Five Tips for Better Biotech Trading & Understanding the BioCatalyst Process

http://www.BioRunUp.com

Tip #1 Do Not Trust the Message Boards

An absolute key to great trading is access to accurate information. The worst place on the Internet to find unbiased and accurate information is on free message boards (ie: Yahoo Finance Message Boards).

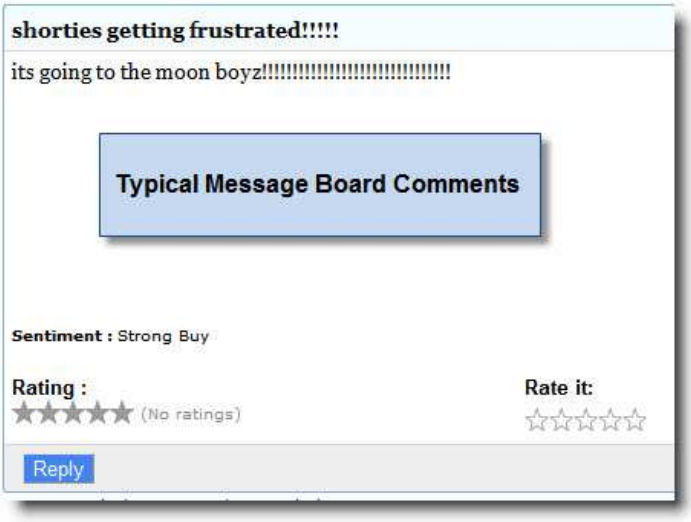
With every stock there are traders spreading mis-information on both sides- You have those who hold the stock and will say ANYTHING to attempt to get others to buy the stock and increase the share price. On the opposing side are those who are short on the stock, gambling on a price decrease, and attempted to scare people away, or out of their position.

Relying on these message boards for information is dangerous for many reasons, these include:

- Anybody can sign up for a Yahoo Account, there is ZERO accountability

- Information presented as FACTS are rarely back up with links and evidence

- There are proven cases where companies or individual investors have hired out work as 'bashers' to create accounts and post slanderous information about companies



- These boards are usually WRONG. From experience when message boards are full of bullish trades who are emotionally attached to a stock they usually end up on the losing end of a position.

- They are vulgar. By no means are we prudish, but the language and maturity level of these communities are on par with a Freshman High School locker room.

Tip #2 If You See it on the National News, it is Too Late

There is a very old and wise saying in the stock market, which is “Buy on the rumor, sell on the news”. More often than not this is very accurate. In the case of Biotech stocks, generally the price has “Run-Up” in anticipation of the regulatory catalyst which has just been announced. Once the news is out, many of the short term traders are exiting their positions and sell out of their positions to lock profits, as the facts rarely end up being as attractive as the upper limits of the rumor. When you have more sellers than buyers, the price drops. Observing this shocks many who are new to trading, but it is not a surprise to experienced traders. On various forums you will read comments like “Why is this tanking, this news is great???” and “What happened? They got FDA Approval!”.

An absolute key to successful Biotech trading is to **get in before everybody else, and get out before everybody else.** This will maximize gains and protect profits.

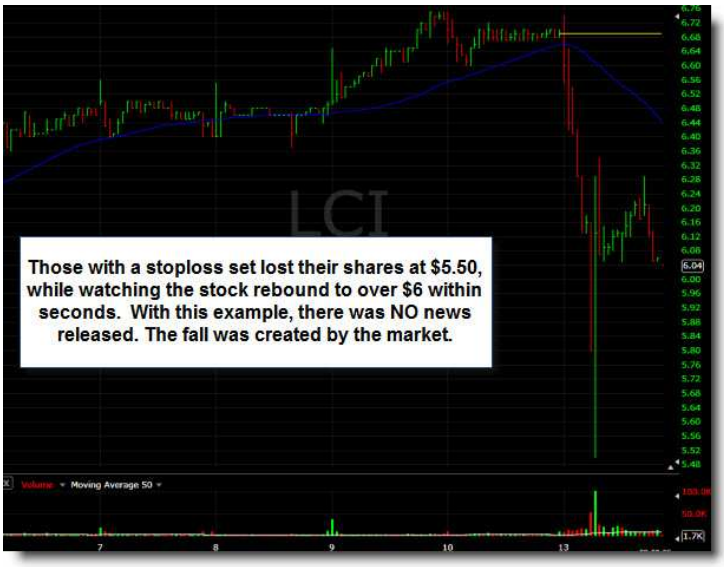
If you are watching CNN and you see that the FDA has approved a weightloss drug, do NOT run to your computer and buy the stock. There has been years of trading leading up to this point, and jumping in to stocks you know nothing about is a recipe for disaster. This is one of the most common mistakes that a beginning trader can make.

Each purchase must be made only once you are informed and comfortable with the stock. A trader needs to be comfortable with many facets of the company, including: company history, potential drug market, cash on hand, outstanding share, financing, and much more. Until you understand these fundamentals, you can not make an informed decision.

Tip #3 Setting a Stop-Loss Will Not Protect You From Bad News

A common mistake that many beginning biotech traders make is by setting a “Market Stop-Loss” on their positions. This is an order placed with a broker to sell a security when it reaches a certain price. A stop-loss order is designed to limit an investor's loss on a security position. For example, a common belief is this stop-loss will protect the trader from bad news such as a surprise early FDA rejection. Their thought may be “*I paid $3 for ABC stock, I will set my stop loss at $2.50 so I will NEVER lose more than $.50 per share.”*

Let us make this clear: We do not **EVER** do this. If this incredibly bad news hits, the price of the shares will drop and your order will be executed at “Market” price, as the price is now under $2.50. This will sell your position at the worst possible time for the worst possible price, as generally the worst of the panic is on this opening drop. There are many cases where a stock initially tanks, only to recover within seconds. You will lose your shares at the lowest price of the day.



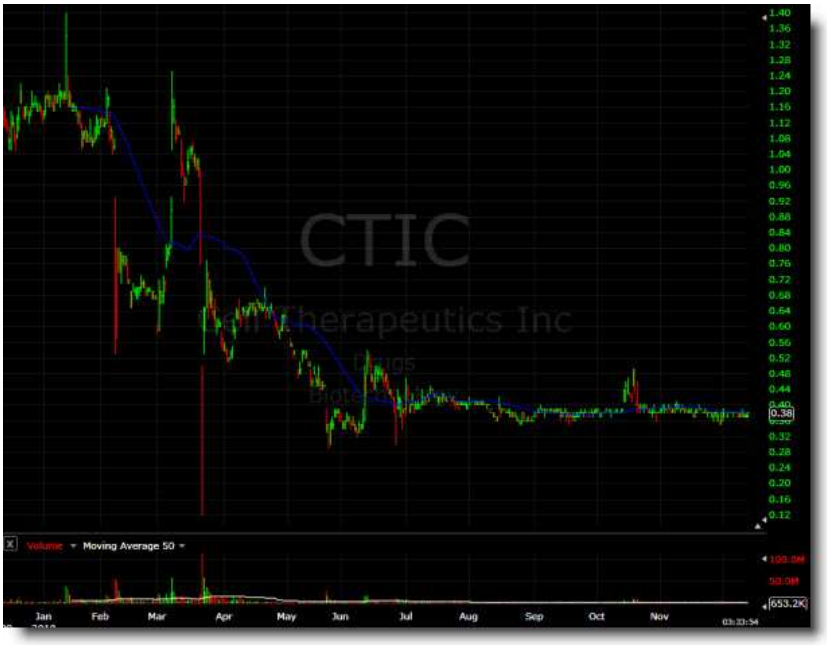
The above example is only one reason why this is bad, there is another more compelling argument. Often before a major catalyst a stock price will unexpectedly dip. We call this a “Stop-Loss Shake-out”. The market can be a very manipulate place, and this happens usually once in every run-up play. The price will drop for absolutely no reason, causing panic and triggering these stoplosses to fire off. Informed traders quickly see the panic is not legit and scoop up all the shares for a discount price. The stop-loss holders are left with no shares and a loss.

Tip #4 Do Not Get Emotionally Attached to a Stock

Traders can develop strange relationships with a stock. When you spend endless hours researching a stock, you end up knowing the intricate details of a company as well as the product. You understand how the drug works, its history, clinical trial results, potential market cap, and much more. Likely you have researched and discussed the company on message boards across the Internet. All this time may create a bond. You can not allow this to happen.

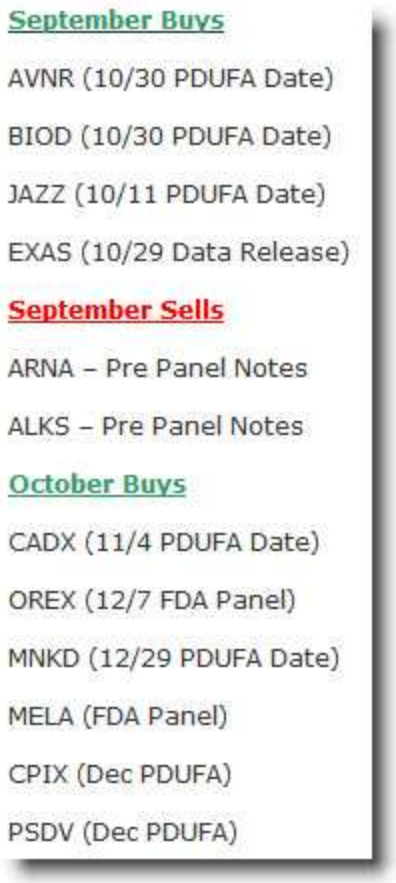
Trading is a business. You can not get emotionally attached to a stock. At a moments notice you must be ready to cut your losses or take your profits and move on to the next play. Once a stock has reached a certain level or a catalyst has occurred, it is time to move on. In the biotech sector there are too many other plays that will offer greater percentage gains.

The stock **CTIC** is an excellent example. Many traders become very wrapped up in its cancer drug in late 2009 and early 2010. The FDA Advisory effectively squashed this companies hopes with a 9-0 “No” vote for the recommendation of approval in March of 2010. Despite this, many traders became so mentally attached to CTIC that they have refused to let go, holding the stock up to this day, all while it has traded in a tight trading range of $.38 - $.40. **<u>Move On!</u>**



Tip #5 Have a Trading Plan

Before you even open a position you should have a general plan in place calculating your exit. This may be based on a target increase in share price, or based on timing. For example the stop ABC has a decision expected from the FDA on or around April 30. The current share price on January 30 is $2. At the moment of purchase you should know that, for example, you will start thinking of selling at $4.50, and you will definitely exit your position before April 15th. Having a plan in advance will make you a better trader.



Remember though, that these plans must be adaptable and flexible. Besides planning the exit of a current position it is wise to plan future purchases. The biotech industry, by design, it filled with clinical and regulatory catalysts. This one of the unique features of the industry, which allows for the Run-Up method, and allows to plan a "Roadmap" of trades.

By researching upcoming events, such as expected clinical results or defined FDA catalysts, you can know months in advance where you plan on moving your trades. This is similar to a chess player planning his moves well in advance. Advanced planning will also aid in the tendency to become attached to a company or stock. Take yours gains (or cut your loses) and move on to the next play.

See our example trading roadmap for the second half of 2010 (to the left).

PART II - Understanding the BioCatalyst Process

Overview of New Drug Development and Clinical Trials

ClinicalTrials.gov is a registry of federally and privately supported clinical trials conducted in the United States and around the world and offers up-to-date information for locating federally and privately supported clinical trials for a wide range of diseases and conditions. A clinical trial can be summarized as a research study conducted in human subjects in order to answer specific health questions (e.g. does an experimental treatment provide any benefit to patient, what are the side effects associated with a treatment, is one treatment better or safer than another in the treatment of a disease).

Phase I Clinical Trials: the drug is introduced into healthy human subjects or, on occasion, patients and is tested for safety, stability, dose tolerance, and metabolism;

Phase II Clinical Trials: the drug is introduced into a limited patient population to determine the efficacy of the product in specific targeted indications, to determine dosage tolerance and optimal dosage, and to identify possible adverse effects and safety risks; and

Phase III Clinical Trials: the clinical trial is expanded to a larger and more diverse patient group at geographically dispersed clinical trial sites to further evaluate clinical efficacy, optimal dosage, and safety.

The drug sponsor, the FDA, or the independent Institutional Review Board (IRB) at each institution at which a clinical trial is being performed may suspend a clinical trial at any time for various reasons, including a belief that the subjects are being exposed to an unacceptable health risk. The results of preclinical animal studies and human clinical studies, together with other detailed information, are submitted to the FDA as part of the NDA.
Based on average estimates from a variety of white papers and published research, there is an estimated one in six (17%) chance of successfully developing a new drug from Phase I clinical trials through FDA approval. **The average duration for successful development is 7-8 years at an estimated cost of $1 billion.**

Overview of medical device / diagnostic development

Medical Devices are classified into Class I, II, and III. Regulatory control increases from Class I to Class III. The device classification regulation defines the regulatory requirements for a general device type. Most Class I devices are exempt from Premarket Notification 510(k); most Class II devices require Premarket Notification 510(k); and most Class III devices require Premarket Approval (PMA).

Products requiring PMAs are Class III devices, classified as high risk devices that pose a significant risk of illness / injury or those found not substantially equivalent to Class I and II predicate devices already cleared for marketing through the 510(k) process. The PMA process is more involved and includes the submission of clinical data to support claims made for the device.

A 510(k) is a submission made to FDA prior to marketing in order to demonstrate that the device is at least as safe and effective (substantially equivalent) to a legally marketed device that is not subject to PMA. For a successful FDA 510(k) submission, the medical device company must compare their device to one or more similar legally marketed devices in order to support the claim of being substantially equivalent to a device already cleared for marketing by the FDA (predicate device). A device is classified as being substantially equivalent based on the following…

- has the same intended use as the predicate; AND
- has the same technological characteristics as the predicate; OR
- has the same intended use as the predicate; AND
- has different technological characteristics, but the information submitted to FDA does not raise new questions of safety and effectiveness AND demonstrates that the device is at least as safe and effective as the legally marketed device.

FDA Section 513(f)(2) refers to the Evaluation of Automatic Class III Designation provision (also known as the "de novo" or "risk-based" classification) and is intended to be applied to low-risk medical devices that have been classified as Class III because they were found not substantially equivalent (NSE) to any identifiable predicate device. Devices classified as NSE due to lack of a predicate may be placed in Class I or Class II if sufficient information is provided by the Company to support a reasonable as-

surance of safety and effectiveness in order to avoid the more timely and expensive clinical trials to support Class III PMA clearance.

A recent report on medical device development in the US estimates an average of $24 million is spent for each successful FDA 510(k) submission while PMA submissions can cost as much as $94 million, based on a survey of 204 medical technology companies. Based on the experience of US medical device companies, the average duration from initial filing to FDA 510(k) marketing clearance is 10 months (compared to FDA guidance for 90 days). The average duration from first FDA communication to PMA marketing clearance is much longer at 54 months (compared to FDA guidance for nine months), reflecting the significant additional time and cost required to conduct clinical trials under IDE clearance for the PMA process.

Overview of FDA approval process

Below is a summary of key terms associated with the FDA approval process…

NDA = New Drug Application
BLA = Biologics License Application or Therapeutic Biologic Application,
sNDA / sBLA = supplemental NDA / BLA,
ANDA = Abbreviated NDA (Generic Drugs)
SPA = Special Protocol Assessment
CRL = Complete Response Letter
PMA = Pre-Market Approval (Medical Devices / Diagnostics)
REMS = Risk Evaluation and Mitigation Strategy
IDE = Investigational Device Exemption
IND = Investigational New Drug Application
ODD = Orphan Drug Designation
RTF = refusal to file

New Drug Applications (NDA)

The new drug approval process generally involves (1) the completion of preclinical laboratory and animal testing in compliance with the FDA's GLP regulations; (2) submission to the FDA of an Investigational New Drug (IND) application for human clinical testing that must become effective before human clinical trials may begin; (3) performance of adequate and well-controlled human clinical trials to establish the safety and efficacy of

the proposed drug product for each intended use; (4) the satisfactory completion of an FDA pre-approval inspection of the facility or facilities at which the product is produced to assess compliance with the FDA's cGMP regulations; and (5) the submission to and approval by the FDA of an NDA.

The NDA also must contain extensive manufacturing information, and the FDA may approve or disapprove the NDA if applicable regulatory criteria are not satisfied or it may require additional clinical data (i.e. a complete response letter or CRL). Once approved, the FDA may withdraw the product approval if compliance with pre- and post-market regulatory standards is not maintained or if problems occur or are identified after the product reaches the marketplace. In addition, the FDA may require post-marketing studies to monitor the effect of approved products and may limit further marketing of the product based on the results of these post-marketing studies.

The Prescription Drug User Fee Act (PDUFA) of 1992 is legislation that allowed FDA to collect fees associated with new drug and biological agent filings. The PDUFA goal action date is a performance metric that seeks to review all NDAs, BLAs, sNDAs, or sBLAs within 6 months for priority review and 10 months for standard review. In response to CRL, the guidelines include two months for a Class 1 Resubmission and six months for a Class 2 Resubmission, based on the amount and nature of information submitted (e.g. additional clinical data would be a six-month review while labeling / REMS issues would likely be a two-month review).

Supplemental NDAs or BLAs are filed to obtain FDA marketing clearance for a new use, strength, or formulation of an already approved drug or biological agent, and the Agency typically responds within two months to formally accept for review and issue a PDUFA goal action date for all new drug or biological agent filings.

Abbreviated New Drug Applications (ANDAs): An ANDA is similar to an NDA except that the FDA generally waives the requirement of complete clinical studies of safety and efficacy. However, it may require bioavailability and bioequivalence studies. Bioavailability indicates the rate of absorption and levels of concentration of a drug in the bloodstream needed to produce a therapeutic effect. Bioequivalence compares one drug product with another and indicates if the rate of absorption and the levels of concentration of a generic drug in the body are within prescribed statistical

limits to those of a previously approved drug.

Under the Hatch-Waxman Act, an ANDA may be submitted for a drug on the basis that it is the equivalent of an approved drug regardless of when such other drug was approved. The FDA will approve the generic product as suitable for an ANDA application if it finds that the generic product does not raise new questions of safety and effectiveness as compared to the innovator product. According to a June 2010 presentation given by the FDA's Office of Generic Drugs, the current review time for ANDAs exceeds two years (26 months). When a generic drug company files an ANDA with the FDA, it must certify that no patents are listed in the Orange Book, the FDA's reference listing of approved drugs and listed patents.

An ANDA filer must certify one of the following... (1) that no patent was filed for the listed drug (a "paragraph I" certification), (2) that the patent has expired (a "paragraph II" certification), (3) that the patent will expire on a specified date and the ANDA filer will not market the drug until that date (a "paragraph III" certification), or (4) that the patent is invalid or would not be infringed by the manufacture, use, or sale of the new drug (a "paragraph IV" certification). A paragraph IV certification (patent challenge) must be provided to each owner of the patent that is the subject of the certification and to the holder of the approved ANDA to which the ANDA refers. A paragraph IV certification can trigger an automatic 30 month stay of the ANDA if the innovator company files a claim which would delay the approval of the generic company's ANDA.

Section 505(b)(2) NDAs: For a drug that is identical to a drug first approved after 1962 (e.g. a new formulation of an existing drug that may be an extended-release or delivered in a novel manner), a prospective manufacturer is not required to go through the full NDA procedure. Instead, it may demonstrate safety and efficacy by relying on published literature and reports where at least some of information required for approval comes from studies not conducted by the applicant, thereby reducing the time and money required for potential approval through this route.

GRASE (Generally Recognized As Safe and Effective) or Grandfathered Drugs: GRASE products are those "old drugs that do not require prior approval from FDA in order to be marketed because they are generally recognized as safe and effective based on published scientific literature." Similarly, Grandfathered products are those which "entered the market before the passage of the 1938 act or the 1962 amendments to the

"effectiveness requirements [of the act] if its composition and labeling have not changed since 1962 and if, on the day before the 1962 amendments became effective, it was (1) used or sold commercially in the United States, (2) not a new drug as defined by the act at that time, and (3) not covered by an effective application." Recently, the FDA has increased its efforts to force companies to file and seek FDA approval for these GRASE products (e.g. aspirin and morphine).

Rotating run-up trading strategy for bio-catalyst events

This is an active, long-only trading strategy with a targeted basket of 3-7 stocks with pending FDA or clinical trial catalyst events that seeks to rotate / position trade (i.e. sell gainers and buy or add to a position for catalyst stocks of interest with stock prices that are down or flat) based on market conditions and stock prices. The information flow includes the clinical / regulatory catalyst calendar database as the primary research source, which is refined to near and long-term stock watch lists and a 3-7 stock portfolio that is updated based on new developments and stock prices.

The basket of 3-7 stocks is chosen approx. 2-3 months ahead of an FDA event (decision or advisory panel event) or clinical trial catalyst (preferably late-stage or pivotal studies) with a goal of achieving stock price gains and profits by selling ahead of the catalyst event. The exact timing of stock buys ahead of the catalyst date is not as important as screening for stocks that are preferably trading near or below the mid-point of their 52-week price range and at low or average trading volumes, which indicates that the stock is largely unnoticed by traders with the potential to experience increases in both share price and trading volume as the catalyst date nears.

Searching for under the radar bio-catalyst stocks

Related to the bio-catalyst, rotating run-up strategy is searching for under-the-radar bio-pharmaceutical or medical device companies that are largely unnoticed by investors and the research analyst community. There is no magic formula for identifying these companies, but such stocks often trade at low average trading volumes (e.g. 100,000 shares or less per day) and below the mid-point of their 52-week stock price range.

Investing in under-the-radar stocks at 2-3 months ahead of their FDA or clinical trial catalyst events can be an effective method of minimizing risk while maximizing potential reward in the form of share price gains as the catalyst date approaches and such stocks attract more attention from investors and possibly research analyst coverage.

A classic example of an under-the-radar stock is medical device company Nephros (OTCBB:NEPH), which traded at less than 10 cents in early 2009 (through May) and peaked at over $2 per share within less than six months based on greater awareness of its pending FDA 510(k) decisions for medical devices associated with dialysis and filtration.