Trends in Mid-Stage Biotech Financing

Independent Study – Winter 2011

Michael D. Hamilton

Tuck School of Business at Dartmouth
# Table of Contents

List of Abbreviations ........................................................................................................ 2

Introduction ...................................................................................................................... 3

Mid-Stage Biotech Financing .......................................................................................... 4
  Sources of Mid-Stage Development Capital ................................................................. 5

Recent Challenges to Mid-Stage Biotech Financing ...................................................... 6
  The Financial Market Crisis of 2008 ............................................................................. 6
  Failed Models .................................................................................................................. 7
  Increased Investment Risk .............................................................................................. 8

The Capital Markets Respond ......................................................................................... 9
  Venture Capital .............................................................................................................. 9
  Private Equity ............................................................................................................... 11
  Investment Banks ......................................................................................................... 12
  Established Biopharmaceutical Companies ................................................................. 13

Analysis and Critique ..................................................................................................... 15

Conclusion ....................................................................................................................... 18
## List of Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRO</td>
<td>Contract Research Organization</td>
</tr>
<tr>
<td>CVC</td>
<td>Corporate Venture Capital</td>
</tr>
<tr>
<td>IPO</td>
<td>Initial Public Offering</td>
</tr>
<tr>
<td>LP</td>
<td>Limited Partner</td>
</tr>
<tr>
<td>M&amp;A</td>
<td>Merger and Acquisition</td>
</tr>
<tr>
<td>PIPE</td>
<td>Private Investment in Public Equity</td>
</tr>
<tr>
<td>PE</td>
<td>Private Equity</td>
</tr>
<tr>
<td>POC</td>
<td>Proof Of Concept (Phase IIa clinical trials)</td>
</tr>
<tr>
<td>RDO</td>
<td>Registered Direct Offering</td>
</tr>
<tr>
<td>VC</td>
<td>Venture Capital</td>
</tr>
</tbody>
</table>
Introduction

The success of small, independent biotech companies is dependent upon outside sources of capital to fund the long and costly process of bringing a new drug to market. Over the last decade, factors both internal and external to the industry have had a large impact on the availability of capital, particularly for those biotechs with candidates in the mid-stage of drug development.

This paper is divided into three sections. The first section examines the current state of mid-stage biotech financing and the factors that have led to the current financing environment. The second section highlights how venture capital firms, private equity groups, investment banks and established biopharmaceutical companies have adapted their investment strategies in light of these factors and finally, the third section analyzes the implications of these strategies and how mid-stage biotech financing may evolve in the future.
Mid-Stage Biotech Financing

The biotech industry has seen incredible growth over the last 30 years despite the large capital requirements, lengthy timelines and high risk associated with drug development.¹ For mature firms, R&D is financed using reinvested profits in the hope of producing new products and continued revenue growth in the future. However, for small, independent biotech companies² with no marketed products, the only option is to fund R&D using external sources of capital.

Although capital is difficult to come by for any small biotech, firms with drugs in the “mid-stage” of development have a particularly difficult time raising funds. The mid-stage of drug development typically refers to phase II clinical trials; however, late phase I or early phase III clinical trials are sometimes also included (Figure 1). The mid-stage of drug development is a particularly challenging time to raise capital as there is minimal clinical data, yet mid-stage trials require large amounts of capital and have relatively high attrition rates. For an investor, this is not an attractive combination. However, if a drug successfully completes mid-stage trials, its value greatly increases, opening up the possibility of an acquisition or IPO and a handsome return for investors. This combination of high risk and high reward is enough to convince many in the capital markets to fund promising, mid-stage biotech companies.

Figure 1: Hypothetical Drug Development Valuations³

---

² Although the term “biotech company” usually refers to a small firm whose goal is the development of new protein-based drugs, this paper will use the broader definition to include those firms developing any new drug, be it a biologic or small-molecule.
³ Valuation estimates were taken from: Christoffersen, R., “Biobootcamp 2009”, April 2009
Sources of Mid-Stage Development Capital

Although there are many providers of capital for mid-stage biotech companies, this paper will focus on the four major sources. Table 1 includes a list of these sources of capital along with the typical funding structures offered. It is important to note however, that not all of these funding structures are available to all biotech companies. The financial state of the company and/or market conditions will often make certain structures unavailable or highly unattractive.

<table>
<thead>
<tr>
<th>Source of Capital</th>
<th>Typical Funding Structure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Venture Capital</td>
<td>Equity Investment</td>
</tr>
<tr>
<td></td>
<td>Venture Debt</td>
</tr>
<tr>
<td>Private Equity*</td>
<td>Equity Investment</td>
</tr>
<tr>
<td></td>
<td>Project Financing</td>
</tr>
<tr>
<td></td>
<td>Milestone Monetization</td>
</tr>
<tr>
<td>Investment Banks</td>
<td>Initial Public Offerings (IPOs)</td>
</tr>
<tr>
<td></td>
<td>Follow-on Offerings</td>
</tr>
<tr>
<td></td>
<td>Registered Direct Offerings (RDOs)</td>
</tr>
<tr>
<td>Established Biopharma Companies</td>
<td>Equity Investment</td>
</tr>
<tr>
<td></td>
<td>In-Licensing/Co-Development</td>
</tr>
</tbody>
</table>

*For the purposes of this paper, “private equity” refers to all “non-venture capital” private equity

Table 1: Sources of Capital and Typical Funding Structures

Over the last decade the capital markets have undergone many changes that have made it increasingly challenging for biotechs to raise capital. This paper is not an exhaustive examination of all the changes that have occurred, but rather, will highlight those changes that have had, or are having, the greatest impact on mid-stage biotech financing. Many of these changes have been driven by factors both internal and external to the biotech industry. The following section will discuss some of these factors and how they have impacted the funding landscape.
Recent Challenges to Mid-Stage Biotech Financing

The Financial Market Crisis of 2008

The collapse of the US financial system in late 2008 had wide reaching impact on the economy as a whole, but it also had specific consequences for biotech companies in need of mid-stage capital.

A Source of Capital Dries Up

Venture capital and private equity (VC/PE) groups who invest in biotech companies obtain their capital from what are called “limited partners”: pension funds, college endowments and other institutions with large pools of capital and a need for diversified investment options. As a result of the financial market crisis many of these limited partners were unable to meet their capital calls or chose to liquidate their investments in order to meet investment allocation targets or short-term cash flow needs. For those VC/PE firms looking to raise new capital, many limited partners who had invested heavily in the past, stopped investing in VC/PE entirely.\(^4\) This forced many VC/PE firms to scale-back current investments and many have capped new funds at below target levels.\(^5\) This has trickled down to mid-stage biotech firms who are now either unable to raise money from VC/PE firms or, of those who have already received funding, have been told to delay further capital requirements for as long as possible.\(^6\)

Depressed Public Equity Valuations

Ever since the biotech bubble burst in the early 2000s, many investors have shied away from public biotech equity due to the high volatility and the spectacular failures of what were once promising companies.\(^7\) The financial crisis only made the situation worse, pushing valuations of public biotech companies to historic lows. These low valuations eventually led to the “closing” of the IPO market in 2008 and since reopening in 2009, IPOs have regularly failed to achieve target prices.\(^8\) Figure 2 summarizes the subsequent returns generated by the most recent US biotech IPOs since the market reopened, with 68% of the companies’ share prices below the IPO price. It should be noted that of the IPOs with the most impressive post-IPO returns, Zogenix (ZGNX) has already received FDA approval for its lead product and AVEO Pharmaceuticals (AVEO) is in late phase III development.

The impact of these low valuations is twofold: first, mid-stage biotech companies who wish to raise capital through either an IPO or a follow-on offering are only able to do so through highly dilutive offerings. Second, VC/PE firms who count on IPOs as an exit strategy are unable to realize acceptable returns in the public markets and are left with one less exit option.

\(^4\) Morrison, C., “For Funds Close to Empty, Filling Stations May Be Hard to Find”, Start-Up, Sept. 2009
\(^5\) Bonanos, P., “As Some VCs Run On Empty, Other Are Topping Off The Tank”, Start-Up, July 2010
Failed Models

**Biotech Venture Capital**

Beyond the fund raising and public equity market challenges discussed previously, the biotech VC industry is facing the much greater problem of a loss of confidence by limited partners that investing in biotech VC will generate the returns promised. Although very large returns were realized at the height of the biotech bubble, many of the VC investments made since have failed to produce the lofty returns many investors believed they would. Figure 3 shows the trend of decreasing returns for biopharmaceutical VC investments since early 2000.

---

9 BIO, Factset, Jan 3, 2011
Biopharmaceutical Research and Development

Despite an ever increasing investment in R&D by the large biopharmaceutical companies, there have been a dwindling number of new drugs coming to market. In 2009, only 26 new drugs were approved, down 54 percent from 1996, one of the highest years on record (Figure 4). This has left the large biopharmaceutical companies in a precarious position. How will they continue to grow earnings? One way is through the acquisition or in-licensing of promising new drugs being developed by small biotech companies. The large biopharmaceutical companies are also in a cash-rich position due to existing revenue streams from blockbusters that have yet to reach the end of their patent life. This has created a unique environment where these companies have both the need and the means to increase their levels of deal-making to boost their pipelines.

**Figure 4: US Drug Approvals 1996 - 2009**

Increased Investment Risk

In the past, the biggest risk of investing in a mid-stage biotech company was the clinical risk: could the drug be proven safe and effective? If so, FDA approval was likely as the regulatory body had reasonably predictable standards for approval. However, as a result of a number of highly publicized and embarrassing recalls of drugs already approved by the FDA (Vioxx and Baycol being two of the most notorious) the FDA has further increased its scrutiny of new drugs up for approval.\(^\text{12}\) The two major consequences of this increased scrutiny are: one, acquiring enough safety and efficacy data to satisfy the FDA has increased the cost of development and two, there is an increased level of uncertainty as to whether the clinical data that is generated will be enough to satisfy the FDA. This increase in both development costs and regulatory risk has placed an even higher hurdle to new drug approval.

---

\(^{10}\) PricewaterhouseCoopers/National Venture Capital Association MoneyTree™ Report, Data: Thomson Reuters (Jan 2011)

\(^{11}\) “Filling The Gap Between Academic Discovery and Commercial Licensing: The Role of Novel Financing and Development Structures”, Frankel Group presentation at Rutgers, Feb 2010

\(^{12}\) McArdle, M., “No Refills”, The Atlantic, July/Aug 2010
In addition to the regulatory risk posed by the FDA, concerns about high drug prices have led to an increase in reimbursement risk. Even if a drug is approved by the FDA and found to be safe and effective once on the market, third-party payors such Medicare/Medicaid and the private insurers are now demanding increasingly steep discounts and even refusing to reimburse for certain products that they believe provide an unsatisfactory cost to benefit ratio. Although this risk can often be mitigated through careful research and consultation with third-party payors before investing, the risk still remains that a future product may drastically change the reimbursement levels previously agreed to and severely impact revenues and subsequent return on investment.

The Capital Markets Respond

As a result of the changing investment landscape, each of the sources of capital previously described adapted their investment strategies to the new economic realities. This section will examine the most impactful strategic shifts that have occurred. The reader will note that while many of the challenges impacted a specific constituent, the effect rippled throughout the capital markets and caused a number of secondary responses by the other constituents.

Venture Capital

Although investment strategies vary greatly across biotech VC firms, a number of notable shifts have occurred in both what biotech VC firms invest in and how they structure their investments. These changes mainly addressed the key goal of VC firms: to provide generous returns for their limited partners. Three common shifts in strategy were identified: lower risk investments, improved capital efficiency and early exit planning.

A Move to Lower Risk Investments

Many VC firms have changed their investment strategy to focus on what are generally regarded as lower risk investments. The most direct way to reduce risk is to invest in later development stages and avoid the highly risky pre-clinical to phase II stages. This shift of investment dollars was particularly evident in the post-financial crisis environment. Late-stage investments not only have less overall risk, they are also more attractive acquisition targets for the large biopharmaceutical firms, making an exit more accessible. This is especially true in 2011, as many large biopharmaceutical companies are aggressively searching for products that are close to entering the market and have the ability to fill the near-term revenue shortfalls caused by patent expiration.

Another method VC firms have used to reduce risk is to invest in biotechs that are targeting therapeutic areas that have inherently lower clinical and reimbursement risk. For example, a drug used to treat an orphan disease which has no currently available treatment options will often be held to lower safety and efficacy standards by the FDA, due to the high unmet need. In addition, the small patient population

---

often leads to fewer reimbursement issues, as with even very expensive therapies the total cost for third party payors is only a small percentage of overall drug expenditures.

It should be noted that many VC firms have resisted this trend and continue to invest in innovative, high risk technology that has a large upside, the so-called “game changers”. Versant Ventures, Third Rock Ventures and Polaris Ventures all subscribe to this strategy and believe that if they invest in the right technology, the returns will justify the risk.16

**Improved Capital Efficiency**

The cash crunch that many VC firms face and their goal of improving returns have led many to focus on maximizing the capital efficiency of investments. Two emerging trends in this area are the “virtual biotech” model and the “lean proof-of-concept (POC)” model, both of which have attracted serious attention from the VC community.

The virtual biotech model is not a new idea, but it has become much more popular as those investing in drug development attempt to reduce costs. At the heart of the model is the management team: a group of seasoned industry veterans who have both the in-depth knowledge and real-world experience required to rapidly advance a drug through the development process. This group coordinates all development activities which are, for the most part, out-sourced to CRO firms who perform the actual studies.17 The benefit of this model is that the infrastructure typically required for a biotech: scientists, equipment and laboratory space, is minimized. The end result is that a promising candidate can be taken through the POC stage, where failure is most likely to occur, with minimal capital costs. Only after the necessary data has been acquired and the candidate is deemed to be worthy of continued development are larger capital investments made.

The second model, lean POC, was originally born out of the large biopharmaceutical companies’ desire to reduce development costs by performing only the key studies that help inform the go/no-go decision. If those studies return positive data, then a more robust development program is undertaken. Although many biopharmaceutical companies have adopted various aspects of the lean POC model, Lilly went so far as to form a separate unit named “Chorus” which successfully reduced time to POC by 18 months and reduced cost to POC by $20M, compared to the industry standard.18 This was enough for Versant Ventures to back Flexion, a start-up formed by the former Lilly scientists who headed Chorus. The $3M unsyndicated seed round was followed up by $33M Series A round that included Versant Ventures and two other VC firms.19

**Early Exit Planning**

As a result of the closure of the IPO market and its subsequent anemic return, VC firms have increased their focus on formulating an exit strategy before they invest. According to one VC principal, in the past,  

---


exit planning was only given a moderate amount of thought prior to an investment. Now, with IPOs still a mostly inaccessible exit option, VC firms are now taking specific steps to improve the likelihood of an exit by acquisition. New investments are now increasingly focused on biotechs developing products for diseases that fall within the established biopharmaceutical companies’ portfolio strategies. In addition, many VC firms are taking a greater interest in the development plans of the biotech they invest in, with the goal of generating a product profile that will attract potential acquirers. Going even further, some VC firms are partnering with large biopharmaceutical companies so as to receive guidance on how to design critical development stage studies.20

**Private Equity**

Non-venture capital private equity firms typically invest in mid-stage biotech companies using specific financing structures that mesh well with the level of risk. The major trend for PE firms investing in biotech has been an increased focus on providing capital in the form of project financing and revenue interest financing.

**Project Financing**

Project financing provides a unique source of non-dilutive capital for mid-stage biotechs, with the most visible firm in this space being Symphony Capital. The deal structure works as follows: Symphony Capital purchases the rights to one or more candidates in phase I development from a biotech, forms a joint venture company around the assets and then hires the biotech to conduct the phase II studies with varying degrees of assistance from both Symphony Capital’s advisors and its CRO partner, RRD International.21 Upon successful completion of phase II clinical trials, the biotech then has the option to re-acquire the candidates at a pre-determined IRR. The key to Symphony Capital’s model is that by producing positive phase II clinical trial data, the joint venture has now reached a major value inflection point and the biotech should be able to raise sufficient capital on the public markets to repurchase the asset.

The most successful application of Symphony Capital’s model was its deal with ISIS Pharmaceuticals in 2006. The PE firm acquired three phase I clinical candidates from ISIS for $75M and formed the joint venture company Gen Isis to develop them with a guaranteed IRR of 32% for Symphony Capital if ISIS re-acquired the assets. After obtaining positive phase II clinical data, Johnson & Johnson expressed interest in two of the candidates leading ISIS to re-acquire all three for $80M up-front (using cash from J&J) and $40M in stock which provided an overall IRR of 70% for Symphony Capital.22

Not all of Symphony Capital’s investments have produced such stellar returns. The fickle public equity market’s resistance to reward positive phase II clinical trial data in Symphony Capital’s later investments with Alexza, Dynavax, Lexicon and Oxigene, resulted in re-acquisition of the assets by the respective biotech in either stock heavy or all stock transactions.23 This left Symphony Capital unable to return cash to limited partners until such time that the equity positions could be liquidated. However, a

---

22 Osborne, R., “Symphony’s Project Financing Model Adapts”, IN VIVO, Jan 2009
23 Ibid.
partner at major PE firm noted that this equity position has the advantage of providing greater upside if the candidates continue to produce positive clinical data.

An interesting note is that Symphony Capital’s financing structure is not new. In the early 1980’s, the immature biotech industry needed capital to run clinical trials and had difficulty raising it through VC firms or the public markets. A financing structure called R&DLPs (R&D Limited Partnerships) were developed which allowed investors to buy a drug candidate, hire the biotech back to develop it, and if successful, gain financially when the biotech later re-acquire it. Companies such as Genentech, Genzyme and Amgen all utilized these financing structures during their early years. Eventually, these financing structures fell out of favor when the tax code was changed and eliminated the substantial tax benefits to investors.

Revenue Interest Financing

For companies with highly promising products already on the market or in late stages of development, revenue interest financing is an attractive way to raise relatively inexpensive, non-dilutive capital. Revenue interest financing works by turning over future royalty payments (e.g. from a partnership agreement with an establish biopharmaceutical company) or a percentage of future product revenue (a “synthetic royalty”) in exchange for an immediate cash infusion. Most of these investments are in low risk post-phase III or marketed products and as a result, private equity firms such as Paul Capital Partners and Royalty Pharma have produced exceptional returns in past years.

Revenue interest financing is typically not available to biotech companies with only mid-stage assets due to the high clinical and regulatory risk. However, there is a trend by PE firms to invest in assets earlier in the development pipeline. Cowen Healthcare Royalty Partners (CHRP), launched in 2007, has a goal of investing 10% of its funds in assets that are in phase III studies. As the market for revenue interest deals becomes more competitive, it will remain to be seen if this trend towards earlier stage investing continues.

Investment Banks

Health care investment banks offer a variety of financial services to mid-stage biotech companies including assistance with M&A activity, IPOs, follow-on offerings, PIPES, RDOs and private placements. In spite of the weak public equity markets, follow-on offerings have picked up considerable pace with more capital raised in 2009 than in 2006, mainly driven by companies who have reported positive clinical data. Surprisingly, there has not been a large increase in PIPE deals as apparently the low public equity valuations aren’t considered low enough by those with money to invest.

---

24 Morrison, T., “Financing Comes Full Circle; R&DLP Resurgence in Works?”, BioWorld Today, Nov 2010
27 Micklus, A., Morrison, C., “For a Look at IPO Future, Follow the Follow-on?”, Start-Up, Sept 2009
One interesting trend in health care investment banking is the move into the more specialized investment structures that are typically the realm of PE firms, specifically revenue interest financing.

Lowering the Cost of Capital

Vertex entered into an agreement in 2006 with Johnson & Johnson to market their not-yet-approved hepatitis C anti-viral candidate VX-950 (telaprevir). At the time, VX-950 was in phase II trials and the $165M up-front payment helped fund continuing clinical trials that if successful, would garner an additional $380M in milestone payments and a 20% royalty on ex-US and Japanese sales. Three years later, in 2009, with VX-950 in phase III trials and a continuing need for more capital, Vertex entered into an agreement with Morgan Stanley whereby it received $250M through the issuance of a note backed by the J&J milestone payments. If the drug does not reach these milestones, the company is not required to repay the loan.

According to a VP at a major health care investment bank, the move into revenue interest financing came about from the lucrative returns the private equity firms were generating. With health care investment banks moving into the space, the greater competition has driven down the cost of revenue interest financing capital from approximately 30% to 15%.

Established Biopharmaceutical Companies

The established biopharmaceutical firms, with their deep pockets and a need to fill their pipelines, have taken on a greater role in the financing of mid-stage biotech companies. The major strategic shifts noted are an increased focus on corporate venture capital investing and, on the acquisition side, a move towards deals that include earn-outs.

A Growing Role for Corporate Venture Capital

Corporate venture capital (CVC) arms are not new in the biopharmaceutical industry. Johnson & Johnson and GSK established their venture arms in 1976 and 1985, respectively. However, since 2000, a number of new CVC groups have been formed by companies including Genentech (2002), Sanofi Aventis (2004), Biogen Idec (2004), Amgen (2004), Merck (2009) and most recently Boehringer Ingelheim (2010).

Although there hasn’t been a noticeable increase in CVC funding as a percentage of total VC raised by biotechs, there has been an increase in the number of deals. Members of the VC community interviewed for this paper confirmed an increase in deal activity by CVC groups, particularly in earlier stage investments. There is a general belief that CVC groups have been filling in the gap left by traditional VC firms as they move towards later-stage, less-risky investments.

---

30 Hughes, J., “Morgan Stanley Unveils $250M Securitization”, FT.com, July 2009
31 Van Brunt, J., “Corporate VCs Help Lift Young Biotechs”, Signals, Oct 2010
Beyond CVC, an interesting shift in Lilly’s investment strategy has been to take on the roll of an LP and invest directly in outside VC firms. Lilly plans on investing up to $50M (to a maximum of a 19.9% stake to avoid accounting issues) in three separate VC firms who will create a portfolio of early to mid-stage candidates, half coming from Lilly itself. The fund will develop the portfolio and upon achieving positive clinical data, Lilly will have the right to claw-back its own compounds, plus 20% of the non-Lilly candidates (matching its equity stake). Lilly’s strategy mirrors an on-going trend among established biopharmaceutical companies who wish to not only acquire new technology, but to also out-license internal candidates for further development by outside investors.

**Acquisition by Earn-Out**

Due to the weak public equity markets, many investors in mid-stage biotech companies have come to rely on acquisitions by established biopharmaceutical companies to provide an exit for their investments. However, the structure of these acquisitions has been rapidly changing and has had a large impact on the mid-stage biotech financing environment.

Although not a new phenomenon, acquisitions are increasingly structured to include “earn-outs”. Five years ago, acquisitions were typically lump-sum payments made to acquire an entire company including all clinical, regulatory and commercial risk. Now, most deals include a modest up-front payment with the remaining sum contingent on the acquired candidates reaching clinical, regulatory and commercial milestones. Of the 2009 deals where terms were publically available, 75% of the acquisitions included earn-outs. This trend is likely to continue into the future as established biopharmaceutical companies take advantage of the lack of other exits for investors and carefully structure deal terms to avoid taking on a majority of the risk.

---

Analysis and Critique

In light of the challenges described and the response of the providers of capital, this section will attempt to draw conclusions as to how mid-stage biotech financing will evolve in the near-term.

Established Biopharmaceutical Companies to the Rescue?

Despite a lack of R&D productivity and the threat of drastically reduced earnings, the actions of the established biopharmaceutical companies don’t suggest a sense of urgency in financially supporting mid-stage biotechs that one might expect. In a recent article, Kevin Kinsella of Avalon Ventures slammed the established biopharmaceutical companies for their “short-sighted, brass knuckle negotiating tactics” when it came to acquisition deals.36 In addition to bad faith negotiations, Kinsella decried the earn-out structure of acquisitions that offer up-front payments that barely match the capital already invested and the rejection of any risk sharing. A cynic might attribute this behavior to the arrogance of fading giants or a lack of foresight, but the author believes that this behavior is a consequence of the realities facing established biopharmaceutical companies.

It is true that in the world of biotech M&A, it’s a buyer’s market. Largely insulated from the impact of the financial market crisis, large biopharmaceutical companies are in an enviable position with large cash reserves and plentiful short-term revenues to fund acquisitions. Despite their privileged role as the most promising exit option, large biopharmaceutical companies have not dramatically increased their acquisition of the now cheap and desperate biotechs. Why? For two reasons: earnings considerations and a new diversification strategy.

It is true that established biopharmaceutical companies have the cash to take advantage of the bargain-priced biotech companies. However, one must remember that as public companies, earnings are king. When a large biopharmaceutical company acquires a mid-staged biotech that won’t produce any revenue in the short-term, consolidation of the acquired company’s balance sheet has only a negative impact on earnings. With the on-going consolidation of the industry and shrinking sales, any transaction with a negative impact on earnings has to be carefully weighed. Gino Santini, SVP of Corporate Strategy and Business Development at Lilly, was quoted as saying “Our balance sheet money...is readily available given our strong cash position, but our P&L money, where we take on the burn of the biotech and all the development costs, is expensive. So while it seems that these biotechs should now be a lot cheaper to buy, in reality that’s not true.”37 The impact of P&L considerations is also reflected in the increasing trend of established biopharmaceutical companies to out-license internally developed candidates to outside investors for development. These deal structures allow firms to leverage their discovery capabilities, but with minimal impact on earnings as these out-licensing deals are structured to keep the assets off the out-licenser’s balance sheet.

Related to the P&L issue is the current strategy of established biopharmaceutical companies to diversify through the acquisition of businesses such as generics firms in emerging markets.38 These acquisitions are meant to boost earnings, diversify risk and enter new markets, but most importantly they don’t have

36 Bigelow, B.V., “Avalon’s Kinsella Calls Out Big Pharma for “Bad Behavior” That’s Pushing Biotech Ventures Almost to Point of Extinction””, Xconomy.com, Feb 17, 2011
38 Rubenstein, S., “Big Pharma Adds to Generics Medicine Chest”, WSJ Health Blog, May 2009
the same P&L cost as mid-stage biotech acquisitions do. This means that mid-stage biotechs looking to the established biopharmaceutical companies to come to their rescue may be left in the lurch as more attractive acquisition targets take precedence.

**A More Challenging Venture Capital Environment**

Biotech VC firms have had a difficult last few years: returns to limited partners aren’t meeting expectations, raising funds is becoming more difficult and exits are scarce. There are exception of course; in the second half of 2010, Third Rock Ventures and SV Life Sciences each closed funds of $426M and $523M respectively, both over-subscribed.\(^{39,40}\) However, entrepreneur’s changing opinion of VC and the increasing number of academic collaborations being forged by the established biopharmaceutical companies are likely to make biotech VC investing more challenging in the future.

If one speaks with entrepreneurs and reads the biotech industry publications, it is impossible to ignore the growing sense of distrust of VC firms. Despite providing much needed capital, there is a belief that VC money brings problems as well. Daphne Zohar of PureTech Ventures outlined the issues she sees in a recent article: deliberately structuring tranches to avoid paying for value inflection milestones, liquidation preference multiples and VC controlled boards.\(^{41}\) Among the entrepreneurs interviewed, the viewpoint is similar: VC firms must be carefully vetted because if you don’t, you will be taken advantage of. This adversarial relationship has led many biotech firms to seek alternative sources of capital or to structure their company so as to keep the need for VC money to a minimum. One interviewee, a founder of a firm that helps commercialize new technologies, recently shifted strategy and intends to avoid taking VC money if possible and is now focused on partnering with established biopharmaceutical firms early on using licensing deals to support the capital needs of the start-up. This firm is not alone in its approach: Zurich-based HS LifeSciences, who also pursues the VC-less development model, was started by the founders of Neurimmune Therapeutics AG which successfully developed a promising antibody technology without VC money, then immediately partnered with Biogen Idec in a milestone-based deal worth $386M.\(^{42}\) According to Edward Stuart, CEO, the company will “never need equity financing again”.

Another issue that VC firms face is the increase in collaborations between established biopharmaceutical companies and academic institutes. In late 2010, Pfizer announced the first of five planned academic collaborations, valued at $85M, under its Global Centers for Therapeutic Innovation (CTI) strategy.\(^{43}\) Beyond just funding, Pfizer will setup a CTI unit at the UC San Francisco campus that comes equipped with both development technology and Pfizer staff to help utilize it. Milestone payments will help fund academic projects and in return, Pfizer will receive an exclusive option to license the technology.

From the perspective of VC firms, they are being squeezed from both sides. Entrepreneurs are reaching out to large biopharma companies and the large biopharma companies are reaching back. Does this

---

40 McBride, R., “SV Life Sciences Closes $523M Fund”, Xconomy Boston, June 2010
42 Senior, M., “Biotech Models: Bypassing VCs to Deal Direct with Pharma”, Start-Up, Jan 2009
43 Ratner, M., “Pfizer reaches out to academia—again”, Nature Biotechnology, Jan 2011
spell the end of biotech VC as we know it? No. There will always be promising technology that needs capital and VC firms will continue to provide it. However, biotech entrepreneurs are starting to realize that VC is not the only way to raise money. For those VC firms who aren’t willing to work collaboratively with entrepreneurs and focus on developing innovative technologies rather than just a return, the future looks bleak indeed.

New Financing Models Needed

The author believes that the only way to develop an effective mid-stage biotech financing ecosystem is through the introduction of new financing models that address the current realities of drug development. This process has already started with the development of project financing and revenue interest financing, but more work is required. The key issues that need to be addressed going forward are: long-term capital support and appropriate risk sharing.

The capital costs and timelines for drug development are only increasing in response to the increased regulatory demands imposed by the FDA. The result is that biotech companies require even larger investments over longer timelines. One of the major difficulties for biotech companies is finding investors who are not only willing to finance the current stage of development, but also the following stages until the company can either be acquired or go public. A closer collaboration between the providers of early stage capital and the established biopharmaceutical companies would go far in addressing this mid-stage funding gap. This would not only improve the opportunity for an exit through acquisition, but also address the lowvaluations of biotech public equity. According to a VP at a biotech hedge fund, one of the key reasons for the depressed public equity market is the mid-stage funding gap. Mid-stage biotechs who raise public equity and fail to obtain target prices often doom the company’s share value as investors know that the capital raised will not be enough to bring the company to the next value inflection point.

The second issue is risk sharing, which was briefly touched on in the previous section. The key requirement for new financing models is an effective sharing of risk among investors. If VC firms continue to demand liquidation multiples and established biopharmaceutical companies continue to off-load risk through the use of earn-outs, no financing model will be successful. Only when all investors equally share risk, will new capital flow into the system.
Conclusion

Despite the multitude of challenges facing mid-stage biotech financing, the author is quite optimistic about the future of the biotech industry overall. Since the dawn of the industry, thousands of new biotech companies have failed, yet there are still numerous investors willing to risk their money on the promise of new therapies. The strategic changes undertaken by the providers of capital in response to the current environment are a mix of both self-preservation reactions that only make the problem worse and creative new models that effectively address financing needs. What is required going forward is the continued development of new financing models that not only address the current challenges, but are flexible enough to address those that will be faced in the future.