Parenteau BioConsultants, LLC

-WHITE PAPER-

EIGHT WAYS TO EVALUATE BIOTECHNOLOGY'S READINESS FOR THE CLINIC

Nancy L. Parenteau. Ph.D.

Clinical trials are generally viewed as a sign that a company has progressed to the next stage and investors usually perceive it as very important validation of a technology and team. Indeed, venture investors often measure a small biotech company's suitability for investment based on the estimated time to the clinic. But entry into the clinic can be a positive, progressive step or a costly step towards a company's end. Many times, you'll read announcements about an investment round of hundreds of millions of dollars that you know is based on a company's entry or near entry into the clinic. Yet many of those investments will not be successful – possibly tainting investment interest in a whole class of promising products in the process. Can one really tell what entry into clinical trials are harbingers of a costly misstep, or a true step forward for the company and its investors? In many cases, yes! Here are a few ways you can evaluate whether those plans for clinical testing represent progress or a potential pratfall.

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1. Be clear on what a company has really achieved.

Entry into clinical trials means that the company has enough ducks in a row to satisfy Institutional Review Boards (IRB) and the US FDA for an Investigational New Drug (IND) application in the US. Meeting these requirements is highly commendable and it likely means there is a good development and regulatory team on board. However, it says nothing about the clinical or commercial value of the product. One can meet IND requirements and still have a clinically meaningless and commercially unworkable product. Look for more.

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2. Look for evidence of preclinical proof of principle.

The proof of principle referred to here can take many forms and does not necessarily mean extensive in vivo preclinical testing. For many problems, truly valid *in vivo* preclinical tests don't even exist. Appreciate that you are looking for information beyond the safety data that regulators require. Depending on the drug or therapy, valuable proof of concept could come from data establishing the target as biologically legitimate and then demonstrating the relationship of the drug to the target, for example. This evaluation does require skill to pull together and analyze the evidence objectively, but it can be done, particularly if one has a good understanding of the biological priority of the target to the specific problem at hand. Evidence can also come from a comparison to a "gold standard". For example, how does the body sometimes solve the problem? What is the biological process in the way or the desired outcome? How potent does my intervention have to be to short-circuit or replace it?

Where should the primary interface between therapy and the in vivo mechanisms of response be for maximum potency and safety? Be careful of even "promising" *in vivo* preclinical studies without connecting the dots based on everything you are observing at multiple levels of experimentation and what is seen in humans. Work with human cells as early and as often as you can.

3. **Be sure the product is what everyone thinks it is.**

This may sound funny, but be sure the company knows what their product really is and be sure to examine how they have defined the product. Practical objectives can sometimes drift away from the established scientific objective on the road between the bench discovery that established the scientific basis for a therapeutic approach, and the development process. Be sure the technology is still on target.

4. **Purge notions and assumptions and ask specific questions.**

Don't take the claim that cell A will cure ailment B, or that target X is significant to disease process Y at face value. Begin with no assumptions, even if you are excited about certain reports on the remarkable importance of A or X. You need to be in a "no spin zone." You should evaluate the biological basis for any claim. You may not be able to get all the answers, but you'll be amazed how much can be deciphered from available data and knowledge. **If you are evaluating a new therapy's ability to succeed commercially, a company or research group that can deliver a strong biological basis for why it should have impact, is probably a more valuable company three years away from the clinic than one entering the clinic without it.** The best development skills in the world used to implement a biologically weak strategy will always deliver a weak product. Understanding the biological basis for a product will also help you evaluate whether the clinical trial is targeting the right patient group and whether the trial is designed to give the product its best chance.

5. **Just because one company succeeds or fails in an area does not mean another one will. Beware of the bandwagon - positive or negative.**

Look at each company and technology with a fresh eye. Be sure to understand the *biological* differences between a product, target or drug

strategy as nature will be the final arbiter of success in all bioscience products. Product design and process matter.

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6. Distinguish true Phase I from Pilot trials.

Be sure to examine the process. As mentioned above, IND approval signifies that certain aspects of the process are in place but it does not judge whether the process is ultimately approvable. If the company does not have a potentially approvable (this does not refer to a GMP process but rather a process that has basic safety and functional aspects addressed) process in place, it is a pilot trial. Many clinical trials get stuck in the Biologics division of the US FDA because there are aspects to their product or process that have no hope of approval, let alone commercial potential. Even pilot trials should be well designed and contribute to the commercial advance of the product. Otherwise they can be red herrings, positive or negative.

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7. **Learn how to recognize when a company or your company has jumped the gun. Look for the biological elephant in the room.**

Too often biotech companies are under pressure to get their product into patients as quickly as possible. This has the potential of burning a tremendous amount of the company's resources in the wrong places at the wrong time while yielding little valid indication of a technology's potential. And, if a technology fails under these circumstances, there is always the nagging question of whether it could have succeeded with a little more homework and patience. Even the largest pharmaceutical companies in the world can fall prey to jumping the gun when it comes to pressure to produce the next biopharmaceutical blockbuster. The failure of Pfizer's torcetrapib to raise HDL levels is an $800M example.[1]

Does this mean a company has to spend years trying to answer every scientific question? Not at all. It means the company should recognize and address the *pivotal* questions that will help establish a biological basis, early – before the emotional and financial investment in the project prevents the company from dealing with that elephant. If a company gets to that point – they have already jumped the gun and added risk that

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1 (See the Forbes online articles by columnists Matthew Herper and Robert Langreth:, *Behind Pfizer's Failure* (http://www.forbes.com/business/2006/12/03/pfizer-heartdisease-drug-biz-cx_mh_1204torcetrapib.html?boxes=author) and *Pfizer's Warning Signs* (http://www.forbes.com/2006/12/07/pfizer-cholesterol-drug-biz-cz_mh_1208pfizer_print.html).

could have been avoided.

8. **There are often rather simple ways to gain confidence in the value of a technology, target or drug before entering a clinical trial.**

A clinical trial is one of the fastest ways to spend money and drain internal resources. You want the result to be worth the investment. When evaluating a new technology, be sure to perform a biological analysis as part of your evaluation. The goal: to understand enough about the biological basis for the drug or therapy in question to have a sense of where it fits in the disease process your are hoping to influence. This analysis can often be performed using existing internal and external data without the need for additional experimentation if the analyst is skilled in knowing how to interpret and integrate biological data, which now can be greatly facilitated with AI. Skill in interpretation and prioritization is key yet you are unlikely to find the type of analysis you need in the scientific literature or even from ChatGPT. Academic science is concerned with describing a murder scene and understanding what happened. You, on the other hand are interested in piecing together the evidence that will tell you who the murderer is and locking them up!

For Companies:
Parenteau BioConsultants is committed to helping translate great science into trailblazing medicine. If you represent a biotechnology company looking for some sound advice on whether you are ready to enter the clinic or the most derisked way to get there, book an exploratory call with Nancy Parenteau.

For Stakeholders:
If you are an investor trying to understand and protect your investment, consider partnering with Dr. Parenteau for a uniquely insightful brand of strategic due diligence that will empower wiser investment decisions.

Book a free exploratory call: https://calendly.com/nlp-pbc/30min

Dr. Nancy Parenteau
+1 (617) 312-2540 mobile
nlp@parenteaubc.com

www.parenteaubc.com