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## Why killing “above average” projects is the only way to rescue biotech’s return on investment

**Across the whole sector, the return on investment in biotech (broadly defined to encompass diagnostic and medical device companies, as well as therapeutic developers) is poor, whether you look at publically traded stocks or private investments through venture capital funds. So poor, in fact, that no ‘generalist’ investor would touch biotech as an asset class.**



**Silver Medal Companies:**  
Successful... but not successful enough?

This, according to Stuart Duty of Piper Jaffrey, is the reason why the IPO window closed for biotech companies, and will likely remain closed for the foreseeable future. This inability to attract ‘generalist’ capital to buy our companies at the end of the life cycle blocks up the whole biotech company pipeline. And there is only one solution: improve the return on investment of the sector so that it becomes competitive with other asset classes.

That much is obvious. Less obvious is how this is to be done. DrugBaron’s prescription is to kill more projects before they consume ultimately non-productive capital. The key is to recognize just how high the barrier has become for commercial success, and that even “above average” projects are unlikely to ever achieve profitability. This prescription is easy to swallow in theory, but difficult to implement in practice. Killing companies (crystallizing losses) is difficult to do when they are obviously failing – so doing it when they are apparently succeeding (just not succeeding enough) requires a special kind of insight... and no small measure of bravery.

A quick survey of companies in the sector that achieved an IPO in the last five years illustrates the scale of the problem: almost every one of them is underwater compared to the pricing of the initial offering, and in many cases the value has fallen by 50% or more. Its true that the variation between companies is substantial, and that one or two have shown stellar gains – but across the board you would lose more than you had gained. For a few die-hard specialists in the area, these rare big wins are enough to keep playing: if you believe you understand how to pick those winners and invest in them selectively, then you can earn handsome returns for that specialist knowledge. By contrast, the ‘generalist’ investor just racks up the average losses of the sector as a whole.

Small wonder then, that there are only a handful of takers for the IPOs that do get away. And the small number of takers, coupled with their relatively modest bite-sizes, severely limits the amount of capital you can raise on the public markets, as well as creating a buyers market that drives down pre-money valuations.

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## **“The key is to recognize just how high the barrier has become for commercial success”**

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The obvious alternative to the public markets for an exit is an acquisition. But a survey of acquisitions in the sector over the last five years is scarcely more encouraging than the survey of public companies. On the surface, the valuations of the companies that did engineer a sale looks promising – the majority of transactions return more than twice the invested capital in the upfront, with 3-5x still to come in milestones. But the number of such transaction has remained stubbornly low: less than 10 per annum. Considering how many private biotech companies there are, you certainly cant rely on being one of the small percentage that get acquired.

Lets assume that big pharmaceutical companies are “smart customers” (though the performance of many of the assets they have acquired stretches the credibility of this assumption almost to breaking point). They will pick the cream of the crop – things with the greatest potential – before those companies are ready for the public markets. By the time a company is sufficiently low risk to be publically financed, the risk has largely disappeared and value is calculated as a multiple of sales based on fairly narrow projections of future growth, limiting the upside – in other words, the market should be efficiently valuing any publically-traded stock which makes acquisitions of those companies by big pharmaceutical companies less likely, at least at any significant premium.

So if, on the one hand, big pharma takes out the very best companies before they are mature enough to even consider going public, while on the other hand the worst companies simply fail and disappear, then reaching the public markets is a difficult to achieve path – you have to keep succeeding enough to survive but not succeed enough, at least early enough, to be taken out.

By this analysis, then, publicly traded biotech companies are not the winners but the silver medalists. Is it any wonder, perhaps, that the return on investment they offer after going public usually disappoints?

The fact is that the bar you have to clear to be successful is much higher than it used to be, and industry insiders have been slow to recalibrate their radars. DrugBaron, together with other industry commentators such as Roger Longman and Jeff Bockman, has already [laid out the arguments](#) why getting regulatory approval is no longer sufficient to expect commercial success. Companies need proof-of-relevance rather than just proof-of-concept.

There are a number of factors underpinning this shift, but two dominate: firstly, the Great Patent Cliff is seeing more and more highly effective, standard-of-care medicines going generic (Plavix™ and Lipitor™ will be the biggest, but there are literally dozens of others). At a stroke, the incremental benefit ratio you will need to demonstrate to sustain a premium price in these major indications will double or triple. And this effect will only be re-enforced as the tsunami of cost effectiveness assessment-based pricing spreads out from its UK epicenter.

Equally important, but perhaps less visible is the big pharma store-cupboard. Looking at new drug launches, its easy to think that the billions of worldwide R&D expenditure has simply “disappeared” but that’s not really the case. Pharma companies have generated hundreds of product candidates that could achieve regulatory success, but whose incremental benefit is considered too low to justify the vast expense of commercial launch.

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## **“The plain fact is that big pharma will not buy things unless they are clearly superior to their own cast-offs”**

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Big pharma may have a huge need to products that show commercially-relevant incremental benefit (caused by the failure of their internal R&D engines to generate enough of them), and they may also have plenty of cash to make such acquisitions. But the plain fact of the matter is that they will not buy something that has only similar potential to their own store-cupboard of perfectly good product candidates that were mothballed for commercial, rather than technical, reasons.

What this means is that too many biotechs are developing products that while approvable, and even somewhat superior to the current standard-of-care, are nevertheless not really superior to this vast, but largely hidden, reservoir of still-born internal projects inside the big pharmaceutical companies.

The best ones may survive long enough to get to market and go public, before finding disappointing sales that precipitate the negative returns for the brave souls that purchased their initial public offerings. An odd one may discover something surprising about their product quite late in the development process, and be the rare gem that the dedicated public healthcare investor is able to sniff out. But for the majority, their fate was sealed when they failed to exceed the early acquisition hurdle simply because the potential purchasers had something as good, or very nearly so, somewhere in the deep freeze.

Because later stage companies consume more cash, these silver medal companies add substantially to the capital-at-work denominator for the sector, without adding much in the way of returns. They are the source of the low return on investment for the sector as a whole.

The solution therefore is to apply a sharper scalpel, and cut off these capital-drains earlier. The gold medalists will continue to romp home, just as before, but the total capital at work in the sector will reduce with concomitant improvement in return on investment, to the point where 'generalists' will be drawn into the market expanding the number of "shots on goal" that biotech can have at developing real, commercially viable innovation.

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## **The real barrier to implementing this solution lies with the taste of the medicine DrugBaron is prescribing.**

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Anil Gaba, an economics professor at INSEAD who studies behavioural factors in economic judgments, illustrates how unwilling people are to crystalize loses. Faced with a theoretical problem where a manager has to choose between saving 2,000 jobs, or taking a gamble that has a 33% chance of saving 6,000 jobs and 66% chance of saving none, the majority of people (and he is using smart people as his guinea pigs) plump for the certain saving. Phrasing the same options in terms of loss, though producing a strikingly different outcome: ask them if they would choose to lose 4,000 jobs (thereby saving 2,000), or else take a gamble where they have 33% chance of losing none and a 66% chance of losing 6,000, now the same people vote two to one in favour of taking the gamble. Quite simply, the stark option of an unavoidable loss is something people have a strong aversion to.

The same applies to investors in biotech companies. If things are a total bust, they will take their medicine and swallow their loss (there is, after all, little option). But all too often there is an option: management provide a plan that, with further investment, they can 'rescue' the situation and all will be well. Sometimes of course, this is exactly the right course of action: if every company was cut adrift the minute something didn't work out, there wouldn't be many survivors. But the loss aversion means that too often the prospect of crystalizing the loss lead to the decision to invest further.

Professor Gaba offers some innovative solutions to this problem. Most importantly, he suggests that the decision to make a new investment should be made independently of the sunk cost, considering the proposition exactly the same way you would consider a de novo investment opportunity. Given that this is so hard to do in practice, he recommends that a different team make the second decision from the guys "on the hook" from the first round. And many institutions are starting to implement this advice with positive results.

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## “Publicly traded biotech companies are not the winners but the silver medalists”

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This works to overcome the “loss aversion” component of the faulty decision making – but it doesn’t overcome the miscalibration of the “success radar”. The fact is that loss aversion and a continuing belief that “better than average” is good enough act synergistically to promote the allocation of capital to ultimately non-productive companies in the biotech space, leading in turn to the poor investment returns.



A “Silver medal” company is like a modern day succubus – it looks attractive, but it will bleed you dry by consuming resources without building value

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The key to turning around the biotech model, then, lies in killing things that would have been valuable five or ten years ago. But only killing them after you have spent enough to make a reliable guess about the future potential. The sector can’t improve productivity by taking less early stage bets: if anything, more of the promising early stage opportunities need to be taken through the first steps of the process to see if they can yield anything that is genuinely innovative and has the potential to be “top one percent”. It is at the next stage that the axe must fall much more ruthlessly than at present. Of ten such opportunities progressed to proof-of-concept, even the second best (the one that might make it to IPO, the silver medal company) probably isn’t good enough to do anything but consume large quantities of ultimately non-productive capital. Only the real gems should be retained – then sold at a substantial profit.

No-one is denying that it’s hard to kill something that might have value, that might be rescued, that might be lucky. But experience has proven time and time again that trying to turn silver-medalists into winners is a very expensive and time-consuming activity that rarely succeeds.

It is these silver-medal companies that are the real threat to the biotech business model. They are like a modern-day succubus – dressed up by eager and enthusiastic management to look like real beauties, until they draw you in, then bleeding you dry as they consume resources with

no hope of ever being successful enough to offer a decent return on the capital employed. Next time you see such a creature of the night, be brave and drive a stake through its heart.

*This article was inspired by a number of excellent presentations at the recent 11th Novo Biosummit in Copenhagen, Denmark, an invitation-only biotechnology conference organized by [Novo Ventures](#), one of Europe’s leading life sciences venture investors.*

