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Too Much Skin in the Game?

There are very few rules for the biotech investor that win universal approval. But the first commandment attracts few dissenters: the inventors and developers of the technologies in which you invest your cash must, as a condition of attracting the cash, invest their life and soul in parallel with your money. Or as its usually expressed, they must have as much skin in the game as possible. It may be orthodoxy, but is it right?

The reasons for wanting the inventor's skin in the game are pretty obvious. Imagine an inventor and developer who has two different inventions, one you have invested cash behind and one in the portfolio of a major competitor. Its going to be pretty disastrous if, a year in (with perhaps two or three million dollars burnt), he decides that the other opportunity is playing out better. Where is his focus, his energy and his intellect going to be? Driving forward something in which you have no stake.

The solution is simple: one investable opportunity per inventor or development team. With nothing else to drive their returns, you the investor can be pretty confident they will do they best they can to make a success of your chosen technology..

The first commandment of biotech investing is that the inventors of the technologies you are backing must invest their life and soul into the project

Turn the tables for a moment, though, and the situation is not so rosy from the perspective of the inventor. Why do investors need a portfolio? For the most part, it is for risk diversification rather than just to get enough capital to work. Most biotech investors will tell you that no matter how clever you are, its impossible to pick only winners. You might, if you are good at what you do, enrich the pool with good opportunities, but if you asked an investor to put everything he owned behind even his best opportunity, he would laugh out loud.

The idea, then, that the inventor (or ultimate owner or developer) of a technology will invest all of their resource behind one technology only works for a certain kind of inventor: one with a belief that the thing they invented is the best thing since sliced bread (or atorvastatin, if that's the biotech analogue of sliced bread).

For an inventor (most often academic in origin) whose life's work has culminated in a single invention, this works well enough. The idea that they have to commit completely behind that invention to attract investment in it is an excellent filter to distinguish those who peddle the commercialization of their invention as a ruse to attract money for more early stage research from those who really believe in the potential for their technology as a life-changing product.

Put simply, this uses the power of “skin in the game” to optimize the selection of the right ideas to back with your investment capital.

The most precious assets in an investor’s portfolio are not the individual technologies, but the development teams that will operate on those assets.

But the validity of this approach is predicated on two assumptions. Unfortunately, the first assumption may not always be true. And the second assumption might never apply. Perhaps its time to ask whether the one inventor, one investment model is always the right one? Iconoclastic as it may sound, maybe going the other way, demanding less skin in the game, might optimize investment returns in some circumstances?

The first assumption, obviously, is that you improve your selection of investable technologies by insisting the owners back them with their careers. It may achieve a degree of positive selection. After all, presumably those ideas where even the inventor has doubts about boarding the ship before it sets sail seem inherently less promising. But counterbalancing this positive effect, there are negative ones of similar or greater magnitude: fanatical belief in an idea, needed to drive the inventor to put all his eggs in the single basket, is hardly compatible with a continual critical re-appraisal of progress in light of each new piece of data that is generated. The person who understands the technology the best is a critical component in the machinery that determines which technologies continue to deserve further support. But a monomaniac, obsessed with the intrinsic value of his invention, is scarcely likely to acknowledge its flaws, even in the face of mounting evidence to the contrary.

And being now ‘trapped’, with all their skin in that one particular game will likely only compound the problem. Do you really believe that, seeing the consequences of admitting to the mounting skepticism around the technology, that the inventor will appraise his Board of Directors with a honest assessment of the prospects? The very characteristic that gave you confidence during the initial selection of the technology for investment now scares you to death: how will I know if my golden technology is made only of iron pyrites? Certainly the inventor is unlikely to tell you.

One solution is to trade a little of the power of the “skin in the game” filter on new opportunities for a little more honesty in the progress reports after investment. If you say to the inventor “Hey, bud, we are going to back you no matter what. But it doesn’t have to be this one technology. If ever you see something you believe has a better chance, tell us and we can switch horses.” With this *modus operandi*, the inventor still has all his skin in the game, but if his confidence in the original technology falls the likelihood of safe harbor in the event of a storm make him more likely to report the advancing weather front that he is the first to spot.

This kind of solution works well if you have inventors smart enough to develop multiple technologies, and self-aware enough to rationally assess the prospects of their own project. And those are the kind of inventors you wanted to be investing in from the beginning.

**To fail because you picked the wrong asset is unavoidable.
To fail because you mis-handled that asset is the cardinal sin.**

The second assumption, though, is more challenging to deal with.

The use of the “skin in the game” filter assumes that the step in the process of successful investing that it aids (selecting the best opportunities) is the main determinant of the outcome. It’s a widely held belief – but is it actually true?

What are the key steps in the pipeline of successful investing? First you have to select an asset to work on; secondly you have to operate on that asset so it moves through a value inflection optimizing simultaneously on development cost and risk and lastly, you need to sell the asset for a decent multiple of what it cost to purchase and develop.

A simple three step roadmap to successful biotech investing.

Interestingly, different investors focus on different steps of the pathway. If you asked for a show of hands, the selling process would probably attract the greatest number of votes as the most important. On the face of it, if you have a fantastic asset, then disposing of it profitably ought to be the easiest part of the process. But experience tells us that few things are so magnificent that they sell themselves. Almost every asset needs to be sold, rather than bought. Matching the right asset to the right buyer remains a mysterious art, possessed by only a few with the Midas touch. As a result, most investors dedicate themselves to managing the exit process. After all, without a good exit to realize the accumulated value, the rest of the process is for naught.

A close second in the lottery, though, would be selecting the right technology in the first place. Like securing the exit, this is a step in the process that VCs internalize (not least because, unlike the actual development of the asset and its subsequent sale, there is no one else who can do the original selection of opportunities). A great deal of time and resource is committed to getting this step 'right'. DrugBaron has recently witnessed an early stage investor spend almost as much money on due diligence on a preclinical asset as they plan to invest, at least during the seed phase, in its development.

It is this selection stage that is widely perceived as the determinant of success – successful investors pick the right opportunities to invest in. Unsuccessful investors made too many “bad calls”. If that assumption is correct, then using the “skin in the game” filter to bolster the success of the selection filter makes perfect sense (even if it comes with the cost of damaging the progress monitor).

But is it correct? Is picking the right opportunities to invest in really the key difference between success and failure?

Quite obviously, eliminating the hopeless candidates is a pre-requisite for success. If the basic premise is flawed, or the product candidate, though technically feasible, solves a problem that doesn't exist, then an investment is unlikely ever to be successful. Fortunately, eliminating the definite losers is fairly easy to do for the experienced investor. But eliminating the nailed-on losers is not the same thing as picking the winners. Once the duds have been ejected, how do you find the one in twenty of the remainder that will win big?

DrugBaron is of the opinion that you cannot. No matter how clever your scientific advisers, how commercially savvy your investment partners, there are no factors that predict the winners. Picking the winners out of the pool, once the losers have been eliminated, is down to luck – pure and simple. As Kevin Johnson, partner at Index Ventures, succinctly put it “Even with the insight of Nostradamus more early stage projects will fail than succeed, simply because there isn't enough data to make a better call.” As a result, there are dozens of potentially successful opportunities out there – far more than ever get invested in.

All the benefits of asset-centric investing come from isolation.

All the benefits of company building come from synergy.

**Isolation and synergy are mutually exclusive:
so how do you get the best of both worlds?**

So does that mean that the difference between the successful investor and the less successful one is just luck (assuming both were equally capable of eliminating the duds)? That would be depressing. And completely inaccurate.

The key is the middle step in DrugBaron's 'successful investing' paradigm: the work performed on the initial asset to create the saleable product.

When a project fails (and most do, of course), the easy explanation is that the underlying technology was flawed in a way that could not have been predicted at the outset. Everyone involved shrug their shoulders. 'C'est la vie'. Technology investing is a high-risk business and this, after all, is why the portfolio model is the only way to invest. Everyone knows its impossible to pick the winners.

Such an attitude is comfortable for managers – they can move on to a decent salary in another company, working on another technology.

But hang on a minute. Can your really tell if it was an unavoidable failure or actually a self-inflicted wound? What happens if the management picked the wrong clinical trial, in the wrong indication? If they used the wrong dose? If they picked the wrong end-point? Or underpowered the trial? The problem with these questions is that they are experimentally hard to verify. Only by doing a better trial with an asset that has already failed once would you be able to determine whether the underlying technology was truly doomed to failure or was just mismanaged by its custodians. And doing that is something that investors are (reasonably enough) loathe ever to do.

But doing the wrong thing in clinical development is endemic. There are so many ways to get it wrong that it should come as no surprise that teams get it wrong, one way or another, almost every time. And getting it wrong isn't just the preserve of biotech entrepreneurs. Big pharmaceutical companies do it too – as DrugBaron recently [noted](#), comparing the development strategy for two ostensibly identical Factor Xa inhibitors, one (Eliquis™) which is headed for failure and the other (Xarelto™) which is headed for the stars.

While its usually possible to distinguish a flawed asset from a flawed development plan once billions have been spent, it is much harder to know why a biotech project failed. But in the absence of data, it's a fair bet that the reason was poor decision making at least as often as it was in-built flaws in the technology.

The bottom line, then, is that making the right operational decisions (more often than not) to convert the initial asset into a saleable package is the real determinant of success in life science investing. Its not about selecting the right assets to operate on – as long as you avoid the real duds its impossible to choose among the rest. Instead, its about successful implementation of the right development plan for each asset to maximize the chances that you properly express the true underlying worth of that asset. To fail because you picked the wrong asset is, for the most part, unavoidable. To fail because you mis-handled that asset is most definitely avoidable.

The best analogy comes from horticulture: faced with a packet of seeds that are difficult to germinate, the challenge for the gardener is to extract the maximum potential from those seeds through application of right degree of heat, light and water. If you visit your gardener friend six months after you gave him the seeds, and he has no plants, you will never know if the seeds were sterile or he simply failed to water them. But you will have your suspicions!

“Even with the insight of Nostradamus more early stage projects will fail than succeed, simply because there isn't enough data to make a better call.”

Kevin Johnson, Index Ventures

What has all this to do with “skin in the game”? Quite a lot.

It means that the most precious asset in an investor's portfolio is not any of the individual technologies, but the development teams that will operate on those assets. The quality of those teams, rather than of the assets themselves, will determine the success of portfolio. Everyone always said "you invest in the team, not in the technology". But its easier to say than it is to do in practice.

Why? Because high quality development teams are much more scarce than high quality technology candidates. As the Eliquis™ story shows, even the world's biggest pharmaceutical companies don't have enough teams that are good enough.

The one product per team model, maximizing the skin the game, only makes this shortage of development expertise more acute. This model makes perfect sense if investable assets are rare and first-rate management teams are ten a penny. But in the reverse scenario, you need to leverage the capabilities of your star developers and push as many assets through their well-oiled machine as you can possibly muster.

