Late Stage Biotech Companies

**Late Stage Defined:** what stage of development must a company have achieved to be considered a “late stage” biotechnology company?

- **Stage 1:** Management is in pursuit of an idea or plan grounded in some initial product development; company has no product revenues to date.
- **Stage 2:** Company lacks product revenues, but has some expense history to confirm that product development is underway.
- **Stage 3:** Company shows revenues (e.g., through licensing) but still operates at a loss; proof of concept.
- **Stage 4:** Company has product and/or licensing revenues; potentially operating with a profit.
Challenges in Securing Financing

- Capital intensive
- Long gestation period
- Difficult to value assets
- FDA providing increased scrutiny

Recent Trends

- Lagging IPO Market
- Slow Stock Performance
- Increase in Strategic Partnering and Mergers & Acquisition (M&A)
- Increased Globalization
### Recent Industry Trends - IPO Market

**Venture Backed Biotechnology IPO’s ($MM): Biopharmaceuticals and Medical Devices**

- **2000**: $4,502, 58 Co’s.
- **2001**: $800, 11 Co’s.
- **2002**: $766, 8 Co’s.
- **2003**: $474, 8 Co’s.
- **2004**: $2,123, 39 Co’s.
- **2005**: $1,005, 21 Co’s.
- **2006**: $1,364, 28 Co’s.
- **2007 (Q1)**: $418, 5 Co’s.

*Source: Dow Jones VentureSource*

### Recent Industry Trends - IPO Market

**Biopharmaceuticals and Medical Devices**

- **2003**: $563M, 11 IPOs
- **2004**: $2,045M, 37 IPOs
- **2005**: $1,503M, 33 IPOs
- **2006**: $1,659.18M, 32 IPOs

### Sampling of 2006 IPO’s

<table>
<thead>
<tr>
<th>Company</th>
<th>% Change At Year End</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acorda Therapeutics (ACOR)</td>
<td>+ 164%</td>
</tr>
<tr>
<td>Vanda Pharmaceuticals (VNDA)</td>
<td>+ 147%</td>
</tr>
<tr>
<td>Achillon Pharmaceuticals (ACHN)</td>
<td>+ 40%</td>
</tr>
<tr>
<td>Artes Medical Inc. (ARTE)</td>
<td>+39%</td>
</tr>
<tr>
<td>Altus Pharmaceuticals (ALTU)</td>
<td>+ 26%</td>
</tr>
<tr>
<td>Targacept Inc. (TRGT)</td>
<td>+ 1%</td>
</tr>
<tr>
<td>Novacea, Inc. (NOVC)</td>
<td>- 13%</td>
</tr>
<tr>
<td>Catalyst Pharmaceutical (CPRX)</td>
<td>- 20%</td>
</tr>
<tr>
<td>SGX Pharmaceuticals (SGXP)</td>
<td>- 42%</td>
</tr>
</tbody>
</table>

### Recent Industry Trends - Biotechnology Stock Performance

**NASDAQ Biotech Index vs. NASDAQ Composite 2004 - 2007**

Source: Wall Street Journal
Recent Industry Trends - Biotechnology Stock Performance

AMEX Biotech Index vs. AMEX Composite 2004 - 2007

<table>
<thead>
<tr>
<th>Date</th>
<th>Open</th>
<th>High</th>
<th>Low</th>
<th>Close</th>
<th>Volume</th>
<th>Total Traded</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 12/4</td>
<td>$95.7</td>
<td>$95.12</td>
<td>$95.39</td>
<td>$96.03</td>
<td>...</td>
<td>$126,411.17</td>
</tr>
</tbody>
</table>

Source: Wall Street Journal

Recent Industry Trends - Increases in Strategic Partnering and M&A

Venture Backed Biotechnology Mergers & Acquisitions ($MM): Biopharmaceuticals and Medical Devices

Source: Dow Jones VentureSource
Recent Industry Trends - Increasing Globalization

Number of Public Biotechnology Companies (Reporting Positive Revenue) in the United States and Abroad

- U.S. Public Biotechnology Companies
- Foreign Public Biotechnology Companies

Financing Options
September 27, 2007

- Venture Capital
- Strategic Alliances & Partners
- Federal Funding Sources
The Financial Investor: Venture Capital

Pros and Cons of Venture Financing

Benefits:
- Contacts
- Experience

Drawbacks:
- Focused on an exit
- Loss of Control

The Venture Capital Market

There is a significant amount of funds available for investment in the biotechnology sector.

VC’s who specifically focus on late stage biotechnology companies.

Sampling of Bay Area Based VC’s Focusing on Later Stage Biotechnology Investment
The Venture Capital Market - Investors

Top 5 Bay Area Based VC’s Focusing on Later Stage Biotechnology Investment*

1. Delphi Ventures - 98
2. Interwest Partners - 78
3. Panorama Capital - 56
4. Burrill & Company - 52
5. Institutional Venture Partners - 52

Source: Dow Jones VentureSource

* Based on number of investments made

Venture Investment Totals Segregated by Industry Type 2000-2006 (Q3)

Source: Dow Jones VentureSource
The Venture Capital Market

Biotechnology ventures are capital intensive throughout a company’s life.

High risk has meant that biotechnology companies have avoided traditional sources of funding and relied on venture capital funds to meet a large portion of the financing needs of the biotechnology industry.
Venture Investments (All Stages) in Biotechnology (Pharmaceuticals/Medical Devices) Companies ($MM) 2000-2006

Structure of VC Financing

**Structures:**

- Equity
- Debt
- Convertible Instruments (notes, warrants, options)
Preferred Stock VC Financing

Equity and in particular the sale and issuance of preferred stock is the most common vehicle for venture capital investments.

Preferred Stock VC Financing - Common Terms

- Milestone Based Funding
- Representations and Warranties
- Use of Proceeds
- Dividends
- Liquidation Preference
- Conversion
- Anti-Dilution
- Redemption
- Control Issues
  - Protective Provisions
  - Voting
  - Board Composition
- Registration Rights
- Drag Along Right
Preferred Stock VC Financing - Common Terms

Milestone Based Funding: VC’s are requiring that their investment be provided to the company in trenches subsequent to closings, upon satisfaction of certain performance milestones

Representations and warranties: The representations and warranties are often more extensive with a late stage, more developed company, particularly in relation to the intellectual property representation.

Make sure rep’s and warranties have knowledge qualifiers where necessary and material adverse effect qualifiers, particularly with respect to IP infringement. Ex:

- Accurate in all "material" respects
- To the "best of company knowledge"

Limit: "no undisclosed liability" and "full disclosure" reps.

Require company management to conduct its own level of diligence in preparing disclosure schedules.
Preferred Stock VC Financing - Common Terms

Use of Proceeds:

- Investors invest with an exit strategy in mind
- Typically has specified steps in mind and a desire to have the investment dollars applied in a manner aimed to achieve such steps
- With late stage investments proceeds provisions are more tailored and funds may be earmarked for a particular purpose

Liquidation Preference

- Liquidity events are much closer with late stage companies
- Heavy focus on these provisions
- Participating preferred rights are often demanded by late stage VC’s

Conversion

- With focus on a liquidity event, late stage VC’s focus on the requisite price and proceeds in an IPO in connection with a conversion of the preferred to common
Anti-dilution:

- In today’s market, companies/investors typically agree to “weighted average” anti-dilution provisions, whether broad based or narrow based.
- Late stage companies that are not cash starved will not accept “full ratchet.”
- Given multiple rounds of financing common in late-stage companies, investors carefully consider any anti-dilution adjustments effected.

Redemption: VC’s want to ensure an exit within a specified time period, and they will require redemption of their preferred stock in case IPO or M&A gets pushed further out.

Typically structured as:

- Company required to redeem by a specified date; or
- Preferred stockholders have an option to redeem after a specified.
Preferred Stock VC Financing -
Common Terms

Control Issues: Protective Provisions, Voting, Board Composition

Protection typically sought by investors against:

- increase in authorized number of shares of Preferred Stock
- authorization, issuance, or reclassification of shares that would have priority over Preferred Stock
- payment or declaration of dividend on shares of Common Stock
- any alteration of Certificate of Incorporation or Bylaws that would adversely affect the Preferred Stock
- any significant company transaction without company approval
- company repurchase of shares except in certain cases from directors, officers and employees

Registration Rights & Drag Along Rights:

- Provisions will receive greater scrutiny and often be required in light of near term applicability and VC’s desire to attempt to control exit process which is more imminent for a late stage company
Preferred Stock VC Financing - Other Key Issues

Valuation

Due Diligence

Exit Strategy

Valuation: Critical negotiation point because of its effect not only on the amount of potential funding a company may receive but also the amount of dilution that may be suffered by pre-money investors.

No single defined standard for valuing biotechnology companies:

- Cash flow analysis
- Market capitalization
- Multiples of comparable companies
- Share trading performance
- Sector volatility
- Performance of IPOs
**Preferred Stock VC Financing - Other Key Issues**

**Valuation:** Several market measures typically used in conjunction, along with more subjective measures to provide a more accurate and complete picture. Process is inherently subjective and thus can be a key point of negotiation

- **5 Factors to Get Ahead in Valuation Negotiations**
  1. Quality of IP Assets
  2. Potential for Licensing/Big Pharma Deal
  3. Market Size and Penetration
  4. Management / Research Team
  5. Possibility for More Rounds of Financing / Burn rate

**Preferred Stock VC Financing - Other Key Issues**

**Due Diligence:**

- Depth and breadth of business and legal due diligence review, particularly in regards to IP, becomes more intensive with late stage companies
- Deal Killers
Strategic Alliances as an Exit Option

Types of Strategic Alliances

- Distribution/Sales, Marketing, Manufacturing
- Licensing/Research & Development
- Joint Venture
- Acquisition of Product/Product Lines
- Acquisition of Equity or the Business Enterprise
Industry Participants

Universities
Pharmaceutical Companies
Other Biotech Companies

Pros/Cons of Strategic Alliances

Benefits:
- Reduction in costs
- Access to financing and technical resources
- Reduce time to market
- Emphasizing complimentary technologies
- Boost in reputation/credibility
- Access to legal/regulatory advice

Drawbacks:
- Incompatible goals
- Loss of control
- Rewards reduced when split
The Strategic Investor: Licensing Arrangements

Vary in structure and involve different combinations of participants

Late stage companies may license technology to Big Pharma or other biotech companies in exchange for licensing fees, royalties or other consideration

Often serve as a key source of revenue for biotechnology companies

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Key Legal Issues

Elements of a Typical Licensing Agreement:

- **Scope**: Subject Matter; Field of Use; Territory; Exclusivity
- **Ownership**: Maintenance; Right to Enforce; Improvements on Licensed Material
- **Payment**
- **Assignment**: Sub-Licensing; Change of Control
- **Warranties**: Indemnities and limitations of liability
- **Term and Termination Rights**
Key Legal Issues

**HSR may be implicated**

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Key Legal Issues

**Confidentiality Provisions**

- Keeps information confidential for a specified period of time
- Limits use of information to contemplated purposes
- Prohibits disclosure to third parties
- Prohibits competition between parties to licensing agreement
- May provide for forms of sublicensing
Key Legal Issues

**Intellectual Property Provisions**

- Basis of licensing arrangements
- Licensor must perform adequate IP diligence
- Should contemplate business models and liquidity events
- Who directs strategy for licensed IP and oversees patent prosecution?
- Competition between parties to the agreement

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The Strategic Investor - Research and Development Agreements

**Two Basic Types**

1. One party undertakes the R&D while the other contributes funds or other resources to the project
2. Both parties contribute in varying degrees to the R&D process and funding.
Key Legal Issues

Elements of a Typical R&D or Collaboration Agreement

- Project management and control
- Licensing of Intellectual Property Existing or That May Arise
- Payment
- Exclusivity
- Term and Termination

Legal Issues to be Addressed

Define the scope of what is to be undertaken
- Filing of patents
- Unexpected outcomes
- Timing of payments
- Day-to-day operations
- Control over products and technologies
- Defining milestones and determining whether they have been achieved
- Exit Strategies/Wind-Up
**TIPS**

Deal with intellectual property rights which may arise as a result of the collaboration at the beginning or additional licenses may have to be negotiated later.

Consider competition law issues, take time to define the scope of the agreement.

Address worst case scenarios (i.e., rejection of the licensed material).

Be willing to renegotiate the agreement if it no longer reflects the commercial reality that the parties face.

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**The Strategic Investor: Joint Venture Arrangements**

Relationships formed by multiple parties for the purpose of engaging in a single activity or a limited number of activities.

**Two Primary Concerns:**

- Entity Selection & Tax Implications
- Operational Concerns
Entity Selection and Tax Concerns

Creation of a Separate Entity

- Provides tax advantages, additional liability protection and flexibility in product pricing
- May make deal difficult to negotiate, complex to administer collaboration, not as easy to wind down

Separate Entities

- Corporation, Partnership, Joint Venture, LLP, LLC

Contributions of co-venturers to new venture

Operational Concerns

How do the parties get into the deal and at what amount?
How will governance be handled?
Compensatory and distribution issues
Exit Strategies
Limitations on competition between participants
TIPS

Deal with intellectual property rights which may arise as a result of the collaboration at the beginning or additional licenses may have to be negotiated later.

Consider competition law issues, take time to define the scope of the agreement.

Address worst case scenarios (i.e., rejection of the licensed material).

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The Strategic Investor:
Acquisition of Equity or the Business Enterprise

Trend is Increasing in Popularity

Two Main Driving Forces:

1. Biotechnology companies searching for new exit strategy as IPO market declines

2. Big Pharma needs to fill diminishing product pipeline
**M&A Gaining Popularity**

**Venture Backed Biotechnology Mergers & Acquisitions**

($MM$: Biopharmaceuticals and Medical Devices)

<table>
<thead>
<tr>
<th>Year</th>
<th>Value</th>
<th>Co’s.</th>
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<tbody>
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<tr>
<td>2001</td>
<td>$1,426</td>
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<td>$4,981</td>
<td>73</td>
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<tr>
<td>2006</td>
<td>$4,693</td>
<td>87</td>
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<tr>
<td>2007 (Q1)</td>
<td>$1,654.53</td>
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</table>

Source: Dow Jones VentureSource

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**M&A Process**

**Due Diligence**
- Material Agreements, etc.

**Negotiations**
- Confidentiality Agreement, etc.

**Engage an investment bank**

**Execute final agreement**

**Announce transaction**
PROCESS FOR ALL FORMS OF STRATEGIC ALLIANCES

Goals and Objectives
Due Diligence
Confidentiality
Defining the Nature of the Arrangement
Documenting the Deal

Positioning for Financing
September 27, 2007

Protecting Intellectual Property and Navigating Regulatory Hurdles as Precursors to Late Stage Financing
## Intellectual Property

### Patents
- Most important biotech benchmark
- Right to exclude
- Development, protection and exploitation of patent portfolio
- Globalization requires patent protection abroad
- Limited time for protection

### Licensing of Biotechnology
- Patent alone does not guarantee commercialization
- Holder may lack resources to bring to market
- Development may exceed $500M
- Licensing allows for recoupment of costs and commercialization

## Regulatory Challenges

### FDA Approval Process
- Time to market may exceed 10 years
- Less than one-percent of compounds discovered in the preclinical stage will make it through the entire approval process
- Company costs require not only covering the cost of the successful drug but also all of the unsuccessful ones
Phases in the Approval Process

PreClinical Phase: 3 years
• Search for potential new compounds; if found tests conducted on animals and living tissue; filing of Investigational New Drug Application (IND)

Phase I: 1 year
• Drug tested on small number of healthy humans

Phase II: 2 years
• Effectiveness for targeted disease tested on small number of human patients

Phase III: 3 years
• Tests run on larger population. Effectiveness and side effects reviewed; large scale production considered; company files New Drug Application (NDA)

Phase IV:
• FDA approval received; drug is marketed to general population; short and long term side effects continue to be monitored

Trends in FDA Regulation & Getting a Product to Commercialization

<table>
<thead>
<tr>
<th>Year</th>
<th>Number of New Drugs Approved by the FDA</th>
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</thead>
<tbody>
<tr>
<td>2000</td>
<td>24</td>
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<tr>
<td>2001</td>
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<td>21</td>
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<td>2003</td>
<td>36</td>
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<td>2004</td>
<td>20</td>
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<tr>
<td>2005</td>
<td>18</td>
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</table>

Source: U.S. Food and Drug Administration
Exit Strategies and the Path to Commercialization

September 27, 2007