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Editorial

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A shortage of funding or not enough healthcare projects?

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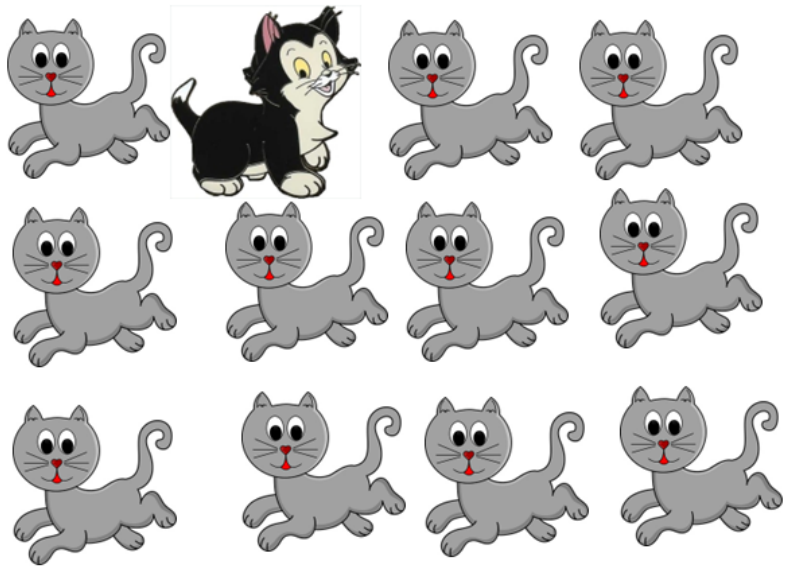
Graphical Abstract



Healthcare Investment - finding the extraordinary amongst the ordinary.

Abstract

The author, having worked in pharmaceuticals for several decades, has advised, in confidence, both investors and small to medium-sized enterprises on transitioning healthcare research projects into commercial development, mainly in Europe. He is now semi-retired. This note is written in the hope that his experience will improve the success of small and medium-sized enterprises in their attempts to get non-academic investment funding and make life easier for investors. Whilst the article focuses on drugs, the broader advice is relevant to other healthcare areas, such as diagnostics and devices.

Keywords: Pharmaceuticals, development, funding, investments, strategy, R&D, USP, development proposal writing

Purpose, Rationale, and Limitations

This article offers a practical and important guide for professionals who wish to transition their successful research project to commercial development. This necessitates obtaining non-academic funding from investors, which is often inadequately addressed, resulting in failure to obtain financial support.

Introduction

What are the chances for healthcare development public funding?

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All big investors want early clinical efficacy data to invest. This leaves a funding gap for small and medium-sized enterprises (SMEs) between the end of the research phase and development leading to the clinic, often called the Valley of the Death[3]. This is usually bridged by a wide range of organisations using non-industrial money in a process that involves industrial assessment to a lesser or greater extent. Assessors' written feedback should be truly valued, as it includes knowledge of unpublished know-how and what works and what doesn't. These days, it is particularly challenging to give helpful and politically correct feedback in any format to inventors - especially where the investment net is cast widely.

Discussion

An investor's success is monitored, *inter alia,* by the short-term return on investment. Unsurprisingly, this information is hard to access.[1,2]

Much of early healthcare research is carried out in academia and spin-offs, with little knowledge of industrial healthcare development. This results in a high percentage of publicly funded healthcare research that is not translatable (for various reasons), even with commercial advice. This is reflected in the high rate of rejected proposals by industry-based investors, although the feedback is unlikely to state this clearly. There may well be an investment shortfall - but not knowing what investors seek also contributes to the applicants' failure. One could also question whether this process is efficient, getting advice so late in the day.

Healthcare research is, by definition, applied research, and one would have thought that academia would want to know how to apply their basic research skills to help patients. The majority of academic papers are written by graduate students who wish to display their plethora of skills and the ability to solve complex problems instead of focusing on the usefulness and reproducibility of the data.

Improving the interface between Academia and Industry

SMEs and startups provide new ideas for healthcare companies; however, most leading academic research laboratories provide little training on the most expensive part of healthcare – development or preparing for development. Attempts have been made in Europe to involve the university's relevant industrial contacts to advise on funding from a dedicated fund. In this author's opinion, this led to a two-to-three-fold improvement in translatability, but it was not continued. Another initiative created a consultancy offering translational advice but not funds. Again: discontinued.

Only the very best drug candidates go beyond research, and when accepted into development, all related research should stop - or be strictly controlled by development. Development is a costly process, and there is no scope for a backup to enter development simultaneously. This point must be emphasised. There is scope for formulation changes, different salt forms, etc., but the specification should not change much. In other words, investors want their money put on the top candidate.

In a perfect world, public or private funding applicants should accurately benchmark their projects upfront. At its most basic, this would indicate whether the project was at the creativity, research, or development stage. Often, there is a discrepancy between what investors seek and what is on the offer. This has been discussed elsewhere[4,5] but is worth mentioning here again.

1. Ideation is the first proof of concept.
2. Research is the precise identification of a drug candidate.
3. Development is taking it to the clinic and market.

The critical test:

If you don't exactly know what you are developing, you are still in research.

To fund a new drug to go through research into development without a thorough review only occurs in academic- or sometimes, unfortunately, in national or international public funding. The result is that commercial investors are very wary and even sceptical of the outputs of such financing. Changing global bureaucracies to align with industrial norms is very hard. To do this would be invaluable, but changing processes requires political decisions, and this is not on the radar.

How to write a good proposal for development investment?

Clarity is everything. I have read hundreds of proposals for development funding; it is clear

that applicants need help understanding the differences in formats required between an academic proposal and a proposal for significant investment to develop a new drug. In development, all research options have already gone, and it should, therefore, in theory, be easier to describe what needs to be done, using a set of criteria. The project must have extreme clarity regarding the drug, the indication, and the route. Investment advisers do not want to spend several hours reading a project without a clear idea of the invention and its USP – Unique Selling Proposition.

The text should be ultra-focused. Evaluators are intelligent and experienced—they do not need long-winded market backgrounds taken from the internet—sometimes generated with AI. The space provided should be optimised to sell the concept with extreme clarity. The use of user-defined acronyms should be avoided. Please avoid references and ambiguities! IP ownership should be clear, and Freedom to Operate, plus patent background and foreground, should be commented on by a competent authority.

Many projects mention industrial advisors helping with them. If you are using their reputation, it is prudent to involve them.

Many senior scientists are not good salespeople. (Sales is a different profession.) Lately, I have noticed that a few top organisations are actively managing their proposal writing to sell their projects, and this approach really works.

Storytelling should be adapted to the audience; figures and diagrams can be invaluable but must help to sell the project and not distract. Figures, if used, should be fully explained and not just copied from an academic paper. Investors will want to see a project that will progressively de-risk the concept for investment and increase its USP.

I have not seen a single proposal in which a claim for a cheaper drug worked as a unique selling proposition. A cheaper drug is not a compelling justification for investors, either. Bear in mind that drugs are relatively inexpensive to manufacture, and this includes Biologicals. Biologicals also have a much longer half-life *in vivo,* i.e., a smaller dose. For a therapeutic to enter development, there must be compelling evidence of efficacy in an appropriate animal model.

As a negative example - binding drugs to cells in vitro or organ targeting, as shown by qualitative imaging studies, is insufficient for drug development. Tumour volume reduction is much less attractive than survival data in xenograft studies. The barriers are (rightly) much higher for development as the financial gamble is enormous. Key experiments should be really well done and ideally blinded to avoid bias.

In general, projects should focus on useful milestones that reduce the research options and speed up the route to the market. It is a shame there is so little development training in the academic world—it is an opportunity missed! Funding platform projects, with many complicated options (whilst great for research), are confusing and extremely discouraging for investment. This is very commonly seen in funding proposals.

Milestones, of course, are project and commercial area-related, but they should add value and decrease the risk of the project. Possible drug milestones are discussed elsewhere [3,4], but some examples with reasoning are listed here:

1. Proof of Mechanism: Regulators are very reluctant to accept a drug these days with no known basis for how it works or at least a hypothesis.
2. Chemical Manufacturing and Control - a statement that the drug entity can be repeatedly manufactured to an acceptable specification and at a viable cost from a qualified individual.
3. Direct and Quantitative proof of concept in a relevant disease model. Imaging is a diagnostic, perhaps, but is not compelling evidence of therapeutic efficacy.
4. A strong IP position with respect to competitors and a lack of prior disclosure by academic publications. Indeed, the topic of future publications is a negative one for investors. Publications should not feature as a future work program – this is a red flag for investors.
5. Evidence that this is the best possible drug and it is in pole position for the indication and that a better/more potent drug is likely outside the development timescale. Investors will not readily fund work to find a better candidate. There is only one shot at the target! Quantitative data is required – with the potential for comparison with competitors.

Proof that a market exists

For some blue-sky projects, the market may not exist yet, which requires the investor to take a bigger risk. This is their job and perhaps the best bit, but it can be made easier by the support (the more formal, the better) of one or more Key Opinion Leaders.

Conclusion

It is essential that project leaders looking for investment do not leave it up to the investor to make their mind up based on the data presented because investors often don't have a deep understanding of the technical details of the research. Instead, the narrative should lead the reader to specific data; less is often more understandable. The initial funding request is always in writing; however, funding face-to-face meetings have been very successful in providing more training and clarity, albeit at a marginally higher cost. The project leader should be a good writer and a salesperson. The use of AI is commonplace now, but at this point, AI-written texts are recognisable, and LLMs do not understand the technical side: AI repeats what it has been told. For now, a good writer still has the edge!

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