17, 2017. While our board of directors has unanimously recommended that stockholders approve the Charter Amendment and all current directors and executive officers are supportive of the Charter Amendment, we cannot assure you that we will be able to obtain requisite stockholder approval of the Charter Amendment. The warrants will be exercisable on any day on or after the date that we publicly announce through the filing of a Current Report on Form 8-K that the Charter Amendment has been approved by our stockholders and has become effective. The warrants will expire five years from the date the warrants are first exercisable. In the event our stockholders do not approve the Charter Amendment, the warrants will not be exercisable and may not have any value.</p> <p>Our common stock is listed on The NASDAQ Capital Market under the symbol "APRI." On April 20, 2017, the last reported sale price for our common stock on The NASDAQ Capital Market was \$1.37 per share. There is no established public trading market for the warrants, and we do not expect a market to develop. In addition, we do not intend to apply for a listing of the warrants on any national securities exchange. The public offering price per unit will be determined between us and the underwriter at the time of pricing, and may be at a discount to the current market price of our common stock.</p> <p>Investing in our securities involves a high degree of risk. Please read "Risk Factors" beginning on page 4 of this prospectus and in the documents incorporated by reference into this prospectus for a discussion of factors you should consider before buying our securities.</p> <p>Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.</p>		
	Per Unit	Total
Public offering price per unit	1.40	\$ 7,042,000
Underwriting discounts and commissions ⁽¹⁾	0.098	\$ 492,940
Proceeds, before expenses, to us	1.302	\$ 6,549,060

The company stated in its Form 424B4, *"We are offering 5,030,000 units, consisting of one share of our common stock and a warrant to purchase 0.75 of a share of our common stock at an exercise price per share of common stock equal to \$1.55. The shares of our common stock and the warrants that form part of the unit are immediately separable and will be issued separately in this offering."*

"We do not currently have a sufficient number of authorized shares of common stock to cover the shares issuable upon exercise of the warrants being offered by this prospectus. As a result, before any warrants can become exercisable, we need to receive stockholder approval of an amendment to our Amended and Restated Articles of Incorporation to increase the number of authorized shares of common stock to a total of 30,000,000 shares (the "Charter Amendment") at our next annual meeting of stockholders."

Now, the firm underwriting this offering would now go to its institutional investors and would ask whether they want to buy shares of APRI at \$1.40, with a warrant to purchase 75% of a share of its common stock at an exercise price of \$1.55. However, the Apricus did not currently have enough authorized shares of common stock to cover the shares if those warrants were exercised. Consequently, the company would now need to receive shareholder approval to increase the number of authorized shares to 30M. The company also noted that the warrants would expire five years from the date when the warrants are first exercisable.



Here's a look at APRI's performance after the offering:



The company filed its Form S-1/A that noted it would now include warrants in its offering on April 20, 2017, and you'll notice how the stock traded lower after. Apricus priced its secondary offering on April 24, 2017 at \$1.40 per share, and investors would also receive a warrant, but the stock traded well below that offering price.

The reason being? Supply and demand. The markets are based on different opinions, and prices are based on whether more traders and investors are bullish or bearish on the stock. Here, we notice that there was not a lot of demand for APRI, causing it to trade below the offering price.

Now, this is just a taste of what you'll need to know before investing in biotechs. You should have an idea, by now, of what some biotech terms mean, how to find catalyst events and

analyze a biotech company. This is not a be-all and end-all. You'll need to learn a lot more before going out and trading biotechs... So check out the next section to see what to do next.





What's Next?

What's Next?

If You're Reading This, Congratulations!

Biotech trading can offer massive opportunity... but the truth is, it's not all roses. Any opportunity that offers huge wins also come with the opportunity to lose big. You need to do your homework and know what you are doing. That's why the next step after reading this ebook is to take my free training course.. where I give you more insight into how exactly I turned \$15,253 into over \$2,900,000... and how you can grab your share of the profits.

In this training I'll reveal my exact 3-Step Plan that organizes my entire process into an actionable roadmap for you to use. This training will tell you the 3 steps I followed religiously to attain my 18,000% ROI in 4 years.

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- The 3-Step Plan for winning biotech trades
- Where to hunt down the perfect catalyst event
- Ways to isolate a high-probability bullish pattern

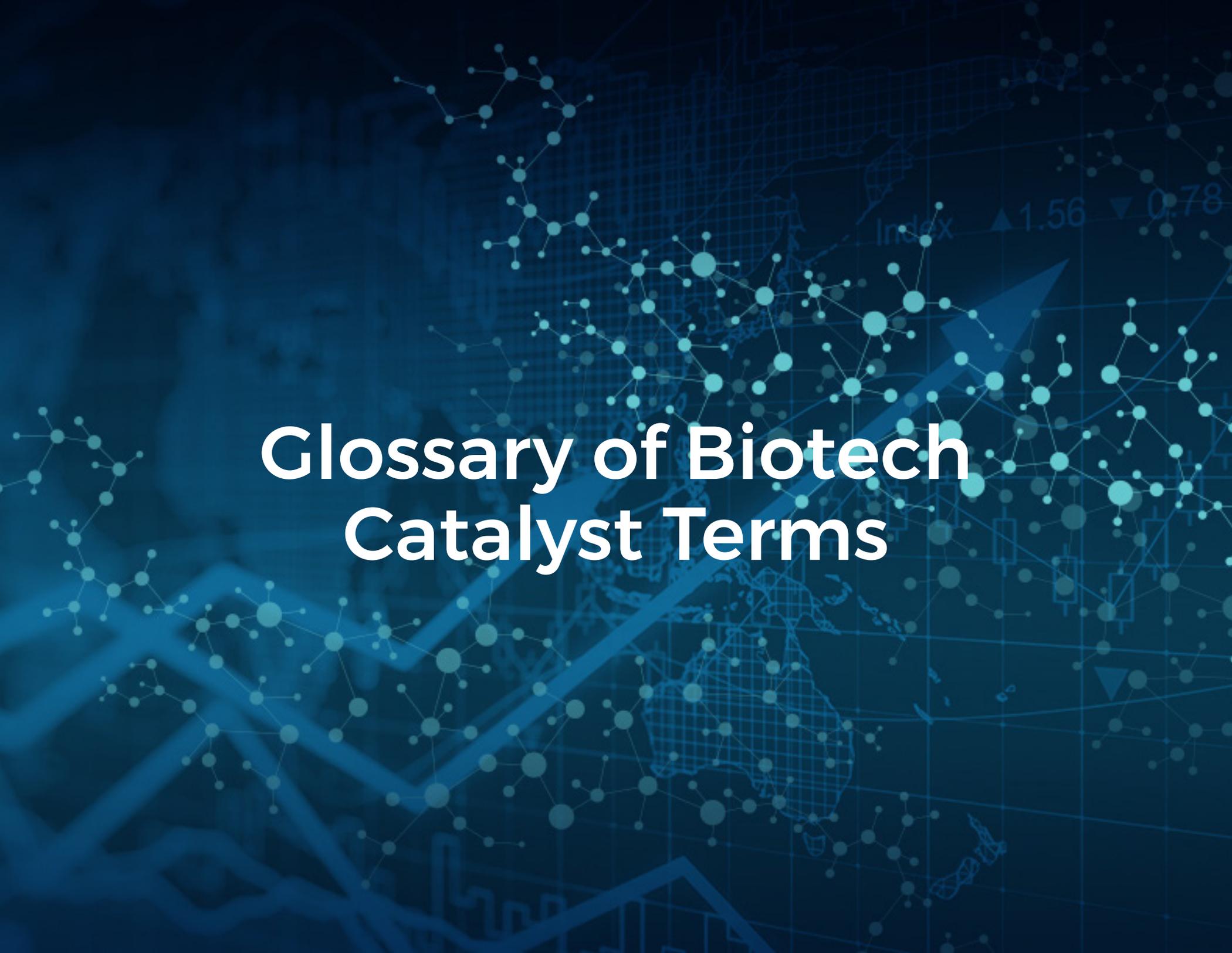
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Glossary of Biotech Catalyst Terms

Biotech Glossary

In no particular order, let's take a look at some terminology that you'll need as a biotech investor.

The clinical testing, or testing stage of a drug candidate on humans, is comprised of three trials. You probably could figure out Phase I is the first stage.

A **Phase I trial** is typically a dose testing trial conducted in healthy volunteers. The end goal of this trial is to determine the maximum tolerable dose in healthy humans. In this trial, the company conducts a PK/PD study. Let's move onto what a PK study is. PK, or pharmacokinetics, is used to determine how the human body metabolizes, in other words, removes the drug from the body. While PD, or pharmacodynamics, helps to determine effect of the drug on the human body, in terms of safety and tolerability. If the company gets the okay to move onto a **Phase II trial**, a small patient population would be used to determine the safety, and sometimes the efficacy, of the drug.

The **Phase II trial** is divided into Phase IIa and IIb, sometimes. A Phase IIa trial is primarily conducted in order to test the dosing requirements in patients. On the other hand, a Phase IIb done to test the initial efficacy. If the company moves onto the **Phase III stage**, there would be a large scale, full-fledged, and often pivotal, trial to test the efficacy and safety, which standardly uses

a drug arm and a control arm, ideally the current standard of care, or, barring that, a placebo. In short, the Phase III clinical trial is conducted to confirm the effectiveness, monitor the side effects, as well as compare the drug to other commonly used treatments. Consequently, data would be collected to determine whether the drug or treatment could be used safely.

Now, you've probably heard of the word **placebo**. In this context, a **placebo** is a drug that has no pharmacological action on the body, think of it as something like a capsule filled with water, it should have no effect on your body, other than hydration. The so-called placebo effect occurs when there is improvement in disease condition despite using just placebo. That in mind, this effect is, quite simply, an improvement in wellbeing in a group that's treated with a placebo, compared to a similar group, which would ideally be randomly assigned, that is not treated at all. Especially in neurological diseases, the placebo effect is more evident. Often, in clinical trials, the placebo effect may reduce statistical significance of the drug arm.

NDA, or New Drug Application, is an application made by the sponsor of a drug candidate to the FDA before or during the pivotal trial of the drug candidate. When the application is made during the pivotal trial, it is called a rolling NDA, which could be used to shorten the process. The pivotal or final trial is usually a Phase III trial. However, it could sometimes be a Phase II trial. This application is supported by data from the pivotal trial, requesting the FDA to approve the drug candidate for the market

based on that data.

The primary goals of an NDA are to determine whether the treatment is safe and effective, and if the benefits of the treatment outweigh the potential risks. Additionally, the NDA should provide the FDA with enough data for it to determine if the proposed labeling is appropriate and what other information it should contain. Moreover, there should be data that describes the manufacturing methods and quality control.

Now, the approval process could take around 10 months, for the standard pathway, and 6 months for the priority review designation. The total time for new molecular entity (NME) NDA and original BLA submissions is set at 12 months following the filing, which is comprised of a 60 day filing period and a 10 month review.

If the NDA is approved, the sponsor can market the drug in the U.S. On the other hand, the application could be rejected outright. However, this is quite rare. The FDA could also ask for more data, or another trial, or for further clarifications. This is usually done through the issuing of a CRL or Complete Response Letter, but sometimes it could be conducted through meeting with the sponsor where the data requested is simple to produce.

A new molecular entity, or **NME**, is a drug that has an active moiety - molecule or ion responsible for therapeutic benefit - that has never before been approved by the FDA. On the other hand, a **new chemical entity**, or **NCE**, is a drug that contains no

active moiety that has ever before been approved by the FDA.

An NME could contain an active moiety that has been approved before, but it must contain at least one active moiety that has never been approved. An NCE, in contrast, is not required to have a single previously approved active moiety. So, an NCE is the broader category in some respects. Receiving an NCE, from the FDA, rewards the sponsor with five years of marketing exclusivity regardless of the patent situation, during which the FDA will not accept any ANDA or 505(b)(2) for that drug.

The **ANDA**, or Abbreviated New Drug Application, is used to apply for marketing approval of generic version of an approved drug. It's labeled "abbreviated" because it doesn't require preclinical or clinical trials to prove safety and efficacy. However, according to the Waxman-Hatch Act, it simply needs to prove bioequivalence.

The **priority review designation**, sometimes referred to as priority review pathway, is granted to drugs that could potentially offer advances in the treatment of a neglected disease or a rare pediatric disease. This designation can be used for another NDA, BLA, or 505(b)(2) pathway, and can be sold to another party. Moreover, the priority review designation generally reduces approval time from 10 to 6 months, and in actual practice, it could reduce by up to a year. These days, priority review vouchers are purchased for hundreds of millions of dollars to gain first-mover advantage.

A **BLA** is the NDA equivalent for biologics. It is applied for the introduction of a biologic or biopharmaceutical drug to interstate commerce.

The **CRL**, or **complete response letter**, from the FDA replaces the old “approvable” and “non approvable” letter, and tells the sponsor that the NDA has been reviewed and cannot be accepted in its present form. The CRL describes specific deficiencies and, when possible, outlines recommended actions the applicant might take to get the application ready for approval.

The CRL is often resolvable, as in the case of manufacturing issues, or when new analyses on existing data are sought. However, sometimes, like in the case of Cempra’s solithromycin, a CRL may demand additional trials, which may not be feasible to undertake, which would effectively reject the drug. The problem with the CRL for investors is that it is not made public by the FDA, and sponsoring companies are free to make public as much, or as little, of the letter as they want. This tends to create some confusion during a taxing period, and therefore, investors are left to figure out whether their investment has any value left after a CRL has been issued.

Most drugs are developed through the FDA’s 505(b)(1) pathway, which could take 15 years and billions of dollars in development costs. However, the **505(b)(2) pathway** targets a specific set

of indications, which could potentially let drugs come to the market in as little as 30 months. These drugs may rely on data from pre-existing drugs for part of their application, which could reduce time and costs. Unlike generic drugs, which only get 180-days exclusivity, these drugs can get up to 7 years exclusivity. Pediatric versions of adult drugs that can demonstrate similarity in action and safety between adult and pediatric settings could use the 505(b)(2) pathway. This also works for modified forms of a disease, or other populations, like age variances, etc.

IND, or **Investigational New Drug Application**, is an application filed by the sponsor of a drug candidate to the FDA, after the preclinical studies are completed. The IND requests the FDA’s permission to conduct human trials of a drug candidate, which is planned for marketing in the U.S. However, the trials may be conducted in any country, but is done so under the FDA’s guidance, especially in later stages. Data supporting the IND comes from in vivo or in vitro studies, or both. In vivo is when the drug is studied in live animals, and in vitro is when it is studied in the lab in a petri dish scenario.

sNDA is an application for an already approved drug that asks for changes in packaging, labeling, dosages, ingredients or new indications, especially the latter. A drug is often used off-label for a disease for which it does not have an approved NDA. Although this may sound illegal, it’s quite the contrary. This is actually perfectly legal, the law being that if a drug is approved for one indication, it can be legally prescribed by a physician for any

indication. However, a company cannot legally market a drug for off-label use. If they want to do so, they need to file an sNDA/ sBLA. The off-label use of the drug then becomes additional on-label use. Often, small companies strategize by getting a drug approved for an easier indication, and then they attempt to file an sNDA for a tougher indication.

Bioequivalence is proven by showing that the generic drug does the same action as the original drug. Typically, this is done by showing bioavailability, either in the bloodstream, or topically, of the same amount of active ingredients in the same amount of time as the original drug.

Besides bioequivalence, the manufacturer of the generic must certify that the original drug is either (a) not patented, (b) has an expired patent, (c) has a patent expiry date before which the generic will not be sold, or (d) has an invalid patent or a patent that the generic does not infringe. In the last case, there's a 30-month litigation period during which the generic cannot be approved.

Form 510(k) is a premarket approval notification, in theory, that has to be filed by manufacturers of a new medical device, if the device is "substantially similar" to an already approved device, which also did not require a premarket approval form. However, as regulations have become stricter, the FDA has started asking for more and more data for the 510(k), making it almost equivalent to an early approval form.

The FDA began the **accelerated approval program** in order to expedite the approval process of critical drugs targeting life-threatening diseases like cancer. The basic concept here is that instead of a primary endpoint like survival or other measures of clinical benefit, an accelerated approval uses a surrogate endpoint to approve a drug.

Let's use high cholesterol as an example. It's well known that high cholesterol could lead to a higher risk of heart attack. Therefore, it's commonly assumed that reducing cholesterol could reduce the risk of heart attacks. This is probable, but not proven. However, to effectively measure this hypothesis with a cholesterol-reducing drug may take 20 years. Since that will be a major "drug lag," reduction of cholesterol itself is used as a surrogate endpoint to accelerate the approval process.

A surrogate endpoint is assumed to lead to clinical benefit, but may not always do so. So, for example, tumor mass as a surrogate endpoint is thought to lead to clinical benefit in cancer patients, and often does so. It's faster, and simpler, to assess a drug against a surrogate endpoint, reducing the clinical trial duration. A drug receiving accelerated approval can be marketed, but needs to do a Phase IV confirmatory trial, which is a full-scale trial for efficacy and safety. If the drug fails this trial, the FDA may withdraw approval.

"Drug lag" is the difference between the date of European and

U.S. adoption of a drug by their respective regulatory authorities. Drug lag occurs tends to occur due to the European agency's efficiency, in relation to the U.S. FDA. The European agency takes 7 months, instead of 10 for approval. **Drug loss** is the result of FDA's regulatory action which reduces the number of approved drugs in the market. In recent times, for example, two well-regarded drugs did not get approval, solithromycin from Cempra and Heplisav-B from Dynavax.

Fast track is another designation granted by the FDA to a drug candidate targeting a serious or life threatening condition, in which there is an unmet medical need. In other words, the condition either has no other approved treatment, or the approved treatment can be shown to have deficiencies that the drug candidate will address, in terms of safety or efficacy. A Fast Track gets the sponsor more frequent meetings and communications with the FDA, as well as accelerated approvals where conditions are met, and rolling submissions.

Breakthrough Designation is another FDA designation granted at the IND stage to a drug candidate targeting a life threatening disease, which has shown some signs of effectiveness in the preclinical stage. The designation will expedite the approval process, including through rolling NDA submissions and smaller trial requirements. The drug isn't meant to be considered a therapeutic "breakthrough." Rather, it's simply a technical term. However, smaller drug companies with a breakthrough designation often abuse this designation, for marketing

purposes.

Orphan Drug status: A rare disease, as defined by the Orphan Drug Act, is one that affects less than two hundred thousand Americans. This includes diseases as familiar as cystic fibrosis, Lou Gehrig's disease, and Tourette's syndrome, and as unfamiliar as Hamburger disease, Job syndrome, and acromegaly, or "gigantism." There are around 6,000 such rare or orphan diseases, and while there may be as few as a few hundred people worldwide with some of these diseases, the total number of Americans with an orphan disease is assumed to be around 20 and 30 million.

Although the market here is small, individually, drug development may cost as much as, if not more than, non-orphan drugs. To give drug manufacturers incentive to conduct research and development (R&D) on orphan drugs, the Orphan Drug Act, and other acts were made into law. These gave a number of tax breaks, funding, and 7-year market exclusivity to orphan drugs. The market exclusivity is for non-superior drugs, and therefore, provides the sponsor a lucrative monopoly right to the small market. To recover development costs, these orphan drugs are often extremely expensive. However, getting an **orphan drug designation**, or **ODD**, is very important for drug sponsors. For example, Alexion's Soliris, which treats the orphan disease paroxysmal nocturnal hemoglobinuria, costs around half a million dollars per year, and made about \$3B in 2015. That's probably from less than 10 patients.

SPA, or Special Protocol Assessment, is an advanced declaration from the FDA that an already-discussed Phase III trial design, endpoints and statistical analyses are acceptable to the FDA. If the sponsor follows those pre-agreed rules and arrives at the agreed upon endpoint, then the FDA must necessarily approve the drug candidate. Now, if a sponsor conducts a clinical trial with, say, a surrogate endpoint, then at the PDUFA, the FDA may not accept that trial as conclusive. However, if the sponsor previously discusses this with the FDA and persuades it to agree to the trial design/endpoints, then they are rewarded with an SPA, which basically makes the process less risky for the sponsor. So, if a company has an SPA from the FDA, that increases their chance of getting approval.

PDUFA, or **Prescription Drug User Fee Act**, is both a law and a procedural step. As a law, it is an Act passed by Congress, which allows drug sponsors to pay the FDA a fee to study their NDA and approve or reject the drug candidate. As a procedural step, it is the particular day on which the FDA makes this decision, and it's one of the most important catalysts in the premarket lifecycle of a drug candidate. **PDUFA** takes 10 months for the standard path, and 6 from the accelerated path, from the date of submission of the complete NDA. The NDA may be submitted within months or even years of the topline results from the Phase III trial. The PDUFA is often preceded by an adcomm, or an advisory committee meeting, where outside experts, sponsor spokespersons, patients and the community come together to

discuss the drug, and the 13-expert panel votes to approve the drug. Although the FDA is not bound by the adcomm decision during its PDUFA, it often follows it.

An **Adcomm**, or **Advisory Committee meeting**, is often convened by the FDA a month before the PDUFA and consists of a dozen or so outside experts, a patient's advocacy representative, and a non-voting industry expert. These meetings are open to the public, and at the end of the discussion, they vote to approve or reject a drug. This decision is non-binding for the FDA, but is often indicative of the PDUFA decision. Before the adcomm, briefing documents are submitted from the sponsor as well as from the FDA, bringing to light, for the first time, considerable data and opinions about the drug candidate. An adcomm is a critical catalyst for a drug sponsor.

An **MAA**, or **Marketing Authorization Application**, is the European equivalent of an NDA. The drug sponsor makes this application to the CHMP, or Committee for Medicinal Products for Human Use. The MAA procedure takes 7 months, after which the CHMP makes a decision to approve or reject the drug candidate. If this is an orphan drug, the application is made to the COMP, or Committee on Orphan Medicinal Products. An MAA approval grants the sponsor authority to market the drug in the entire European Union, which is a market roughly equivalent to the U.S., in terms of both population and GDP. As such, it is the second most important medical market in the world. Similarly, for pediatric-use only products, there's a special application called PUMA instead of the MAA. **PUMA** stands for **Pediatric Use**

Marketing Authorization.

The **CHMP**, or Committee for Medicinal Products, for Human Use is a part of the EMA or European Medical Agency, which is, more or less, equivalent to the FDA. However, unlike the FDA, which is a mostly monolithic organization, the EMA has multiple branches, one for general products (the CHMP), one for orphan drugs and one for pediatric-use only drugs. However, the FDA does have the CDER, the Center for Drug Evaluation and Research, which handles the NDA review process. The CHMP is solely responsible for approval of non-orphan, non-pediatric drugs.

IRB, or **Institutional Review Boards**, are set up for every sponsored drug candidate at a research institution or a hospital. Their main task is to review the drug candidate during trials to approve it, on an ongoing basis, based primarily on safety and efficacy. FDA has strict regulations on IRB membership. Now, the IRB must include at least five members including at least one scientific member, one non-scientific member, at least one person not affiliated with the research institution, no members with conflicts of interests, both genders if at all possible, and so forth.

An **IDE** or investigational device exemption is used to gain approval for medical devices, just like an IND is for drugs. An IDE allows companies to sell and use a limited number of devices for clinical trials. The IDE exempts the device not only from the premarket approval regulation, but also from a host of other

reporting and recording regulations.

Off-label use: As we've stated earlier, FDA approved drugs do not necessarily need to be prescribed for treatment that it was specified for. A number of FDA approved drugs are used for indications, which are not approved. Some antibiotics are used to treat stomach ulcers, and aspirin is used to prevent heart attacks and as an anticoagulant. These are off-label uses for the drugs, and are perfectly legal. However, at least until a while ago, marketing a drug for off-label use was disallowed by the FDA.

OTC drug simply a drug that is available to the consumer without a prescription. As recently as 1940, all nonnarcotic drugs were available over the counter.

Biological drugs (or biologics) are genetically derived from living matter. They include vaccines, blood and blood components, allergenics, somatic cells, gene therapy, and recombinant therapeutic proteins, and can be composed of sugars, proteins or nucleic acids or even living entities like cells and tissues. They usually do not have "composition of matter" patents, and are theoretically more susceptible to generic competition, i.e., biosimilars. A number of the most cutting edge drugs today - Humira, Remicade, Herceptin - are biologics.

Generic drugs: Once a drug's patent expires, any manufacturer could produce a drug that is similar in composition and action.

This can be sold under the innovator drug's chemical or generic name, but not the brand name. Generic drugs drastically reduce the price of the innovator drug, and companies adopt a variety of means known as "evergreening" to block introduction of generic versions of their drugs. An ANDA needs to be filed before a generic is approved, and since these must be filed before a drug's patent expires, ANDAs are often followed by patent infringement lawsuits. The Hatch-Waxman Act gives 180-day market exclusivity to the first filer of an ANDA.



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