



Examining an Innovative Financing Alternative for Mid- Stage Biotechs

By: Yuti Dalal & Scott Orn

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“The best time to raise money is before you need it...and [developing a product] takes twice as long and costs twice as much as you think.”

-- Tom Churchwell, Managing Director, ARCH Venture Group¹

Introduction

In June 2005, Symphony Capital, a private equity fund, and Exelixis, a mid-sized Biotech, announced a joint venture that received little fanfare outside of the Biotechnology Industry. Inside the industry though, CEO's, Business Development Officers and General Counsels were scrambling to understand this new financing alternative that yielded \$80M in proceeds for promising, but cash constrained Exelixis. Over the last year, Symphony announced another deal, this time with highly regarded Isis Pharmaceuticals, and analyses like the one to follow have exposed the merits and costs of Symphony Capital's new financing vehicle. As the details have come into focus, it is our belief that this type of deal will become very popular in the Biotech Industry.

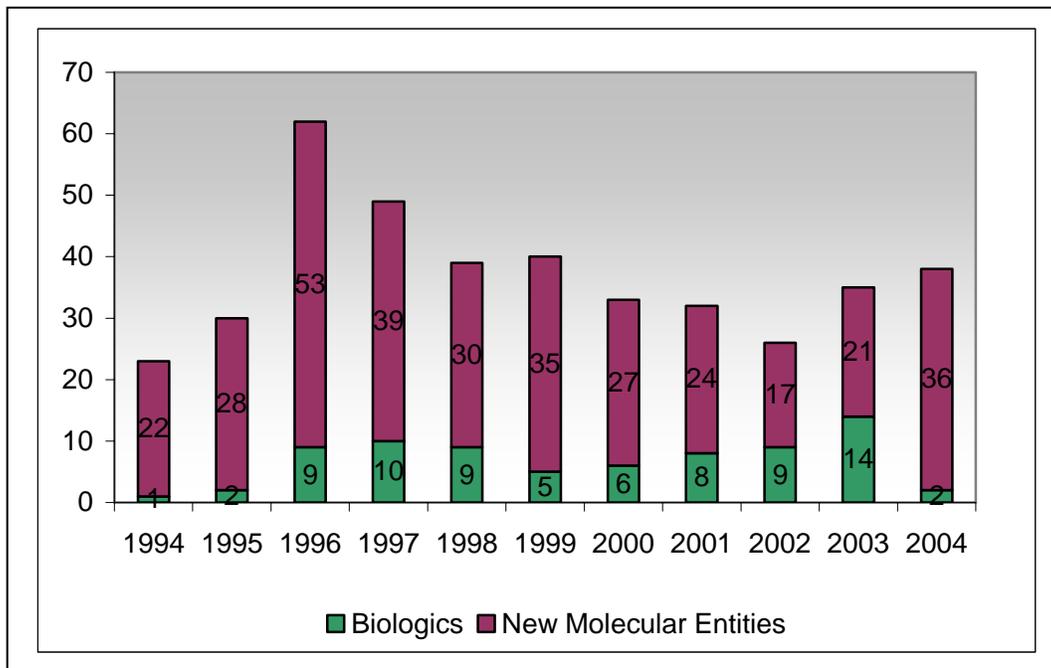
Industry Background

Drug development is one of the most difficult, risky and expensive businesses in the world. Industry experts estimate that new active substances (NSAs) entering clinical evaluation have an 11% chance of being approved and reaching the market. Only 16% of NSAs entering Phase II reach the market and the failure rate is still very high at Phase III, when only 44% of all NSAs in Phase

¹ “ARCH chief is addicted to making start-ups go,” Jon Van, Chicago Tribune, 5/21/06 (<http://www.chicagotribune.com/business/chi-0605210018may21.1.2295747.story?coll=chi-business-hed>)

III are approved and marketed.² Industry estimates put the cost of developing a drug that reaches the market at approximately \$800M and after it reaches the market, even more money must be devoted to marketing support and Phase IV studies to prove ongoing safety.³ Over the last ten years, pharmaceutical companies have responded to the long odds and high costs by merging to generate research and development and marketing scale and cost efficiencies. However, Exhibit 1 shows the number of new FDA drug approvals has been flat over the last 8 years, and new molecular entities, traditionally the domain of pharmaceutical companies, make up a declining portion of the approvals.

Exhibit 1: New Drugs Approved 1994 – 2004



Source: Abbott Laboratories Presentation (1/23/06)

Out of this abyss of Pharma’s declining productivity, cost cuts, and a singular focus on “blockbuster drugs,” another approach has emerged and even

² “Industry Success Rates 2002,” GA Ashton & PJ Joshua, CMR International, p. 2.

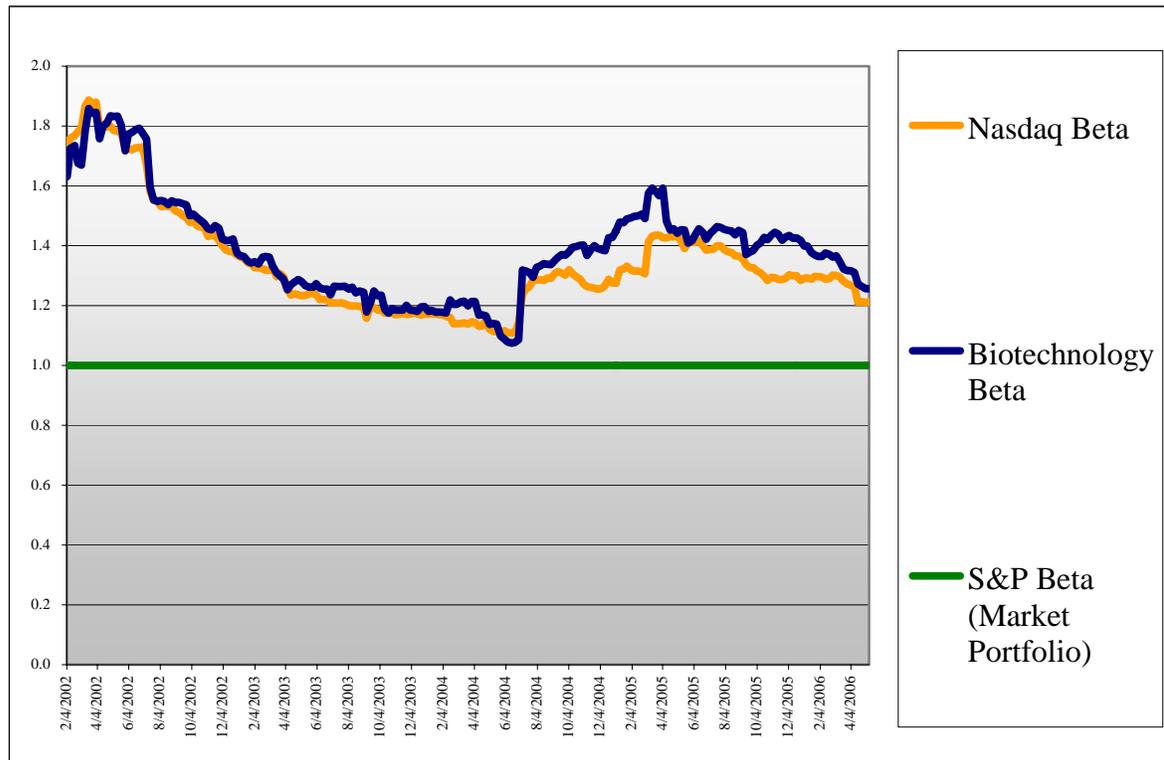
³ “Cost of Developing Drugs Found to Rise,” Gardiner Harris, Wall Street Journal, 12/3/01

flourished. By embracing cutting edge science, harnessing an entrepreneurial spirit and solving difficult problems, Biotechnology companies have become the driving force of innovation in drug development. The grandfather of Biotech, Genentech, now 30 years old, is a fully integrated drug company with an \$84B market capitalization and \$7B in revenue.⁴ Amgen, Gilead and Biogen IDEC, the other giants of Biotech, have a combined market capitalization of \$120B, revenue of \$18B, and all are profitable and self-sustaining.⁵ Still, new approaches cannot completely overcome the underlying risk profile of the drug development business. Unexpected FDA approvals and rejections, coupled with technology breakthroughs that change the landscape overnight, still result in a much higher degree of volatility than the broader market. Exhibit 2 compares the American Biotechnology Index's Beta to the S&P 500 which is a proxy for the broader market, and the NASDAQ 100, another highly volatile, growth company oriented index.

⁴ Yahoo! Finance

⁵ Yahoo! Finance

Exhibit 2: AMEX Biotechnology Index Volatility (Beta) vs. NASDAQ 100 & S&P 500

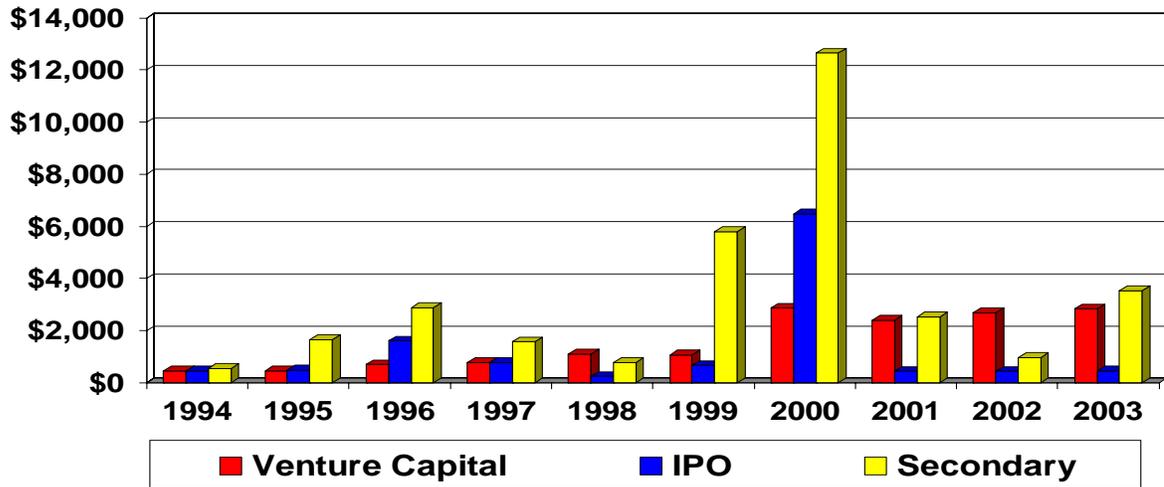


Source: Underlying Data from Yahoo! Finance

The successes of the “Big Four” pave the way for investment capital and credibility for the other side of the Biotech spectrum - startups. Biotechnology startups are typically founded upon a breakthrough piece of science, usually out of a University lab. Venture Capitalists supply the high risk/high reward capital, work with the entrepreneur to develop a “go to market strategy,” hire professional management at the appropriate time, and help with additional capital raising from the VC community and Pharmaceutical companies anxious to get access to the newest technology and drugs. Biotechnology venture funding is driven by the Industry Benchmarks performance (heavily influenced by the Big Four), the recent performance of Initial Public Offerings (IPOs) and at the margin, scientific breakthroughs and fads feed a herd mentality that can unhinge valuations from

reality, and drive financing activity to spectacular highs. Exhibit 3 demonstrates the correlation between Venture Capital Funding, IPO Market, Secondary's (Post IPO capital raisings).

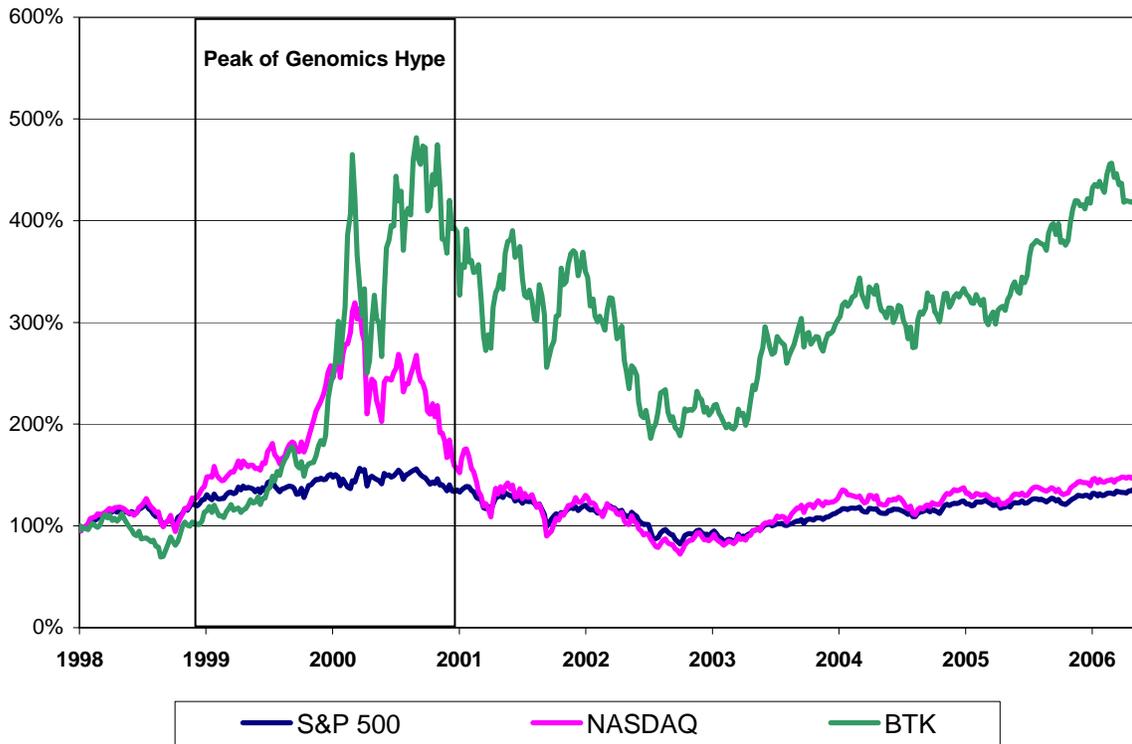
Exhibit 3: Biotechnology Financing Activity



Sources: BioWorld

Exhibit 4 charts the stock performance of the Amex Biotechnology Index (BTK). Stock performance and it is no coincidence that the amount of capital raised (Exhibit 3) shifts into overdrive as the Genomics fad reaches its apex in 1999 & 2000.

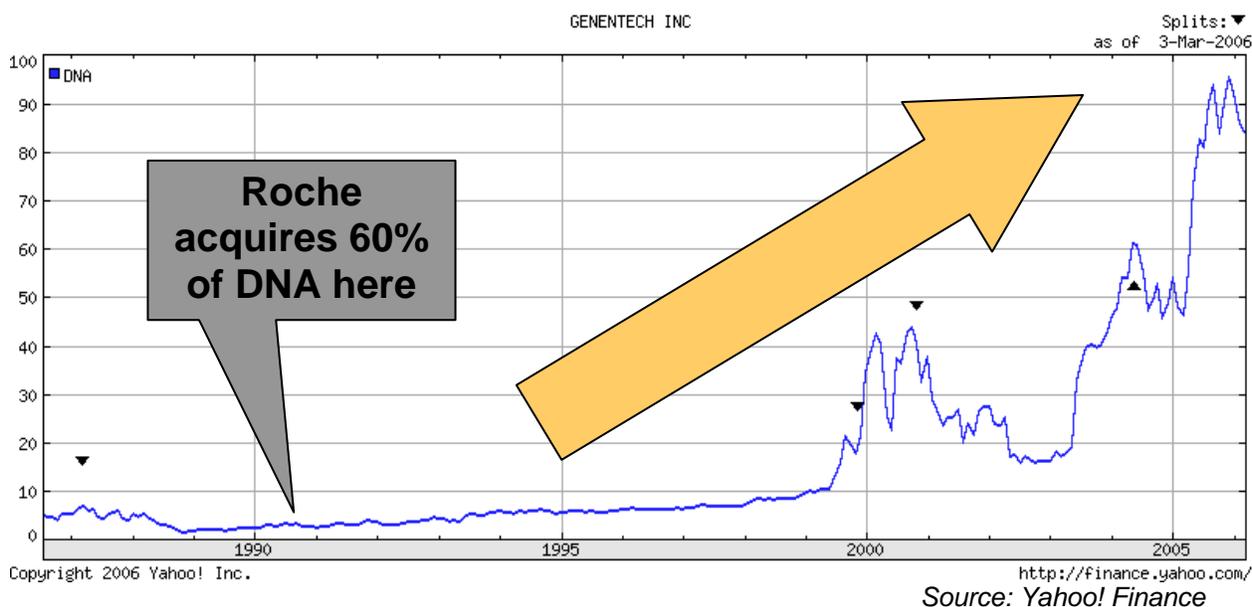
Exhibit 4: Biotechnology Relative Industry Benchmark Stock Performance



Source: Underlying Data from Yahoo! Finance

The Biotechnology Beta, Financing Activity, and Benchmark Performance Exhibits all demonstrate the feast or famine nature of the sector. Most Biotech executives have suffered through the funding lulls of the 80's and early 90's, when even the best business plans couldn't raise capital, and are conditioned to raise money whenever it is available. However, while the companies keep approximately 1.5 to 2 years of capital on hand at all times, the funding droughts often last 3 to 5 years, so even the most conservative and well managed Biotechs usually have trouble raising capital at least once in their lifecycles and pay the price of heavy dilution.

Exhibit 5: How Could Genentech Retain More of this Upside?



Genentech was no exception to this syndrome and was forced to sell 60% of itself to Roche on September 7, 1990.⁶ Roche's opportunistic investment yielded an approximate return of 22x its initial investment.⁷ The Roche-Genentech example demonstrates that the ability to vet good science and understand the Biotechnology funding cycles can be highly profitable.

The funding cycle has remained relatively stable recently and despite the dearth of IPO's since 2001 reflected in Exhibit 3, venture financing has stayed relatively consistent. The consistency of venture investors is partly due to the tremendous returns venture capital generates by getting into the companies early and at low valuations, relative to future exit valuations. For the most part, venture investors will stick by good companies during funding droughts, continuing to nurture promising ideas. However, there is a group of Biotechs that lack the luxury of this type of investor base.

⁶ Genentech Website: www.gene.com

⁷ Yahoo! Finance, DNA's Stock Price of \$3.62 (9/6/90) & \$82.60 (6/1/06).

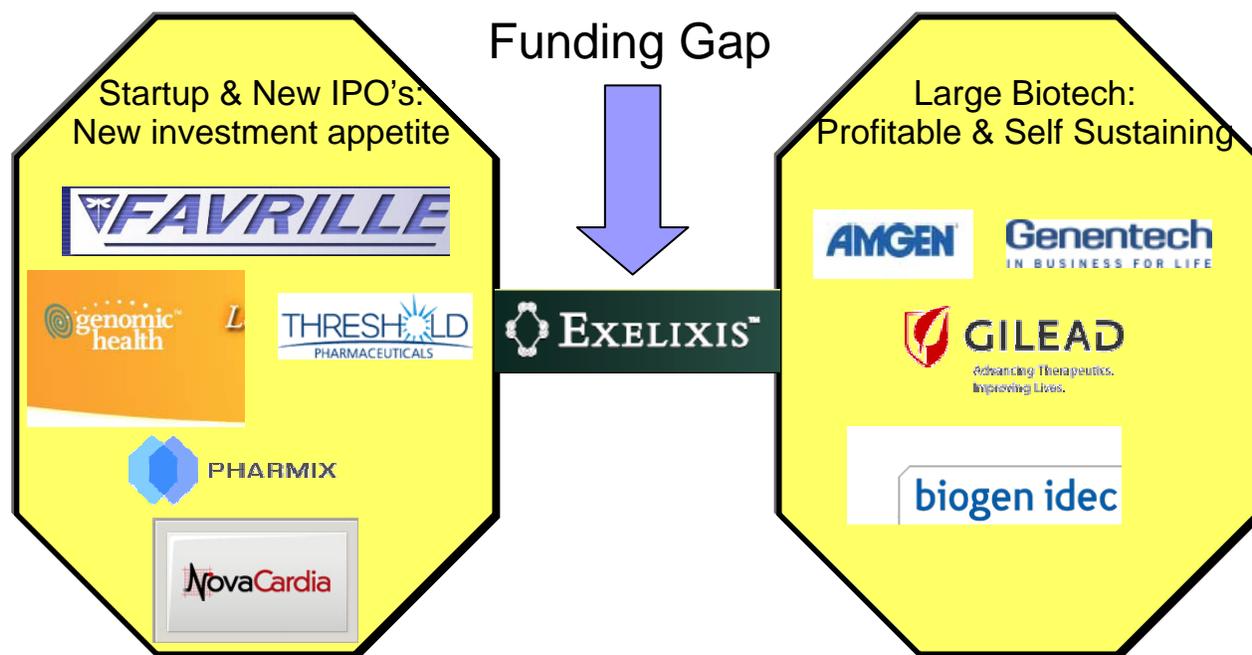
Stuck in the Middle – Mid-Stage Biotech’s Funding Gap

Between the venture backed startups with high return potential and patient investors who are oriented towards investing new capital, and the large Biotechs that are profitable and self sustaining, lies a group of approximately 170 companies that are traded publicly and have market capitalizations between \$50M and \$900M.⁸ Approximately 60 of these companies are profitable, but none to the degree that allows them to embark on broad new product initiatives without raising additional capital.⁹ Those that are not profitable struggle to support their existing candidates in expensive trials and rely on the cash they generated in an IPO and through large Pharma partnerships. Tapping the equity markets is difficult because their investor base consists of a combination of venture capitalists trying to exit the investment and institutional investors who are holding the stock in the hopes of surpassing the *next* milestone and capturing the associated valuation inflection point. Neither group is looking to invest more capital, except in the most dire situations. These companies are caught in the Mid-Stage Biotech Funding Gap (Exhibit 6). Rather than languish in the Funding Gap, the management team of one of Mid-Stage Biotech’s most promising companies, Exelixis, has taken a proactive approach to its financing challenges.

⁸ JPMorgan Trading Comparables Analysis, March 1, 2006

⁹ Ibid, March 1, 2006

Exhibit 6: Mid-Stage Biotech's Are Caught in the Funding Gap



Exelixis Overview

Exelixis, Inc. is a development-stage Biotechnology company, founded in 1994 based on biological insights into fruit flies and focused on developing drugs for cancer, metabolic disorders and cardiovascular diseases. The Company had its IPO in 2000, during the peak of the genomics hype, raising \$126 million.¹⁰ Its stock price skyrocketed to \$50 per share, giving Exelixis a market cap of \$2.5B, before the price settled to single digits, currently hovering between \$9 and \$12.¹¹ Like so many other venture backed companies, it leveraged its key technical insight, the biology of the fruit fly, to raise money and expand its scientific capabilities through collaborations with large Pharma and Biotech. Six years after its IPO, it has \$200M in Cash, but is burning approximately \$120M per year.¹² It

¹⁰ Exelixis Website: www.exelixis.com

¹¹ Yahoo! Finance

¹² Exelixis, Inc. Form 10-K filed with Securities & Exchange Commission, March 9, 2006, p.41

still lacks an approved product and its only sources of revenue for the foreseeable future are executing on existing partnerships to trigger milestone payments and signing more partnerships. However, the Company has one of the most promising drug pipelines in all of Biotech. Exelixis is the classic Mid-Stage Biotech, mouth-watering pipeline potential, but capital constrained and a cash runway of only 1.5 years. Yet, with all of its major drug candidates partnered, it has precious few ways to raise more money.

Pipeline Basics & Development Capabilities

According to Exelixis, its compounds, all but one of which was formed through its own discovery and clinical development initiatives, have first-in-class and best-in-class potential. It currently has 13 high-quality internally generated compounds in development - 8 in clinical trials, and 5 new development compounds in preclinical phases. The Company's proprietary structure-based drug design techniques and approaches to pharmacodynamics and pharmacokinetics enable it to move these leads into the clinic very quickly. In the last two years alone, Exelixis has filed 8 investigational new drug applications (IND) and it believes its technology capabilities will allow it to file another 3 INDs per year for the foreseeable future.¹³

Its clinical development pipeline includes seven compounds in cancer and renal disease. XL119 (originally Rebeccamycin), its most advanced compound, is in a Phase III clinical trial in patients with inoperable bile duct tumors and was exclusively licensed to Helsinn Healthcare SA with the option to reacquire

¹³ Exelixis Presentation – First Annual R&D Day, December 6, 2005

commercial rights for North America. Six other compounds - XL647, XL999, XL880, XL820, XL844, and XL184 are in Phase I or very early Phase II trials.¹⁴

The Company's preclinical pipeline comprises six programs. The preclinical oncology programs consist of development candidates that focus on inhibiting the RAF (XL281), Akt/S6k (XL418), and IGF1R (XL228) kinases that are implicated in various cancers. In preclinical metabolic disease programs, which consist of Liver X Receptor, Farnesoid X Receptor, and Mineralocorticoid Receptor programs, the Company is developing small molecules that modulate nuclear hormone receptors implicated in various metabolic and cardiovascular disorders.¹⁵

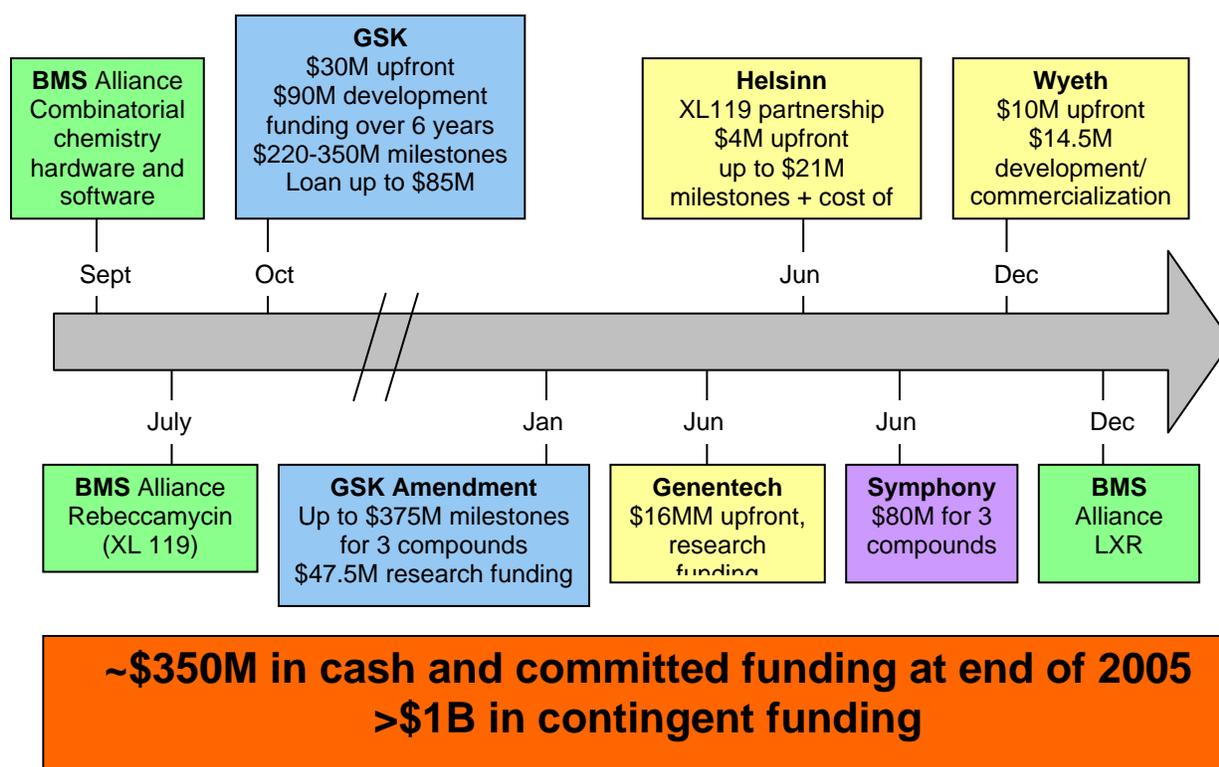
Strategic Alliances/Business Development History

Exelixis' technology has been validated through alliances with major pharmaceutical and biotechnology companies (Exhibit 7), including GlaxoSmithKline (GSK), Bristol-Myers Squibb (BMS), and Wyeth.

¹⁴ Exelixis Website: www.exelixis.com (Pipeline)

¹⁵ Exelixis Website: www.exelixis.com (Pipeline)

Exhibit 7: Exelixis Collaborations



The Company received its lead drug candidate in a September 1999 deal with BMS as well as a total of approximately \$180M in cash and commitments over the life of the collaboration and combinatorial chemistry hardware and software, along with related intellectual property rights. In return, Exelixis granted BMS a limited sublicense to use Exelixis' proprietary worm and fly technology which has helped BMS get two products into the clinic.¹⁶ Exelixis has leveraged its chemistry capabilities to develop the previously discussed pipeline and it is eligible for royalty payments on the sale of products commercialized under the collaboration.

¹⁶ Exelixis Website: www.exelixis.com (Strategic Alliances)

The Company's October 2002 deal with GSK, which was later reworked in January 2005, yielded approximately \$325M in cash and commitments.¹⁷ In exchange, Exelixis will deliver 32 validated targets and GSK has the right to select up to three compounds at proof-of-concept (completion of Phase IIa clinical development). Exelixis retains rights to all collaboration compounds not selected by GSK.¹⁸ Exelixis' December 2005 deal with Wyeth brought in \$10M upfront and potential milestone payments of approximately \$147M in milestone payments, as well as royalties on the sale of products commercialized.¹⁹ Wyeth will be responsible for all further preclinical and clinical development, regulatory, manufacturing and commercialization activities for the compounds.

Exelixis has clearly executed on its strategy of partnering to validate its technological approach and to bring much needed cash and other capabilities into the firm. However, the Company's approach will receive its most important blessing when a drug developed entirely in-house is approved. That milestone is still many years and millions of dollars away, and despite having over \$350M in cash and committed funding at the end of 2005 and over \$1B in contingent funding, there is no guarantee it will get there without incurring serious dilution. An innovative new private equity fund called Symphony Capital might be Exelixis' best chance of reaching its goal.

¹⁷ Exelixis, Inc. Form 8-K filed with Securities & Exchange Commission, October 28, 2002 and January 10, 2005

¹⁸ Ibid

¹⁹ Exelixis, Inc. Form 8-K filed with Securities & Exchange Commission, December 22, 2005

Symphony Capital Overview

Symphony Capital was founded in 2002 by five former pharmaceutical, biotechnology, contract research organization and law executives who together, have participated in over 100 FDA-approved products and over 400 clinical trials during their careers.²⁰ Symphony has raised one fund of \$315M of capital from large endowments, foundations, pension funds, other institutional investors in the United States and Europe.²¹ The fund has consummated transactions with Guilford Pharmaceuticals, Dynavax (\$50M) Exelixis (\$80M) and Isis Pharmaceuticals (\$75M) to date.²² Symphony has recognized the Mid-Stage Biotech Funding Gap and has found a way to make healthy returns while helping its partners move their programs along in the clinic.

Symphony's investing thesis consists of the team leveraging its technical background and clinical trial experience to vet partnership opportunities with cash strapped Biotechs that have high potential programs in early stage clinical trials. Then the business development and law professionals structure a deal that satisfies the cash needs of a specific clinical trial for its Biotech partner while simultaneously taking ownership of the drug candidate. These deals are very unique because the Biotech has the option of buying back the candidate after it has met a clinical milestone at a predetermined premium that assures Symphony of a compounded annual return of between 25%-35%. Depending on the transaction, Symphony is also issued warrants in the Biotech that should become very lucrative if the molecule hits the endpoint. Symphony also negotiates

²⁰ Symphony Capital Website (Biography): www.symphonycapital.com

²¹ Symphony Capital Press Release – January 5, 2005

²² Symphony Website: www.symphonycapital.com

downside protection in the form of “walk away” payments and warrants should the Biotech not exercise its option.

A Hybrid Model

To take advantage of the Funding Gap opportunity, Symphony has structured itself as a hybrid private equity firm, combining the best attributes of venture capital funds, hedge funds and highly structure oriented private equity firms. Like a venture capital firm, Symphony invests in early stage and other risky but potentially very profitable programs. The downside in these deals is staggering – almost a complete lost of principal (i.e. \$50M), however, the pay off is enormous and a few big wins can subsidize a big loss. Symphony behaves like a hedge fund by only investing in public companies, which means there is more information about the compounds and technology underpinnings than in a little known startup. Additionally, investing in public companies means the warrants and stock compensation they receive can be registered and made liquid much faster than if they had to wait years for a company to go public and then another 6-months to 2-years for the lock-up to end. Finally, just as private equity or leveraged buyout funds depend on the structure of the deal to limit their downside while still preserving their upside, Symphony is very careful and innovative when designing its deals.

A Groundbreaking Partnership: Symphony Evolution

On June 9, 2005, Symphony and Exelixis formed a joint venture called Symphony Evolution, Inc. In exchange for an upfront cash payment and contingent capital, Symphony took ownership of three Exelixis drug candidates.²³ At the time of the deal, all three compounds were in Phase I, and one has since moved into Phase II. The deal is subject to some early buyback options that will be discussed but generally, Symphony will own the compounds through Phase II, at which time Exelixis can buy them back.

This deal has home run return potential for Symphony yet unlike an earlier stage biotech, the compounds have already received some early validation and Symphony can diversify away some specific compound risk by tying up the bundle of three. From Exelixis' point of view, it is raising much needed capital at potentially less dilutive levels through the option components and can offload some early trial risk. This deal has the potential to be the proverbial "win-win" for both parties.

Deal Specifics²⁴

- Closing Date: June 9, 2005
- Three Phase 1 Cancer Programs
 - XL784, XL647 and XL999 all inhibit receptor tyrosine kinases
 - XL647 and XL999 targeted anti-cancer agents, through Phase I and Phase II studies in multiple tumor types

²³ Exelixis, Inc. Form 8-K filed with Securities & Exchange Commission, June 9, 2005, p. 2.

²⁴ Ibid, p. 2-3

- XL784 in diabetic nephropathy, through Phase I and Phase II studies.
- Symphony is making up to \$80M of capital available to Exelixis
 - \$40M drawn down at signing
 - \$20M required to be drawn down in the first year with up to \$40M available
- Exelixis can repurchase the programs at its option
 - Beginning on the 1-year anniversary of Closing Date and running for 3 more years
 - Exelixis is required to pay back all invested capital and additional payments equal to an annually compounded return of 25%
 - Repurchase can be made in cash and stock (up to 33% of total and at market price per share)
 - Company has 18 months from Closing Date to reacquire one of the three Programs and will make a pro-rata payment to Symphony consistent with the deal terms
- Other consideration
 - \$3M structuring fee to Symphony on Closing Date
 - 5-Year Warrants²⁵ to Symphony for 750,000 shares of EXEL priced at \$8.90 (market price on Closing Date)
 - Another 5-year warrant for between 375,000 to 750,000 shares will be issued upon the 2nd draw, depending on whether \$20M or \$40M is drawn respectively

²⁵ Warrants give the holder the right to purchase stock at a predetermined price. If the current stock price is above the exercise price, the warrant is “in the money” and can be exercised for a profit.

■ Symphony Downside

- If Exelixis doesn't buy back the programs, then Symphony is issued another warrant for 500,000 shares, to be exercised at a 125% premium to Exelixis' share price at that time.

Symphony Key Value Drivers

Given that Symphony is taking up to \$80M of risk in this transaction, the assumption is that they will have diligenced the compounds quite heavily. However, as previously discussed, in Biotechnology, failure is a regular occurrence and often the reasons cannot be isolated, let alone predicted, so there is real risk here for Symphony regardless of its technical team's skill. The payoff has three components:

- 1) \$3M Upfront Structuring Fee which means they are only advancing \$37M (potential for \$77M total), mitigating some risk and enhancing the IRR because it will be calculated on a lower capital base.
- 2) The 1.0M to 2.0M in warrants with strike prices ranging from \$8.90 to 125% of stock price at the time of issuance have tremendous value because they have an extended maturity of 5 years and Exelixis' stock has been highly volatile. Based on Black Scholes (Exelixis historical stock volatility of 50%, stock price at the time of issue of \$8.90, and risk free interest rate of 4.6%), each warrant has an implied value of \$4.40, so total warrant portfolio value is between \$4.5M - \$8.4M. Furthermore,

should the compounds in the trial hit their end-point, Exelixis' stock should rise and the warrants will be "in the money" and even more valuable.

- 3) Symphony receives a guaranteed 25% compounded annual return if Exelixis exercises the option to buy the compounds back. To understand the magnitude of that return, if Symphony advances the full \$80M for a 3 year period, Exelixis will be paying back \$156M, a profit of \$76M without factoring in the warrants and structuring payment.

Symphony's return profile depends on the dates Exelixis exercises its buyback options (if at all), but warrant compensation and structuring fee drive the overall return above 25% per year as long as Exelixis does exercise and in Part 3 above, we've demonstrated that the multiple on investment, or cash on cash return is very attractive as well.

Exelixis Key Value Drivers

Exelixis is paying a heavy price for this capital, but as previously discussed, it has very few alternatives. The drivers for Exelixis are:

- 1) The deal allows them to offload some trial risk, but this is not a big value driver because the firm and its shareholders have already committed to these compounds, if they fail, the damage to Exelixis will be much more profound than an \$80M loss. Still, every bit of risk mitigation helps.
- 2) More important than risk mitigation, is that without this deal, Exelixis would have had to raise capital at a prohibitive cost. The Company could only raise equity in an emergency, because raising equity now, before a

milestone is reached would be seen as a signal of something gone awry and would have been highly dilutive. An Exelixis Executive explained, “We got killed when we issued \$50M of new stock to existing investors last year.”²⁶ If the compounds hit their endpoints, Exelixis will exercise its option to buy them back, then turn around and deliver them to GSK, which will trigger huge milestone payments and provide the funds to payback Symphony. Furthermore, as part of the GSK deal, GSK will handle all Phase III development costs so Exelixis will be free to spend its money on other programs.

Symphony’s Future

Symphony’s flexible fund structure and rare combination of deal experience and technical insight translates to a strong market position versus other sources of capital. In addition, the Exelixis deal has generated a tremendous amount of press and subsequent deal flow for the firm. The firm now has non-disclosure agreements with over 60 Biotech firms.²⁷ Furthermore, Symphony just announced a \$75M deal with Isis Pharmaceuticals around Isis’ highly regarded anti-cholesterol drug, on which it has spent more than \$500M to get through Phase I.²⁸

The fund still has over \$100M in dry powder remaining and in the near term, Symphony should focus on diversifying away its specific disease state risk. Since

²⁶ Exelixis’ Presentation to Kellogg Biotech Trek, January 18, 2006

²⁷ “Biotech Companies Revive Option to Share Costs, Benefits of Pharmaceutical Trials,” Susan Thomas, Wichita Business Journal, 5/6/2006 (<http://www.bizjournals.com/wichita/stories/2006/05/08/focus3.html>)

²⁸ “Looking For Cash, Isis Strikes Rare Licensing Deal,” Christopher Hinton, Dow Jones Newswire, 5/3/06

it already has deals in Cancer, Cardiovascular, and Neurology, it should look for exposure in other areas. Longer term, Symphony will be looking to raise another fund. If the first three deals perform, the business model will be validated and the Mid-Stage Biotech Funding Gap, which 170 firms fall into, is big enough to sustain at least a \$1B fund.

Conclusion

As pharmaceutical companies struggle with declining new product yields for a host of reasons, Biotech companies have become the major innovation drivers in the drug development industry. Large, profitable Biotechs can fund their own research and development and are well positioned to maintain their new product development pace. At the same time, startups can attract funding because they are founded on the most exciting new technologies and venture investors are willing to invest multiple times and be patient with the companies because the low valuation they are investing at means the returns will still be strong if the company makes significant progress.

In between these two groups lies Mid-Stage Biotechs, which lack the support of venture investors because they are trying to exit the investment, yet don't have the profit streams to sustain investment. Exelixis is a fine example of a Mid-Stage Biotech with an exciting pipeline, but very few remaining sources of capital. Symphony Capital has recognized the opportunity, and executed a deal with Exelixis that should be very positive for both, contingent on the clinical data of course. Symphony's alternative financing model has solved Exelixis' funding challenge, and as evidenced by the recent Symphony & Isis deal, will become an

important source of capital for many other Mid-Stage Biotechs in the coming years.