
Financing as mother's milk for international biotechnology start-ups

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Abstract: This paper uses interviews of biotechnology investors and entrepreneurs to investigate the role of four investor types and eight financing vehicles across four stages of firm evolution. The choice of financing vehicle can have a differential impact on speed to market, control of direction, degree of technological risk, and capability development. This framework will be helpful for entrepreneurs, policymakers, academics and the international trade community in anticipating the impact of financing on firm and technology development – particularly as biotechnology firms are developing the next generation of drugs, therapeutics, devices, tools and diagnostics for curing human disease.

Keywords: biotechnology; financing; technology development; firm evolution.

Reference to this paper should be made as follows: Banerjee, P.M. (2009) 'Financing as mother's milk for international biotechnology start-ups', *Int. J. Technoentrepreneurship*, Vol. 2, No. 1, pp.45–63.

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1 Introduction

Recent statistics indicate that not only are developed economies such as the USA, Canada, UK and the European Union building life sciences hubs, but also the BRIC (Brazil, Russia, India, China) countries have surged in capital investments in the life sciences. For example, in May 2007, the Wall Street Journal reported that San Francisco-based Burrill & Co. raised as much as \$200 million for an India-focused health-care fund. As the influx of capital fuels significant growth of and focus on life sciences businesses in both developed and developing countries, a number

of fundamental questions arise. What are investor expectations regarding the creation of value in biotechnology start-ups? How do different types of financing influence the development of underlying technologies? What is the role of investors in shaping technology development in life sciences?

'Founding conditions' are important to the viability of life sciences start-ups. In his seminal paper, Stinchcombe (1965) articulated that founding conditions have a disproportionate effect on young firms and their high propensity to fail. According to Stinchcombe, these founding conditions affect the ability of new firms to adjust to new roles and working relationships. Founding conditions include, but are not limited to, scientific and technological proprietary know-how (Liebeskind et al., 1996; Baum et al., 2000), structures of founding teams (Ruef et al., 2003); founding team experience (Delmar and Shane, 2006); location advantages (Lomi, 1995; Stuart and Sorenson, 2003); and environmental conditions at founding (Swaminathan, 1996).

In this light, financing has been an overlooked 'founding condition'. Financing typically is thought of as a resource that must be obtained in order to grow (e.g., Wernerfelt, 1984). Yet, financing can have a critical role in developing life sciences firms by forming social networks (tying the start-up firm to other actors in the industry) and providing mentoring (advise on how to run the business) (e.g., Clercq et al., 2006). Moreover, the various financing vehicles selected can differentially impact the way in which companies choose to develop technology. This is particularly true in new life sciences start-ups because the application area, target market, business model and drug development strategy are tied to the financing vehicles selected by the firm. These are the constraints of the financial scenario in which the firm operates.

Financing is a fundamental constraint to technology development. The scarcity of financing is exacerbated as investors – who are naturally skeptical or cautious about choice and timing of investments – grapple with the ever exploding set of technology opportunities. This hurdle is heightened by the complexity created by multiple disciplines, i.e., chemistry, biology, physics, marketing, financing, etc., and across multiple geographies. With the internationalisation of financing (Holaday et al., 2003; Pandey, 1998; Pardee, 1987), small firms are forced to grow in new and novel ways based on their available financing options. These financing options do not come with 'no strings attached'. Financing is not just a resource. Like mother's milk, financing determines how strong the firm's bones are (technology core), as well as ultimate success in the world once weaned. This paper looks at financing as determining technology development and at investors as shapers of infant firms into adults.

This paper does not investigate the impact of investing in general but specifically explores the nature of investing in biotechnology. The term biotechnology refers to any technological application that uses biological systems, living organisms, or derivatives thereof, to make or modify products or processes for specific use.¹ Thus, the biotechnology industry consists of all firms that apply the principles of engineering and technology to life sciences. Using grounded theory (Glaser and Strauss, 1967; Glaser, 1998) based on in-depth interviews using snowball sampling method (Biernacki and Waldorf, 1981) of players in biotechnology start-up financing, the choice of financing in biotechnology is found to involve a two-stage decision. The emphasis of grounded theory is on exploration and investigation. Findings are inductively and empirically derived directly from the data, rather than from interpreting the data in light of some existing theory. Hence, the analysis resulting from grounded theory is intimately and directly linked to the data in explicating themes, patterns and categories.

First, the decision of the type of investor who finances biotech companies is highly firm lifecycle- or stage-dependent; and second, the decision of type of financing is dependent on technology development needs.

This paper contributes to biotechnology innovation strategy and financing. Biotechnology and the resulting products have great potential to directly affect human well-being. As Pisano (2006) describes:

“The latest digital camera may delight you, but it is unlikely to save your life. A buggy piece of software may aggravate you, but it is unlikely to kill you (although it may raise your blood pressure!) Because drugs have the power to save or improve your life or the potential to harm you, the stakes are higher than for other kinds of products.”

Moreover, this paper stresses the importance of understanding financing and strategic decisions to be taken therein. A great innovation quite often does not win in and of itself. Innovations need to find markets and applications to address, they need to be financed, then developed, validated (often through partnerships), productised, and commercialised by capable management teams. All of this is against a backdrop of uncertain capital markets and financing availability, threats from competing technologies and therefore risk of obsolescence, and a dynamic market environment. Understanding that even great innovations and ideas require a set of appropriate pre-existing conditions to develop, to find and build new markets, to change customer behaviours and attitudes, and transform existing paradigms, is critical for innovators, management and investors to fully appreciate. Meanwhile, policymakers, regulators, government agencies, academia, and the international community, need to be prepared to understand and play the appropriate role in cultivating great innovations.

2 Investors and expectations

For the firm, the choice of *investor* represents the first decision in the financing process. Interviews have elucidated the range of investors to include angels, venture capital firms, corporate investors, and institutional public investors. These investors are largely constrained or guided by their investment mandates to finance companies at pre-defined stages of maturity. For example, Catalyst Health and Technology Ventures in Boston, MA was founded with the mandate to invest in seed-stage technologies as the initial institutional founder. Therefore, Catalyst invests exclusively in Series A rounds (first round of institutional funding) and takes dominant ownership positions (>40%) in their portfolio companies. Conversely, Baird Venture Partners in Chicago, IL was founded with the mandate to finance mezzanine or growth-stage life science companies gearing up for product commercialisation. Therefore, Baird invests primarily in Series C and subsequent rounds (third round and later institutional funding) and is usually the ‘last money’ into an investment prior to a liquidity or exit event.

2.1 Investors and what each investor wants

Angel investors. Angels are typically high net worth individuals who provide initial capital for seed-stage ventures (Clercq et al., 2006; Holaday et al., 2003; Sudek, 2006). At the time of angel investments, most ventures are no more than

a concept or a business plan. Angels generally back specific entrepreneurs or individuals with a particular known expertise or a track record of past value creation, which may include friends and family. At this stage, angel investors can provide between \$ 5,000 to \$ 500,000 per venture and expect liquidity over a ten-year timeframe (Freear et al., 1995). Angels employ a portfolio approach whose success hinges on one wildly successful venture to generate 100–500-fold returns vs. 99 other failed ventures.

Venture Capital firms (VCs). VCs usually represent the earliest institutional backers of companies once an underlying technology has been sufficiently defined (Clercq et al., 2006; Kaplan and Stromberg, 2001). In other words, VCs seek out ventures that may be high risk (although lower risk than angel investors) with some level of validation. However, like Angels, VCs expect disproportionate returns including the cost of failures. Expecting a 10–100 fold return on an individual investment, even if only 10–20% of a VC portfolio is successfully exited, can represent performance success. VCs typically demand large stakes (>40% ownership) in their portfolio companies and bring capabilities, access to management talent, and industry know-how in addition to financing sources. Over the past ten years, VCs have continued to move into later-stage opportunities recognising new opportunities in product development.

Corporate investors. Corporate or ‘strategic’ investors, as they are often called, are large public or private life science companies that provide financing to biotechnology companies at all lifecycle stages. These financing vehicles (described later) can include project financing for technology development, strategic equity (for example, see Dushnitsky and Lenox, 2005), as well as licensing (for example, see Arora et al., 2001) and merger/acquisition activity (for example, see Rothaermel and Deeds, 2004). Corporate investors usually seek out a portfolio of investments with strategic coherence that enables them to retain option value on products and technology for future corporate activity. Corporate investors have flexibility in the range of companies, stage of development and amount invested. In the last ten years, most pharmaceutical and biotechnology companies have established independent corporate investment or corporate venture groups.

Institutional public investors. Institutional public investors include mutual funds and hedge funds. Examples of institutional public investors include Fidelity, T. Rowe Price, Janus, Blackrock and ING. These investors seek out public and private companies that are likely to generate superior investment returns in terms of stock price performance (Hansen and Hill, 1991; Kochhar and David, 1996; Lukas, 2002; William, 2003).

3 Investment vehicles by stage

Before reporting the first findings from interviews, it is important to fully define the term ‘technology development’. Based on interviews with investors and entrepreneurs, technology development in the biotechnology industry refers to the process of discovering and developing novel compounds and drugs, medical devices, clinical diagnostics, as well as tools required for life sciences research and bringing them to market. Similar to the high tech industry, most biotechnologies go through multiple stages of development including technology conceptualisation (also called ‘proof of principle’ in the biotech industry), validation (biotech vernacular is ‘proof of concept’),

commercialisation and maturity. The biotechnology industry is somewhat unique in that companies with validated technologies yet no marketed products can in fact successfully IPO and become public entities. This occurs largely because often public investors provide 'cheaper' capital (i.e., higher valuations) to biotechnology companies than traditional venture capital firms.

There are roughly four stages of a biotechnology start-up based on status of technology development: seed stage (founding), development stage (pre-commercial), mezzanine stage (growth), and maturity stage. At the seed stage, the firm has only a technology concept which may be as yet untested. Development-stage firms are defined as those conducting early technology design and drug discovery research. At the mezzanine stage, the entrepreneurial firm has completed full-scale development, received regulatory clearance, and is commercialising products. At maturity stage, for most biotechnology companies, the firm has commercial products and is driving sales growth.

The set of investment vehicles employed to fund biotechnology companies across these stages seem to segregate both by the financing source as well as the stage of firm and technology development. Interviews highlighted that new financing vehicles are constantly being developed to creatively monetise technology. As depicted in Table 1, this paper will focus on eight primary financing vehicles: seed capital, institutional funding, project financing, Corporate Venture Capital (CVC), alliances/licensing, Mergers and Acquisitions (M&A), Initial Public Offerings (IPOs), and structured financing.

Table 1 Biotechnology financing vehicles by investor and technology stage

	<i>Seed</i>	<i>Development</i>	<i>Mezzanine</i>	<i>Maturity</i>
Angel investors	Seed capital	N/A	N/A	N/A
Venture capital	Project financing	Institutional funding	Institutional funding Structured finance IPO	Structured finance
Corporate investors	Project financing	CVC M&A/Alliances	M&A/Alliances Licensing	M&A/Alliances Licensing
Institutional public investors	N/A	N/A	Institutional funding IPO	Institutional funding IPO

Seed capital. Founding capital that represents the initial source of financing for a venture prior to any institutional funding sources. Angel investors, acquaintances, friends and family members are the most common source of seed capital.

Institutional funding. Any investment from an accredited public or private investor (which includes venture capital, institutional public investors, etc.) can be categorised as institutional funding.

Project financing. As the name suggests, project financing is the funding of technology development by development-stage companies. Sponsors for project financing include VCs and corporate investors.

Corporate Venture Capital (CVC). The explosion in CVC is an important recent trend. Public and private corporations alike have created internal venture capital groups, for example, Novartis Ventures, GlaxoSmithKline's S.R. One, Pfizer Ventures and Merck Capital, which invest in private, development-stage or mezzanine-stage ventures.

Alliances/Licensing. Partnerships, like strategic alliances, enable collaborative development and provide equity financing to both private and public firms. In these agreements, technology, product, or commercialisation rights are transferred or licensed in return for funding. These agreements are often structured to include up-front cash payments with additional earn-outs (or royalties) that are based on achievement of specified technological or commercial milestones.

Merger and Acquisition. M&A typically occur with later-stage clinical programs once technology or market risk has been 'wrung out'. M&A enables particularly big pharma to reap the future upside of product development without incurring technology risk. Two specific variations of merger and acquisition transactions include Reverse Mergers and Specialty Purpose Acquisition Companies (SPAC). Reverse mergers enable private companies to access public capital by acquiring an existing public entity, usually a 'shell' or distressed entity (Brenner and Schroff, 2004). SPACs are similar to reverse mergers where the acquiring entity is a public shell that purchases private companies. SPACs are funded by a concentrated set of institutional public investors. The mandate for a SPAC is to invest its capital by purchasing a private or public company within a preset 18-month timeframe, else the capital is returned at face value to the original investors. Once an acquisition is made, the acquired company effectively begins trading under the SPAC's registration and stock ticker, simulating the effect of a reverse merger for the acquired company.

Reverse mergers and SPAC deals are executed similar to typical M&A transactions. Examples of reverse mergers since 2004 include Micromet and CancerVax, Cyclacel and Xcyte, Panacos Therapeutics and VI Technologies, Infinity Pharma and Discovery Partners International, EpiCept Corp and Maxim Pharma, and Solexa and Lynx Therapeutics. The advantage of these financing options are significantly lower costs, shorter timeframe to public trading than an IPO, no risk of IPO withdrawal due to market conditions or SEC rejection, less investor scrutiny, and less ownership dilution. The primary risks of a reverse merger or SPAC are lack of institutional support, research coverage, or trading in the stock – primarily due to limited involvement of investment banks – in addition to company liabilities or shareholder suits associated with distressed acquisitions.

Structured financing. Defined as the use of an established development company as an independent, private financing company specifically formed to drive product development in collaboration with a life sciences start-up. A seminal example is the Exelixis and Symphony agreement consummated in 2006. This type of financing broadens the funding capability for promising internally or in-licensing clinical programs and offers value-added clinical trial management expertise and capacity, transfers development risk to external investors, preserves future control, and prevents loss of value through licensing or sale of programs.

Initial Public Offering (IPO). IPOs are a vehicle for private companies to secure financing from public investors and sources. IPOs offer the cheapest cost of capital for early-stage ventures; create greater liquidity and access to broader sources of capital;

allow the firm to use stock as currency in transactions; raise potential valuation; and enhance the proposition to attract management talent. However, the 'bar' for taking a company has consistently risen due to several high profile public biotech failures in the last several years. IPOs also incur higher regulatory and administrative costs and stringent reporting requirements.

4 Investment vehicles and development of underlying technology

As the diversity of financing vehicles suggests, technology development is significantly impacted by the choice of financing vehicle. Specifically, interviews highlight four main areas of impact on the underlying technology and its development: speed to market, control, risk, and capability development. In other words, each type of financing affects

- the speed with which technological development is completed and subsequently converted into commercial products
- the level of control retained by the entrepreneurial firm in setting the direction of technology development, including application areas and target markets
- the degree of technological risk undertaken by the entrepreneurial firm
- the extent to which the entrepreneurial firm can build capabilities through either direct interactions with investors or resources that investors provide to the firm.

4.1 Speed to market

The vehicles by which biotechnology and life science companies are financed – and specifically the expectations of investors who provide financing – have an important influence on the speed of technology development and the resultant timing of investment returns. Interviews suggest that angel investors and venture capital firms typically have the longest time horizons. One interviewee remarked:

“[Angel and VC] investors typically fund development-stage technologies that may not even have specific applications in specific markets, but near-term represent interesting technology concepts or potential breakthroughs.”

For example, in mid 2007, the institutional venture capital funds, Polaris and Flagship co-led a Series A investment into T2 Biosystems, a Boston-based technology startup spun out of M.I.T., that is developing a label-free biosensor-based detection system for genomic and proteomic analysis. The core technology for T2 has been scientifically validated by M.I.T. researchers and academic labs, however, the large commercial market applications in proteomic and genomic research for pharmaceutical and biotechnology drug discovery, as well as in molecular diagnostics applications, are still unproven. For investments at this stage, venture funds such as Polaris and Flagship would have a technology development horizon of 2–4 years, followed by application validation and commercial launch within an additional 1–3 years. The patience for enabling technologies to adequately mature and reach full validation is also reflected by the minimum five to ten-year 'lockup' (the minimum time period before an investor can redeem their funds) that venture capital firms require from their investors.

Therefore the impact of these financing vehicles can be characterised as low due to the long lead times and technology development cycles that are acceptable or expected.

At the other end of the spectrum from angels and venture capital firms are the institutional public investors who have relatively shorter investment time horizons. Institutional public investors can have anywhere from a 6-month to 3-year time horizon for their investments depending on market and industry dynamics. Consequently, they look to invest in companies where technology development is near complete or ready for commercialisation, or where technology development cycles are relatively short, in order to more rapidly realise returns. This explains in part why biotechnology companies with advanced-stage drugs (e.g., phase 3 drug candidates nearing FDA review and less than two-years from commercial launch) see more success in IPOs and stronger stock price performance, than companies in earlier stages of drug development. Moreover, the investment horizon for institutional public investors – and therefore expectations for speed of technology development and investment returns – continues to shorten for several reasons:

- more institutional funds themselves are publicly traded entities and therefore need to demonstrate quarterly and semi-annual returns in order to retain and attract their own investors and limited partners
- the growth in global liquidity and availability of investment-grade options means institutional funds must compete more to attract investors and therefore have less leverage to set long lock up periods for their limited partners and investors
- the emergence of institutional hedge funds, which are growing as a source of public funding for higher risk (and by implication, high reward) life science and biotechnology companies, also require shorter payback horizons and therefore will demand more rapid technology development from the companies in which they invest.

Between the spectrum of venture capital firms and institutional public investors are Corporate Venture Capital (CVC) investors, project financing, and structured finance investors. These investment vehicles are typically designed to finance technologies in mid-stage development (also called ‘bridge’ investments, or investments that bridge a technology from concept to commercial). These financing vehicles are structured to reward the achievement of a specific set of technological- and development-based milestones, which creates incentives for entrepreneurial companies to more rapidly complete technology development to meet these requirements. These financing vehicles can be characterised as having medium impact because their requirements for speed of technology development are shorter than venture capital or angels but longer than institutional public investors.

4.2 Control of direction

Most financing vehicles for entrepreneurial firms demand a high degree of control, therefore significantly impacting the direction of technology development. Interviews indicate that control can take several forms, for example:

- formal positions on the company's Board of Trustees
- financings based on technological and business development milestones that can also be used to determine compensation for entrepreneurs and executives
- retaining the option to replace existing management teams with their own entrepreneurs if specific milestones are not met, and/or
- in joint venture or alliance situations, a joint governance committee may be put in place to drive technology development to ensure mutually beneficial outcomes.

Each of the financing vehicles exercises varying degrees of control using the methods outlined above.

According to interviews, institutional venture capital firms exert the highest level of control over technology development. This should come as no surprise because, according to an investment banker,

“VCs encounter the triple threat of risk-reward-liquidity in a company's financing lifecycle. VCs invest the largest up-front dollars in unproven companies at a time when the underlying technology is often no more than a concept, sometimes even before a target market or commercial use has been identified, and usually several years away from any exit or foreseeable liquidity event ... such as an IPO or sale of the company. VCs mitigate risk by investing behind talented management teams and by playing active Board roles in their companies. And, more often than not, [VCs] will step in as the interim CEO of a portfolio company if [this is] required to right a sinking ship.”

Venture capital firms codify their controlling rights in term sheets – whether for technology development, business development activities, or Board voting rights – as a prerequisite to making the investment. In short, venture capital firms have the most at-stake in development-stage ventures and therefore exert the highest control over technology and corporate development.

After venture capital, in terms of impacting technology development, project financing and structured financing arrangements, exert the next highest level of influence. These financing vehicles are structured to achieve a specific set of mutually beneficial or pre-set objectives, often financed through milestone-based arrangements. Accordingly, the entrepreneurial firm is contractually bound to use the financing proceeds for project-based objectives or to meet specific milestones. For example, US Genomics is an early-stage biodefense company that is developing a novel genomics-based test system to rapidly detect hostile airborne microbes, bacteria or other biological weapons for terrorism. Since 2003, US Genomics has received project financing from the US Federal Government DARPA project under the Department of Defense to develop a system that can be placed in airports, train stations, office buildings or other public venues worldwide to provide instantaneous detection of biological terrorism agents. Although US Genomics's technology has other highly promising applications potentially in molecular diagnostics, hospital-based infection detection, epidemic detection, etc., the DARPA financing limits the range of technology development to focus on biodefense, with other applications to be pursued opportunistically with alternative funding.

Alliances, joint ventures and licensing partnerships, which can also be extended to include CVC, play a role in direction of technology development, however, these investment vehicles are more flexible than project and structured financing approaches. Alliances, joint ventures and licensing agreements are typically structured and led by joint committees composed of the relevant parties, while CVCs are setup with periodic committee-based reviews, which collectively are responsible for ensuring that technology development is consistent with the objectives of the partnership. In biotechnology, these financing vehicles are frequently structured on a non-exclusive basis that does not restrict the entrepreneurial firm from pursuing additional or alternative avenues of technology development without consequence to the joint financing arrangements.

Reverse mergers, which can result from alliances or licensing partnerships, can similarly have medium to high impact on the direction of technology development. According to interviews with investment bankers, reverse mergers are usually backed by a small group of new investors who provide a private company with access to additional capital as a public company, provide prior investors liquidity (opportunity to sell their shares to new investors), and also enhance visibility as the company will trade on the public markets. However, as one investment banker described,

“There is substantial risk in a reverse merger or SPAC to the group of new investors: first, since the company became public through a reverse merger instead of an IPO underwritten by investment banks, the company is less likely to have institutional or trading support as a public entity; second, in a traditional IPO, the company will receive attention and coverage from equity research analysts who provide valuable visibility for the company with a broader group of institutional investors – that rarely happens in reverse mergers; third, the small group of new investors may be left holding all the shares of the new public company without the liquidity to exit at some future time – this is not the case with a typical public investment.”

Consequently, the Boards of reverse merger companies are composed of the members of the new investment group. Through their Board roles, the investment groups can influence the direction of technology development, choice of target markets, and deployment of company resources.

By contrast, in an IPO the most likely investors (composed of institutional public investors) have limited to no involvement in setting the direction of technology development. In interviews with institutional public investors, it appears their focus and capabilities are best suited to conducting analysis into companies and markets to select the best investments. Institutional public investors are not equipped with the expertise to set the direction of technology development. As one investor described,

“[We] almost never – and in fact prefer not to – have formal positions or influence on company Boards. In addition to all the regulatory and compliance issues relating to the [Securities and Exchange Commission], setting strategic direction within our target companies is simply not what we do best.”

Institutional public investors prefer to evaluate among companies, an approach that does not lend itself well to investing the time to influence a particular company or technology’s direction of development. Consequently, institutional public investors have little to no role in impacting a company’s technology development strategy.

Finally, angels have the absolute lowest level of control in determining the direction of technology development. This appears largely due to the fact that angels finance based on individual relationships often with entrepreneurs who are identifiably within a defined network of their acquaintances. Angels appear to place substantial faith in the founding entrepreneur or team to set the direction and course of technology development.

4.3 Degree of technological risk

One of the central rules of investing is said to be “buy low, sell high”. However, more sophisticated investors believe this tenet to be incomplete because it suggests a desired performance outcome, not a decision criterion. The decision criteria that lead to successful investment outcomes are more often a function of those factors that maximise reward while minimising risk. The risk-reward decision is critical and unique to each financing vehicle, and appears to be reflected in the degree of technological risk that investors are willing to accept.

As interviewees described, angels and venture capital firms are at the highest point of the risk-reward tradeoff. These investors accept a very high degree of technological, market and business risk across many investments in exchange for the potential to achieve extraordinary returns on a very small number of investments. Therefore, angels and venture capital firms often encourage companies to pursue high levels of technological risk in order to enhance the likelihood of a breakthrough discovery, game-changing innovation, etc. In biotechnology, angels and venture capital firms are the primary and nearly exclusive backers of the highest risk technology opportunities, for example, companies pursuing novel and unprecedented drug targets. Sirtris is such an example. Sirtris was founded in 2004 following the discovery at M.I.T. and Harvard of sirtuins – a family of biological molecules that control aging and metabolism and are naturally occurring within mammalian physiology. At the time, the science of sirtuins was in a highly nascent state, wholly unproven yet seductively promising, as early preclinical testing showed that regulation of sirtuin genes resulted in rats living 20–30% longer lives with 40–70% enhanced metabolism (on par with marathon runners). The implications for human longevity and metabolism were staggering. As one interviewee explained, “this is the pharmaceutical equivalent of the fountain of youth!” The publication of these early results led to a flood of financing interest in Sirtris, which in 2004 received a seed investment from M.I.T. and in 2005 closed its first institutional venture funding round. Between 2005–2006, Sirtris raised \$120 million in venture funding – one of the most heavily and fastest financed private companies in the history of biotechnology – from well-known venture funds including Polaris, Skyline, Bessemer, TVM, Three Arch, and Cargill (Interestingly, Sirtris attracted corporate venture funding from Genzyme, Novartis, and GlaxoSmithKline, all vying for the option to license future sirtuin drugs from the company). With a substantial funding base secured, Sirtris was able to take significantly greater technological risk in sirtuin discovery by simultaneously advancing several drug programs into human clinical trials in 2007. In early 2008, Sirtris agreed to be acquired by GlaxoSmithKline for \$720 million. Sirtris’s rapid technological progress was underpinned by the high risk-high reward opportunity that angels and venture capital firms were uniquely positioned to support.

Outside of funding by angels and venture capital firms, most financing vehicles seek out lower risk technologies and more predictable investments. For example, interviews indicate that most CVCs, project financing and structured financing vehicles prefer technologies that have achieved an acceptable level of validation or proof-of-concept (defined in the biotechnology industry as achieving phase 2a – i.e., the drug is proven safe and generally effective in humans). CVCs, project financing and structured financing can be characterised as having a medium or moderate impact on technological risk. (The investments into Sirtris by Genzyme, Novartis and GlaxoSmithKline appear to be an aberration rather than the norm, as biotech and pharma CVCs seem to prefer funding programs once the technology risk is largely wrung out.) Companies generally advance their drug programs into later-stage clinical trials prior to seeking funding from CVCs, project financing or structured financing vehicles. “[This approach] serves the dual purpose of providing the company maximum leverage in retaining better economics in either a financing or licensing transaction”, according to an interviewee.

In contrast, among all the financing vehicles and investor types, institutional public investors appear to exhibit the lowest appetite for technological risk. At the stage when entrepreneurial companies need to make the most significant decisions regarding technological development risk, institutional public investors are largely irrelevant as a financing vehicle due to their risk profile. Because of this investment stage mismatch, institutional public investors have the lowest impact on the degree of technological risk decision by entrepreneurial companies. In interviews with institutional public investors, there was a clear consensus that they would willingly take on market risk or business execution risk. As one investor described, “... both [market and execution] risks can be diligenced” and is “strongly preferred to taking on any real technological risk”. Companies looking to secure funding from institutional public investors will thus need to be at a near-commercial or revenue-generating stage (with a defined path to cash flows) where technological risk is largely mitigated. This conversely could explain why, for example, there are a very small number of pre-revenue medical device companies that have successfully completed IPOs (Dexcom, Northstar, Hansen, and Enteromedics) on the US Nasdaq market in the last five years.

4.4 Focus on capability development

Thus far, this discussion highlights that the impact of financing vehicles on technology development is strongly biased to favour investors’ objectives. Or, said another way, the focus has been on the impact of technology development *only* insofar as it serves the objectives or constraints of the financing vehicle or investors. For example, first we focused on the urgency or speed of technology development to reflect the holding period or investment horizon of the financing vehicle or investor (i.e., speed to market). Second, we focused on the control exerted on technology development by investors such that it meets their objectives for future liquidity (i.e., control of direction). And third, we focused on how investors’ decision criteria for technological risk in investments are largely a function of their intrinsic risk-reward appetite (i.e., degree of technological risk).

A fourth consideration is the focus on capability development. Capability development is a strategic contribution that importantly refocuses the discussion from investors’ objectives and financing vehicles to more squarely on the best long-term impact on technology development for the firm. Building capabilities goes beyond

the pure capital or financing contributions that any investor or financing vehicle can provide. Consequently, the relative priority and contributions of each type of financing vehicle to technological capability development merits further exploration.

For similar reasons outlined in the “Control of Direction” section, venture capital firms have the highest impact on technological capability development. Several elements are core to the life sciences venture capital model beyond the financing, specifically VCs provide entrepreneurial companies with: access to talented management teams and technical entrepreneurs; technology acquisition, licensing and regulatory expertise; technology development and management tools; access to potential technological partnerships or key customer trial opportunities; technology infrastructure including access to resources; and smart entrepreneurial business sense to translate the technology into commercial value. As one seasoned entrepreneur described,

“The best VC funds like Polaris, Frazier, MPM, Domain, Versant – they all have reputations for building market leading companies with world class management teams. There is a rigorous focus on building real and lasting capabilities within the company backed by a winning culture. This is true of all the best VCs and their best portfolio companies.”

That VCs place great emphasis on capability development is reinforced by the experience and background of most VC partnerships. It appears that most VC partnerships feature a complementary mix of industry veterans with significant operating experience, proven technological entrepreneurs, savvy finance experts, as well as external network of experts to provide cutting-edge technological expertise. This combination of people and technical know-how ensures that venture capital firms have the highest and most significant strategic contribution to entrepreneurial firm capabilities.

At the other end of the spectrum, angels and institutional public investors have possibly the least meaningful impact on capabilities for technology development. As discussed in the “Control of Direction” section, angels are largely composed of investors who rely on the entrepreneur for direction and execution, provide little monitoring or support outside the financing, and are relatively autonomous and hands-off in governance (for example, angels rarely take Board positions).

Meanwhile, institutional public investors seem to be both structurally and practically constrained from strategic contributions to technological capability development. Increasingly, financial market authorities such as the Securities and Exchange Commission (SEC) regulate the depth and nature of interactions between companies and public investors – for example, through Regulation Full Disclosure (‘RFD’) which requires that a company executive can only share publicly available information with any external constituent or investor; if a company executive shares any non-public information, that immediately is considered grounds for future insider trading litigation, unless the executive immediately files a full disclosure statement with the SEC that makes the information publicly available to all investors and constituents. In addition, institutional public investors are practically constrained from contributing to firm capabilities because this is not their core competency nor are these types of long-term investments justified given the relatively shorter investment horizons for these financing vehicles. The only exception is the recent emergence of ‘crossover’ investors, i.e., institutional public investors who invest in private late-stage technology companies or in IPOs for technology-stage companies, as a passive form of contribution to development of technological capabilities.

Most of the other financing vehicles – such as CVC, project financing, and structured financing – share a variable impact on development of technological capabilities, depending on the specific objectives of the financing vehicle. Alliances and licensing vehicles seem to exhibit a surprisingly limited impact on new capability development. Biotechnology research alliances between startups and big pharma are, according to conventional wisdom, viewed as joint partnerships between large diversified capability-rich corporations and small entrepreneurial resource-poor companies. However, contrary to expectations, biotechnology research alliances or licensing arrangements may have a low to negative impact on development of new technological capabilities in entrepreneurial firms. Biotechnology firms tend to be built around a specific type of technological knowledge, capabilities or know-how, which is lacking within large pharmaceutical companies (large pharma specialise in clinical drug development, regulatory and commercial expertise). This explains, in part, why

“the top ten pharmaceutical companies have spent more than \$60 billion cumulatively from 2003–2006 buying biotechnology companies for their early-stage drug candidates, knowledge and capabilities,”

according to an industry executive. The biotechnology licensing market is also quite significant: as one investor pointed out, “nearly 60% of blockbuster drugs [defined as global sales greater than \$1 billion] marketed globally today were in-licensed by big pharma from early-stage biotechs”. Large pharmaceutical companies license a specific product or technology from a biotechnology firm (with up-front payments and defined future milestone payments) and effectively take over the development and regulatory approval of the drug. Licensing as a financing vehicle detracts from entrepreneurial firm capability development because the firm does not build later-stage drug development, regulatory and commercial capabilities; and in most cases, the large pharmaceutical company has no future or trailing requirements to continue to build or enhance the technological capabilities of the entrepreneurial biotechnology firm.

Reverse mergers and SPACs have been cited by the cynical investor as a poor outcome for a private entrepreneurial firm because of the lack of capability development following the successful consummation of the financing. This view may still be applicable to traditional reverse mergers where a single management team is formed and assets of the combined businesses are merged. However, heightened investors’ requirements for payback from reverse mergers demand that companies rapidly drive technological and commercial synergies, often requiring a strong focus on capability development. The view of SPACs as narrow financing vehicles is rapidly changing as well. SPACs today appear to be increasingly attracting seasoned Boards composed of technology experts, industry veterans, and savvy financiers – more closely resembling venture capital partnerships. Moreover, SPACs place emphasis on retaining management teams and executives in the acquired business in order to ensure continued development of capabilities and continuity. Although general awareness and knowledge of SPACs seems to remain low, these combined factors increasingly make SPACs a valuable financing and strategic vehicle for developing capabilities for greater technological impact.

Table 2 summarises the discussion from this section by outlining the full range of financing vehicles according to their level of impact on technology development.

Table 2 Technology development matrix

		<i>Impact on technology development</i>		
<i>Financing vehicle</i>	<i>Speed to market</i>	<i>Control of direction (market/application and novelty)</i>	<i>Degree of technological risk</i>	<i>Focus on capability development</i>
Seed capital	Low Willing to tolerate long development cycles	Low Autonomy given largely to founding team and entrepreneurs	High Invest without expectation of immediate returns (high risk portfolio)	Low Reliance on entrepreneurs; no mentoring, autonomous governance
Institutional funding – VCs	Low – Medium Focus to invest and grow early-stage firms and technologies	High Active role in technology and market development; typically take Board positions	High Incubate early technologies prior to value inflection or proof of concept	High Priority given to building world-class teams and companies for value creation
Institutional funding – public investors	High Cash-flow driven results; seek value inflection and liquidity	Low to None Investments made on technology merits; no impact on direction aside from shareholder votes	Low Prefer targets with minimal technology risk and maximum market upside	Low to None Not the business model; holding periods typically do not justify long-term investment
Project financing	Medium Focus on major milestone achievement	High Funds earmarked for specific project purposes with defined outcomes	Medium Varies by nature of technology and project	Medium Focus on building capabilities if it achieves goals
CVC	Medium Longer holding period enables focus on technology development	Medium to High Influencing technology assets to reflect strategic priorities of the corporation	Medium Priority given to technology development over payback horizon	Medium Varies by CVC; more focus on capability development in strategic assets
Alliances/ Licensing	High Earn-outs drive demand for rapid investment returns	Medium to High Control preference given structure of technological milestones for royalty payments	Medium Prefer minimal technology risk	Low Focus insofar as affects value of underlying licensed assets
Reverse mergers – traditional	High Demand from investors creates impetus to generate rapid returns	Medium to High Active control by board and management but limited flexibility as a public entity	Low Favour commercial cash-flow generating assets with minimal risk	Medium Varies by goal and technology/market needs of the combined entity
Reverse mergers – SPACs	High Earn-outs and expectations drive demand for fast returns	Medium to High Capital managed by board with varying level of influence on technology development	Low Prefer to trade off technology risk for management execution risk	High Retain business teams and management to retain and grow internal business capabilities

Table 2 Technology development matrix (continued)

<i>Impact on technology development</i>				
<i>Financing vehicle</i>	<i>Speed to market</i>	<i>Control of direction (market/application and novelty)</i>	<i>Degree of technological risk</i>	<i>Focus on capability development</i>
Structured financing	Medium	High	Medium	Medium to High
	Medium term time frame for investment returns	Creative joint-venture structure for mutually beneficial results	Technology risk mitigated by high control requirements	Focus on building the combined entity and drive capabilities
IPO	Medium	Low	Low	Medium
	Growing appetite for pre-revenue companies	Investments made on technology merits; no impact on direction	Cheapest source of capital; public investors prefer lower risk	Focus on capabilities insofar as it enhances R&D or technology development

5 Discussion

The key insight that arises from this research is that “one size does not fit all”. The choice and availability of financing vehicle needs to be matched to ensure the desired outcome for both the entrepreneurial firm and the investor. If, as this research suggests, financing is an under-appreciated factor in determining the course of technology development, entrepreneurial firms may benefit from a broader review of available financing vehicles, particularly as the landscape for financing options continues to evolve, for example, with the emergence of CVCs, SPACs, as well as structured and project financing in the last five years.

Several normative insights with regard to the impact of alternative financing vehicles on technology development can be drawn from research and interviews with biotechnology investors, investment bankers and industry executives. Perhaps not surprisingly, it appears that seed- and development-stage firms should continue to seek out angels and venture capital firms, respectively, as their primary source of financing. Venture capital firms provide not only initial financing, but also capabilities for technology development, a valuable external network of experts and customers, access to management teams, coupled with a long-term investment horizon to adequately develop and mature technologies. The only trade-off it appears is the demand for greater control and ownership that venture capital firms bring.

For mezzanine and maturity-stage biotechnology companies, the range of available investor choices has expanded beyond traditional venture capital and institutional public investors in recent years. Biotechnology firms can now tap CVC, project financing and structured financing vehicles, potential alliances or licensing arrangements, or reverse mergers into SPACs or other public entities. In addition, institutional public investors are increasingly exploring cross-over investments into mezzanine-stage private companies with mitigated technology risk. Several of these financing vehicles such as project financing and structured financing, as well as SPACs, seem to be gaining visibility and popularity with private biotechnology companies. These financing vehicles, if structured appropriately, can provide a primary or secondary source of financing to drive technology development and build capabilities that are consistent

with the long-term interests of the firm. Finally, it appears there will be an ongoing role for institutional public investors in biotechnology as they provide the cheapest source of capital. However, firms need to be cognizant of the potential tradeoffs associated with relatively shorter holding periods and investment horizons, wariness toward technology development risk, and ambivalence toward capability development.

This discussion of financing vehicles for the firm would be incomplete without considering the socially responsible role of investors in building biotechnology firms. Interviews suggest that investors need to look beyond profits to long-term technology development and value creation. The financing of entrepreneurial life science companies – where the next generation of therapeutic drugs, devices, tools and diagnostics for curing human disease are being made – is ultimately a ‘public goods’ problem as these companies’ products provide social benefits. Policymakers, regulators, government agencies such as the FDA, academic universities and their affiliated entrepreneurial engines (e.g., licensing offices, etc.), as well as the international community, must be cognizant of these changes to anticipate the business, scientific and social consequences of these ventures.

6 Conclusion

In conclusion, financing looks to be more than a resource; it emerges as a tool of evolution. Financing seemingly determines long-term firm and technology development, especially when concerning biotechnology start-ups. In-depth interviews with industry players, in a grounded theory investigation, indicated four main alternatives for investor sources: angels, venture capital firms, corporate investors, and institutional public investors. Each of these investors utilises different financing vehicles at different stages of the firm. There are roughly four stages of the firm: seed stage, development stage, mezzanine stage, and maturity stage. There seem to be eight key financing vehicles employed that affect technology development: seed capital, institutional funding, project financing, Corporate Venture Capital (CVC), alliances/licensing, Mergers and Acquisitions (M&A), structured financing and Initial Public Offerings (IPO). Each of the eight financing vehicles either has a low, medium or high impact on speed to market, control of direction, degree of technological risk taken, and focus on capability development for future success. These findings have implications for entrepreneurs, investors, strategic entities including potential MNC acquirers, and governmental agencies.

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Note

¹United Nations Convention on Biological Diversity as found on Wikipedia.