

Biotech Survival Guide: Successfully Navigating the Downturn

By Roland Andersson and Frank Deane

Not all hope is lost. Biotechs that adapt to the current market and capital realities and focus on the most value creation activities will be able to survive and excel once market conditions improve.

Biotechs are feeling the crunch as volatile market conditions and recessionary fears are causing investors to keep their wallets close to the vest. Risk-averse investors are driving up prices of low-risk assets, putting significant pressure on higher risk assets—such as biotech equities and lines of credit.

Biotech equities declined by 12 percent on average on the NASDAQ Biotechnology index (NBI) during 2008. Small cap biotechs (\$500M-\$2B) and micro-cap biotechs (<\$500M) declined even more, by 26 percent and 41 percent respectively. Borrowing costs have increased nearly ten-fold as measured by the TED spread (the difference in basis points between the yield on 3-month LIBOR and 3-month Treasury bills). Even blue-chip Large Pharma is not immune, as evidenced by Pfizer's sky-high borrowing cost for the Wyeth acquisition. Risk aversion and higher costs of capital are causing innumerable difficulties for life science companies of all sizes and sectors.

Risk aversion has also reduced overall venture capital (VC) funding, although it is still available from select VCs for the right investments. According to Bob Parente, Head of VC Services at Leerink Swann, "It's a tough time for VCs. We're hearing from our clients that funding is tight and biotechs are under duress. In fact, overall flow of VC money into the biopharma industry has dropped ~30 percent, from \$5.9B in 2007 to \$4.2B in 2008." In December 2008, Mr. Parente conducted a Leerink Swann survey amongst 36 leading Life Science VC funds. Eighty-two percent of the VCs were not actively seeking investments, and 60 percent reported concerns from limited partners about sector over-exposure. In response, VCs were more actively managing their portfolio risk. Survey responses also suggested that early stage investments will decline from 73 percent in H1 2008 to 58 percent in 2009, and that late stage investments will increase from 24 percent in H1 2008 to 34 percent in 2009. In parallel, VCs were also showing an increased appetite for private investments in public equities (PIPEs) due to near-term liquidity concerns. This may benefit public biotechs seeking PIPEs, but is bad news for

private biotechs seeking additional capital.

Waiting For Godot

Akin to waiting for Godot, VCs waiting for an IPO in this market do so in vain. Per Leerink Swann's survey, VCs do not expect the IPO market to open until 2010 or beyond, assuming general stabilization and recovery of the economy. However, there is at least one bright spot for biotechs to focus on: Mergers and Acquisitions (M&A). M&A will continue to serve as the primary exit for VCs, with 88 percent of VCs anticipating at least one portfolio company exit during 2009.

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We expect a potential uptick in M&A activity over the coming years, as Large Pharma has cash on the sidelines and depleted pipelines that need bolstering. M&A activity is also expected to increase as biotechs may be more willing to accept deal terms they once would have rejected. However, time to exit appears to be increasing. VCs funded companies for 5.5 years in 2005 and 7 years in 2008 on average, according to a recent START-UP analysis.

In light of current market conditions, biotech management and VC investors will need to adapt quickly and strategically build for the long-run. We recommend the following strategies to help extend the runway and create value in the midst of a downturn:

- Align the portfolio risk profile with current investor risk appetite;
- Create sustainability via alternative financing and strategic partnerships;
- Selectively reduce burn rate.

These strategies will not only help biotechs weather the current storm, but also pave the way for future acquisitions.

Aligning Portfolio Risk Profile With Current Investor Risk Appetite

Biotechs need to lower their risk profile to better align with investor risk appetite. De-risking means

accepting lower rewards (market yield) for lower risks (increased commercial and regulatory success). To be more attractive to investors, biotech management teams and VCs should de-risk their companies using draconian pipeline prioritization. De-risking of a biotech pipeline can be done by phase, by therapeutic area (TA), and by mechanism of action (MOA).

First, when possible, we recommend focusing on specialty pharma therapeutic areas. Large Pharma is increasingly looking for specialty pharma products with the realization that primary-care driven blockbusters are less common. Oncology has long been the preferred area of investment, but interest may diminish slightly as treatment options improve and cancer assets face an increasingly crowded marketplace. Central Nervous System disorders, cardiovascular disorders, and metabolic disorders all require large trials with substantial safety data. Specialty markets require smaller trials and allow for staging of sequential indications. By TA, biotechs should focus on core areas of expertise and de-prioritize non-core assets.

Second, by development phase, attractive post proof of concept assets should be progressed at all costs, earlier clinical assets should be critically evaluated for progression, and pre-clinical ones may need to be tabled. It also may be necessary to suspend basic research. There are trade offs to be made between placing few big bets versus more medium and smaller ones. In the current environment, we recommend focusing on the medium and smaller bets investments. Where possible we recommend pursuing lower risk trial designs and pursuing indications in sequence.

Third, by MOA, biotechs should prioritize assets in proven, or at least better understood, MOAs, over novel and riskier novel MOAs. Freed resources should be allocated to priority assets, which drive future valuations, or eliminated, to free cash. Importantly, to maintain scientific esprit de corps, biotechs should earmark select funds for tangential areas of investigation.

Taking de-risking a step further, biotech management may want to evaluate selective mergers with similar sized biotechs operating in the same TAs. Mergers between biotechs with overlapping VC investors may be the most palatable. If a strategic fit exists, a merger would provide more shots on goal and could free up cash through cost-cutting synergies. A larger and highly focused biotech with multiple post POC (proof of concept) assets would be an attractive acquisition candidate.

Creating Sustainability Via Alternative Financing And Strategic Partnerships

The current cash-constrained environment has drained traditional sources of biotech funding and created acute operational shortages: ~380 public biopharma companies have less than a year of cash remaining. At best, we suspect the situation is comparable for private biotechs, but is likely worse. As a first step, cash-hungry biotechs should strive for cash neutrality by delaying outlays and reducing burn. Second, they should not be afraid to present their funding needs to existing VC investors, which are jointly rewarded for success. Failing these, biotech may want to consider alternate approaches to accessing capital and resources. These include venture development, royalty financing, and Large Pharma strategic partnerships and options deals. Experience suggests that royalty financing and venture development can be expensive ways to access capital, with options deals perhaps offering the most promise.

In venture development, a biotech creates a separate development company with a combination of capital and resources from a third party investor. In exchange, the biotech trades IP or ownership of the development asset(s) for the option to re-purchase these rights back from the development company at pre-ordained milestones. Symphony Capital, a private equity firm, pioneered this approach and manages a \$315M fund to invest in early phase clinical programs. Symphony typically invests \$40-80M, with a target return of 25-30 percent. Symphony expresses a strong preference for novel preclinical and Phase I assets, and solicits biotech without the capital and/or clinical expertise needed to bring early stage pipelines through development. A standard deal structure involves creating a Development Corporation (DC) as a joint venture with the biotech. IP is then in-licensed from the biotech to the DC, which provides capital and a buy-back option for the biotech. Symphony expects to influence development through DC board presence, exerts day to day operational control via a proprietary CRO, and retains equity or warrants in the biotech to protect downside. We know of investors raising capital to pursue similar models: one targeted at pre proof of concept (POC) assets and the other seeking POC to Phase III assets. In December, Goldman Sachs publicly expressed interest in investing in this space.

Royalty financing is available to those biotechs with revenues. Here, the biotech exchanges a share in the stream of future product revenues for upfront capital. For example, in August 2007, Enzon Pharmaceuticals

sold 25 percent of its worldwide royalty stream for PEG-INTRON A to Drug Royalty for \$92.5M. Other investors also offer similar financing arrangements, including Paul Capital.

Large Pharma strategic partnerships offer many benefits to biotechs. They provide access to cash, validate the biotech's assets (and thus intrinsic value), and may increase likelihood of future acquisition. Biotechs retain the most flexibility by partnering on specific assets. Multiple partnerships with different Large Pharmas may preclude future acquisition and multiple partnerships with a single Large Pharma may deter future potential suitors. To pursue this route, biotechs first need to identify and approach Large Pharma companies with interest in a specific asset or TA. Tactically, it is important to engage with both relevant scientists at the Large Pharma and business development teams, as both are required to champion a partnership.

Options deals may be of particular interest for cash strapped biotechs. Under such arrangements biotechs receive funding, but sometimes also resources and expertise, in exchange for offering the Large pharma certain guarantees. The biotechs typically offer the pharma a first right of refusal to license a particular asset or set of programs within a pre-arranged price range at select milestones. GSK's Center External Drug Development (CEEDD), Novartis' Option Fund, and Eli Lilly actively seek these types of arrangements.

For example, in October 2008, GSK and AFFiRiS announced a collaboration agreement granting GSK exclusive rights to AFFiRiS's Alzheimer's disease vaccine programs. GSK is acquiring exclusive rights to develop and commercialize two Alzheimer's disease vaccine candidates that are currently in Phase I clinical and an exclusive option to develop and commercialize other candidates in preclinical development. Under the terms of the agreement, AFFiRiS will receive an up-front payment of €22.5 million and could be eligible for future milestone payments and royalties.

Selectively Reduce Burn Rate Focus On Value-Creating Clinical Development

A critical step for all Biotechs is to reduce burn rates. We recommend this be done strategically and in a focused manner. We first recommend looking at Contract Research Organization (CRO) and Contract Manufacturing Organization (CMO) expenditures in the context of asset prioritization. After reducing clinical spending we recommend looking at sundry expenditures. While difficult, pruning expenses builds stronger companies, provides management

with accurate cash flows, and creates a platform for further action. Experience suggests that 10-15 percent reductions are achievable without disruptive operational impact. Importantly, during any burn rate reduction exercise employee morale needs to be managed so as to create buy-in and shared ownership. In biotech, burn rate reduction should not be done very selectively as it can be disruptive to asset progression.

Burn rate reduction begins with an accurate view on monthly cash flows. We recommend a data guided and orderly approach. As a first step we suggest management critically evaluate which outlays can be postponed. Optimally, this exercise should be coordinated with portfolio prioritization decision making. Second, after determining which costs can be delayed, management should focus on reducing burn across all expense categories.

Tactically we encourage management teams to take a divide and conquer approach—focusing on the highest cost categories first. In biotech the largest outlay will likely be on Contract Research Organization (CRO) and Contract Manufacturing Organization (CMO) services, but substantial savings can be achieved from the traditional line items: rent, equipment leases, professional service fees, insurance premiums, and sundries. As a last resort, management may want to consider headcount and compensation. Headcount reductions should align with portfolio prioritization decisions, and changes in compensation need to be shared and overly communicated.

We recommend multiple implementation approaches, including: re-negotiating/re-bidding contracts, consolidating vendors, and implementing usage protocols. For example re-negotiating/re-bidding contracts can be effective at reducing CRO/CMO services, rent, equipment leases, professional service fees, and insurance premiums. Consolidating vendors and implementing usage protocols can be effective at reducing sundry expenses, such as travel, office/lab supplies, and utilities. Additionally, management may want to consider offering suppliers equity in lieu of cash. For example, Quintiles offers CRO service risk sharing arrangements through its partnering group, Novaquest. Professional service organizations may also be willing to enter into such arrangements. Last, economies of scale matter in reducing costs. Because many biotechs, particularly private ones, have limited negotiation leverage with suppliers we encourage VCs to take an active role with their portfolio companies. We suggest VCs raise the issue of burn rate reduction with management across all portfolio companies, and

lead consolidated negotiations of big ticket items, for example CRO/CMO services.

A Proactive Response

These recommendations are not made lightly, and will require substantial time investments by biotech management and VC investors to implement. In summary we recommend management seek to:

- Align the portfolio risk profile with current investor risk appetite;
- Create sustainability via alternative financing and strategic partnerships;

- Selectively reduce burn rate.

Based on previous downturns, it is plausible to expect biotech re-investment will lag investment in other sectors. From this perspective, we recommend biotech management take proactive actions and actively involve investors and employees. The alternative, taking reactive actions with less cash and no time to spare, will be harder and more damaging to employee morale, asset progression, and diminish company value. Not all hope is lost, especially for adaptable leadership teams. ■