## Factors Influencing Superior Returns Achieved through Mergers & Acquisitions of Corporate Spin-Outs in the Life Sciences

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Submitted to the Harvard-MIT Division of Health Sciences and Technology in Partial Fulfillment of the Requirements for the Degree of

MASTER OF SCIENCE IN HEALTH SCIENCES AND TECHNOLOGY at the

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### Abstract

Corporate spin-outs have become more frequent in the contemporary business environment as an alternate source of risk diversification and value creation for both the parent and external investors. Once established, corporate spin-outs are often perceived to be of higher quality than their counterparts in the industry; previous studies have shown that they tend to receive higher valuations in financing, faster financing and higher preference by prestigious Wall Street investment banks when they decide to go public.

The primary objective of this thesis was to compare the net proceeds associated with successful liquidity events (IPO or M&A) for US based therapeutic-focused corporate spin-outs to industry averages and test the hypothesis that corporate spin-outs generate superior returns. A database containing information on 186 corporate spin-outs within the life sciences (founded from 1990 – present) was generated for the purpose of testing this hypothesis. Net proceeds from corporate spin-out liquidity events were compared to median net proceeds of all biotech/pharmaceutical liquidity events for a given vintage year and type of liquidity event (IPO vs. M&A). Liquidity events were observed with a higher frequency than overall industry averages. Results indicated that net IPO proceeds were similar to industry averages, while M&A proceeds were above the median vintage year value for every case observed. When normalizing by the most advanced clinical stage program, a similar trend was observed in three of the five cases. In addition, internal rate of return (IRR) and cash on cash exit multiple for Series A investors was substantially higher in corporate spin-outs than industry averages.

In order to understand why acquisitions of corporate spin-outs appeared to generate sizable excess returns relative to industry averages, qualitative interviews were conducted with former executives involved in these transactions.

Key insights from these interviews indicate that a seasoned management team, prestige of parent company, high quality syndicate of investors, clinically proven technology and a clear regulatory path to approval are all elements that help drive excess valuations of corporate spin-outs in the life sciences.

We conclude that corporate spin-outs do generate superior returns through M&A exits compared to venture-backed start ups, while proceeds from IPO's were similar to case controls.

I dedicate this thesis to my parents, Gil and Ellen Magnani, and my wife, Kate Rubins, for their continued support and encouragement throughout the years.

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# **Chapter One: Characteristics of Corporate Spin-Outs**

## Overview of Corporate Spin-Outs

Corporate spin-outs have become more frequent in the contemporary business environment as an alternate source of risk diversification and value creation. Increased global competition, free information flow and technology savvy capital markets have all contributed to the evolution of corporate spin-outs. The graphic below provides a high level framework for the basic mechanics of a corporate spin-out (Tübke 2004); a process which many have compared to cellular division or mitosis.



Figure 1 - Illustration of Corporate Spin-Out Process

Previous reports have estimated that 12.9% of all new firm formations in the European Union are the result of corporate spin-outs. Once established, corporate spin-outs tend to exhibit superior headcount and financial growth when compared to venture backed start-ups (Moncada 1999). Factors which influence these superior returns are widely debated in academic literature, but may include technical (Klepper & Sleeper 2005) or non-

technical (Chatterji 2008) skills transferred from prior management experience at large companies.

Certain industries appear to be more receptive to the creation of corporate spin-outs. Previous studies have investigated the role of corporate spin-outs in the semiconductor (Braun & MacDonald 1978), disk drive (Agarwal 2004, Chesbrough 1999, Christensen 1993), laser (Klepper 2005), medical instrumentation (Garnsey 2006) and automobile (Klepper 2007) industries. Some of these industries appear to benefit from a spin-out's ability to rapidly innovate (high tech) while others adopt this business model in response to geographic concentrations of human capital and relative dissatisfaction with their current employer's attitude towards innovation (automobiles).

Establishing a new company requires entrepreneurs to obtain financial and human capital from external sources which have little ability to assess their relative quality. Interorganizational endorsements have been employed extensively in the biotechnology industry as a mechanism to signal the quality of a new venture (Stuart 1999). Strong relationships with established corporations provide a positive signal to the market regarding the underlying technology of the newly formed corporation. This study showed that corporations which received inter-organizational endorsements were more successful in generating capital than companies who were unable to secure such endorsements.

Other commonly cited factors which influence the development of corporate spin-outs include barriers to market entry, regulatory influences and tax incentives imposed by local governments.

Companies employ numerous tactics with respect to non-core technologies. Three of the most common tactics employed are listed below.

• **Divestiture:** Technologies which are deemed non-core or out of strategy for a given organization can be out-licensed to another corporation for development

and commercialization. This tactic enables the parent company to monetize the value of these technologies while simultaneously alleviating any future P&L burden associated with the program.

- Stagnation: Companies in competitive markets often make initial investments in multiple technologies. As these programs progress, the company eventually decides to focus resources on one particular program. To prevent the other, potentially competitive, technologies from entering the market the parent corporation may simply 'park' the assets and discontinue internal development. While this option prevents the parent company from monetizing the technology and alleviating future P&L burden, it also prevents or delays a competitive product from entering the market.
- Spin-Out: In certain instances companies will spin-out technologies into a new corporate entity. This option provides an interesting mix of benefits to the parent company. Equity in the new corporation is generally retained by the parent, along with options or rights of first refusal to the technology being developed.
   Programs continue to be developed externally, sparing the parent company's P&L exposure. In the event that the technology is effective, the parent company has the option to either re-acquire the spin-out or sell the company to another entity for a profit.

In this study, we are indifferent as to the reason why a spin-out of the underlying technology was chosen. Our purpose is to examine the chronology of events and subsequent liquidity events that these spin-outs eventually achieved.

#### Corporate Spin-outs in the Life Sciences

Within the life sciences, corporate spin-outs have become more prevalent over the past twenty years, as can be seen in the figure below. Fourteen spin-outs were incorporated in 2008 alone; almost as many as were established during the first five years of this data set.





Spin-outs have been established in at least 20 countries around the globe. The United States is the most frequent location of incorporation, representing 57% of all spin-outs established to date. The United Kingdom and Canada have also been home to approximately a dozen spin-outs over the past twenty years. Other countries which have incorporated multiple spin-outs include Germany, India, Australia and Sweden. We hypothesize that government regulations may be less stringent in these geographies, though no thorough analysis has been conducted to support this hypothesis.





We have also explored the relative geographic proximity of spin-outs to their parent companies. Our analysis shows that spin-outs are generally located in relatively close proximity to the parent company (see charts below). Approximately 60% of the spin-outs in our data set were located within 250 miles of the parent company, while fewer than 30% of the spin-outs were located 1,000 miles or further from the parent. Since 1990, approximately 186 corporate spin-outs have been established in the life sciences worldwide.





Median Distance from Parent Company = 43 Miles (N=98)

An exploration of the specific states of incorporation was also performed in this study. California recorded the highest levels of spin-out activity, with 42 companies incorporated since 1990. Fifteen spin-outs were recorded in Massachusetts during the same time period. Several other states had moderate levels of spin-out activity, as can be observed on the heat map below. The propensity of spin-outs to incorporate near their parent company may have influenced the geographic concentration of spin-outs into a few select states.



Figure 5 - Distribution of US Corporate Spin-Outs by State (Heat Map)

Source: Google Maps

One potential explanation for the increased incidence of corporate spin-outs could be an increased risk profile associated with the underlying research. Many commonly known pathways have already been exploited in the development of older therapeutics. Without any 'low hanging fruit' remaining to be developed into a new drug, companies must embark on new research targeting new pathways. Historical evidence has documented that equity investments have been used in R&D collaborations to share risk or clinical uncertainty surrounding pre-clinical or clinical stage programs (Pisano 1989). Other studies have shown that smaller biotechnology firms often consult with prominent scientists as a mechanism to signal the legitimacy of their underlying technology to the industry (Higgins & Gulati 2003). However, as uncertainty continued to rise due to the novelty of the underlying research, companies began to deploy a spin-out strategy as a more prudent mechanism to minimize exposure to these uncertainties.

Another potential catalyst for the higher frequency of spin-outs is Wall Street's decreasing tolerance for clinical and regulatory risk. Much of this perceived risk has been exacerbated by the capital markets and translates into depressed stock prices on public exchanges. Prior high profile clinical failures have cost investors millions of dollars; with no systematic mechanism to predict clinical outcomes investors are

becoming less tolerant of these deals and more vocal in their displeasure with management teams that persist in these activities.

One recent study was able to demonstrate that new government regulation on agricultural biotechnology products significantly reduced share prices for companies engaged in these activities (Dohlman 2002). Another study investigated the impact of receiving a Refusal to File (RTF) letter for ImClone's blockbuster drug Erbitux (Reynolds 2002). The immediate effect was a 20% decrease in share price, representing a \$4 Billion loss in market capitalization.

#### Primary Objectives of Corporate Spin-outs

Primary motivations for corporate spin-outs can be sorted into three categories:

#### **Motivations to Spin-Out**

Restructured Spin-Outs – These events occur in response to ongoing
restructuring efforts at the parent company and are generally initiated to help
regain corporate focus. In many cases, the parent company provides support and
encouragement to the spin-out management team.

In December 2008, Protein Design Labs (PDL) elected to spin-out their therapeutics division into a new operating entity called Facet Biotech. The parent company would remain focused on the collection of royalties from their intellectual property estates on manufacturing monoclonal antibodies. The spinout was accomplished through a pro rata stock dividend to PDL's stockholders of the common stock of Facet Biotech Corporation. The primary goal of this transaction was to enable investors to invest in and realize the benefits of each business model separately. • Financial Spin-Outs – In certain instances, a parent company will operate as a shell and spin-out partial equity stakes in technologies that they own. In contrast to the restructured spin-outs, these scenarios do not involve any corporate efforts to refocus corporate strategies, but are merely an alternative vehicle for capturing value through public capital markets.

Following completion of an acquisition by Amgen in 2007, several copolymer programs from Ilypsa were slated for immediate termination due to a lack of strategic interest by Amgen. The original syndicate of venture investors for Ilypsa approached Amgen with the concept of spinning out the shelved assets into a new company. In exchange for out-licensing the rights to these programs, Amgen would retain an undisclosed equity stake in the new company, Relypsa. Participation in future venture financing rounds was an option afforded to Amgen to prevent further dilution.

• Entrepreneurial Spin-Outs – Entrepreneurial spin-outs are driven by individuals from the parent company who wish to pursue technologies which are out of scope or not being pursued by the parent. These ventures do not necessarily receive support from the parent company, and often times encounter hostility in the early stages of venture formation.

CoGenesys was incorporated due to this motivation. The company was initially spun-out of Human Genome Sciences shortly after HGS appointed a new CEO, Tom Watkins. Watkins quickly determined that albumin-conjugated protein based therapeutics were out of HGS' long term strategy and refused to dedicate resources to those programs. Through a persistent effort by Steve Mayer and Craig Rosen (former CFO and CSO of HGS respectively), Watkins eventually conceded to licensing out the technology and providing a bridge loan to cover operations for six months while the team secured venture financing. The company was eventually sold to Teva for \$400 Million.

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## Inclusion/Exclusion Criteria for Selecting Corporate Spin-out Activities

Given the vast array of business transactions that involve potential 'spin-out' activities, it is essential to delineate our target universe of activities for analysis. For the purpose of this thesis, we have defined the universe of corporate spin-outs to include a pre-defined set of activities as listed in the table below.

Activity	Description
	Partial or complete privatization of a firm, which is led by incumbent
Buy-Out	management (management buy-out), former employees (employee buy out) or
	investors (leveraged buy-out).
	Parent company sells equity of existing or newly created company through an
Equity Carve-Out	Initial Public Offering (IPO)
	Stock distribution by parent of an existing or newly created entity to
Equity Spin-Off	shareholders on a pro-rata basis.
Latant Smin Off	Part of an existing company is spun out and operates semi-autonomously while
Latent Spin-OII	remaining fully owned by the parent.
	A transaction in which some, but not all, parent shareholders receive shares in a
Split-Off	subsidiary in exchange for relinquishing their parent company shares.
	Complete spins-off of all subsidiaries by parent to shareholders and cessation of
Split-Up	operations.

#### Figure 6 – Execution / Tactics Included in Spin-Out Analysis

The following activities were excluded from the analysis as they were not considered true "corporate spin-outs". Most of these activities do not result in the creation of a new separate operating entity and were deemed out of scope for the present study.

#### Figure 7 - Execution / Tactics Excluded in Spin-Out Analysis

Activity	Description
Corporate	A new venture is incorporated within the confines of the parent
Venturing	A new venture is incorporated within the commes of the parent
Internal Spin-Off	Transfer of a division within parent company (Internal transfer)
Internal Subsidiary	Creation of an internal subsidiary which remains controlled by the parent
Outsourcing	Externalization of non-core capabilities
Sell-Off	Sale of company assets to another (pre-existing) firm

## Factors Influencing Spin-Out Creation and Performance

While it has been postulated that corporate spin-outs perform better, on average, than pure start-ups, publications identifying specific factors which contribute to this success have been sparse. A recent publication by Alexander Tübke has provided the most comprehensive review of this topic to date, though his analysis was focused on European companies and spanned several industries. Through a careful analysis of 211 detailed surveys, the following five factors were identified as influencing the decision to spin-out:

- Information asymmetries between management of the parent and spin-out (differences in opinion between parent and spin-out employees can decrease shareholder value if spin-out is not executed)
- High rate of successful firm creation in the industry
- Low government regulation/deregulation
- Market or product relatedness missing between parent and spin-out
- Type of motivation behind spin-out (entrepreneurial, financial, restructuring)

In addition to identifying specific factors which were correlated with the decision to spinout a new company, Tübke also found the following factors influenced the degree of success a corporate spin-out following incorporation:

- Capacity to create alliances and partnerships with other companies
- Innovativeness of spin-off's core competencies
- Knowledge transfer from parent
- Organizational design (focused vs. mixed structures)
- Organizational freedom before separation
- Overall activity within the business sector (emerging vs. mature industries)
- Parent's attitude towards entrepreneurship / pre-existing spin-out policy
- Protection of the spin-off's business
- R&D intensity
- Regulatory / legal environment (affects parent more than spin-out)
- Remarriage of ownership and control
- Spin-off motivation (customer driven vs. parent driven)

Unfortunately, none of the companies surveyed were in the business of manufacturing therapeutics. This raises the question of what different factors and influences exist in that industry. The goal of this study is to perform a similar exercise and identify factors which influence successful corporate spin-outs in US-based therapeutics companies. Due to the small sample size available, this thesis will not contain calculations of statistical significance but will employ a mix of quantitative and qualitative observations. Naturally, factors which were identified through the course of primary market research may be subject to sample bias and should not be extrapolated beyond the scope of the present study.

### Hypotheses

As discussed earlier, the underlying hypothesis for this body of work is that corporate spin-outs which focus on the development of therapeutics experience superior returns upon successful liquidity events when compared to *de novo* venture-backed start-up

companies. (Specific liquidity events studied in this thesis included initial public offerings (IPO's) or merger & acquisition (M&A) by a larger corporate entity. The perception that corporate spin-outs are of higher quality than start-ups has been expressed by numerous individuals in various aspects of the healthcare industry, but a formal study has not been conducted to accept or refute the validity of the statement.

In addition to ascertaining the relative value of IPO and M&A proceeds associated with therapeutic-focused corporate spin-outs, a second hypothesis for this body of work is that a series of common factors exist within these companies which account for their relatively higher valuations. A relatively low absolute number of spin-outs within this sector prevents statistical analyses to be sufficiently powered. While statistical significance is unlikely to be achieved, trends and similarities will be identified. The following hypotheses will be the basis of the analysis performed in this thesis:

- For Mergers & Acquisition (M&A) transactions, therapeutic-focused corporate spin-outs have been perceived to be of superior value by venture investors when compared to pure start-up companies. The assumption held by many in the industry is that these technologies have been well vetted by their parent and therefore should command a premium valuation upon liquidity. This assumption, however, has not been fully tested with a robust data set. We propose a quantitative analysis of returns achieved through M&A for all therapeutic-focused corporate spin-outs, and subsequent comparison to a matched set of industry transactions for a given year. *Our hypothesis is that superior returns will be observed when compared to median industry proceeds.* (The relatively low absolute number of transactions available for analysis prevented calculations that reach statistical significance.)
- For Initial Public Offerings (IPO's), we will also analyze net proceeds of corporate spin-outs and compare those values to net proceeds of all biotech IPO's for a given year. Our hypothesis is that superior returns will be observed when compared to median industry proceeds. (Again, the relatively low absolute

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number of transactions available for analysis prevented calculations that reach statistical significance.)

3. Qualitative interviews with former executives and venture capitalists associated with these companies have been conducted in order to ascertain the specific factors which they believe influenced the superior valuations observed in these transactions. Our hypothesis is that a common series of factors will emerge in the therapeutic-focused corporate spin-outs which are associated with superior returns upon M&A or IPO exit.

#### Rationale for Study

Corporate spin-outs within the life sciences have become more frequent as large companies continue to face mounting pressure from capital markets to reduce overhead and maximize R&D efficiencies through divestiture of non-core programs. They provide the parent company with an option to minimize liability and risk associated with technological innovation while maintaining an option to reacquire the assets once they are more developed. A detailed analysis of US based therapeutic-focused spin-outs founded subsequent to 2000 has shown that these companies experience supra-median returns upon successful acquisition by a larger organization.

In addition to conducting an analytical assessment of net proceeds associated with liquidity events for corporate spin-outs, qualitative interviews were conducted with senior executives involved in these transactions. The decision process that executives must undertake to determine whether they should position the company for acquisition or continue to develop their programs internally remains poorly defined. Interviews with senior executives and venture capitalists directly involved with the formation and liquidation of these companies helped to elucidate some of the factors which were evaluated in making the decision to exit.

## **Chapter Two: Methodology**

## SpinCo Database Generation from Sources

In order to generate a comprehensive database of corporate spin-outs within the life sciences, information was gathered from several secondary sources, as detailed below. Transactions which met the following initial screening criteria were included in the database:

- Deal Type: Spin-out
- Deal Date: January 1990 Present
- Deal Status: Completed
- Industry Classification: Biotechnology (Windhoovers), Biotech (SDC Platinum), Biotechnology (VentureXpert)

The database generated from this initial query contained 186 records. (See Appendix for complete list of transactions.) Companies were broadly categorized based on their primary business strategy into one of six categories.

- Diagnostics: 10
- Drug Discovery: 14
- Healthcare Services: 20
- Medical Devices: 23
- Therapeutics: 96
- Other: 23

Among these transactions, 96 were based on therapeutics and 54 were US-based spinouts. Due to changes in the healthcare environment over the past twenty years, we have decided to focus on spin-outs founded subsequent to the year 2000, thereby restricting the experimental arm to 32 transactions. These companies form the primary data set of this thesis; their ability to generate financial returns through IPO or M&A will be compared against other companies in similar therapeutic areas with liquidity events in the same year.

#### IPO/M&A Databases

In order to provide a control group for comparison of overall performance of the Spinouts, a comprehensive list of IPO's and M&A activity within the US life sciences industry was constructed. Data was merged from Windhoover's and SDC platinum to provide a comprehensive list of transactions from 1990 - 2008.

### Commercial Databases

- **Capital IQ**: Comprehensive financial database containing information on corporate spin-outs, IPO's and M&A activity across several industries.
- **CRSP**: The Center for Research in Security Pricing [Graduate School of Business, University of Chicago]: Database containing comprehensive pricing information for stock of US & foreign publically traded companies.
- MedTrack: Database of clinical development status for US companies.
- **SDC Platinum** [Thompson Financial]: Mergers & acquisitions across several industries.
- VentureXpert [Thompson Financial]: Comprehensive database of information covering venture, buyouts, private equity funds, firms, executives, portfolio companies and limited partners around the world.
- Windhoovers: Windhoovers is a financial database focused on the healthcare sector. It provides a comprehensive list of business development and financial transactions within the life sciences.

### United States Food and Drug Administration (FDA)

- FDA Center for Biologics Evaluation and Research (CBER) & Center for Drug Evaluation and Research (CDER)
  - Drugs @ FDA (<u>http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm</u>)
  - o Orphan Drug Designation (http://www.fda.gov/orphan/index.htm)

## Target Respondents for Market Research Interviews

Data from the aforementioned sources were used to identify a target list of companies to profile; former corporate executives, venture capitalists and staff from companies which subsequently acquired the spin-outs were identified and recruited to participate in telephone interviews. The primary objective of the interviews was to ascertain the specific criteria or rationale for 1) pursuing the corporate spin-out initially and 2) identification of specific factors or elements which they believe contributed to the valuation upon successful exit.

Company	Interviewee	Title
AkaRx	Robert Desjardins	Former President & CEO
MGI Pharma	Mary Lynne Hedley	Head of R&D
Barrier Therapeutics	Al Altomari	Former President & CEO
Clarus Ventures	Nicholas Simon	Managing Director
Cerexa	Dennis Podlesak	Former President & CEO
Domain Associates	Eckard Weber	Partner
CoGenesys	Steven Mayer	Former CEO
Teva	Ram Petter	Director, Strategic Planning and New Ventures
Facet Biotech Corp.	Faheem Hasnain	CEO
Symyx Therapeutics Inc.	Iou Shonard	Former President & CEO
(Changed to Ilypsa)	Jay Shepard	Former President & CLO
5 AM Ventures	Scott Rocklage	Managing Partner
Amgen	Andy Davis	Director, Business Development

#### Figure 8 - Subjects for Market Research

Note: Records indented on the above table represent investors or acquirers of a given spin-out company.

## **Chapter Three: Results**

### Experimental Group Selection

We have identified a set of 32 corporate spin-outs that were incorporated in the US from 2000 to present with a primary business focus on the discovery and development of novel therapeutics. These companies will serve as our experimental group with regards to examining the factors which influence their higher degree of overall success when compared to case-matched control companies.





A critical review of the frequency with which these nascent companies successfully completed an Initial Public Offering (IPO) or acquisition identified that over 40% of this sample (13/32) have accomplished one (or both) of these events.

SpinCo	Parent	Launch Year	IPO	M&A
Evivrus	Enzon	2008	Canceled	
Facet Biotech	Protein Design Labs	2008	12/5/2008	
Forsight Vision 3	ForSight Labs	2008		
Mirina	Accelerator	2008		
Myriad Pharmaceuticals	Myriad Genetics	2008	Pending	
Abraxis BioScience	APP Pharmaceuticals	2007	11/14/2007	
Basic Services	Eaton Laboratories	2007		
CPEX Pharmaceuticals	Bentley Pharmaceuticals	2007	07/01/2008	
iBioPharma	Integrated Biopharma	2007	08/18/2008	
MDRNA	Nastech Pharmaceuticals	2007		
Relypsa	Amgen	2007		
Abbey Pharmaceuticals	Acadia Pharmaceuticals	2006		
CombinatoRx Singapore	CombinatoRx	2006		
Macroflux (Zosano Pharma)	Alza	2006		
Rxi Pharmaceuticals	CvtRx	2006	03/12/2008	
Text Thanhaceuteus	Yamanouchi Pharmaceutical.	2005		01/00/2008
AkaRx	Fujisawa	2005		01/09/2008
Cerexa	Peninsula Pharmaceuticals	2005		12/13/2006
CoGenesys	Human Genome Sciences	2005		01/22/2008
Tioga Pharmaceuticals	Merck KGA	2005		
Pharmacopeia Drug Discovery	Accelrys	2004	04/30/2004	
Aerovance	Bayer	2004		
Light Sciences Oncology	Light Sciences Corporation	2004		
Pecos Labs	Siga Technologies	2004		
Osteologix	Nordic Bone	2003	05/24/2006	
Symyx Therapeutics (Ilypsa)	Symyx Technologies	2003		07/18/2007
Barrier Therapeutics	Johnson & Johnson	2002	04/29/2004	06/23/2008
Ribapharm	ICN Pharmaceuticals	2002		
Affymax	GSK	2001	12/15/2006	
Ceregene	Cell Genesys	2001		
Calando Pharmaceuticals (Insert Therapeutics)	Arrowhead Research	2000		
Perlegen Sciences	Affymetrix	2000		

## Figure 10 - Corporate Spin-Out Target Universe

#### Initial Public Offerings in Biotech

In order to ascertain the relative success of these liquidity events, we have generated a comprehensive database of all healthcare related IPO's and M&A activity from 1990 – 2008 (see Methods section for more details). Comparison of liquidity events by year helps to normalize data and accounts for macroeconomic trends (recession, poor capital markets, war, etc...) that might otherwise influence the relative abundance of capital for these types of transactions.

As can be seen in the chart below, net proceeds associated with initial public offerings (IPO's) for corporate spin-outs roughly follow the median value for all life sciences IPO's of a given year.<sup>1</sup>





Note: Numbers in superscript represent the value percentile of that IPO relative to all life science IPO's in that year. (\* Net proceeds estimated by deducting average % of gross proceeds for other IPO's in that year.

Source: Windhoover's, SDC Platinum, SEC Filings, Company Press Releases

<sup>&</sup>lt;sup>1</sup> Affymax, Intermune, Osteologix and Panacos are considered outliers in this example, but yield no statistical significance to the overall trend.

#### Mergers & Acquisitions in Biotech

In contrast to the observation that net proceeds from IPO's are roughly equivalent in corporate spin-outs when compared to the market overall, net proceeds associated with merger and acquisition (M&A) activity during the same period yield a very different conclusion. While only five examples within our cohort have successfully completed an acquisition, all five cases beat their median vintage net proceeds – some of which exceeded the  $75^{\text{th}}$  percentile for transaction value in their vintage year. These five case studies have been circled in the chart below and will be profiled in depth in the next chapter.





M&A for Corporate Spin-Outs

Note: Numbers in superscript represent the value percentile of that deal relative to all life science M&A deals in that year. Source: Windhoover's, SDC Platinum, SEC Filings, Company Press Releases

#### Initial Public Offerings by Lead Program Phase of Development

Since spin-out companies often inherit programs from the parent company which are at an advanced pre-clinical or clinical stage of development, it was essential to take this into account. Data from MedTrack provided information on lead compound status for 515 US based companies. This information was merged with the 790 IPO records from Windhoover's to generate a list of 270 companies with both IPO information and clinical stages of development.



#### Figure 13 - Overlap of IPO & Pipeline Databases

Using this merged data set, control comparators were identified (where available) for each of the spin-out companies which have completed an initial public offering to date. Where specific cases could not be matched to all three dimensions (year of liquidity, phase of development of lead program and therapeutic area of lead program), therapeutic area was not filtered out. The table below summarizes the key findings for our nine spin-outs that have successfully completed an initial public offering.<sup>2</sup>

<sup>&</sup>lt;sup>2</sup> We have assumed in this study that information available from online databases is complete, current and accurate.

SpinCo	IPO	Net Proceeds	Lead Program TA	Status Comparable Firms		Net Proceeds	TA of Comps	
					3SBio Inc.	\$107.0	Cancer	
Abraxis	2007	\$700.0	Oncology	Market	Simcere Pharmaceutical Group.	\$168.6	Cancer	
CPEX	2008	\$33.0	Endocrine	Phase III	Only endo IPO in 2008			
Pharmaceuticals		++++++			Bioheart, Inc.	\$4.3	CV	
iBioPharma	2008	\$4.5	Infections	PC	IR Biosciences Holdings Inc (1 for 10 reverse stock split)		Derm/Infections	
Rxi	2008	\$47.9	Neuro/Metabolic/	PC	CPEX Pharmaceuticals, Inc.	\$69.9	Endocrine/Metabolic	
Pharmaceuticals		-	Cancer		China Sky One Medical, Inc.		All TAs	
					Cytokinetics Inc	\$95.9	Cancer/CV/Circ	
					Dynavax Technologies Corp	\$48.1	Cancer	
Pharmacopeia	2004	\$43.8	Cancer/Autoimm	Phase II	Metabasis Therapeutics Inc	\$32.6	Blood & Lymphatics	
Drug Discovery	2001	<b>V</b> IOIO	Cardio		Auxilium Pharmaceuticals Inc	\$36.6	Kidney	
					Alnylam Pharmaceuticals Inc	\$30.2	Blood & Lymphatics/Resp	
					Inhibitex Inc	\$36.0	Resp/Infections	
Osteologix	2006	\$10.0	Osteoporosis	Phase I	Altus Pharmaceuticals Inc	\$97.7	Kidney	
					Biosyntech Inc (Pink Sheets)			
					GPC Biotech AG	\$95.3	Cancer	
					ACADIA Pharmaceuticals Inc	\$31.3	CNS	
Barrier					Corcept Therapeutics Inc	\$49.1	CNS	
Therapeutics	peutics 2004 \$68.0 Dermatology	Dermatology	rmatology Phase III	SCOLR Pharma Inc		CNS		
					Dynavax Technologies Corp	\$48.1	Infections	
				Corcept Therapeutics Inc	\$49.1	Endocrine/Metabolic		
						MannKind Corp	\$81.4	Endocrine/Metabolic
					Auxilium Pharmaceuticals Inc	\$36.6	Muskuloskeletal	
					Trubion Pharmaceuticals Inc.	\$48.4	Al/Cancer	
					Cleveland Biolabs Inc	\$9.2	Cancer	
					Micromet Inc		Cancer	
					Osiris Therapeutics	\$35.8	CV/Circulatory/endo/musc ulo/resp	
					Indevus Pharmaceuticals Inc	\$32.3	CNS/Substance Abuse	
Affymax	2006	\$98.9	Kidney	Phase II	Neuro-Hitech Pharmaceuticals Inc		CNS	
Anymax	2000	\$30.5	Runey	r nase n	Targacept Inc	\$41.9	CNS	
					Raptor Pharmaceuticals Corp.		Digestive/endo	
					Achillion Pharmaceuticals Inc	\$55.3	Infections	
					Altus Pharmaceuticals Inc	\$97.7	Endocrine/Metabolic	
					Catalyst Pharmaceutical Partners Inc.	\$18.7	Substance Abuse	
Zymogenetics	2002	\$111.6	rh Factor XIII &	PC	TapImmune, Inc.		Cancer	
	LUUL		thrombin		Proteo Inc		Dermatology	

### Figure 14 - IPO Comparables Based on Lead Program Phase of Development

## Mergers & Acquisitions by Lead Program Phase of Development

A similar exercise was attempted to identify appropriate comparable M&A transactions for our five case studies which were successfully acquired. Unfortunately, very little overlap existed between recent M&A transactions in Windhoovers and clinical pipeline data on MedTrack.

To provide a similar comparator group for further analysis, an initial list of all life science M&A transactions which took place during the time horizon of our target liquidity events (2006 – 2008) was generated in Windhoover. This data set included 210 transactions, approximately 99 of which were based on non-therapeutic products (basic research, invitro diagnostics or molecular diagnostics). One deal was terminated before consummation and thirteen had no data on deal values. The remaining 97 transactions were analyzed to determine the phase of development of their lead program at the time of the transaction. SEC filings and press releases were reviewed to ascertain the lead stage of development and target indications for the target company's product pipelines.

Lead Status	2006	2007	2008
Pre-clinical	3	5	5
Phase I	4	4	5
Phase II	11	9	7
Phase III	4	2	5
Market	11	8	12
NDA Submitted		-	2

Figure	15 -	Merger	&	Acquisition	Deals	by	Lead	Program	Phase	of Devel	opment
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Source: Windhoovers, SEC Filings, Press Releases

Using this information, we were able to determine the median deal values for companies experiencing an M&A liquidity event by year and lead program phase of development. Superimposed on this chart are the net proceeds associated with each of the five corporate spin-out M&A events. They are coded to indicate the vintage year of the liquidity event. Unfortunately, due to the low sample size it was impossible to isolate indication-specific data for valuations by stage of lead program.

Based on this data we conclude that AkaRx, CoGenesys and Ilypsa all generated supramedian returns when adjusted for lead program phase of development and year of liquidity event. Barrier Therapeutics and Cerexa were unable to generate supra-median returns when adjusted for these factors. Barrier Therapeutics had already successfully closed an IPO in 2004 and was financially constrained at the time of their ultimate acquisition by Stiefel Laboratories. This forced the company to accept the acquisition on less than ideal terms. Cerexa's exit was considered by many in the investment community to be among the most lucrative in the history of the biotech industry. Several other large M&A deals closed in 2006 as well, raising the median deal value in 2007 to \$2.125 Billion.

Figure 16 - Merger & Acquisition Comparables Based on Lead Program Phase of Development



Note: Colors in the table above correspond to the vintage year of the M&A exit for each of the spin-outs profiled. The median value for 2007 M&A with a lead compound on the market was \$2.125 Billion due to several abnormally large transactions (Medimmune/AstraZeneca, MGI/Eisai, Pharmion/Celgene, New River/Shire and Reliant/GSK.)

Source: Windhoovers, SEC Filings, Press Releases

#### Internal Rate of Return for Corporate Spin-Outs

Another dimension that is often used to measure investment success is the internal rate of return (IRR). IRR incorporates the magnitude of an investment's return over a finite time horizon, and is calculated by the following formula:

NPV = 
$$\sum_{t=0}^{N} \frac{C_t}{(1+r)^t} = 0$$

Typically investments will incur negative cash flows ( $C_t$ ) in the early years and experience a liquidity event that produces a positive cash flow later in the investments time horizon. The IRR is determined by taking the net present value of future cash flows, setting the equation equal to zero and solving for the appropriate discount rate. The tables below provide information on the Series A investments for several corporate spin-outs as well as their subsequent liquidity events and respective IRR's.

		Series A					
Company	Date	\$ Raised	Post \$	Date	\$ Raised	IRR	Multiple
Intermune	4/30/1999	\$2.30	\$18.00	3/24/2000	\$125.00	758%	6.9
Esperion	7/6/1998	\$0.50	\$2.34	8/10/2000	\$63.00	380%	26.9
Versicor	7/1/1995	\$0.06	\$0.37	8/3/2000	\$50.00	162%	135.1
Panacos	11/14/2000	\$3.25	\$6.10	3/11/2005	\$120.88	100%	19.8
Osteologix	6/1/2003	\$2.00	\$4.00	5/24/2006	\$10.00	36%	2.5
ONYX	4/16/1992	\$5.00	\$12.50	5/9/1996	\$32.10	26%	2.6
Targacept	8/22/2000	\$30.40	\$41.08	4/12/2006	\$45.00	2%	1.1
Barrier	5/10/2002	\$46.00	\$83.00	4/29/2004	\$68.00	-10%	0.8
Therapeutics							
ZymoGenetics	11/1/2000	\$150.00	\$367.00	1/31/2002	\$111.60	-61%	0.3
Sources:	VentureSource.	Windhoovers,	SEC Filings				

Figure 17 – Internal Rate of Return fo	Corporate Spin-Outs Experiencing IPO's
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Internal rates of return for IPO activity varied from -60% to over 750%. With the exception of Barrier Therapeutics and ZymoGenetics, the remaining corporate spin-outs profiled generated a positive IRR through completion of an IPO. Return multiples ranged from 0.3 - 135X across this data set.

Figure 18	- 1	Internal	Rate o	f Return	for (	Corporate	Spin-Outs	Experiencing M&A	L
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		Series A		Liquidity Event						
Company	Date	\$ Raised	Post \$	Date	\$ Raised	IRR	Multiple			
Cerexa	8/23/2005	\$50.00	\$70.00	1/11/2007	\$493.60	309%	7.1			
AkaRx	8/12/2005	\$15.50	\$20.00	1/9/2008	\$300.00	207%	15.0			
CoGenesys	6/9/2006	\$55.00	\$115.00	2/21/2008	\$400.00	108%	3.5			
Barrier	5/10/2002	\$46.00	\$83.00	8/7/2008	\$148.00	10%	1.8			
Ilvpsa	5/9/2003	\$10.00	\$60.00	7/18/2007	\$420.00	59%	7.0			
51 G	VanturaCourses	Windhoonorg	CEC Eilinge							

Sources: VentureSource, Windhoovers, SEC Filings

The five case studies profiled above generated IRR's of 10% - 309% through completion of an M&A event. With the exception of Barrier Therapeutics, IRR values were far in excess of traditional biopharmaceutical venture investments (see explanation below). Return multiples were equally impressive, with a range of 1.8 - 15X.

Information from VentureSource has been included in the subsequent table to serve as a control measurement for overall IRR across all investments in the biopharmaceutical space on an annual basis. Despite erratic returns for pharmaceuticals and biotechnology R&D through the late 1990's, general IRR's have been in the 10-20% range. Healthcare software investments also experienced an abnormal return in 2003, though general IRR's in this segment are approximately 10%.

# Figure 19 – US Venture Capital Dollar-Weighted Internal Rate of Return on Vintage Year Companies

Industry	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007
Biotechnology/Biopharma R&D	37.10	34.33	10.15	37.09	70.25	0.61	8.81	15.10	28.97	10.37	33.46	26.55	0.25
Healthcare Devices	28.30	6.72	9.15	13.97	7.84	9.38	5.70	10.85	10.76	9.72	11.95	8.35	4.69
Healthcare Services	10.27	0.95	10.09	11.15	6.36	8.00	13.63	7.19	25.41	18.97	18.35	11.71	3.90
Healthcare Software	(4.52)	26.70	26.46	0.22	4.61	(0.48)	1.03	6.21	55.52	14.16	20.55	(0.91)	14.26
Pharmaceuticals	35.42	117.30	25.82	70.41	23.14	8.72	17.32	(2.35)	9.17	27.21	1.07	31.46	3.54

As of 9/30/2008 Pooled gross means of companies receiving initial investment in:

Source: Cambridge Associates, LLC

In response to these observations, we have focused the remainder of this thesis on profiling the five spin-outs which achieved a successful M&A event and identifying the qualitative factors that influence the overall success of corporate spin-outs through M&A activity within the life sciences. This thesis reviews contemporary literature and integrates insights from qualitative interviews with former corporate executives associated with many of the spin-outs being investigated.

## **Chapter Four: Corporate Spin-Out Profiles**

The following chapter provides a brief chronology of events for five case studies of corporate spin-outs which achieved a successful exit via acquisition by a larger corporate entity. The chronology includes a summary behind the genesis of the initial spin-out as well as the strategic rational behind their subsequent acquirer.

The survey methodology employed in our study has resulted in non-parametric data across the companies profiled. To prevent inappropriate comparisons across the companies we have organized the profiles into the following primary categories:

- Rational for Incorporation
- Initial Capitalization
- Product Development
- Acquirer's Interest in Spin-Out
- Deal Structure
- Summary

Minor variations to this format have been included to capture additional insights from specific interviews. In addition to these sections, a tabular summary of each liquidity event has been included at the end of each company profile.

### AkaRx Corporate Profile

AkaRx was incorporated in 2005 following the completion of a merger between Yamanouchi Pharmaceuticals and Fujisawa Pharmaceuticals. The company was lead by a former executive from Yamanouchi, Robert Desjardins, and was developing a clinical stage program in thrombocytopenia. Approximately three years after incorporation, the company was successfully acquired by MGI Pharma for approximately \$300 Million.

#### **Rational for Incorporation**

The primary rational for the incorporation of AkaRx was to maintain continuity of two ongoing NDA submissions to the FDA. In February 2004, Yamanouchi had submitted two NDA's which were under review and pending approval at the time and Fujisawa announced their intention to merge. In tandem with this announcement, the headquarters of the new company (Astellas) would be located in the current Fujisawa headquarters; the Paramus, NJ offices would be closed. Despite significant retention bonuses, key personnel involved with the two NDA submissions were being heavily recruited by other companies.

A group of senior management from Yamanouchi proposed the creation of a spin-out to the chairman of Astellas. The newly created entity would retain key personnel until Yamanouchi's ongoing NDA submissions were approved. In exchange, Astellas would out-license drugs that were out of their strategic focus to the newly created spin-out. The key drug that was out-licensed was YM-477 (renamed AKR-501) and was being developed for thrombocytopenia. Specific target population included idiopathic thrombocytopenia pupura (ITP), chemotherapy-induced thrombocytopenia and hepatitis-induced thrombocytopenia.

#### **Initial Capitalization**

The company was launched with a bridge loan from Yamanouchi in December 2004. A syndicate of venture investors was subsequently assembled, with InterWest Partners and Sutter Hill Ventures leading the investment. Yamanouchi's equity stake in the company was reduced to approximately 10% following the initial tranche. Key management from Yamanouchi was retained in order to continue monitoring of the two outstanding NDA's. (These two NDA's were subsequently approved and have been successfully marketed for several years.)
#### Figure 20 - Capitalization Timeline for AkaRx



#### **Product Development**

AkaRx filed an IND for their lead drug and began clinical development in mid-2005. By the end of the year, clinical data was available showing dose response and pharmacokinetic profile. A phase II clinical study was initiated shortly thereafter which also demonstrated promising results.

During this same time period, Amgen and GSK were developing competitive products. As AKR-501 continued to advance in the clinic, the company realized that they lacked sufficient capital resources to continue development alone. Upon initial discussions with potential co-development partners, it became clear that an acquisition was preferable.

## **MGI Pharma's Interest**

The current CEO of MGI Pharma had a close relationship with a managing partner at Interwest, a majority shareholder of AkaRx, and was able to facilitate an introduction of the two companies. Following the first company presentation, MGI believed that AkaRx desired a higher valuation than they were worth. Approximately six months later AkaRx returned to MGI for a second presentation, during which they indicated that they were willing to execute a transaction on more realistic terms. (This may have been influenced by additional clinical results of the two competing drugs that were released following the first road show, which widened the gap between AkaRx and competition.)

The rationale behind MGI's interest in AkaRx was primarily to fill their complementary commercial bandwidth in hematology and oncology. In 2006 the company received FDA approval for Dacogen and began to detail the product in the hematology/oncology

markets. Despite strong sales uptake, the company believed that the sales reps had sufficient capacity to add a second product to their portfolio in the space. With targeted indications for AKR-501 including ITP and chemotherapy induced thrombocytopenia, there was a strong overlap in the managing physicians between the two drugs.

## **Deal Structure**

Shortly following the second company presentation, the two parties agreed to consummate an option structured deal, whereby MGI paid an upfront fee and continued to finance the development of the lead program in thrombocytopenia. The option was exercised in the Fall of 2007, though took until January 2008 to close the deal. (In the Fall of 2008, MGI was acquired by Eisai.)

## Summary

AkaRx was incorporated to retain key personnel who were actively involved in two ongoing NDA submissions to the FDA. In exchange for their assistance, Yamanouchi Pharmaceuticals agreed to out-license AKR-501 and float a bridge loan to the new entity. AKR-501 entered clinical development in 2005 and was eventually acquired by MGI Pharma in 2007.

# Figure 21 - Summary of Liquidity Event for AkaRx

Deal Date	1/9/2008
Description	MGI Pharma Inc. was granted exclusive rights to develop AKR- 501, a novel, small molecule thrombopoietin mimetic being developed for the treatment of thrombocytopenia, and an option to acquire AkaRx at MGI PHARMA's sole discretion at any time up to January 8, 2010. This option was exercised on 1/9/2008.
Value	\$45M up front and \$255 at time of option exercise. (Total Deal Value: \$300M)
Management	<ul> <li>Robert Desjardins – President &amp; CEO (Former Chief Development Officer, Yamanouchi Pharmaceuticals)</li> <li>Donna Tempel – COO (Former VP Project Management, Yamanouchi Pharmaceuticals)</li> <li>Rudolph Lucek – EVP Regulatory Affairs &amp; QA (Former VP Regulatory Affairs, Yamanouchi Pharmaceuticals)</li> <li>Steven Silbert – EVP Operations (Former Sr. Director, Clinical Administration and OA, Yamanouchi Pharmaceuticals)</li> </ul>
# of Employees	13
Lead Program	Phase I
Market	Thrombocytopenia
0 1 D /	· ·

Orphan Drug/ Accelerated	No Orphan Drug Designation	
Approval	1	

#### **Barrier** Therapeutics Corporate Profile

Barrier Therapeutics was spun out of Johnson & Johnson in September 2001. The company constituted J&J's entire Dermatology R&D arm and included two products with full phase III data packages ready for submission to the FDA.

#### **Rational for Incorporation**

The primary reason for creating Barrier came from the observation that Johnson & Johnson was unwilling to dedicate resources to the development of their internal pipeline. Dedicating 15-20 full time equivalents (FTE's) to research was considered to be a source of distraction within the organization. The corporate culture within the firm was focused on obtaining innovative products through acquisition as opposed to internal R&D.

One additional catalyst for the creation of Barrier Therapeutics was the assertion that dermatology was out of Johnson & Johnsons commercial strategy. The company had significantly devalued these assets which provided an opportunity for a financial arbitrage by outside investors.

## **Initial Capitalization**

During the first year of incorporation, Barrier was seeking venture investors with the assistance of the Johnson & Johnson Development Corporation (JJDC) an internal venture capital arm of the parent company. TL Ventures was the first firm to review their business plan and agreed to invest as well as arrange the syndicate. Through contacts established by JJDC, Barrier was able to close a \$46 Million Series B in May 2002.

A large factor in the success of raising money can be attributed to the close ties to the parent organization; the underlying patents, technology, NDA's, management and manufacturing facilities were all coming from Johnson & Johnson and provided investors with a sense of security. In exchange for spinning out the assets, Johnson & Johnson retained an equity stake of ~35% in Barrier, and was entitled to receive pre-defined milestone payments and royalties on future product sales.

Bridge Loar \$0.15 M F	n (10/01) Series A \$46.0 M \$83.0 M	(5/02) Raised (Post \$)	Series B (10/03) \$32.0 M Raised	IPO (4/04) \$75.0 M Raised \$345.81 (Post \$)			Acquisiti \$148 I	on (6/08) Million
2001	2002	2003	2004	2005	2006	2007	2008	

## Figure 22 – Capitalization Timeline for Barrier Therapeutics

#### **Product Development**

The pipeline of products that were initially spun out to form Barrier included two products with a full Phase III data package that was ready for FDA submission, as well as several other products in earlier stages of clinical development. (Johnson & Johnson retained any dermatology products which were already on the market.)

Barrier's initial product development strategy was to focus on developing and commercializing topical dermatology products first. Revenues from these products could then help reduce the burn rate and be funneled into R&D efforts for oral drugs.

#### Leveraging Capital Markets to Fund R&D

In April of 2004 the company successfully completed an initial public offering (IPO) which generated net proceeds of \$75 Million. The IPO was led by JP Morgan, Morgan Stanley and Bank of America. One source of value creation for the public markets was the perception that the company was being lead by former Johnson & Johnson executives. Another factor which caused all of the banks to compete for this IPO was the importance of keeping the parent company happy.

Following completion of the IPO, Barrier was in a more secure cash position to continue their product development efforts. Unfortunately, delays in the clinic prevented some of

their topical products from coming to market on time. This placed a large R&D burden on their P&L; eventually the company's burn rate approached \$50 Million annually which required them to complete a secondary offering. As the economic climate became less receptive to follow on deals, the company was faced with a choice on how to minimize the cash burn: 1) sell the business or 2) acquire something big that can drive revenue growth in the near term.

## Stiefel Laboratories' Interest and Deal Structure

In June 2008, the company was acquired by Stiefel Laboratories for approximately \$148 Million. Despite representing a 73% premium to the trailing 30 day stock price, this liquidity event was not considered a tremendous success by either the management team or the investors. Stiefel's primary interest in Barrier was on the pipeline, with a particular interest in high quality Johnson & Johnson products.

The deal was structured in two transactions; a tender offer for outstanding shares of Barrier Therapeutics followed by a merger of the two companies into a separate operating entity called Bengal Acquisition Inc.

#### **Summary**

Barrier Therapeutics was established because Johnson & Johnson was unwilling to dedicate resources to the development of their dermatology pipeline; their corporate culture emphasized obtaining innovative products through acquisition as opposed to internal R&D.

The company successfully raised over \$78 Million in venture financing and completed a \$75 Million IPO in 2004. Barrier was eventually acquired by Stiefel Labs in 2008 for \$148 Million. Stiefel's primary interest in Barrier's was its pipeline of Johnson & Johnson products.

Figure 23 - Summary of Liquidity	Event for Barrier	Therapeutics
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	<b>IPO Date:</b> 4/29/04 (\$75M in gross proceeds)					
Deal Date	M&A Date: 6/23/08					
Description	<ul> <li>Sold to Stiefel Labs in a 2 part transaction:</li> <li>Tender offer</li> <li>Merger of Barrier into wholly-owned subsidiary (Bengal Acquisition Inc.)</li> </ul>					
Value	\$148M in cash (73% premium to trailing 30 day close price)					
Management	<ul> <li>Al Altomari – President and CEO (Former GM, Ortho Neutrogena)</li> <li>Charles Nomides – COO (Former Director, R&amp;D Consumer</li> <li>Products Worldwide, Johnson &amp; Johnson)</li> <li>Braham Shroot – CSO (Former CSO, DFB Pharmaceuticals &amp;</li> <li>President, Galderma)</li> </ul>					
# of Employees	115					
Lead Program	<ul> <li>3 marketed programs:</li> <li>Solagé (solar lentigines)</li> <li>Vusion (diaper dermatitis)</li> <li>Xolegel (seborrheic dermatitis)</li> </ul>					
Market	Dermatology					
Orphan Drug/ Accelerated Approval	Orphan Drug designation for liarozole (congenital ichthyosis) – 6/18/2004					

## CoGenesys Corporate Profile

CoGenesys was founded in 2006 as a spin-out from Human Genome Sciences (HGS). The company continued to develop albumin-conjugated protein based therapeutics which were deemed to be out of strategy by the parent company. Approximately two years after incorporation, the company was successfully acquired by Teva for \$400 Million.

Human Genome Sciences was originally focused on gene discovery and development of protein therapeutics from those newly discovered genes and EST's. HGS had a unique business model which included wet chemistry labs which cloned all of the genes being

discovered. This enabled the company to leverage both bioinformatics and an extensive clone library to enable more rapid identification of new potential lead compounds.

Using homology comparisons and other techniques, the company was able to systematize and prioritize the development of a sub-set of the lead compounds based on likelihood of clinical success and overall market potential. Many of these compounds were submitted as IND's to the FDA and entered early clinical development.

In addition to the core technology at HGS, the company also acquired technology which enabled the generation of albumin-fusion proteins developed at Princepea. This technology helped to boost the half life of many therapeutic proteins, and also simplified the purification process.

#### **Rational For Incorporation**

In 2004, Bill Haseltine retired as CEO of HGS and was replaced by Tom Watkins. Watkins came to HGS from TAP, and employed a very different management philosophy than Bill Haseltine. Shortly following his appointment as CEO, Watkins began to prioritize the numerous active IND programs and identified a set of key products to focus on. His primary objective in this process was to minimize the near term burn of capital resources and maximize the chance of creating revenue generating marketable products. Albuferrin (albumin interferon alpha), lymphostat (antibody), albumin GLP (diabetes) were the primary drugs that HGS decided to focus their efforts on.

In tandem with the ongoing cost restructuring, many of the staff scientists affiliated with programs that were deemed out of strategy were being laid off. This was of concern to Craig Rosen, who approached Steve Mayer in hopes of finding a creative solution to remedy the situation. They mutually decided to create a 'Skunk Works' group which leveraged an empty facility and a core group of top scientists. The primary objective was to screen the newly shelved products and create new lead derivatives. These new derivatives could either be re-entered into the HGS pipeline or sold to 3<sup>rd</sup> parties.

## **Initial Capitalization**

Despite having the support of Mayer and Rosen, the process of gaining internal support from senior management proved to be quite difficult. The costs associated with the 60-70 FTE unit was estimated to be \$20 Million per year and ran counter to Watkins' primary objective of cutting near term expenses. Mayer suggested that HGS enact an 'intrapreneurship' model, whereby a wholly owned subsidiary is created for the purpose of developing these products and senior management is provided with an equity stake in the new corporate entity. (The stock price for HGS had been sufficiently suppressed that it no longer offered the correct incentive to management. This option allowed for the creation of a new currency and provided an increased level of motivation for the team.)

The spin-out option was subsequently presented to the Board of Directors. This model enabled the newly created company to do the following:

- 1. Establish collaborative research initiatives with third parties
- 2. Seek external financing
- 3. Provide a real option value to HGS if programs succeeded in the clinic

Despite these benefits, Watkins was uncomfortable with engaging in this type of transaction, but was willing to have Mayer and Rosen buy the rights directly from HGS. Under the terms of the contract, the new company assumed all responsibility for the employees, retained the building and equipment which was not being utilized and obtained a broad license to various genes, EST's and the albumin fusion technology. HGS agreed to finance the venture for the first six months, during which Mayer and Rosen were seeking venture capital. Following the successful completion of fundraising, HGS received a licensing fee for the technology as well as payment for the cash burn from the previous six months of operations.

The separation was completed in June of 2006 and CoGenesys closed on a \$55 Million round of financing. One compelling proposition to the venture capitalists was their

unique business strategy of focusing on product developing through Phase II. By leveraging cost estimates from the latest Tufts study, Mayer estimated that building a fully integrated biopharmaceutical company would cost approximately \$700 Million and take 12 years. This estimate was broken into three primary phases of company development:

- 1) Initial company development and preclinical research (5 years, \$200 Million)
- 2) Early clinical development (2-3 years, \$100 Million)
- 3) Phase III and commercialization (5 years, \$400 Million)

Mayer was able to illustrate this concept by using an S-curve to show the capital requirements as a function of the likelihood of receiving FDA approval. In tandem with the time and cost estimates, he also incorporated the risk profile and was able to show that both phase I and phase III generated a low internal rate of return for different reasons. (Phase I is low cost but high risk while Phase III is high cost and low risk.) CoGenesys was focused on developing products from IND through Phase II, which maximized the IRR to the investors.

From the outset, CoGenesys was targeting M&A as a liquidity event over IPO due to the differential valuations accorded by pharmaceutical companies. Another concern with an IPO exit in the contemporary business environment was the ongoing burden associated with being a publicly traded company.

#### Figure 24 - Capitalization Timeline for CoGenesys

Series A (6/06) \$55.0 M Raised \$115.0 M (Post Money)

Acquisition (2/08) \$400 Million

2006

2007

2008

#### **Product Development**

The two primary products being developed by CoGenesys were a long-acting beta natriuretic peptide and long acting G-CSF. These programs were being developed in the clinic until 2008, at which point the company's capital resources were sufficiently depleted to warrant pursuing a Series B round of venture financing or negotiate a successful liquidity event. When the company received an offer by Teva Pharmaceuticals, they decided to pursue that option and were subsequently acquired in 2008 for \$400 Million.

## **Teva's Interest in CoGenesys**

Teva Pharmaceuticals was historically known to be a small molecule based generic company. However, the company's long term strategic plan was to develop a core competency in the manufacture of protein based therapeutics in order to compete in the biosimilar market. In order to facilitate knowledge transfer and maximize the chances for success, 100% of the CoGenesys employees were retained following the acquisition. The senior management team from CoGenesys is currently engaged in providing consulting services until September 2009 on an 'as needed' basis. This arrangement was designed to provide Teva with the necessary expertise when needed, while enabling the former executives to pursue other entrepreneurial ventures.

#### Summary

CoGenesys was founded in 2006 in response to a shift in senior management at the parent company, Human Genome Sciences. The new CEO determined that albumin-conjugated protein based therapeutics to be out of strategy and refused to dedicate resources to those programs.

Approximately two years after incorporation, the company was successfully acquired by Teva for \$400 Million. Teva was interested in expanding into the biologics manufacturing space.

Figure 25 - S	ummary of	Liquidity	Event fo	or CoGenesys
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Deal Date	1/22/2008	
Description	Acquisition of assets for \$400M	
Value	\$400M in cash	

Management	<ul> <li>Steven Mayer – CEO (Former CFO, Human Genome Sciences)</li> <li>Craig Rosen – CSO (Former CSO, Human Genome Sciences)</li> <li>Indra Sanyal – CTO (Former VP, Process Development, Human Genome Sciences)</li> <li>Alain Cappeluti – CFO (Former VP, Financial Operations, Human Genome Sciences)</li> </ul>
# of Employees	72

Lead Program	Phase II		
Market	Neutropenia		
Orphan Drug/ Accelerated Approval	No Orphan Drug Designation		

## Ilypsa/Relypsa Corporate Profile

Ilypsa was founded in May of 2003 as a spin-out from Symyx Technologies. The initial team included two former Symyx employees, Gerrit Klaner and Dominique Charmot.

## **Rational for Incorporation**

Symyx Technologies was currently engaged in the application of their proprietary technologies in polymers, ceramics, and other non-pharmaceutical materials. Two entrepreneurs within the parent organization believed that the technology had significant

potential in the pharmaceutical space, but the company was not interested in developing those capabilities internally.

#### **Initial Capitalization**

The company was initially capitalized with 5AM Ventures and Sprout Ventures (now New Leaf Ventures). Vijay Lathi, Managing Partner at New Leaf Ventures, took a lead role in licensing the Symyx technology for applications in the pharmaceutical sector. In exchange licensing the technology, Symyx received a straight royalty position in the new venture, but was not provided with any claw back options or rights to future products.

## Figure 26 - Capitalization Timeline for Ilypsa

Series /	A (5/03)	S	Series B (6/05)	Corp Loan (4/06)	Debt (3/07)	Acquisition (7/07)
\$10.0 M	I Raised	\$	36.0 M Raised	\$22.0 M Raised	\$1.5 M Raised	\$420 Million
2003	2004	2005	2	2006	2007	2008

#### **Product Development**

Once incorporated, the company focused on identifying specific markets where the technology could provide a source of differentiation. One area that appeared to be attractive involved the regulation of salts and ions in the gastrointestinal tract; phosphate binders in particular were thought to represent a very attractive market opportunity. The current market leader, Renagel, was being marketed by Genzyme and generated annual revenues in excess of \$500 million dollars. Genzyme acquired the product in an M&A transaction with Geltex Pharmaceuticals in September 2000. The product was capable of binding phosphate, but had very little selectivity and consequently bound many other ions and salts as well.

The team thought they could use the polymer technology to design a superior (more selective) phosphate binder. This would potential provide the following benefits:

- 1) Lower dosing regimen
- 2) Improve patient compliance
- 3) Reduce side effect profile

High throughput screens were initiated to identify more selective phosphate binders; the final lead compound was able to bind approximately 80% phosphate by weight, compared to Renagel's 20% binding by weight.

Once a lead polymer was identified through HTS, the corporation began to focus on the development of a pre-clinical data package and ultimately commencing clinical studies.

With clinical development underway, it became apparent that the company would need to seek out additional financing to maintain operations. Once the program entered Phase I of clinical development, the team decided to raise a Series B. In June of 2005, the company was able to close a \$36M round with new investors including USVP and Delphi Ventures.

#### **Business Development Initiatives**

In tandem with raising a Series B, the company was also initiating discussions with several Japanese companies for rights to their technology in Japan. Two companies progressed through the diligence and arrived with term sheets for Ilypsa. Ultimately, the company chose to partner with Astellas. Terms of the licensing agreement provided total aggregate proceeds of \$92 Million to Ilypsa, including a \$22 Million up front payment and royalties in the mid-teens on future product sales. (The company received approximately \$35 Million over the first two years of the license.) They continued to seek out strategic partnerships around the world, but opted to keep US rights with Ilypsa.

In December 2005 the company hired Jay Shepard as CEO to provide assistance with corporate partnering, product development and commercialization. (Prior to this event, Scott Rocklage had served as acting CEO since the company's inception.) Based on the

precedent established by Astellas in Japan, the terms that Ilypsa was considering for partnerships seemed quite high to other potential firms. It wasn't long before companies began to determine their receptivity to an acquisition. Lehman Brothers was retained to run the process, which ultimately yielded five bids. Amgen's bid was eventually selected and in June 2007 they announced the completion of the transaction for \$420 Million.

#### **Amgen's Interest in Ilypsa**

Over the past two decades, Amgen has established a strong position in the nephrology space. As a consequence of this strategy, the company was continuously evaluating opportunities for external partnerships to bolster the existing pipeline.

The nephrology space has not seen much innovation over the past several decades, leading to a relatively low deal volume. The landscape of opportunities at the time evolved mostly around erythropoietin stimulating agents (ESA's) (of which Amgen already had two), phosphate binders and calcium mimetics. Amgen's outreach efforts were focused on diversifying their portfolio across these mechanisms of action. Despite being a crowded landscape, Ilypsa's phosphate binder had some characteristics which Amgen thought could be clinically superior to Renagel and their follow on molecule, Renvela.

Several manufacturing and formulation issues were identified early in the diligence process, but scientists at Amgen thought they could be overcome. The deal was initiated around in-licensing ILY-101 as a stand alone product. Since Ilypsa's business was focused on this program, the investors were not very interested in such a deal. The conversations turned to an M&A, due diligence was conducted and a deal was consummated in June 2007. Through the diligence process, Amgen's team investigated the other assets as well (ILY-102 & ILY-105), but the key value driver for Amgen was the phosphate binder, ILY-101.

Despite positive preliminary clinical data, Amgen announced in their 2008 Annual Report that they were reviewing other options for the commercialization of ILY-101

We have reviewed data from recently-completed phase 1 and 2 clinical trials for AMG 223, the product candidate acquired in the Ilypsa acquisition. The results were consistent with what is likely required for registration of a phosphate-binding therapy. However, in the context of our overall development portfolio, the Company will be reviewing other options for the commercialization of this investigational product.

Source: Securities and Exchange Commission

#### Post Merger Integration and the Formation of Relypsa

Following the announcement of the deal, Amgen indicated that they intended to only pursue development of ILY-101; they had no intention of continuing development of any other programs from Ilypsa. Through subsequent conversations between Andrew Gengos, Vice President of Corporate Development & Strategy, Roger Perlmutter, EVP R&D and Scott Rocklage of 5 AM Ventures, the concept of spinning out the other assets into a new venture was introduced. The concept eventually received approval by Kevin Shearer and Relypsa was established in October 2007.

Relypsa was able to retain 40 of the 70 original employees from Ilypsa (Amgen had intended to terminate all 70 employees following the closing of the deal). The entire management team remained intact and was able to successfully raise a \$33 Million Series A. The investment syndicate included 5 AM Ventures, CMEA Ventures, Delphi Ventures, Mediphase Venture Partners and New Leaf Ventures.

Since its inception, the company has pursued development of a lead program in hyperkalemia. In December 2007 an IND was initiated for this program; they have subsequently completed two Phase I and one Phase II clinical studies to date. Prior to establishing Relypsa, Amgen had negotiated an opt-in option for this program, which includes a pre-defined valuation and timeline for exercise. Details of this opt-in deal were not publically available.

## Summary

Ilypsa was incorporated to leverage core polymeric technologies developed by Symyx Technologies in the pharmaceutical space, a market that was out of strategy for the parent.

The company's lead program was a selective phosphate binder being developed for patients with chronic kidney disease (CKD). In 2005, Ilypsa negotiated a \$92 Million strategic alliance with Astellas and closed a Series B of venture financing.

The lucrative terms of this Japan-only deal made other potential suitors consider M&A as a viable alternative to product licensing. The company was eventually acquired by Amgen in 2007 for \$420 Million. Despite preliminary success in the clinic, Amgen has subsequently discontinued development of ILY-101. The other programs being developed by Ilypsa were subsequently spun out into a new corporate entity, Relypsa. Amgen retains an equity stake in Relypsa, but has not contributed any financing to the spin-out.

## Figure 27 - Summary of Liquidity Event for Ilypsa/Replysa

Deal Date	6/4/2007		
Description	Acquisition of assets for \$420M		
Value	\$420M in cash		

	Jay Shepard – President and CEO (Former VP Commercial				
	Operations, Telik)				
	Jeryl Hilleman – CFO (Former VP Operations, Geron)				
	Detlef Albrecht – Chief of R&D (Former VP Clinical				
	Development, ALZA)				
	Gerrit Klaerner – CBO				
Management	Michael Burdick – VP Regulatory				
	Jerry Buysse – VP Pre-Clinical R&D (Former VP Discovery				
	Biology, Microcide Pharmaceuticals)				
	Guido Smeets – VP Clinical Development (Former VP R&D,				
	GMP Companies)				
	George Tyson – VP Pharmaceutical Science (Former VP				
	Manufacturing Operations, Threshold Pharmaceuticals)				
# of Employees	78				

Lead Program	Phase II	
Market Hyperphosphatemia in CKD patients on hemodialysis		
Orphan Drug/ Accelerated Approval	No Orphan Drug Designation	

## Cerexa Corporate Profile

Cerexa was incorporated in 2005 to continue development of novel anti-infective agents. In less than two years the company was successfully sold to Forrest Laboratories for \$494 Million in total remuneration.

## **Rational for Incorporation**

Cerexa was founded in 2005 following the acquisition of the parent company, Peninsula Pharmaceuticals, by Johnson & Johnson. At the time of the acquisition, Peninsula had

two anti-infective products in development; doripenem (Phase III) and ceftaroline (entering Phase I). Johnson & Johnson was only interested in developing doripenem at the time of the deal and was not willing to provide any remuneration for ceftaroline. As a consequence of this decision, the investor syndicate agreed to sell doripenem to Johnson & Johnson, while simultaneously creating a new company to continue development of ceftaroline.

Many members of the senior management team at Peninsula subsequently joined Cerexa following the acquisition. This was a primary consideration from the venture syndicate; they tend to have a predilection to investing in serial entrepreneurs with a successful track record. Often the spin-outs are formed around a single molecular entity that has been out of strategy for the parent company to develop.

#### **Initial Capitalization**

The company was initially capitalized through a bridge loan of \$16 Million in June, 2005. Two months after the bridge loan the company closed a \$50 Million Series A financing which was co-lead by Frazier Healthcare Ventures and New Leaf Partners; other investors included Cannan Partners, Domain Associates, EGS Healthcare Capital Partners and Montreaux Equity Partners.

Figure 28 – C	Capitalization Time Bridge Loan (6/05) \$16.0 M Raised	Series A (8/05) \$50.0 M Raised	Acquisition (1/07) \$494 Million
2005		2006	2007

#### **Product Development**

The company continued to develop ceftaroline while simultaneously in-licensing three other compounds in earlier stages of development. Due to the rapid clinical trial designs for anti-infective compounds, the company was able to complete their Phase I and Phase II clinical studies in approximately one year and attracted Forest Laboratories' interest in the company. Cerexa was subsequently acquired for approximately \$494 Million in December of 2006. This deal has subsequently been touted by the investor community as generating the highest IRR of any therapeutic company to date. Net returns to some investors were approximately 9X over a 12-18 month horizon.

## Summary

Cerexa was founded in response to an acquisition of the parent company by Johnson & Johnson. J&J had placed no value on Peninsula's anti-infective ceftaroline and had no plans to continue development of the drug.

Several members of the senior management team from Peninsula joined Cerexa and continued to advance ceftaroline in the clinic. Less than two years following incorporation, the company was sold to Forrest Labs in 2006 for \$494 Million.

# Figure 29 - Summary of Liquidity Event for Cerexa

Deal Date	12/13/2006	
Dear Date	<ul> <li>Forest acquired all outstanding capital stock of Cerexa in exchange for:</li> <li>Aggregate consideration of \$480 million in cash</li> <li>Assumption of \$13.6 million in expenses and payments related to the transaction</li> <li>A contingent payment of \$100 million if US net sales of ceftaroline products during any twelve-month period within the first five years following the first product launch exceed \$500M</li> </ul>	
Value	\$480M in cash, \$13.6M in expenses (Total Deal Value: \$494M)	

Management	<ul> <li>Dennis Podlesak – President &amp; CEO (Former President &amp; CEO, Peninsula Pharmaceuticals)</li> <li>George Talbot – CMO (Former Founder, Talbot Advisors; VP, Aventis Pharmaceuticals)</li> <li>James Ge – VP Drug Development (Former VP, Pre-Clinical Development, Peninsula Pharmaceuticals)</li> <li>Rick Orr – General Council (Former General Council, Peninsula Pharmaceuticals)</li> </ul>
# of Employees	20

Lead Program	Phase III
Market	Antibiotic
Orphan Drug/ Accelerated Approval	Fast track granted (March 2006)

## **Comparison of Corporate Spin-Outs**

We have provided an in depth profile of five corporate spin-outs which achieved a successful exit via acquisition by a larger corporate entity. The following section contains a summary of factors that each of these companies shared in common as well as other factors which do not appear to have a direct influence on achieving liquidity via acquisition.

The five most commonly cited factors influencing the relative success of corporate spinouts are listed below.

**Established Management Team** – The most frequently cited reason for the overall success of a given company was the management team. Management teams which had previously worked together at a parent company were often the same people tasked to lead the spin-out. Maintenance of continuity within this group appears to exert a strong influence on the attitude and culture of the newly formed organization.

**Prestige of Parent Company** – Perceived quality of the parent company was directly correlated to the perceived value of the spin-out by all respondents in this study. Parent companies of the five case studies included Astellas, Human Genome Sciences, Johnson & Johnson, Peninsula and Symyx; these organizations were all considered 'high quality' and therefore enabled the spin-outs to benefit through association. Benefits included preferential treatment by potential investors, higher levels of receptivity with potential partners and ultimately superior valuations upon exit.

**High Quality Investor Syndicate** – Reputation of the investment syndicate was another factor mentioned by most respondents in this survey as a source of value creation. Institutional investors with strong track records generally have no shortage of companies seeking investments; this enables them to be scrupulous in

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selecting the most promising technologies and management teams to invest in. Investment syndicates of the five case studies profiled contained several influential venture capital firms; one respondent noted that a venture capitalist on their Board of Directors facilitated an introduction to their future acquiring company (AkaRx).

**Proven Technology** – In addition to the prestige of investor syndicates or parent companies, the underlying technology associated with a spin-out is of critical importance to the overall success of the company. Some companies chose to focus on elegance in simplicity of design (Ilypsa) while others leveraged massive HTS screening technology to identify promising targets to develop (CoGenesys). However, a proven technology was unanimously identified as a critical factor in the company's overall success.

**Established Regulatory Path** – One aspect of the business model that is often overlooked in start-ups is the time and cost associated with pre-clinical and clinical development of drug candidates. Given their prior affiliations with leading drug development organizations, most CEOs surveyed felt confident that their regulatory trial strategies were well conceived and executed. This dimension was also frequently cited by individuals in the acquiring companies as a source of significant value creation; it was presumed unlikely that a former J&J executive would allow a poorly designed data package to be sent to the FDA for review.

Interestingly, the following factors were not mentioned by any of the respondents as directly contributing to the overall success of corporate spin-outs. Given the methodology of the survey instrument, respondents were not provided with any factors to rank or consider. All factors mentioned in the course of the interviews were provided in an unaided fashion.

**Fast Track / Accelerated Approval** – Our hypothesis was that companies with an accelerated path to the market would be valued at a premium compared to case

controls. While this was not explicitly stated as a factor to consider, it should not be ruled out as a source of value creation. Comparing the presence/absence of a Fast Track or Orphan designation did not appear to affect the overall value of a spin-outs exit via M&A in our five case studies.





**Therapeutic Area** – Therapeutic areas of focus were also hypothesized to be correlated with a spin-outs success rate. Companies profiled had lead programs in antibiotics, blood disorders and dermatology. Interestingly enough, this factor was not mentioned by any respondents as influencing the overall success of a spin-out company when compared to *denovo* venture start-ups.

However, data from Medtrack was used to identify M&A transactions by therapeutic area and compared to our case studies in the chart below. The bar graphs represent the median net proceeds for M&A transactions in each of the therapeutic areas specified on the X axis. Individual geometric shapes represent the net proceeds for each of the five case studies and are coded based on their lead program's therapeutic area. Based on the data available, the spin-outs outperformed the median net proceeds in every instance observed. This observation can be explained by the presence of a management team with domain expertise in a given disease.





**Company Size** – Another dimension that was hypothesized to positively correlate with deal size was the number of employees at a spin-out. However, data from our five case studies was unable to support this hypothesis (see below). Excluding information from Barrier Therapeutics would lead us to conclude that there was no trend observed, while inclusion of this data point raises the question of a possible negative trend in deal value and company size. Without a sufficiently large sample size, no definitive conclusions can be drawn on the relative importance of company size on deal valuation.

Figure 32 - Company Size vs. Deal Value



# **Chapter Six: Discussion**

In this work, we have analyzed the overall performance of corporate spin-outs in the life sciences in subsequent liquidity events (IPO vs. M&A) to determine whether these corporations tend to outperform median industry values on a vintage year basis. Corporate spin-outs have become more frequent in the contemporary business environment as an alternate source of risk diversification and value creation. Increased global competition, free information flow and technology savvy capital markets have all contributed to the evolution of corporate spin-outs. Recent trends have shown an increase in the number of corporate spin-outs in the life sciences over the past 20 years, with approximately 60% of these companies being incorporated in the United States. It has been suggested by many industry professionals and venture investors that corporate spin-outs are perceived to be of superior value as compared to pure venture backed startup companies, though a data driven analysis of this hypothesis has not been published to date. In this work, it has been demonstrated that corporate spin-outs which successfully complete an Initial Public Offering (IPO) generate net proceeds that approximate the median industry value for a given year, whereas the similar comparison for Merger & Acquisition activity generates super-median returns in most cases. In addition, internal rate of return (IRR) and cash multiples for early investors were substantially higher in corporate spin-outs than industry averages. Our work has made no attempt to predict returns for companies that remain privately held.

In conducting this analysis, a comprehensive database of all IPO and M&A activity within the life sciences from January 1990 – December 2008 was generated. This gave us a data set of 186 corporate spin-outs to analyze. To further refine the target universe, we have concentrated on corporate spin-outs which focus on therapeutic development, are US based and were founded subsequent to January 2000. This reduced our sample size to 32 companies. Of these companies, eleven have successfully completed an Initial Public Offering and five have been acquired. (One company in the data set, Barrier Therapeutics, had an IPO in 2004 and was acquired in 2008.)

Net proceeds associated with successful liquidity events for the target universe were compared to median net proceeds for all life sciences Initial Public Offerings or M&A deals in a given vintage year. These results were mentioned in the first paragraph of this section. In order to take into account the lead program's phase of development in each company, data from MedTrack was merged into our Windhoovers data set. This provided a comparison group of 270 companies with Initial Public Offering net proceeds and lead stage of clinical development. Normalizing for lead program phase of development did not materially alter the results, indicating that capital markets do not appear to favor corporate spin-outs over venture backed start-ups.

In order to perform a similar analysis for corporate spin-outs which were subsequently acquired, we identified 97 of the 210 transactions in the Windhoovers database which met the following criteria: 1) transaction was completed, 2) therapeutic focused company and 3) data available on deal value. Press releases and filings with the Securities & Exchange Commission were analyzed to determine the lead program's phase of development at the time of each deal. When compared against our set of five corporate spin-outs which were subsequently acquired, the spin-outs out-performed the industry medians in three of the five cases observed.

Finally, information on Series A venture financing was obtained from VentureSource for the corporate spin-outs under investigation. This information was merged with data on liquidity events to calculate the internal rate of return (IRR) and cash multiple for each investment opportunity. IRR values and cash multiples exhibited high volatility across the data set, though in general tended to outperform industry averages on a vintage year basis.

#### Factors Influencing Success in Corporate Spin-outs

In this pilot study, respondents were asked to comment on factors which influenced the overall success of their spin-out. Below is a list of the most frequently cited factors along with a critique of their validity in the author's opinion.

**Established Management Team** – An experienced management team was the most frequently cited reason for overall success of a given company, with a particular emphasis on prior work experience in the same company. We believe that continuity and consistency are essential elements in the successful creation of a new corporate culture. In addition, seasoned management teams will bring prior knowledge, industry best practices and attract superior employees and strategic investors.

**Prestige of Parent Company** – Perceived quality of the parent company was directly correlated to the perceived value of the spin-out by all respondents in this study. Much of this preferential treatment has to do with the quality of the data package for underlying therapeutic assets. Given the current plethora of novel therapeutic companies, and present crisis in the capital markets, it is imperative that potential strategic investors conduct extensive due diligence to avoid making poor investment decisions. Spin-outs which emerge from less prestigious parent companies are less likely to conduct pre-clinical and clinical development plans to the exacting standards of rigor that the FDA requires for approval. As a consequence, many studies performed by these companies must be rerun by the new investors, thereby increasing clinical development costs, delaying eventual market approval and reducing potential peak revenues.

**High Quality Investor Syndicate** – Reputation of the investment syndicate was another factor mentioned by several respondents in this survey as a source of value creation. This is a difficult metric to accurately evaluate; as was mentioned earlier in the report, top tier investors are generally afforded the luxury of picking only the most promising technologies to invest in and may therefore serve as a confounding factor in the success rate of their portfolio. That being said, prestigious investors also have deep connections with senior executives in industry and on Wall Street. It is our opinion that a high quality syndicate of investors sends a strong signal to potential acquirers and the capital markets regarding the validity of the underlying technology and clinical programs.

**Proven Technology** – Perhaps no factor is more important in the success of a spin-out than the underlying technology that the company was founded to develop. This study has profiled companies with platform technologies as well as individual compound portfolios. The unifying theme behind these companies is that the technology has been demonstrated to be safe and effective. The current market environment requires that companies demonstrate these elements of their technology before investors consider entering conversations. Given this relatively high barrier to entry, many start-up companies are leveraging non-dilutive financing vehicles such as SIBR grants or other government loans before seeking venture capital investments.

**Established Regulatory Path** – As was mentioned extensively in the company profiles, establishment of a clear regulatory path to approval was another critical element in the success/failure of a start-up company. Regulatory affairs are often overlooked early in the drug development process; a fact that is associated with very negative consequences once the company begins to solicit potential strategic partnerships. We believe this is an important factor for the overall success of a spin-out company, but also believe that it is more easily accommodated by start-up companies through the successful recruitment of a seasoned regulatory affairs executive from a larger company. Additional high profile cases of inappropriate drug approvals by the Food and Drug Administration will likely cause this factor to increase in importance for all companies engaged in the development of therapeutics.

#### Future Directions

This pilot study has provided the analytical framework to test the perception that corporate spin-outs in US based therapeutic companies generate supra-median returns when compared to the overall industry activity on a vintage year basis. When normalizing for lead program phase of development, this is true about 60% of the time.

Future studies should delve deeper into the factors which were considered by each stake holder in the value chain. In particular, the elucidation of a factor-oriented framework to aid in the decision process to determine whether a program should be developed internally or spun-out into a separate operating entity would be of significant benefit to executives in life science organizations who must routinely make these decisions in an impartial and objective manner. Additionally, venture capitalists who invest in these companies are often tapped for their knowledge and experience in building value-added organizations. Incorporation of this framework will be beneficial to these individuals as they determine whether or not to invest in a spin-out.

A second framework could be generated to guide the strategic planning within a spin-out in order to maximize its chance of achieving a successful liquidity event. A series of qualitative interviews with senior executives and venture capitalists directly involved with the formation and liquidation of these companies would elucidate some of the factors shared by the success cases.

The impact to shareholder value of spinning out technologies into novel corporate entities represents yet another interest topic to explore. Most of the parent companies in our data set trade on public exchanges. Changes in share price surrounding the announcement of a corporate spin-out could be measured and compared to the pre-money valuation of the corporate spin-out to determine whether shareholder value was created, transferred or destroyed.

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# Appendix

Discussion Guide

## Introduction

- Thank respondent for participating
- Request if respondent minds that the interview be taped (merely for continuity of discussion and for generation of anonymous quotes)

# A. Background and Overview:

The purpose of this discussion is to better understand the strategic rationale for establishing a corporate spin-out to develop therapeutic products as opposed to conducting the development program internally. I am particularly interested in understanding the thought process behind this decision; the primary objective of the thesis is to determine whether a systematic framework can be established to help others make these decisions in the future.

# **B.** Spin-Out Background:

- 1. Can you please indicate when the spin-out company was incorporated/founded?
  - a. What were the primary stated objectives for the establishment of a separate corporate entity?
    - Specific program development
    - Focus on a therapeutic area that was out of strategy for parent
    - Shareholder activism
      - Other
  - b. Did the firm develop a business plan before incorporating?
  - c. How was the company initially capitalized?
    - Did the parent organization retain an equity position?
    - Did the company secure additional venture backed financing?
      - Was this accomplished through a syndicate or an individual venture capital firm?
    - Are there additional options or rights that the parent company has on any programs in development at the spin-out?
  - d. How was human capital allocated to the spin-out?
    - How many employees of the spin-out came from the parent?
      - What were some of their functional roles?
    - Subsequent to the spin-outs founding, have you hired other individuals from the parent company?
- 2. Can you briefly describe the ongoing projects at your company?
  - a. Are you currently working on pre-clinical or clinical stage programs?
    - What therapeutic areas are your programs investigating?

- Were these TA's out of scope for the parent company?
- b. Does your company currently have any products with Orphan Drug, Fast Track or Accelerated Approval designation?

## C. Management Background:

I would now like to shift the conversation to focus on the management team that was in place at the time of incorporation.

- 3. Can you please let me know what your official title was upon incorporation of the firm?
  - a. Prior to this position, were you previously employed at the parent company?
    - What was your title and responsibility in your prior position?
    - How long were you employed at the parent company?
    - What was the corporate culture like at the parent company?
- 4. Were there other individuals in the founding management team who came from the parent company? (Please identify key roles, CFO, COO, CSO, etc...)

## [ONLY ASK IF MANAGEMENT TEAM CAME FROM PARENT COMPANY]

- 5. Do you believe that your prior work experience has helped the spin-out succeed to date?
  - a. What elements of your work experience have contributed to this success?

## **D.** When to Spin-Out vs. Develop Internally

Now that we have a better understanding of the parent company, the spin-out background and the management team, I would like to delve into some strategic questions regarding the pursuit of a corporate spin-out.

- In your opinion, what elements are required in order for a spin-out to succeed? (Probe for clinical programs, management team, access to capital/resources from parent, etc...)
  - a. How many of these elements were in place in your most recent spin-out?
- 7. Do you believe that your company should have been spun out from its parent?
  - a. If not, what additional elements might have changed your opinion?
  - b. Was the timing right for the company to be spun-out?
  - c. Do you believe that spinning out your company has generated more value overall than if the programs were developed within the parent organization?
    - How has the difference in value creation been split up in the spin-out compared to the parent company?
- E. Risks and Benefits

For the final few minutes of our conversation I would like to develop a better understanding of the relative risks and benefits associated with corporate spin-outs.

- 8. Based on your personal experience, can you please describe the relative risks associated with corporate spin-outs? (Probe for financial uncertainty, regulatory risks, lack of sufficient resources to fully develop/advance programs into clinic.)
  - a. Of the risks that you mentioned above which ones have you experienced first hand in your current company?
  - *b.* Do you believe that your affiliation to the parent company has alleviated or minimized any of these risk factors?
    - Has your association with the parent company been a negative factor to the spin-out in any way? (Probe for lack of interest in corporate alliances or M&A, or difficulty securing investment syndicates.)
- 9. What are the relative benefits of corporate spin-outs when compared to internal development programs at the parent company? (Probe for increased focus/attention on smaller # of programs, dedicated staff & resources, agility and flexibility to change programs quickly.)
- 10. Do you believe that the benefits associated with your current spin-out outweighed the risks? Why?

## Closing

- Any further comments?
- Thank the respondent for participating
| - Comprehensiv | e List of C    | Corporate Spin-Ou         |
|----------------|----------------|---------------------------|
|                | - Comprehensiv | - Comprehensive List of ( |

SpinCo	Parent	Year of Founding	Country of Origin
Agfa	Bayer	1873	Germany
Mead Johnson Nutrition Company	Bristol Myers Squibb	1967	US
Eurand Pharmaceuticals	American Home Products	1969	Italy
Genentech	Roche	1976	US
Penwest Pharmaceuticals	Penford	1986	US
Novavax	IGI	1987	05
Athena Diagnostics	Citocom	1909	115
Cardiac Sciences	Modetano	1991	115
Endocare	Genetics Institute	1991	India
Bone Health Inc	Deprenvl Research	1992	US
Onvy Pharmaceuticals Inc	Chiron	1992	US
USANA Health Sciences	Gull Laboratories	1992	US
Anika Therapeutics	MedChem Medical	1993	US
Cytec Industries	American Cyanamid	1993	US
Genzyme Transgenics	Genzyme	1993	US
Guilford Pharmaceuticals	Scios Nova Inc	1993	US
Zeneca	Imperial Chem	1993	UK
Guidant	Eli Lilly	1995	US
Pharming	GenPharm International	1995	The Netherlands
Vaxgen (Genenvax)	Genentech	1995	US
Versicor	Sepracor	1995	US
Viasys Healthcare	Thermo Electron	1995	Germany
Tripath Imaging (Formerly AutoCyte)	Roche	1996	US
Clinical Labs & Pharma Services	Corning	1996	US
Eligix	Coulter Cellular	1996	US
Maxygen	Glaxo Wellcome	1996	US
Metagen Pharmaceuticals	Schering AG	1996	Germany
MetaXen	Xenova	1996	UK
Modex	CytoTherapeutics	1996	US
Molecular Informatics	National Ctr for Genome Research	1996	US
NeoZyme	Genzyme	1996	US
Aesthetics Technologies Corp	Collagen	1997	05
Crescendo	Alza	1997	Canada
Empsis Neuro i herpaeutics	DuPont Merck	1997	LIS
Endo Pharmaceuticais	OraSura Technologies	1997	115
Exertisis Prant Sciences	University of Kontucky	1997	115
Oakwood Laboratories	Ben Venue	1997	US
OraTol	Cortecs	1997	UK
Pharmetics	Theratechnologies	1997	Canada
Soberics	Brown University	1997	US
Targacept	R.J. Reynolds	1997	US
Volu-Sol	Biomune	1997	US
CliniChem	BioChem	1998	Canada
Cytovia	CoCensys	1998	US
Esperion Therapeutics	Warner Lambert	1998	US
Genzyme Molecular	Genzyme	1998	US
Iconix Biosciences	Microcide	1998	US
Intermune	Connetics	1998	US
Oncolytics		1998	Canada
Varian	Varian Medical Systems	1998	US
Agilent Technologies	Hewlett Packard	1999	US
Artemis Medical		1999	UK
Framingham Genomic Medicine	Boston University	1999	US
Galapagos Genomics	Crucell, Tibotec	1999	Belgium
MelTec	University of Magdeburg	1999	Germany
NsGene	NeuroSearch	1999	Denmark
Oxxon Therapeutics	Oxford University	1999	UK
Panacos	Boston Biomedica	1999	US Franco
Proskena X Castar Thorspoulies	Licond	1000	LIC
A-Ceptor Therapeutics	CuraCon	2000	115
Areadial	Alexion	2000	119
Arradian Resiles Bharmasouties	Pocho	2000	Switzerland
Dasilea Pharmaceutica	ChoGen	2000	US
Ecogenix	Sainte-Justine Hospital	2000	UK
Edward Lifesciences Corn	Baxter	2000	US
Gyros	Amersham Pharmacia	2000	Sweden
Calando Pharmaceuticals (Formerly Insert Therapeutics)	Arrowhead Research Corporation	2000	US
NeuroVive Pharmaceutical (Formerly Neuropharma)	Zeltia	2000	Sweden

SpinCo	Parent	Year of Founding	Country of Origin
Perlegen Sciences Inc.	Affymetrix	2000	US
Benovo	Manchester University	2000	UK
Sophion Bioscience	NeuroSearch	2000	Denmark
Subma Dental	Sybron	2000	US
Sydion Dental	Theratechnologies	2000	Canada
Thereau Edge (Intelligent Thereau tip Solutions)	Triangle Pharmaceuticals	2000	US
Casharas Bissoisnes (Formerly Thormogenic Imaging)	GSK	2000	US
Seanorse Bioscience (Formerly Thermogenic imaging)	BelyMedica	2000	US
Volcano Therapeutics (Cardiotech)	PolyMedica	2000	US
ZymoGenetics		2000	US
Advanced Medical Optics	Allergan	2001	
Affymax	GSK Barristantantantantan	2001	115
bioMosaic	Raven Biotechnologies	2001	Sweden
Biovitrum	Pharmacia	2001	Sweden
Celmed BioSciences	Theratechnologies	2001	Canada
Ceregene	Cell Genesys	2001	Double
Inoxell	Pharmexa	2001	Denmark
Ivax Diagnostics	lvax	2001	05
Meridica	PA Consulting	2001	US
Monsanto	Pharmacia Corporation	2001	US
Poseidon Pharmaceuticals	NeuroSearch	2001	Denmark
Protiva Biotherapeutics Inc.	Inex	2001	Canada
Zimmer	Bristol Myers Squibb	2001	US
Barrier Therapeutics	Johnson & Johnson	2002	US
BioXell	Roche	2002	Switzerland
Codexis	Maxygen	2002	US
CXB Biosciences	University of Dundee	2002	UK
MedCo Health Solutions	Merck	2002	US
Photogon		2002	US
Bibasharm	ICN Pharmaceuticals	2002	US
	Sonic Healthcare	2002	Australia
SciGen	Protein Polymer	2002	US
Spine wave	CoNeS Pharmaceuticals	2002	UK
Xention	Intercell	2003	Austria
Biovertis (Formerly Bioventis)	Abbett Leberatorios	2003	US
Hospira	Abbolit Laboratories	2003	Canada
IDx	Spectral Diagnostics	2003	Germany
Larnax	MediGene	2003	UP
Osteologix	Nordic Bone	2003	US Australia
Probiomics	Mineral Securities	2003	Australia
Revivicor (Formerly Regenecor)	PPL Therapeutics	2003	05
StemPath	Ottawa Research Health Institute	2003	Canada
Symyx Therapeutics Inc. (Changed to Ilypsa)	Symyx Technologies	2003	US
Veryan Medical	Imperial College London	2003	UK
Pharmacopeia Drug Discovery	Accelrys	2004	US
Aerovance	Bayer	2004	US
Avexa	Amrad	2004	Australia
BioPharmica	Grandbridge	2004	Australia
Dia-B Tech	Cardia Technology	2004	Australia
Evotec Neurosciences	Evotec OAI AG	2004	Germany
Izalex	Thuris	2004	US
Light Sciences Oncology	Light Sciences Corporation	2004	US
Novexel	Sanofi-Aventis	2004	France
Pecos Labs	Siga Technologies	2004	US
PowderMed	Chiron	2004	UK
Rhytec	Gyrus	2004	US
Vertical Health Solutions	Dynamic Health Products Inc.	2004	US
AkaRy	Yamanouchi Pharmaceutical, Fujisawa	2005	US
AspenBio Pharma Inc	Cambridge Holdings Ltd.	2005	US
Cereva	Penninsula Pharmaceuticals	2005	US
CoGenesivs	Human Genome Sciences	2005	US
Dettikon Es Holding	EMS-Chemie Holding	2005	Switzerland
Luminous	Inlight	2005	US
Perlecan Pharma	Dr. Reddy	2005	India
Suntavin	HPA	2005	UK
	Primary Corp	2005	Canada
Tiese Desmonution	Marck KGA	2005	US
hoga Pharmaceuticals	Acadia Dhamacouticals	2006	US
Abbey Fnarmaceuticais	Actorna Zantarie	2006	Canada
Atrium innovations	Relience Productions Inc.	2006	119
Aquamer Medical Corp.	Denacasa Productions Inc.	2000	India
Camin Fine Chemicals	CombinateRx	2000	119
CombinatoRx Singapore		2000	Borruda
Covidien	i yco international	2006	Dennuua

SpinCo	Parent	Year of Founding	Country of Origin
CSE Therapeutics	Cleveland Clinic	2006	US
Evesense	Ciba Vision	2006	Germany
I AB Research	LAB International Inc	2006	Canada
Macroflux (Zosano Pharma)	Alza	2006	US
Movetis	Janssen Pharmaceutica NV, Ortho-McNeil	2006	Belgium
Nabriva	Sandoz	2006	Austria
	Akzo Nobel	2006	The Netherlands
Palau Pharma	Uriach	2006	Spain
Puramed Bioscience Inc	Wind Energy America, Inc.	2006	US
Pri Pharmaceuticals	CvtRx	2006	US
Sup Dharma Advanced Research Company	Sun Pharmaceutical Industries	2006	India
Abravis BioScience Inc	APP Pharmaceuticals, Inc.	2007	US
Abrumth	Biofusion	2007	UK
Adapak Ingram Holdings	Tiger Brands I td	2007	South Africa
Accock Ingram Holdings	Brookwood, Targeted Technology	2007	US
Atoriosite Medical Systems	Arteriocyte	2007	US
Anteriocyte Medical Systems	Faton Laboratories, Inc.,	2007	US
Dasic Services, inc.	BMXP Holdings Inc.	2007	US
Bio-Matrix Scientific Group, Inc.	C.I. Corp	2007	South Korea
CDEX Phormaporticals	Bentley Pharmaceuticals	2007	US
CPEX Pharmaceuticals	Novogen	2007	US
Glycotex	Health Enhancement Products Inc.	2007	US
HEPI Pharmaceuticais	Integrated Biopharma Inc	2007	US
BioPharma, Inc.	Market & Research Corp	2007	US
	Nastech Pharmaceuticals	2007	US
MDRNA	Octillion Corn	2007	Canada
Microchannel Technologies Corp.	Piramal Healthcare Ltd	2007	India
Piramai Life Sciences Lifflited	Amaen	2007	US
Relypsa	lypice Inc	2007	US
Thomas Pharmaceuticals Ltd.	Chamacanax Pharmaceuticals Ltd	2007	Australia
Verva Pharmaceuticals Ltd.	Artra Zanaca	2008	Sweden
Albireo	Avago	2008	US
Alverix	Avago	2008	Canada
API	Cardinal Health	2008	US
Cardinal Health, Clinical and Medical Products Business	Cardinal Health	2008	US
Celera	Appleia Enzop	2008	US
Evivrus	Enzon Destain Design Labo	2008	US
Facet Biotech Corp.	Protein Design Labs	2008	115
Forsight Vision 3		2008	US
Mirina	Accelerator	2008	us
Myriad Pharmaceuticals, Inc.		2008	Sweden
Ospol AB	BIOIN AB	2000	Nonway
PCI Biotech AS	PhotoCure ASA	2000	India
Ranbaxy Life Science Research Ltd.	Ranbaxy Laboratories Ltd.	2008	lanan
RaQualia	Pfizer	2008	Japan

Figure 34 - Distribution of US Corporate Spin-Outs by State

Corporate Spin-Outs by State



Figure 35 - Average Distance From Parent for US Spin-Outs

State of Incorporation	# of Spinouts	Average Linear Distance to Parent	Average Driving Distance to Parent
AL	1	0	0
			071
CA	42	//1	0/1
со	1	0	0
СТ	3	1,582	1,893
DE	1	104	122
FL	3	731	881
IL	1	5	7
IN	3	457	519
MA	15	708	822
MD	4	702	820
MI	2	297	381
мо	1	0	0
NC	4	266	311
NH	1	0	0
NJ	8	420	490
NM	1	1,758	1,985
ОН	1	5	5
OR	1	4	6
PA	2	8	10
TN	1	C	0
UT	2	632	710
VT	1	2,568	3,032
WA	4	852	1,019
Wi	1	192	209
Mean		503	587
SD		658	771
Median		282	346

Source: Google Maps, company websites

Parent Company	# of Spin-Outs
Roche	4
Genzyme	3
NeuroSearch	3
Theratechnologies	3
Alza	2
Bayer	2
Bristol Myers Squibb	2
Chiron	2
GSK	2
Pharmacia	2

Figure 36 - Parent Companies with Highest Frequency of Life Science Spin-Outs

Note: 160 other parents each spun out one company in the time horizon studied.





**Biotech IPO Gross Proceeds** 

Figure 38 - Overall M&A Statistics for Healthcare Companies 1991 - 2008



Figure 39 – Internal Rate of Return Analysis for Corporate Spin-outs vs. Industry Averages



Deal			Deal			
Year	Target	Acquirer	Value	Lead Indication	Broad Indication	Lead Status
2008	Nektar Therapeutics	Novartis AG	115.00	COPD	Respiratory	PC
2008	ImClone Systems	Eli Lilly & Co.	6,500.00	Cancer	Cancer	Market
2008	Genelabs Technologies	GlaxoSmithKline PLC	56.79	Hep E	Infections	Phase II
2008	Direvo Biotech AG	Bayer HealthCare LLC	300.00	Protein Engineering	Protein Engineering Kidney/CV/Resp/Al/Canc	N/A
2008	Pharmacopeia	Pharmaceuticals Transcept	73.66	Diab Neph/HTN/COPD/AI/Cancer	er	Phase II
2008	Novacea	Pharmaceuticals				
2008	AviaraDx	bioMerieux SA	60.00	Cancer Diagnostics	Moecular Diagnostics	N/A Deal
2008	ImaRx Therapeutics	Microbix Biosystems	5.00	Acute massive pulmonary embolism Cardiovascular, Diabetes, Women's Health and	CV	Terminated
2008	Sciele Pharma	Shionogi & Co. Ltd.	1,424.00	Pediatrics	CV/Endo/Woman	Market
2008	Nuvelo	ARCA biopharma		heart-failure	CV	Phase I
2008	Prestwick Pharmaceuticals	Biovail	100.00	chorea associated with Huntington's disease	Neuro CV/Endo/Inflammation/Bl	Market
2008	PGx Health Valeant Pharmaceuticals	Clinical Data	66.20	Myocardial perfusion imaging	ood	Phase III
2008	International	Meda AB	425.00	Autoimmune and infection	Al/Infection	Market
2008	Talecris Biotherapeutics	CSL Ltd.	3,100.00	IVIg	Neuro	Market
2008	Curacyte Discovery GMBH	The Medicines Co.	38.96	Surgical blood loss	Blood	PC NDA
2008	Lev Pharmaceuticals	ViroPharma	442.90	Hereditary angioedema	Dermatology	Submitted
2008	SGX Pharmaceuticals	Eli Lilly & Co. Access	61.97	Oncology	Cancer Infection/Cancer/Dermat	PC
2008	MacroChem	Pharmaceuticals	7.78	Diabetic foot infection/ cancer/derm	ology	Phase III
2008	Mirus Bio	Roche	125.00	RNAi	Basic research	N/A
2008	Applied Biosystems Group	Invitrogen	6,409.23	Basic research	IVD	N/A
2008	Immunicon	Veridex LLC	31.00	IVD	IVD	N/A
2008	Third Wave Technologies	Hologic	580.00	IVD	IVD	N/A
2008	Vernalis Pharmaceuticals	lpsen	18.70	Parkinson's Disease	Neuro	Market
2008	Barrier Therapeutics	Stiefel Laboratories	145.95	Dermatology	Dermatology	Market
2008	Innovive Pharmaceuticals	CytRx	20.72	Oncology	Cancer	Phase I
2008	Johnson & Johnson	Amic AB		IVD	IVD	N/A
2008	Protez Pharmaceuticals	Novartis AG	400.00	Infections	Infections	Phase II
2008	Neosil	Peplin Ltd.	6.70	Acne	Dermatology	PC

## Figure 40 - Overall M&A Statistics for Healthcare Companies by Lead Program Phase of Development

Deal						1
Year	Target	Acquirer	Deal Value	Lead Indication	Broad Indication	Lead Status
2008	Amnestix	Sygnis Pharma AG	6.29	Neuroprotection	Neuro	Phase II
2008	Osiris Therapeutics	NuVasive	85.00	Orthopedics	Orthopedics	Market
2008	Critical Therapeutics	Cornerstone BioPharma	64.15	Respiratory	Respiratory	Market
2008	lomai	Intercell AG	171.74	Traveler's diarrhea	Vaccines	Phase II
2008	Kosan Biosciences	Bristol-Myers Squibb Co.	234.61	Multiple myeloma	Cancer	Phase III
2008	Navitas Assets LLC	Gilead Sciences				
			E0 E4	secondary acute myeloid	Cancer	Phase III
2008	Xanthus Pharmaceuticals	Antisoma PLC	52.54			Market
2008	Oryx Pharmaceuticals	Sepracor	70.00	CV/CINS/Pain/Intections	N/A	N/A
2008	OncoGenex Technologies	OncoGenex	20.21	N/A Neutropoutionio	N/A Noutrocouticals	N/A
2008	Calgenex	PanGenex	7.70		Canada	Phase II
2008	Virium Pharmaceuticals	MacroChem	6.64	CRC, prostate, brain	Cancer	Filase II
2008	LifeCell	Kinetic Concepts	1,744.38	Basic research	metabolic neurology	N/A
2008	Sittia Pharmacouticals	GlavoSmithKline PLC	720.00	Diabetes	immunology and inflammation	Phase I
2000	Bolymor Technology Group	DSM NV				
2008	Shimodo Riotoch Bty 1 td	Abravis BioScience	15.00	Post-Surgical Pain	Pain	Phase III
2008	Milloppium Pharmacouticals	Takeda Pharmaceutical	8,167,60	Multiple myeloma	Oncology	Market
2008	Serency	Pfizer	0,101100			
2008	Serenex		9.02	Duchenne muscular dystrophy	Genetic disease	Phase I
2008	Bio Arroy Solutions Ltd		117.00	IVD	IVD	N/A
2008	Tissue Ssienes Laboratories	Covidien Ltd	72.69	Hernia repair	Medical Device	N/A
2008	Provide Science Laboratories	Bruker BioSciences	976.30	Basic research	IVD	N/A
2008	Bruker BioSpin Group	Braker Dioocierices	010.00	Bable Foreland		NDA
2008	Encysive Pharmaceuticals	Pfizer	190.76	Pulmonary hypertension	CV	Submitted
2008	Proprius Pharmaceuticals	Cypress Bioscience	75.00	IVD	IVD	N/A
2008	MiMedx	Alynx Co.		Basic research	Basic research	N/A
2008	CollaGenex Pharmaceuticals	Galderma Laboratories	420.00	Rosacea	Dermatology	Market
				MM, SCLC, colon, pancreatic	Canada	PC
2008	Molecular Discoveries LLC	ImmunoCellular Therapeutics Ltd.	0.82	& ovarian		
2008	NanoMatrix	Organogenesis		l issue engineering	Tissue engineering	N/A Dhasa l
2008	Progen Pharmaceuticals	Progen Pharmaceuticals	21.87	Oncology		
2008	CellzDirect	Invitrogen	57.00	Liver test		IN/A
2008	AppTec Laboratory Services	WuXi PharmaTech Co.	162.70	Lab services		IN/A
2008	Panbio Ltd.	Inverness Medical Innovations	37.00	IVD		N/A
2008	CoGenesys	Teva Pharmaceutical Industries Ltd.	400.00	Neutropenia	Blood	Phase II

Deal			Deel Velue	Lood Indication	Broad Indication	Lead Status
Year	Target	Acquirer	Deal value	Lead Indication	IVD	N/A
2007	Encode Pharmaceuticals	Bennu Pharmaceuticals	5.03	11/2		N/A
2007	BBI Holdings PLC	Inverness Medical Innovations	137.87		No disal Davias	N/A
2007	AcryMed	I-Flow	25.00	Device Coating	Medical Device	N/A
2007	USB	Affymetrix	75.00			N/A
2007	CovX Research LLC	Pfizer	600.00	Oncology/metabolic	Oncology/metabolic	PC
2007	Illumigen Biosciences Adams Respiratory	Cubist Pharmaceuticals	216.20	Нер С	Infections	PC
2007	Therapeutics	Reckitt Benckiser PLC	2,300.00	OTC Respiratory	Respiratory	N/A
2007	MGI Pharma	Eisai Co. Ltd.	3,331.99	MDS, cancer induced nausea	Cancer	Market
2007	Tutogen Medical	Regeneration Technologies	246.94	Basic research	Basic research	N/A
2007	Pharmion	Celgene	2,682.02	MDS	Cancer	Market
2007	Coley Pharmaceutical Group	Pfizer	165.00	NSCLC	Cancer	Phase III
2007	Oncotech	Exiqon AS	41.35	Oncology testing prostate, pancreatic and	Cancer	N/A
2007	Agensys	Astellas Pharma	537.00	bladder cancers	Cancer	Phase I
2007	Reliant Pharmaceuticals	GlaxoSmithKline PLC	1,650.00	Hypertriglyceridemia	CV	Market
2007	Avant Immunotherapeutics	Celldex Therapeutics	75.00	Glioblastoma	Cancer	Phase II
2007	ViaCell	PerkinElmer	283.32		IVD	N/A
2007	Align Pharmaceuticals LLC	Cyclacel Pharmaceuticals	4.90	Radiation paliation therapy	Cancer	Market
2007	Haptogen Ltd.	Wyeth Pharmaceuticals				
	Swedish Orphan International	Que disk Orch an International AP				
2007	Manufacturing	Swedish Orphan International AB	1 50	Multiple concer	Cancer	Phase II
2007	Point Therapeutics	DARA BioSciences	22.00	Multiple cancel	IVD	N/A
2007	Atria Genetics	Celera Group	33.00	IVD	ND	N/A
2007	Spring Bioscience	Ventana Medical	40.00			Ν/Δ
2007	Nabi Biologics	Biotest AG	185.00		Canada	Phase I
2007	Adnexus Therapeutics	Bristol-Myers Squibb Co.	505.00	Cancer		Pliase
2007	Renovis	Evotec AG	160.86	Neuro & Inflammatory Disease	Neuro/Inflammation	PC N/A
2007	IsoTis	Integra LifeSciences Holdings	51.47	Basic research	Basic research	IN/A
2007	Brookwood Pharmaceuticals	SurModics	62.00	IVD		N/A
2007	HemoSense	Inverness Medical Innovations	171.62	IVD		N/A
2007	Iconix Biosciences	Entelos	8.69	Predictive toxicology	Predictive toxicology	N/A
2007	MZT Holdings	Inverness Medical Innovations	38.00	IVD	IVD	N/A

Deal		Acquirer	Deal Value	Lead Indication	Broad Indication	Lead Status
Year	Sustama Madiaina	Coll Thorapoutics	35.00	Cancer	Cancer	Phase II
2007	Systems Medicine	Morek & Co	350.00	CHE	CV	Phase III
2007	NovaCardia	Noven Pharmaceuticals	135.00	Psychiatric disorders	CNS	Market
2007	JDS Pharmaceuticals LLC	Noven Fhamaceuticals	8.40	Cognitive disorders	Neuro	Phase II
2007	Hamilton Pharmaceuticais	Review Pharmaceuticals	4.00	Cell therapy	Basic research	N/A
2007	AmCyte	Reneuron Group FLC	272.50		IVD	N/A
2007	NimbleGen Systems		272.50	Diabatas	Endo	Phase II
2007	Alantos Pharmaceuticais	Amgen	2 119 57	ND		N/A
2007	Ventana Medical Systems	Roche Diagnostics	3,110.57	CKD	Kidpov	Phase II
2007	llypsa	Amgen	420.00		IVD	N/A
2007	Cholestech	Disease NV	290.77	1vD		N/A
2007	Digene	Qiagen NV	1,420.03	NIA	NA	N/A
2007	Exelgen Ltd.		2.15	N/A	Capacr	Market
2007	Bioenvision	Genzyme	345.00	leukemia	Drug Dolivony	N/A
2007	lomed	Empi	22.00	Drug Delivery		
2007	Cytyc	Hologic	6,499.22			N/A
2007	Mytogen	ACT	6.00	heart-failure	CV	Phase
2007	FermaVir Pharmaceuticals	Inhibitex	18.93	IVD	IVD	N/A
2007	Stratagene	Agilent Technologies	245.65		IVD	N/A
2007	Somanta Pharmaceuticals	Access Pharmaceuticals	11.93	Hyperuremia	Blood	Phase II
2007	BioVeris	Roche	600.00	IVD	IVD	N/A
	Therapeutic Human			11/12		NI/A
2007	Polyclonals	Roche	56.50		Nultiple	Markot
2007	MedImmune	AstraZeneca PLC	15,600.00		Multiple	NIA
2007	454 Life Sciences	Roche Diagnostics	152.00	Sequencing		N/A
2007	Tripos	Tripos Discovery Informatics	26.18	Informatics	Basic research	N/A
2007	Hypnion	Eli Lilly & Co.	315.00	Insomnia	CNS	Phase II
2007	Morphotek	Eisai Co. Ltd.	325.00	Cancer/RA/Infection	Cancer/RA/Infection	Phase I
2007		Opko Health		N/A	N/A	N/A
2007	Adeza Biomedical	Cytyc	452.00	IVD	IVD	N/A
2007	Adiana	Cytyc	60.00	IVD	IVD	N/A
2007	<b>BioRexis Pharmaceutical</b>	Pfizer	200.00	Diabetes	Endo	PC

Deal			Deal Value	Load Indication	Broad Indication	Lead Status
Year	Target	Acquirer	Deal value			Market
2007	New River Pharmaceuticals	Shire PLC	2,600.00	ADHD	CNS	Phase II
2007	VIA Pharmaceuticals	Corautus Genetics		atheroscierosis		Fliase II
2007	HemoCue AB	Quest Diagnostics	420.00	IVD	IVD	N/A
2007	Allendale Pharmaceuticals	Synova Healthcare Group	17.00	IVD	IVD	N/A
2007	Molecular Devices	MDS	615.00	PER 201 20 30	IVD	N/A
2007	Syntonix Pharmaceuticals	Biogen Idec	120.00	Cancer/Autoimmune	Cancer/Al	PC
2006	Valera Pharmaceuticals	Indevus Pharmaceuticals	174.19	Prostate cancer	Cancer	Market
2006	Evotec Technologies GMBH Disc-O-Tech Medical	PerkinElmer	30.34	Basic research	IVD	N/A
2006	Technologies Ltd.	Kyphon	260.00	Basic research	Basic research	N/A
2006	Cerexa	Forest Laboratories	593.60	Infections	Infections	Phase III
2006	Osmetech PLC	Idexx Laboratories	44.90	IVD	IVD	N/A
2006	MacroMed	Protherics PLC	25.00	esophageal and brain	Cancer	Phase II
2006	Diagnostics	Luminex	38.74	Molecular Diagnostics	IVD	N/A
2006	Praecis Pharmaceuticals	GlaxoSmithKline PLC	54.80	NHL	Cancer	Phase I
2006	Conor Medsystems	Cordis	1,262.92	IVD	IVD	N/A
2006	Solexa	Illumina	650.00	Gene sequencing	Molecular Diagnostics	N/A
2006	Cabrellis Pharmaceuticals	Pharmion	104.00	SCLC	Cancer	Phase II
2006	iviGene	Oragenics	0.20		IVD	N/A
2006	CoTherix	Actelion Ltd.	420.00	PAH	CV	Market
2006	Tanox	Genentech	905.02	Asthma	Respiratory	Market
2006	Kos Pharmaceuticals	Abbott Laboratories	3,715.21	IVD	IVD	N/A
2006	Sheffield Pharmaceuticals	Pipex Pharmaceuticals	21.25	Wilson's disease	CNS	Phase II
2006	Q-RNA	Neuro-Hitech	10.89	Alzheimer's Disease	CNS	Phase II
2006	Groupe Corneal Laboratories	Allergan	217.00	Dermal Fillers	Dermatology	N/A
2006	Abrika Pharmaceuticals LLLP	Actavis Group	235.00	Drug Delivery	Drug Delivery	N/A
2006	Nottingham Ltd.	Lonza Group Ltd.	460.00		IVD	N/A
2006	RxKinetix	Endo Pharmaceuticals	115.00	Oral mucositis	Cancer	Phase II
2006	Lumigen	Beckman Coulter	185.00	IVD	IVD	N/A
2006	Vision Systems Ltd.	Danaher	520.00	IVD	IVD	N/A
2006	Mvogen	Gilead Sciences	2,244.44	PAH	CV	Phase III

		Deal Value	Load Indication	Broad Indication	Lead Status
Target	Acquirer	Deal value		N/A	N/A
Urigen Pharmaceuticals	Urigen	40.00	N/A		N/A
Genaco Biomedical Products	Qiagen NV	40.00	4145		Dhaso II
Sirna Therapeutics	Merck & Co.	1,100.00	AMD	Oprinalmology	Market
Icos	Eli Lilly & Co.	2,228.60	ED	Reproductive	
ProIX Pharmaceutical	Oncothyreon	39.81	Pancreatic	Cancer	Phase II
airPharma LLC	Meldex International PLC	8.00	Asthma	Respiratory	Market
Berna Products	Crucell NV	16.50	typhoid vaccine	Vaccines	Market
PowderMed Ltd.	Pfizer	230.00	Flu Vaccine	Vaccines	Phase I
TheraPei Pharmaceuticals	Forbes Medi-Tech	50.63	Diabetes	Endo	PC
Bacterial Barcodes	bioMerieux SA			IVD	N/A
Sentigen Holding	Invitrogen	25.93		IVD	N/A
Avidia	Amgen	380.00	Autoimmune and inflammation	Al/Inflammation	Phase I
Sirion Holdings	Sirion Therapeutics				
Enterix	Quest Diagnostics	43.00	IVD	IVD	N/A
Jade Pharmaceutical	AMDL	4.23	Cancer Diagnostics	Molecular Diagnostics	N/A
Tissue Repair Co.	Cardium Therapeutics	2.12	Tissue engineering	Tissue engineering	Phase II
Sytera	Sirion Therapeutics				
Applied Imaging	Genetix Group PLC	25.80		IVD	N/A
		504.47	hematopoietic stem cell	6	Dhaco III
AnorMed	Genzyme	584.17	transplantation	Cancer	Flidse III
Emergent Product	Emergent BioSolutions	470.00	Vaccines	Vaccines	Market
ColBor LifeScience Ltd	OrthoNeutrogena		IVD	IVD	N/A
Confluent Surgical	United States Surgical	245.00	Surgical Sealants	Surgical Sealants	N/A
IN Macri Tachnologies LLC	PerkinElmer	56.65		IVD	N/A
Octoo Piologics	Smith & Nenhew Endoscony	72.30	Basic research	Basic research	N/A
Biscore International AB	GE Healthcare	435.92	IVD	IVD	N/A
Blacore International AB	Giload Sciences	136.76	Manufacturing Eacilities (API)	Manufacturing Facilities (API)	N/A
Agenceut Personal Conomica	Applied Biosystems Group	120.00	manalastannig i sommes ( m i)	IVD	N/A
Agencourt Personal Genomics	Thormo Eichor Scientific	11 775 82	IVD	IVD	N/A
	DerkinElmor	1/ 00	110	IVD	N/A
Spectral Genomics		80.00	IVD	IVD	N/A
	TargetUrigen PharmaceuticalsGenaco Biomedical ProductsSirna TherapeuticsIcosProlX PharmaceuticalairPharma LLCBerna ProductsPowderMed Ltd.TheraPei PharmaceuticalsBacterial BarcodesSentigen HoldingAvidiaSirion HoldingsEnterixJade PharmaceuticalTissue Repair Co.SyteraApplied ImagingAnorMedEmergent ProductDevelopment GMBHColBar LifeScience Ltd.Confluent SurgicalJN Macri Technologies LLCOsteoBiologicsBiacore International ABRaylo ChemicalsAgencourt Personal GenomicsFisher Scientific InternationalSpectral GenomicsAbmaxis	TargetAcquirerUrigen PharmaceuticalsUrigenGenaco Biomedical ProductsQiagen NVSirna TherapeuticsMerck & Co.IcosEli Lilly & Co.ProlX PharmaceuticalOncothyreonairPharma LLCMeldex International PLCBerna ProductsCrucell NVPowderMed Ltd.PfizerTheraPei PharmaceuticalsForbes Medi-TechBacterial BarcodesbioMerieux SASentigen HoldingInvitrogenAvidiaAmgenSirion HoldingsSirion TherapeuticsJade PharmaceuticalAMDLTissue Repair Co.Cardium TherapeuticsSyteraSirion TherapeuticsApplied ImagingGenetix Group PLCAnorMedGenzymeEmergent ProductDevelopment GMBHConfluent SurgicalUnited States SurgicalJN Macri Technologies LLCPerkinElmerOsteoBiologicsSmith & Nephew EndoscopyBiacore International ABGE HealthcareRaylo ChemicalsGilead SciencesAgencourt Personal GenomicsApplied Biosystems GroupFisher Scientific InternationalSpectral GenomicsApplied Biosystems GroupThermo Fisher ScientificPerkinElmerApplied Biosystems GroupSiacore International ABGilead SciencesAgencourt Personal GenomicsApplied Biosystems GroupFisher Scientific InternationalSpectral GenomicsApplied Biosystems GroupThermo Fisher Scientific	TargetAcquirerDeal ValueUrigen PharmaceuticalsUrigenGenaco Biomedical ProductsQiagen NV40.00Sirna TherapeuticsMerck & Co.1,100.00IcosEli Lilly & Co.2,228.60ProlX PharmaceuticalOncothyreon39.81airPharma LLCMeldex International PLC8.00Berna ProductsCrucell NV16.50PowderMed Ltd.Pfizer230.00TheraPei PharmaceuticalsForbes Medi-Tech50.63Bacterial BarcodesbioMerieux SASentigen HoldingInvitrogenAvidiaAmgen380.00Sirion TherapeuticsEnterixQuest Diagnostics43.00Jaiseue Repair Co.Cardium Therapeutics2.12SyteraSirion Therapeutics2.12Applied ImagingGenzyme584.17Emergent ProductDevelopment GMBHEmergent BioSolutions470.00ColBar LifeScience Ltd.OrthoNeutrogena245.00JN Macri Technologies LLCPerkinElmer56.65OsteoBiologicsSmith & Nephew Endoscopy72.30Biacore International ABGE Healthcare435.92Raylo ChemicalsGilead Sciences136.76Agencourt Personal GenomicsApplied Biosystems Group12.00Fisher Scientific InternationalThermo Fisher Scientific11.775.82Spectral GenomicsPerkinElmer14.00AnorMedDerkencesSilead SciencesBiacore International ABGE Healthcare435.92<	TargetAcquirerDeal ValueLead IndicationUrigen PharmaceuticalsUrigenN/AGenaco Biomedical ProductsQiagen NV40.00Sima TherapeuticsMerck & Co.1,100.00lcosEli Lilly & Co.2,228.60ProlX PharmaceuticalOncothyreon39.81ParnareatucalOncothyreon39.81airPharma LLCMeldex International PLC8.00Berna ProductsCrucell NV16.50PowderMed Ltd.Pfizer230.00TheraPei PharmaceuticalsForbes Medi-Tech50.63Bacterial BarcodesbioMerieux SA25.93AvidiaAmgen38.00Autoimmune and inflammationSirion HoldingsSirion Therapeutics43.00Ivitorgen25.93IVDJade PharmaceuticalAMDL4.23Cancer Diagnostics43.00SyteraSirion Therapeutics2.12Tissue Repair Co.Cardium Therapeutics2.12Applied ImagingGenetix Group PLC25.80AnofMedGenzyme584.17Emergent ProductOrthoNeutrogenaIVDCoffuent SurgicalUnited States Surgical245.00Surgical SealantsJN Macri Technologies LLCPerkinElmer56.65565OsteoBiologicsSmith & Nephew Endoscopy7.30Basic researchBiacor International ABGE Healthcare435.92IVDRaylo ChemicalsGilead Sciences136.76Nanufacturing Facilities (API)Agener	TargetAcquirerDeal ValueLead IndicationBroad IndicationUrigen PharmaceuticalsUrigenN/AN/AN/AGenaco Biomedical ProductsGiagen NV40.00N/DIcosMerck & Co.1,100.00AMDOphthalmologyIcosEli Lilly & Co.2,228.60EDReproductiveProl K PharmaceuticalOnordhyreon39.81PancreaticCancerairPharma LCMeldex International PLC8.00AsthmaRespiratoryBerna ProductsCrucell NV16.50typhoid vaccineVaccinesPowderMed Ltd.Pfizer230.00Flu VaccineVaccinesPowderMed Itd.pfizer230.00Flu VaccineVaccinesBacterial BarcodesbioMerieux SAIVDIVDSentigen HoldingInvitrogen25.93VIDAvidiaAmgen380.00Autoimmune and inflammationAl/InflammationSirion Therapeutics2.12Tissue engineeringTissue engineeringSyteraSirion Therapeutics2.12Tissue engineeringTissue engineeringApplied ImagingGenetix Group PLC25.80IvDIvDAnorMedGenzyme584.17VIDIvDConfluent KongelaUnited States Surgical245.00Surgical SealantsJN Macri Technologies LLCPerkinElmer56.65IvDOsteobiologicsSmith & Nephew Endoscopy72.30Basic researchJade PharmaceuticalGenzyme56.65Iv

Deal			Deal Value	Load Indication	Broad Indication	Lead Status
Year	Target	Acquirer			Cancer	Phase I
2006	Conforma Therapeutics	Biogen Idec	250.00	Uncology		N/A
2006	CanAg Diagnostics AB	Fujirebio Diagnostics	100.00		Capacit	PC
2006	GlycoFi	Merck & Co.	400.00	Cancer	Cancer	FC
2006	Fumapharm AG	Biogen Idec	10.00	10.10 L /		N1/A
2006	HaptoGuard Ltd.	Synvista Therapeutics	8.80	IVD	IVD	N/A
2006	Diagnostic Products	Siemens AG	1,860.00	IVD	IVD	N/A
2006	Bruker Optics	Bruker BioSciences	135.00		IVD	N/A
2006	Serologicals	Millipore	1,400.00		IVD	N/A
2006	Rinat Neuroscience	Pfizer	500.00	Neuro	Neuro	Phase II
2006	Holdings	Epix Pharmaceuticals	127.06	Anxiety	Neuro	Phase III
2006	Discovery Partners	Infinity Pharmaceuticals		N/A	N/A	N/A
2000	Neber	Biocon Ltd	5.00	Drug Delivery	Drug Delivery	N/A
2006	NODEX	Cougar Biotechnology			<b>°</b>	
2006	VM BioSciences LISA	VM BioSciences	32.85	N/A	N/A	N/A
2006	Fin Biosciences USA	Serologicals	74.80		IVD	N/A
2006	Linco	Eisber Scientific International	283.00		IVD	N/A
2006	Athena Diagnostics	Pharmas	59.20	IBS	Autoimmune	Phase II
2006	Vela Pharmaceuticais	Weteen Pharmacouticals	1 900 00	Multiple generics	Multiple	Market
2006	Andrx	Durayay Technologian	12.00	Hen B	Vaccines	Market
2006	Rhein Biotech NV	Astallas Dharma	12.00	Tiep D		
2006	Dynogen Pharmaceuticals	Astellas Pharma	175.00		IVD	N/A
2006	Acon Laboratories	Inverness Medical Innovations	72.00	1VD	IVD	N/A
2006	Xenogen	Caliper Life Sciences	73.20	Acute decompensated heart	1VB	
2006	Myogen GMBH	Wulfing Holding GMBH	6.10	failure	CV	Market
2000	Wyogen oner	AngioGenex				
2000	AdagGen AG	OncoVista		IVD	IVD	N/A
2000	Targeted Molecules	Chromos Molecular Systems				
2000	Cana Ohm Spioneos	Becton Dickinson & Co	255.00		IVD	N/A
2006	Montigon Pharmacouticals	SuperGen	40.00	Oncology	Cancer	PC
2006		Dusa Pharmaceuticals	30.00	Acne	Dermatology	Market
2006	Sinus Laboratories	Cancer//av	79.46	Oncology	Cancer	Phase II
2006	wicromet	Gangervax	10.40			