

## Introduction.

Creating a profitable business built on a scientific or technological innovation is a complex task, requiring diverse skills and a lot of time. One of the most challenging aspects of building such a business is navigating the transitions between the three quite disparate types of human endeavor shown in figure 1: research; business creation; and ultimately the management of a going concern (a cashflow positive business).



Figure 1: From science to profits

This article is for those engaged in, or interested in, that process, and lays out a framework for thinking about it. In particular, this article focuses on the initial steps of a voyage which starts with the genesis of a scientific idea; leads to the creation of a product that meets a specific need of a specific class of individual; and results in creation of a profitable business, built on delivering that product to those individuals.

The subsequent transition from viable business to large, stable operating company is also a huge and challenging endeavor. However much has been written elsewhere on that portion of the life of an emerging company, and in this article we focus on the foundation that needs to be created even before such business expansion activities can be launched.

Although the examples in this article are from the field of life sciences, the principles described here apply quite generally to the creation of businesses based on significant product innovation, in fields involving a heavy dose of science.

## The innovation continuum

The innovation continuum of figure 2 starts with basic research, moves through directed research and then enters the more focused product research phase. Only after that does actual product development commence; and subsequently clinical trials, regulatory approval and market acceptance. For science-based products outside the life sciences, the first four stages are the same. However the nature of the market adoption and acceptance phases differ, and depend on the targeted industry and application.

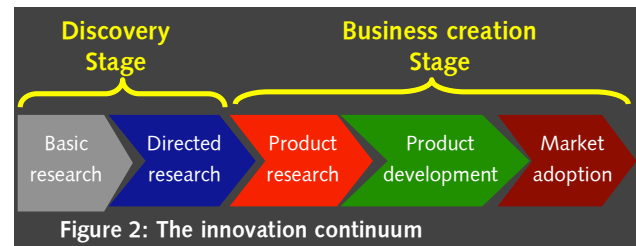


Figure 2: The innovation continuum

As an innovation moves along this continuum, the environment which it needs in order to flourish must change significantly. Management must be prepared to initiate a series of fundamental cultural transitions relating to:

- the extent to which work is focused on meeting a *specific need* (an application focus), rather than on *studying a problem*;
- the nature and magnitude of financing, its source, and the velocity of cashflow; and
- the necessary project team skills, and most likely the very nature of the organization within which the project is based.

These transitions are discussed below.

### From “studying a problem” to “meeting a need”

*An important difference between the early & late phases of the innovation continuum is the extent to which the work focuses on meeting the specific need of a specific target individual, rather than on studying a problem.*

In the initial *basic research phase*, activities are characterized by the pursuit of “knowledge for knowledge’s sake”, and lead to important basic scientific breakthroughs — such as the principles of biochemistry; the description of the double helix; quantum mechanics; and the theory of relativity.

Building on the breakthroughs of basic research, the subsequent *directed research phase* is characterized by a distinct, albeit fuzzy, focus on specific applications. In this phase, activities target the directed pursuit of knowledge, and are about things like understanding basic cancer growth mechanisms, the relationship between islet cell function and diabetes, heart disease risk factors, or the properties of stem cells.

With the knowledge obtained from directed research, investigators can hypothesize specific product concepts, aimed at meeting a specific need of a specific group of individuals. For example: a drug that would act on a specific receptor to inhibit cancer growth; or a laser that can reshape the eye to eliminate the need for eyeglasses.

The work then moves to the phase of *product research*, in which the applications are exceedingly specific but fundamental questions remain. For example, product research addresses questions such as

- does arterial stenting work in an animal model?
- can you use a balloon to unblock a clogged artery?
- can you create a functional cochlear implant that improves hearing?
- will cPAP reduce problems associated with apnea?
- can a laser reshape a cornea in an animal model?

Once a team can answer these questions, it can create a detailed description of a product that meets a specific, targeted need; and can specify the technology on which that product will be based.

Then the project can move on to the *product development phase*. This phase, characterized by a very tight focus on a specific application, has as its outcome development of a specific product, which can be manufactured at a certain price point, and which will reliably accomplish a desired outcome, when used by the targeted customer (a clinician in the case of most life sciences products).

When creating a science-based business, it is very important to be quite clear whether the project is at the directed research, product research, or product development phase. This is because the way the project needs to be managed, the way it should be financed, and the types of skill sets needed all differ enormously as the project advances from phase to phase of the innovation continuum.

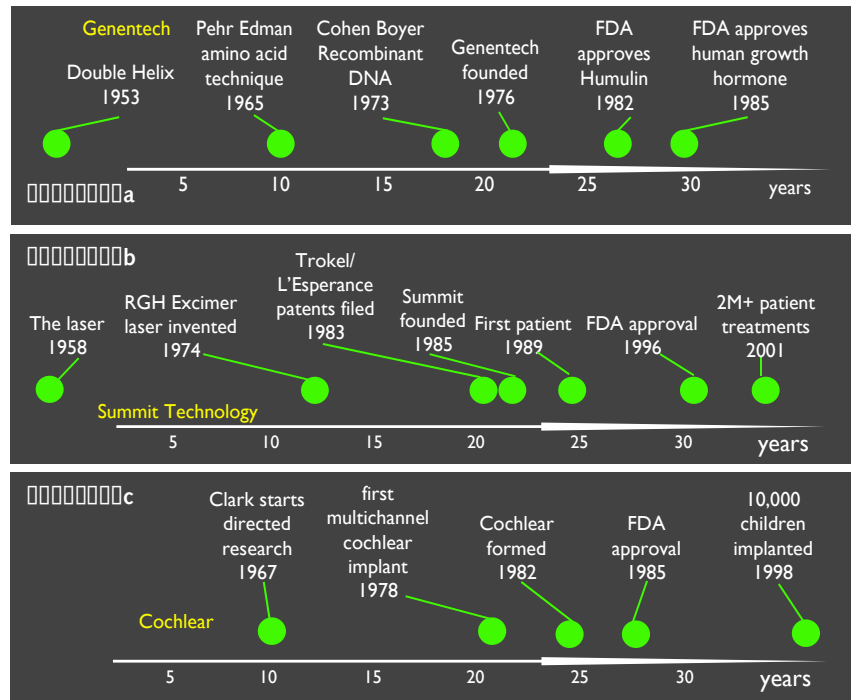
*One of the most common seeds of failure we have observed in science-based, startup businesses is the failure to correctly identify the stage of the project, and the consequent application of inappropriate management techniques.*

*It takes a long time*

Figure 3 illustrates some of the major milestones in the progression of three projects along the innovation continuum. The milestones of 3(a) relate to Genentech: the world's first biotech company; those of 3(b) relate to Summit Technology<sup>1</sup>: a pioneer in the laser refractive surgery business (widely known as LASIK); and those of 3(c) relate to the commercialization of cochlear implants by an Australian company, Cochlear Ltd.

Each of these examples led to creation of businesses with value measured in billions of dollars, and fundamentally changed for the better the lives of many patients.

*As these timelines illustrate, it takes a long time to commercialize a fundamental science-based advance. It is very important for entrepreneurs and investors to have realistic expectations regarding the duration of such a project, or mid course disaster is quite likely.*



**From "common good" to profit-driven investment**

The innovation continuum divides roughly into two parts: the *discovery stage*, encompassing the basic research and directed research phases; and then the *business creation stage*, including the product research,

<sup>1</sup> The author was CTO of Summit Technology from '86-'89.

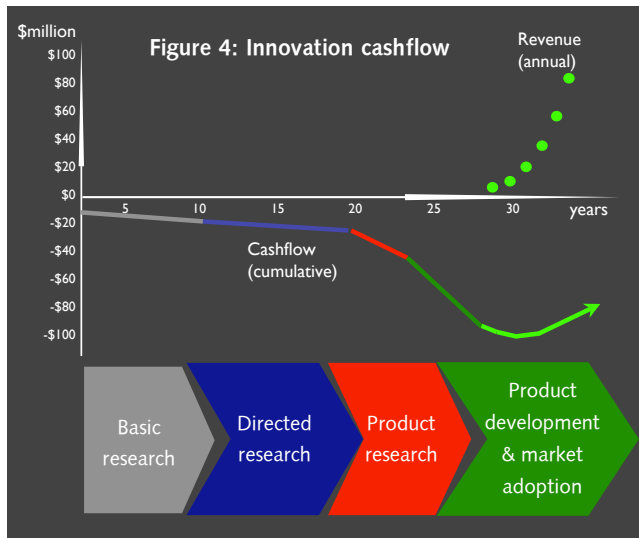
product development, market acceptance and development (figure 2).

While the discovery stage can often be thought of as leading to a “common good”, the business creation stage should be always about creating a profitable business that can deliver a return on investment. Reflecting this difference, both the magnitude of financing and its source differ substantially between these two stages of the process of turning an idea into a profitable business.

*Cashflow is a key metric*

In moving along the innovation continuum, cashflow is one of the two most important project metrics, with the other being a metric of progress towards creation of a sustainable and profitable business.

Figure 4 illustrates the cashflow of a project as it moves along the innovation continuum. During the discovery stage (basic research & directed research), cashflow is relatively slow, relatively stable and predictable, and of course, negative. Once the business creation stage commences (starting with product research), cashflow accelerates alarmingly. As market acceptance and adoption begins, it accelerates still further. Only once revenues begin to grow quite substantially can the business move to a cashflow neutral position.



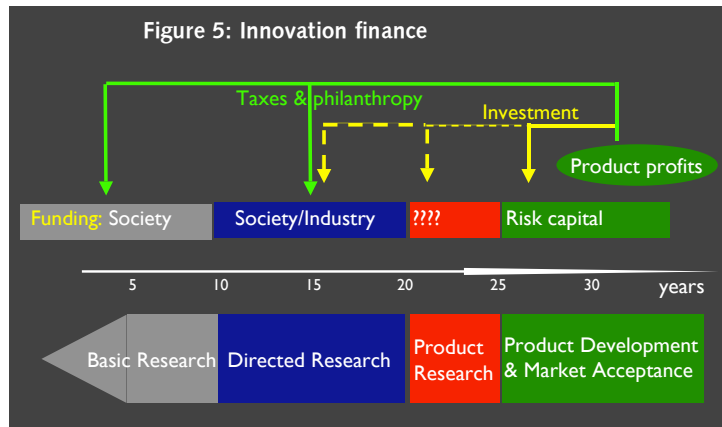
*Where does the money come from, and why?*

The magnitude of investment required to bring a breakthrough, science-based product to market is

substantial. For example, as shown in figure 4, for breakthrough medical devices cumulative investment commonly approaches \$100 million, and recent studies conclude that the costs of developing a successful new drug average \$800 million.

Figure 5 illustrates the model through which differing phases of the innovation continuum are financed, *all ultimately driven by the engine of profits from products that emerge from the continuum.*

Once a project reaches the product development



phase, management and investors can expect that the profits from successful commercialization will be captured primarily by the company which developed the product, if the management team executes effectively. There are thus established, profit-oriented investment capital pools (such as venture capital) that are well suited to investing in the later phases of the innovation continuum.

In contrast, it is quite rare for the financial benefits of breakthroughs in the basic research phase to accrue primarily to those who financed the research. Think of the examples given earlier of the discovery of the double helix or of quantum mechanics, or even of the transistor. While these have spawned large profitable industries, the financial rewards have not been returned to the financiers of the basic underlying research.

There are a number of reasons for this.

- 1) Because of the general nature of basic research and its lack of application focus, such breakthroughs typically lead to significant revenues at best many years after the original breakthrough occurred (reducing time-weighted returns).
- 2) It is hard to construct a financeable vision of the potential financial rewards from basic research, because the ultimate applications are rarely visible to the original researchers.

3) The fundamental nature of a basic research breakthrough often leads to its benefits being distributed across a whole industry (diluting the benefit to the financier). It is very hard to prevent this diffusion of value over the lengthy innovation cycle, as people leave one company and move to another, patent terms expire, and information moves increasingly freely around the world.

Because of this, basic research is best thought of as leading to a common good, much as we think of roads or the police force. Investment in such a common good typically comes from society as a whole (from government, financed by taxes) or from philanthropy.

*While the payoff is far in the future, failure by society to invest in basic research starves the innovation pipeline of the kernels of knowledge on which future profitable businesses will be based, and is akin to eating the seed corn of future generations.*

Between these two extremes are the phases of directed research and product research. As industries move increasingly to open innovation<sup>2</sup> and the world becomes increasingly globalized, it becomes harder for investors to realize a return on directed research. Less and less directed research is being funded by investment capital (which is, by definition, focused on a risk adjusted return). It will be important for society and philanthropy to create mechanisms to adequately fund such directed research as it increasingly becomes a common good.

Product research is a bit of a gray area. This type of activity can be a significant source of competitive advantage, and can definitely justify investment of risk capital. On the other hand, it is often mismanaged and always has high risk, and so is perceived to be a particularly risky type of investment — to be undertaken only by very experienced and risk tolerant investors.

Increasingly available are pools of “common good” financing (such as government research grants, innovation grants, and other industrial policy-related sources of funds) that are earmarked for product research. One can debate whether this is desirable, since (in contrast to their admirable track record financing basic and directed research) governments have a poor track record at deciding what product research merits funding. Furthermore, assuming a finite source of common good financing, this reduces the amount of money available for financing basic research, which

<sup>2</sup> See *Open Innovation*, by Henry Chesbrough.

(unlike product research) has no alternate source of finance.

*Investors need a return*

Investing return-seeking risk capital in basic or directed research most commonly leads to investor disappointment, and usually happens only when the investors (and often the researchers) have incorrectly classified the project as being closer to commercialization than is actually the case. In contrast, the financing of projects from the product research phase on is logically the province of the profit oriented investor, focused on risk-adjusted return.

Name	Revenue '03	Name	Revenue '03
<b>Pfizer</b>	<b>\$45B</b>	<b>Boston Scientific</b>	
Lipitor	\$9B	Taxus stent	\$200M
Norvasc	\$4B		
Zoloft	\$3B	<b>Medtronic</b>	
Neurontin	\$3B	Pacemakers	\$1.6B
Zithromax	\$2B		
<b>Amgen</b>	<b>\$8B</b>	<b>Therasense</b>	
Epogen/Aranesp	\$4B	Blood glucose monitor	\$200M
Neupogen/Neulasta	\$3B		
<b>Genentech</b>	<b>\$3B</b>	<b>Guidant</b>	
Rituxan	\$1B	Implantable defibrillator	\$1.5B

Table 1 illustrates the motivation for investing in early stage business creation projects in the life sciences. Projects which have the potential to create products such as those in table 1 can easily justify the large investment required, and the high risk of failure associated with early stage science.

*However, while most novel, science-based product developments require large investments, only a few have the potential to create blockbuster products, and even fewer achieve that potential. It is vital to carefully evaluate the potential of a product to address large ultimate markets, for without that potential investor objectives for return are hard to satisfy.*

**From discovery to business creation**

Table 2 summarizes the fundamental differences between the discovery stage (basic & directed research) and the business creation stage (product research, product development, market acceptance & expansion) of the innovation continuum. In addition to the differences in the nature of funding, in the speed with

which cash-in-hand diminishes, and in the degree to which there is a focus on an ultimate application, there are two additional factors identified in table 2.

*First: duration.* The discovery stage primarily involves investigating the unknown, and inevitably includes unforeseen developments, and blind alleys. Thus, while basic research *activities* (such as “test 5 mice”) can be scheduled and accomplished according to a predetermined plan and timeline, the attainment of research *outcomes* (such as “cure cancer”) is hard to schedule and inherently unpredictable.

In contrast, product development outcomes can be managed according to predictable timelines. That is just as well, since without predictability the case for an investment is hard to make (yet another reason why research activities are poorly matched to financing by risk capital).

Table 2: Two Paradigms		
	Discovery Stage	Business Creation Stage
<b>Financing</b>	Government, Industrial R&D	VC, public equity
<b>Cashflow</b>	Slow & steady	Fast & accelerating
<b>Focus</b>	Investigating a problem	Meeting a need
<b>Duration</b>	Unpredictable	Scheduled
<b>Skills</b>	Scientific	Technical, marketing, sales, finance

*Second: skills.* The nature of the required human resources changes radically as a project moves from the discovery to business creation stage. In the discovery stage, the needed skill sets are largely scientific (including the management of scientists). Once the project moves to the business creation phase, additional team member skills are needed. These include market assessment, financial management, project management, engineering rather than scientific technical skills, and skills in envisioning and implementing new business models.

As a startup company moves from the discovery stage into the business creation stage, a common error is to underinvest in the human resources that were superfluous to the discovery stage but are essential to the business creation stage. In part this stems from a widespread belief that it is best to focus first on removing the technical risk associated with product development, and only after that on reducing the residual commercial risk<sup>3</sup>.

*This leads to a range of pathologies (most commonly to the development of a product that few customers want to buy), and frequently to the demise of the business.*

*Different cultures, different goals, different organizations*

The business creation and discovery stages differ so substantially, that it is unreasonable to expect a single organization to do both well. This represents one of the greatest challenges associated with managing a project as it moves along the innovation continuum from the discovery stage to the business creation stage.

There is a well established, and successful, cultural and organizational model for conducting basic research: embodied in major research universities such as Stanford, MIT, Harvard, Oxford and Cambridge (to choose some anglo-centric examples). There is also a well proven organizational model for moving through the business creation stage (at least once product research has been completed), embodied in the model of the Silicon Valley startup company, and biotech variants of that model.

Some large companies have had success at creating organizations that excelled at basic research (Bell Laboratories, for example), and others have made major efforts to create strong research centers (Microsoft) that are still in their youth. In most cases success has involved creation of a separate research organizational model, closely resembling that of a research university, which is carefully disconnected from the day-to-day quarterly profit treadmill of the operating business parent.

In contrast it appears to be difficult to create a successful business creation organization within a university parent, and observation suggests that efforts to do so are rarely successful.

As a project crosses the boundary between directed research and product research, the organizational structure within which it operates needs to change if the project is to lead to a profitable business. For example, the project should move out of a university setting and into a commercial environment, such as a startup company.

If a team is to take a project through the discovery stage and on into the business creation stage, then necessary skill sets need to be added early in the transition to business creation, and the leadership baton must be passed from a scientific leader to a more business focused leader. Concurrently, the way the team is managed and the team’s incentives need to undergo a

<sup>3</sup> For more on this topic see *Value Milestone Process*, R.G. Caro

complete transformation: from university-like to customer- and profit-oriented.

*This transformation is exceptionally hard, and rarely proceeds without hiccup. When done well it can create enormous value. The biotech industry provides a fascinating Petri dish within which to observe more and less successful examples of this.*

## About TangibleFuture, Inc.

Innovation has traditionally been a risky process, with a high failure rate<sup>4</sup>. In our experience, a significant portion of these failures occur due to neglect of a critical set of activities that lie at the intersection of technology and the market. We believe that many of these failures could have been avoided, and that the techniques for doing so can be systematized and applied in a variety of situations. *TangibleFuture, Inc.* was formed to take on these tasks, and to be a resource for high-tech entrepreneurs and intrapreneurs. Our goal is to increase substantially our clients' probability of success.

We work with startups, research organizations, and established companies planning to grow by means of new products, new markets, new business initiatives, or acquisitions. We focus particularly on markets and industries in which things are changing rapidly, or new disruptive technologies are emerging and creating turmoil. Our approach generally involves a blend of strategic advisory services, hands-on execution, and analysis — and is uniquely tailored for each engagement to help accomplish a specific, agreed upon, business objective.

Every client we work with is creating something different. And each one has different strengths and weaknesses. Our role is often to help increase the strengths, and fill in for the weaknesses. So what we do varies for each assignment. Please feel free to contact us to discuss *your* plans and to see how we can help.

Our team has a blend of skills, experience and knowledge that makes us particularly effective. These include

- senior management experience in high technology businesses: we know what its like to be in our client's shoes, and what it takes to succeed;
- a track record of successful consulting engagements with clients ranging from startups to large multinational companies: we know how to provide effective help;
- expertise in both technology and market analysis: we know how to find out what customers will need several years in the future, and understand what a technology could be capable of by then. We can help craft

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<sup>4</sup> In his book *High Tech Startup*, John L. Nesheim reports that “the chances are six in one million that an idea for a high-tech business eventually becomes a successful company that goes public”. Clayton M. Christensen, in *The Innovator's Solution*, estimates that only about one in ten successful companies is able to maintain above market growth rates over a period of a decade or more.

a product definition that will maximize the business opportunity, while remaining within the bounds of what time, money and technical capability make feasible; and

- deep industry expertise and a global perspective: we know already a great deal about the industries in which we specialize, and the activities of their key participants in North America, Europe and Asia.

## Biography: Richard G. Caro



Dr. Richard G. Caro is the President and founder of TangibleFuture, Inc., where he helps entrepreneurs and managers create and grow high technology businesses.

Prior to founding TangibleFuture, Richard was Managing Director at RHK, a provider of advisory services to the communications industry, where he was responsible for leading RHK's Communications Components consulting practice and Innovations competency center. Previous roles include CEO (founder) of Vital Insite, a venture-backed start-up company developing continuous, noninvasive blood pressure monitoring devices; Engineering Program Manager at Coherent, then one of the two largest laser manufacturers in the world; and V.P. Technology Development (CTO & employee #5) of Summit Technology, a pioneer in the laser refractive surgery business. Before entering industry, he was a member of the research staff at Stanford University, working in the fields of applied physics, optics and laser development.

Richard has been responsible for the development of a number of successful products, and has 23 issued patents and over 45 peer reviewed publications. He received a B.Sc. (Hons) degree from Melbourne University, Australia, and a D.Phil., in experimental laser physics and nonlinear optics, from Oxford University — where he was a Rhodes Scholar.

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