Do's and don'ts of successful drug development
Reflections of two biotech veterans

Dr Peter French and Dr Kevin Lynch

The challenge of drug development

Gaining approval for a new drug product takes an average of 10–15 years of research and development and costs on average around U.S. $1.3 billion[1]. Despite these significant investments in time and money, 88% of drug candidates in clinical trials fail[2]. It is a high-risk game. After a combined 60 years working in this area and witnessing a few major successes but many more failures, the two authors here review some key areas to consider when a biotech company sets out on the drug development journey.

Start with the end in mind

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One of Stephen Covey's "7 Habits of Highly Successful People" that really resonates is to "start with the end in mind". This applies absolutely to drug development. Studies using laboratory-grade reagents or laboratory-scale processes that generate critical path data will often need to be repeated using the planned final configuration before a regulatory body such as the FDA will approve your drug. This means that any of the technical data to support how well your drug works, or how safe it is, that doesn't utilise the exact product being launched on the market will probably be unusable for regulatory submissions. In some cases that might just be the cost of developing and prototyping and tweaking the innovation, and that's fine. As long as you and the investors understand that, and factor that into the budget and time expectations. However, approaching the regulator with sub-optimal data is a very expensive and time-consuming mistake that can set a program back many months and, if time and funds are critical, could be the kiss of death for a start-up. This is one example of the need for careful planning and forethought towards the ultimate goal of a successful regulatory submission. This rule holds true even where a company intends to proceed only as far as the inflection point that allows a major sale or partnership. In many respects, all other activities that do not contribute to this aim are secondary.

So, what does a successful drug look like? The characteristics of the drug are of prime consideration. These include:

- It should be at least as effective at treating the disease as existing treatments, unless it offers some very major benefits in terms of administration or safety profile, where a slightly less effective drug may be a success
- It is acceptably safe considering the disease severity, and here context is critical: what is an acceptable safety profile for a novel anti-cancer therapy is very different to a new lipid lowering drug.
- It has acceptable tolerability or few (and minor) side effects at the dose that is anticipated to be used in the clinic

In addition to the drug's physical characteristics, there are clear commercial and regulatory considerations that underly future success. These include:

- There is a market potential that offers a strong potential return of investment
- The path to regulatory (and reimbursement!) approval is clear
- There is a clear exit strategy

Ultimately, success is defined by how much (time and cost) it will take to get there.

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[1] Wouters OJ, McKee M, Luyten J, 2020. Estimated Research and Development Investment Needed to Bring a New Medicine to Market, 2009-2018. *JAMA*; 323(9):844-853.

[2] US Congressional Budget Office, April 2021. "Research and Development in the Pharmaceutical Industry". https://www.cbo.gov/publication/57126

Causes of Failure of Drug Development

The main cause is that the drug doesn't work. But there are many other reasons, which we break down into two main categories – failure of the drug candidate and failure of the company. This section examines some of the root causes of each of these scenarios.

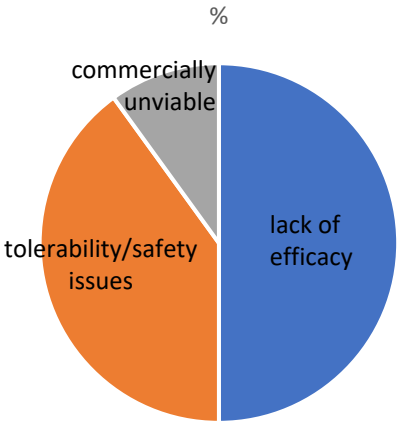


Figure 1. Causes of drug failure.

Root Causes of Drug Failure

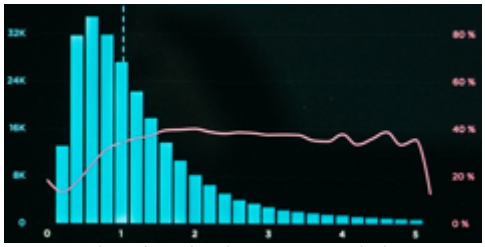
Figure 1[3] shows the potential categories that typically result in drug failure. Each one on its own may not necessarily predict a drug's demise, however, when combined with issues in other domains will increasingly hinder the potential for a drug to succeed. The following are some suggestions as to how to address these issues should they arise.

A. Lack of efficacy

Lack of efficacy is the main reason why drug development fails. The best advice is to find this out as soon as possible, and move on. The most damaging failures in drug development are those that are identified late, especially if the reasons were predictable early on. Don't keep trying to flog a dead horse but prioritise early identification of reasons to fail.
As a note of warning, ff you are licensing the innovation in from an external source, be sure that the data can be reproduced independently or at the very least independently validated.

Lack of efficacy in the clinic despite pre-clinical promise can be due to at least two key issues:

1. Inadequate or flawed basic science, data collection and analysis



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Sometimes a small sample size can produce encouraging results that cannot be reproduced in larger cohorts. This is true in both preclinical and clinical models. Or, technologies and interventions that work very well *in vitro* , or even in *in vivo* animal models, fail to produce the same results when translated into people. It is important to retain some level of skepticism or at least an awareness of the typically poor predictive power of preclinical models before advancing too far into the clinical program. Once in the clinic, the continued evaluation and validation of data will help inform a company when to close down a program or project for lack of efficacy.

In a paper published in 2011 by scientists at Bayer, the authors noted that the success rates for new development projects in Phase II trials had fallen from 28% to 18%, with insufficient efficacy being the most frequent reason for failure[4]. When the authors compared published data with their in-house findings, they found that only in ~20–25% of the projects were the relevant published data completely in line with in-house findings. In almost two-thirds of the projects, there were inconsistencies between published data and in-house data that either considerably prolonged the duration of the target validation process or, in most cases, resulted in termination of the projects because the evidence that was generated for the therapeutic hypothesis was insufficient to justify further investments into these projects. They concluded that literature data on potential drug targets should be viewed with caution, and underline the importance of confirmatory validation studies for pharmaceutical companies and academia before larger investments are made in assay development, high-throughput screening campaigns, lead optimization and animal testing.

[3] Adapted from: Sun D, Gao W, Hu H, Zhou S, 2022. Why 90% of clinical drug development fails and how to improve it? *Acta Pharm Sin B*; 12(7): 3049–62
[4] Prinz F, Schlange T, Asadullah K, 2011. Phase II failures: 2008–2010. *Nature Rev. Drug Discov.* 10: 328–329.

These data confirm the limitations of the predictivity of disease models, and may even raise questions about the validity of the targets being investigated. How can a company identify and avoid the root causes of these irreproducible data?

There are a large number of activities in science that give rise to potentially dubious data. Most of these practices fall into two categories: misrepresentation and bias. Whilst fraud is infrequent, it does occur, however it is more commonly unwitting over-interpretation of data and lack of recognition of bias that results in data that is misleading. Suffice it to say that the raw data needs to be carefully checked before entering into a more detailed and resource consuming project.

2. Flawed study design (endpoints, patient population, dose)

Once the preclinical studies have been thoroughly undertaken, and the drug moves into the clinic, it is very important to ensure that the relevant patient population is selected for the intended end-market (consider race, demographics, disease stage, etc), and critically that the primary and secondary end points are carefully designed to ensure relevance but also to not bias against the chance of success. A trial that does not meet its primary endpoint is considered a failure, even though there may have been evidence of efficacy using a different endpoint. A failed clinical trial often means the end of the drug development investment which is hugely disappointing if the failure is defined by the selection of the wrong primary endpoint.

In recent years, there has also been growing regulatory scrutiny regarding dose selection, inclusive of amount, frequency and route of administration. Indeed, in oncology drug development the FDA has initiated Project Optimus, an initiative that places great emphasis on the need for more robust dose analysis, including randomized dose comparisons, early in a development program and before pivotal trials begin. For drug developers this does pose a dilemma when the drive to identify a recommended Phase 2 dose seems so urgent.

Ensure the CRO you choose to undertake the study is competent to produce and manage the trial to comply with the full relevant regulatory requirements. Effectively managing a CRO is always a challenge and the quality and experience of the individuals who work on your projects is critical in the success of specific projects. Always ensure that you review the backgrounds of project managers and that these individuals are those that will actually be working on your projects. Operations leadership within your organization is key to optimizing the outcomes of CRO managed studies.

3. Poor drug-like properties (ADME)

Your candidate drug's properties of absorption, distribution, metabolism, and excretion (ADME) need to be understood and at an early stage. The level of permeability or solubility needed for oral absorption is related to potency. The relative importance of poor solubility and poor permeability towards the problem of poor oral absorption depends on the research approach used for lead generation[5].

B. Tolerability/Safety Issues

These can be due to:

1. Lack of CMC data

Never underestimate the need to have Chemistry, Manufacturing and Controls (CMC) testing (including analytical monitoring) completed as soon as possible to avoid finding yourself later in development with an unworkable product. Robust CMC characterisation will also minimize the potential need for a costly and delayed switch to a different formulation later in the development program. The identification of a promising chemical/monoclonal antibody (mAb)/ biologic is just the start of a long journey to a successful product approval. While early development is typically focused on pre-clinical and clinical aspects, a continued focus on CMC is essential to ensure a successful product and the shortest path to approval.

[5] Lipinski CA, 2000. Drug-like properties and the causes of poor solubility and poor permeability. *J Pharmacol Toxicol Meth*; 44(1):235-49.

2. Flawed preclinical studies

The animal model does not reflect the potential adverse health effects of the drug in the human population. Just as animal efficacy models can be poorly predictive of outcomes in humans, animal safety data can also be misleading. Animal toxicology studies provide a guide to potential human toxicity, but do not diminish the need for extreme vigilance in the clinic. Mechanistic toxicity considerations are also of importance and help advise those areas that need greatest attention in the clinic. In this respect, bear in mind the need with some agents (notably monoclonal antibodies and biologics) for consideration of both on- and off-target toxicities, especially where a therapeutic target may be expressed differently in different species.

3. Poor drug-like properties (ADME)

See above. For example, problems with excretion can lead to accumulation of the drug (or its active metabolites), and to downstream adverse effects due to toxicity[6].

C. Commercially Unviable

Issues to consider:

1. Insufficient landscape assessment of current standard of care and precedents

Check that you are aware of the current standard(s) of care, as this will be the standard that you will be testing your candidate drug against in Phase 2 onwards.

It is also mandatory for the organization to monitor developments in the field and potential competitors. Some areas can move extremely rapidly, and in some cases the standard of care can change before your own development program is complete. Will your comparators in pivotal studies remain relevant at the end of the study? Importantly, much can be learned from competitor data, both in efficacy and safety determination. Clintrials.gov is a remarkably useful source of information regarding trial design, endpoints, timelines and participant institutions. On this note, be aware as possible of the key influencers in the field and learn from them. This can be in the form of conventional scientific advisory boards, but also informal discussions with experts in different geographies. Seek multiple interactions and remember not to be overly influenced by one strong opinion: many programs have veered off-course under the influence of a loud voice that was ultimately found to be incorrect.

2. Failure to consider pricing/reimbursement needs

Consider: What is your reimbursement strategy?

In Australia, Australian residents are covered for health services by Medicare, which covers a number of programmes. One of these, the Pharmaceutical Benefit Scheme (PBS), assists with the costs of prescription medicines. The programme defines maximum quantities and the number of repeats which can be funded. For some of these medicines, prior authorisation is required. The Therapeutic Goods Administration (TGA), a division of the Australian Government Department of Health and Ageing (DHA), grants marketing authorisations. Manufacturers of prescription medicines have to file an application to the Pharmaceutical Benefits Advisory Committee (PBAC) for their medicine to be subsidised under the PBS. The PBAC must assess whether the medicine is both clinically effective and cost-effective (compared to other treatments) before recommending that a product should be added to the PBS. Manufacturers of prescription medicines have to file an application to the PBAC for their medicine to be subsidised under the PBS. The PBAC considers an economic evaluation, at the price initially set by the manufacturer, to determine whether the product should be included in the PBS list.

Many countries now have well-established national reimbursement processes and, while different, all demand the need to demonstrate value for the drug being prescribed. Value is in turn determined by the benefit delivered in relation to the cost. As a general principle, greater benefit can justify higher prices, and marginal benefit cannot. This is of course context dependent, so in a life-saving intervention even small benefits may result in high value determination. In reimbursed markets, failure to secure reimbursement is closely tied with commercial failure in that country. Therefore, designing pivotal studies that will allow for appropriate comparisons and cost efficacy calculations may be crucial in the future commercial success of the drug.

The USA perhaps stands out in the global pharmaceutical market in that, for many companies, whether your drug is a success or not depends on whether you can get it reimbursed in the USA. The USA accounts for the largest share of drug spending and innovation in the world, and its drug pricing regime is the most complex

[6] Garza AZ, Park SB, Kocz R, 2023. In: "Drug Elimination" https://www.ncbi.nlm.nih.gov/books/NBK547662/

given its multi-payer model and unique overlay of market access requirements that collectively impact drug pricing and reimbursement decisions in the U.S. Additionally, U.S. drug pricing and reimbursement are undergoing significant changes, with recent federal legislation, the Prescription Drug Pricing Reform provisions of the Inflation Reduction Act, significantly altering the pricing regime under certain federal programs. The U.S. health care system includes both private and public health insurance coverage. Whether a drug product is covered, and at what price, is determined by each payer's coverage, coding, and payment criteria for health insurance plans. The largest government-funded programs are Medicare and Medicaid, under which plans are subject to detailed requirements set forth by statute or regulation. Private plans, which cover far more Americans than public plans, have more flexibility to make coverage and reimbursement determinations. All plans implement various cost containment measures which may impact plan beneficiaries' access to certain drug products.

3. The drug is too expensive

What will be the cost of your drug? How often will it need to be administered? What will your drug cost to manufacture? How difficult are the necessary storage conditions? Much will depend on whether it is a biologic or a chemical or a small molecule. You need to understand what options you have for manufacture and the cost and time to obtain sufficient quantities for a clinical trial program. This will depend on the route and frequency of administration. Some small molecules may demand life-long administration. How is that priced in a way that will be acceptable to reimbursement authorities? Conversely, a gene therapy is very expensive to manufacture but it will only be administered once. How will you determine a price for that? Some recent therapeutics (eg CAR-T therapies) are very complicated, patient-specific, and have production costs of tens of thousands of dollars. What price is justified for these agents?

4. It works really well – but nobody needs it

A range of scenarios might give rise to a product that is effective but not really needed. This could be because it is not significantly different to the standard of care, there are multiple highly effective standards of care, generic drugs are available that are effective, safe and extremely cheap, or your innovation is simply too late to market. Being late to market is not necessarily the death knell for an innovation. Best to market will usually beat first to market. In fact, the first product to market can encourage the target customer to be more receptive to change, or pave the way for higher pricing from reimbursement authorities. If, when a better or safer product comes along, the broad customer base is already accepting the value proposition and will be open to change. Unfortunately, if your innovation is a "me too" product, without a compelling value proposition or differentiated benefit, then it is unlikely to be successful.

Strategies to Address the Root Causes of Drug Failure

A. At the pre-clinical stage:

- Conduct an audit of raw preliminary data before committing. Seek independent expert advice.
- Understand the disease biology in the context of your drug. Consider target cell/tissue, the tumour microenvironment for oncology programs, host immune response .... and potential pharmacodynamic measures of drug activity that may allow early determination of drug activity.
- Explore preclinical models but remember their limitations … again, seek expert advice!
- Define a clear development plan - trial design, target patient population, milestones, budgets, timelines
- Define potential safety risks based on biology and preclinical observations and design your protocol to mitigate those risks
- Think about future combination drug needs and plan early
- Careful selection of your CRO is critical – ensure they are competent in the relevant field of drug development, and ensure that you are part of the review team that selects their staff working on your project
- CMC studies are especially important and pertinent for companies which are focusing on mAbs (and other biologics. mAbs cannot undergo complete characterization like in small molecules due to size, while the variable and hypervariable sections are important for antigen binding specificity, as well as displaying potential cross-species differences. This, along with other issues which your development/CMC partner can help to identify, are critical to find early; issues found later on can be very costly in time and money.

- As early as possible in the development of the drug – but importantly after lodging your patent application – you should validate your assumptions about the need for the product with clinicians and/or patients. This will also help to overcome scepticism from potential investors. Even if they need it, will they need it enough to buy it over what they are currently doing? Remember in these early discussions to ask participants to sign a confidential disclosure agreement (CDA).
- Speed to market is important, but value proposition is more so, so take your time and get it right, if you have a truly innovative and differentiated product.
- Monitor potentially competing development programs and learn from them.

B. When (if) the drug reaches the clinic:

- Focus on robust data collection, perform regular quality checks, and be cautious with anecdotes, compassionate use/early access. General advice is, despite enthusiastic investigators, to not open early access programs until there is confidence that you are in the final steps towards regulatory approval. Earlier access programs have the potential to go very wrong where adverse events occur and data collection outside of clinical trials is invariably suboptimal. The best way of giving early access to most patients is through the earliest possible registration.
- Careful investigator selection – for early oncology development, ensure deep experience in first-in-human studies. Seek investigators who are collaborative and communicative ... but always understand that they have different agendas and priorities.
- Watch and learn from competition .... keep an eye on trial design, data, signals in different diseases, toxicities, biomarker developments
- Be realistic with timelines and setting expectations ... just reference the competition to see how long things really take!
- Seek external input .... activities elsewhere may be touching on things you haven't yet thought about.
- Retain clarity and focus on the development path - ask how does this activity move you forward along the route to registration? Everything else is secondary.
- Carefully evaluate dose optimisation .... consider utilizing potentially more than one recommended phase 2 doses (RP2Ds), in oncology development consider the value of optimal biological dose (OBD) vs the need to define a maximum tolerated dose (MTD), conduct early dose-ranging studies to address increasing regulatory scrutiny on this topic.

Root Causes of Company Failure and How to Manage Them

1. Lack of money

This is an obvious reason why drug development companies fail to get their bright idea to market. However, even well-funded programs fail because of financial mismanagement. Careful budgetary control and timeline planning is critical. Determine the likely key inflexion points that may allow for additional fund raising and ensure that your budget comfortably extends beyond that point, and where possible allows for unpredictable delays.

There are many other reasons why this happens. Overcoming the following more fundamental problems will hopefully prevent this situation occurring:

2. Failure to articulate the value proposition of your drug portfolio

There is a lot of money out there for the "killer" breakthrough innovation, but the investors who have the money need to understand why the customer (patient/physician/big pharma) will buy your drug. There is often a large disconnect between what value and attraction the inventor places on an innovation, and that placed on it by the end user. When customers face choices, they base their decisions on the relative perceived value, not the actual or economic value, nor even the great science behind a new product. A big factor in this is that most people are reluctant to change what they are doing, unless there is a compelling reason to do so. How well innovators understand and articulate that compelling reason will influence how likely investors are to put their money in. How do you convince an

investor that you know that the customer will buy your product? You have to have gone out and asked the customer. But that means you have to know who they are.
Your knowledge also needs to be expressed succinctly in some kind of 'pitch' document or slide deck. This needs to tell a compelling story, without initially getting too bogged down in detail. Trigger the interest and then follow up with the detail as requested (and ensure that a CDA is in place before disclosing sensitive or unpublished information). Before this point, ensure that you have a data room that is as complete as possible, is organised in a way that allows the viewer to readily find important materials, and has identified data gaps or weaknesses in advance.

3. Failure to understand who the customer is

In drug development, the customer could be the clinician (GP, medical specialist, surgeon), the non-clinical specialist (pathologist, radiologist), or it could be the ultimate end user – the patient, or the customer could be a big pharma company. What motivates each of these potential customers is very different, so whilst a drug may appeal to a clinician because it is more effective, or has fewer side effects, the patient may not want to pay the premium for it achieves reimbursement. So, when an investor asks who is the customer, a successful innovator will not only know who the customer is, but will also know why they will buy the product.

4. Failure to understand what the customer values

We know Steve Jobs famously said, "*Some people say, "Give the customers what they want." But that's not my approach. Our job is to figure out what they're going to want before they do. I think Henry Ford once said, "If I'd asked customers what they wanted, they would have told me, 'A faster horse!'*" In Jobs' case, he knew exactly who his customer was and was not (the customer was not a computer specialist. The customers were those who wanted to do everyday tasks faster and easier, and who had never bought a computer before). He had a very clear vision and a great feel for the end user. In drug development, it is unlikely that your novel molecule will be a mass consumer item. It will be used by or for people who are suffering from a disease of other medical condition, or who want to avoid suffering from a disease or condition. So, what the end user values is something that they can rely on to improve their lives, and be willing to pay for that. The medical specialist who may be the customer does not want to compromise the patient's health, so they need to be convinced that the innovation will either improve the outcome for the patient, or will provide the same outcome but for a lower price, or faster, or less painfully. The government values the cost savings that the innovation will bring to the health budget. The more indirect these benefits are, the harder it will be to convince a customer to pay for it.

Having determined who your customer is and what is likely to drive their decision based on the value they are looking for, the next thing to do is to get some evidence to support this. This is where "**Voice of Customer**" typically comes in. "*The Voice of the Customer is a process for capturing customers' requirements. It produces a detailed set of customer wants and needs which are organized into a hierarchical structure, and then prioritized in terms of relative importance and satisfaction with current alternatives*"[7]. But caution is required here. If it is done correctly, with the correct customer/end user, then "*it can form a solid basis for design and marketing decisions from concept development through product launch*". If done badly, and/or if the results are seen as absolute, it can doom the product even before it is launched. It must capture what the customer/end user values and what would make them change from what they are doing currently. Remember the 2019 Australian Federal election result, or the 2017 US Election result. The polls in both elections got the wrong result. The Voice of Customer – in this case the Opinion Polling - was wide of the mark. Why? Because the voters changed their minds on the day. Or they gave one answer in a hypothetical situation, but when it really counted – election day – they realised the implications of what they were doing and many of them changed their choice. The same danger potentially lurks in Voice of Customer surveys.

[7] http://www.mit.edu/~hauser/Papers/Gaskin_Griffin_Hauser_et_al%20VOC%20Encyclopedia%202011.pdf

5. Failure to understand the customer's barriers to change

Whilst your potential customers may see the value in your innovative new product, they may simply be constrained by an inability to change for external reasons that have nothing to do with you or your product, and over which you may have little control. Failure to understand these barriers and how long they may take to overcome can seriously impact cash flow projections, with obvious consequences for the business. There may not be any approved reimbursement codes available (this can take up to two years in the US). Healthcare customers (clinicians, hospitals, laboratories) may be locked into business models that depend upon patients accessing existing products. Companies need to do a thorough stakeholder review to identify these hurdles to adoption and ensure key revenue projections are based on solid data.

6. You have the wrong team

In our opinion, a successful innovation needs a team that comprises:

- A visionary leader to think beyond the here and now to what might be
- A technically proficient and rigorous scientist/clinician
- An experienced regulatory professional
- A highly competent operations manager to run the trials and pull all the disparate activities together
- A hard-nosed business and financial leader who can ensure that the company operates within reasonable financial bounds
- An extensive network that can be called upon to help when faced with a potentially insurmountable hurdle
- A board of directors with experience in drug development that advises and challenges senior management on their decision-making

Importantly, these individuals do not need to be operating full time and early in development critical input from some functions may be limited to a few hours per week. Indeed, sometimes, they are all the same person. But very rarely. Alfred Lo, formerly of Sydney's Cicada Innovations commented, "*Great things come when you bring people together from different skills and experience – strong commercial and strategic thinkers combined with researchers and scientists working on breakthrough technologies – that's when you see really successful innovation*".

7. Overpromising and under-delivering

It's an easy and tempting trap to fall into. Promised deliverables will be remembered and held against you. Are the costs and timelines that you are estimating to take a drug to market (or to acquisition by a Pharma company) possible, or even likely? Are the market penetration rates and revenues likely? Remember that investors and potential Pharma partners will be skeptical of revenue projections and expect you to have carefully and realistically appraised your projections. Assess the competition and ask whether your projections make sense. Obviously, there is a fine line to tread here. You should aim to give a range – best and worst-case scenarios, and the middle range. If the worst-case scenario means you don't get as much funding, then it probably tells you that it is going to be a difficult journey. Drug development usually requires long time frames and patient capital before realising projected returns. This is due to a number of factors, some of which are well understood by investors and innovators, and some less so. The time to recruit patients and undertake clinical trials can vary widely depending upon the prevalence of the condition being addressed, the current state of care, the potential risks of the intervention, and on the potential endpoint being pursued. Complex regulatory, reimbursement and procurement pathways require considerable evidence-based data to be collected, and that can be time consuming. It is important for all stakeholders to understand these constraints on drug development. Innovators should be cautious about engaging with investors who don't understand the potential time horizons and are looking for a quick exit. This pressure can cause companies to cut corners, to the long-term detriment of bringing the product to market. Be careful that you can deliver on your promise. One example is seen in off-label use of products. Many drug development companies imply, or factor into their market size estimates, off-label use for their product. However, a company can't promote a product for off-label use, and this results in projections based on this application being overestimated.

8. Underestimating the risks

Write down EVERY risk you can think of. And then write down some more. The World Economic Forum did not have a pandemic threat in its top 20 risks in its 2020 Global Risks Report. COVID-19 rendered that report irrelevant by February. Factor the most likely risks into your estimated time and cost to market entry and return on investment, and your business model. And formulate mitigation strategies to deal with the risks should they arise.

9. Underestimating the regulatory and reimbursement hurdles

Innovators, especially inexperienced Australian innovators, often do not have sufficient knowledge of the USFDA or even the TGA regulatory approval application process. There are a number of paths to FDA clearance or approval. If you do not know, or underestimate what your regulatory path to market approval is, you’ll lose credibility with supporters and investors. Ensure you understand early on what the requirements are that you need to address in your documentation, and plan accordingly. In many countries, market success is predicated on securing national reimbursement. In some cases, this can be even more difficult than a successful regulatory approval. It is important to understand these processes and factor in realistic timeframes for this second and critical ‘regulatory’ hurdle.

10. Partnering too early

There are many benefits of early engagement with potential clinical and commercial partners. By talking to multiple interested parties, competitive tension can be built, insights into what the market wants to see can be gained and further opportunities for your innovation could be identified. However, you usually only get one shot at this, so trying to partner too early with a product that is sub-optimal can undermine your chances of getting the best partnership then and later. Also, first impressions are important, as is word of mouth and reputation. All are hard won and easily lost. It is a judgment call and highly dependent on the urgency of need for partnering, however, in many circumstances we would prefer to impress a potential partner with a compelling semi-finished beautiful swan than going in with an ugly duckling that may have the potential to turn into a beauty.

11. Not exploring all funding options

There are many potential sources of funds for your innovation. Academic grants are very competitive and relatively low level in respect to drug development costs, but can keep a program moving forward as more substantial investment is sought. VC funding is not limited to the small number of operators in Australia, so seek VC discussions outside of this geography and match the stage of your product to the profile of the VC. Biotech and Pharma companies are always seeking highly innovative products with disruptive potential. Seek those companies with therapeutic interest and focus in your area, and identify those contacts where the decision-making occurs in those companies (often not at a local level, but can be facilitated by helpful local staff). Many potential investors will adopt a ‘watch and wait' approach. This is normal and gives you opportunity to revisit the discussion when you have new data. Finally, don’t be perturbed by rejection. Perseverance is key and most successful fund raising occurs after many first pass rejections.

12. Lack of documentation, record-keeping and standard operating procedures

Essentially, there is just one message to know here - if it isn’t properly documented, it didn’t happen. This holds true across preclinical experimentation, clinical work, CMC advances, financial management, and every other company function. The earlier a company understands what needs to be documented and puts in place the systems to document it, the greater the chances are that its development efforts will pay off when it comes to overcoming regulatory obstacles and getting a product onto the market. In this respect, it is also extremely important to identify a suite of internal standard operating policies and procedures in advance of their need. Retrospectively populating data and events is enormously difficult, so have these in place as soon as company activities reach that point.

13. Being too ambitious

Ensure that your resources match your plans to develop your drug. It's best to map out your pathway in order of milestones and then devise strategies to reach those milestones sequentially. Then you need to develop a realistic budget for resources required to achieve each milestone, including money, people and time. Hasten slowly. Ensure that each milestone's dependencies have been covered. Always ask whether your planned activities move you further towards that registration goal and, if they don't, question carefully their need.

14. Not being ambitious enough

Whilst it may be sensible to start small and local, and revenues that result may be sufficient to sustain a comfortable but small business, if your product is truly innovative, plan to expand it outside your comfort zone so that it can benefit a wider range of patients. True innovation and potential will be recognised by investors. Thinking outside the Australian business environment will also have the benefit of expanding your business into a successful multi-geography enterprise and provide investors with a much more attractive potential return on their investment.

Final thoughts

Remember that the road to success is beset by pitfalls and hurdles, no matter how great the underlying science may be. Ask an experienced drug developer and they will tell you that the most successful products they have worked on were still a roller coaster ride of highs and lows. Don't be put off by another roadblock. Analyse it and find a solution. You should aim to control as much as you can during the development phase of your drug to maximize the chances of its success, increase the value of your product and company, and most importantly, to bring your product to market to improve patients' lives and health.

For further information please contact

Dr Peter French:
e: pwf261@iinet.net.au
m: +61 487264328
w: www.drpeterfrench.com

Dr Kevin Lynch:
e. kevinpklynch@gmail.com
m: +61 0412 564 020

