Financing Methods That Drive Innovation in Biotech and Pharmaceuticals: The Meagfund IPO Model

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Abstract

Current research has shown that a mega fund and securitization approach using debt financing can not only mitigate risk in investments in cancer but can also align research and development in the right direction for new and innovative breakthrough therapies. We propose a new application of this megafund biopharma model – the megafund IPO model. There are almost arbitrage-like opportunities for investors where there are heavily discounted investments opportunities which are generated in IPO's. However, these events driven investments are only for the institutional investor and hence pooling capital into a more scalable mega fund structure could generate returns that are not otherwise possible while encouraging innovation in biomedicine.

The investment vehicle is attractive to investors because of the significant amount of alpha that the fund can generate on de-risked basis. Risk is mitigated by the fact that there is an arbitrage like opportunity for the institutional investor in events driven investments for the mispricing of an IPO. We examine a back-testing of ten years examining a long only strategy and later also look at a case study of Monashee Investment Management that currently most closely resembles the megafund IPO model.

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Introduction

The biotechnology and pharmaceutical industry face a growing challenge. Investors are withdrawing capital from the sector. Even though there has been remarkable scientific breakthroughs and understanding of molecular biology and medicine, the financial returns to biopharma investments have been lackluster (Fagnan et al., 2013; American Cancer Society 2011). The process of translating biomedical research into effective drugs is broken and the main driver behind this phenomenon is that the business model for translational research is flawed (Fagnan et al., 2013; Evaluate Pharma, 2010).

The drug development process has become increasingly expensive, lengthy, complex, and risky. These factors have made investing in biotech and pharmaceuticals less interesting. As such, a confluence of these factors can cause significant underfunding for the entire industry. Given these complexities and risks, traditional financing vehicles such as private and public equity are becoming less effective funding sources because the needs of limited partners and shareholders do not align with biomedical innovation (Fernandez et al., 2012).

Fernandez et al., argues that the quarterly earnings cycle, real time pricing, and dispersed ownership of public equities create an environment that has implications so that senior management must create strategies aligned with more immediate payoffs, and potentially move away from speculative transformative research. Private equity may offer more flexibility in terms of pursuing risk taking investments and deferred exits. However, the scale is considerably smaller, the time horizon is shorter than most clinical cycles and funding decisions are driven less by scientific breakthroughs than by business cycles and windows of initial public offerings (Fernandez et al., 2012). Whereas all elements of these arguments may be true, we propose in this thesis a megafund IPO investment model that is a hybrid venture capital/private equity/hedge fund model that can offer solutions to these problems with traditional investment vehicles and that can align innovation in biomedicine.

Quarterly earnings cycle, real time pricing, and dispersed ownership of public equities typically

apply within the domain of traditional long short equity hedge funds that try to gain alpha based on relative value. These funds must closely follow quarterly earnings and make their money based on the portfolio manager's view on the relative intrinsic value of the stock versus how the stock is currently trading. These investors typically follow the value investing principles of Benjaim Graham and Warren Buffett (Graham & Dodd, 2008). However, within the megafund IPO model that we propose, there are no public disclosures of earning results yet and whereas their many be private financials provided in the S-1 registration, these arguments do not apply when investing in early stages. Furthermore, because of the de-risked nature of the arbitrage like opportunity the investment style is designed to take greater risk in companies that generate the greatest amount of alpha which is aligned with companies that have the most innovative products and ideas with high barriers of entry. Although positions are encouraged to be liquidated at most with 1 year holding periods, we propose the lock up periods of 5 -12 years as mentioned in Fernandez et al.'s seminal work that introduced the biopharmaceutical megafund concept. Whereas the thesis presents the megafund IPO model as one application of the megafund concept that has been introduced, ultimately our goal would be to not only offer the product as a standalone investment strategy but to integrate it into Fernandez's megafund model that argues for diversified investments in public and private equity, royalties, and all other aspects of biopharmaceutical investments. We will constantly move back and forth explaining the megafund IPO model as an application to investing in IPOs as a standalone product as well as an integrated megafund model that incorporated into Fernandez's proposal that invests in all aspects of healthcare (Fernandez et al., 2012).

Critics may argue that the megafund IPO model may not be aligned with innovation in biomedicine. However, as mentioned before, investors in the megafund IPO model will have a strong penchant for investing in novel therapies given the fact that more alpha is generated from transformative innovative technologies with high barriers of entry. Furthermore, the fact that the investment strategy is derisked encourages investors in the megafund IPO model to take greater risk in investing in innovative companies that may be riskier.

Critics may also argue that investors in biomedical IPOs are only looking for large market size drugs that are scalable. However, the fact that a drug is scalable is not only favorable because of the revenue stream from serving a large patient base that translates to profits, but also because it implies that there are many cross applications to various therapeutic indications for the same drug. Hence, drugs with large market sizes may indeed be the most optimal place to look for innovation. Moreover, orphan drugs have a very attractive return in the markets as well (Fagnan et al., 2013) demonstrating that scalable technologies are not the only source of innovation that institutional investors are looking for.

Critics may also argue against this model because of the possible short term horizon for profits. The IPO market is often more active when the overall indices are high and investors may only invest in small window business opportunities when the IPO's are looking to perform well (Fernandez et al., 2012). However, the fact that the investment model takes advantage of mispricings in IPO's is more of an alpha play than a beta play that is coupled to the markets. Our model proposes 3 month, 6 months, 1 year holding periods with 5-12 year lockup periods. Even if the holding period of the IPO is short, transferring ownership of equity to another after proceeds have been raised is irrelevant from the perspective of the management of biotechnology and pharmaceutical companies, because they have raised sufficient capital to cover their R&D needs.

Finally, critics may argue that the megafund IPO model may look unfavorably at early stage investments, also known as the valley of death (Fernandez et al., 2012). However, in IPOs, proceeds are generally raised not only for later stage investments but early preclinical studies as well. Even if only IPOs with later stage investments were to be chosen, the contraction in early stage venture investments that sometimes do not continue to participate in later stages of financing is a void that can be complemented by later stage rounds of financing from the megafund IPO model that are necessary for biotechnology companies to continue to thrive. IPO investments could be complemented with private placements, which can also provide heavily discounted opportunities. Furthermore, the

business model we propose have holding periods of 3 months, 6 months, and 1year but have lockup periods of 5-12 years and have to hold 20 projects within the same year at any given time. An RBO backed mega fund that has an IPO investment component will encourage innovation and increase returns while mitigating risk. This megafund IPO model in conjunction with the cancer megafund model, late stage royalty megafund model, and orphan drug megafund model can all be integrated to create better securitization and de-risking techniques that solve the broken link between financial returns and biopharma innovation. New applications and use of megafunds can solve complex problems that evolve in healthcare.

The thesis is materially different from previous biopharma megafund models provided in the literature in the sense that we introduce a new paradigm – the megafund IPO model and analyze risk not just in terms of standard deviation and returns but also within the context of alpha and beta. The megafund IPO model is materially different from a traditional long short equity hedge fund. It is a hybrid private equity/venture capital/hedge fund style that invests in early stages like venture capital, uses leverage to invest in IPOs like private equity, but also can long short IPOs like a hedge fund and use complex derivative techniques that are not typically available in long only products. We use a securitized long only strategy back test for the megafund IPO model as a low benchmark to demonstrate how a long short fund would perform better at a minimum, assuming with active management and hedging strategies the returns would be greater in a long short hybrid hedge fund/private equity/venture capital model. The idea of using a specific type of hybrid hedge fund/private equity/venture capital strategy within the megafund context that can align innovation, contrary to what critics may say, is a novel idea that has not yet been explored in the literature. The thesis also negates past literature that challenges investing in IPOs with an empirical study. Furthermore, we provide a case study of a firm, Monashee Investment Management, that currently participates in this investment strategy and offer the investment analysis in sample deals that would be similar to the deals that the megafund IPO model would participate in to gauge the practicality of

implementing the fund.

Securitization and Portfolio Theory

Core to understanding the megafund model are the principles of securitization and portfolio theory. Securitization is a financial engineering technique in which a pool of investment capital is raised by issuing equity and several classes of bonds with varying risks rewards profiles. Securitization generally involves cash flow transactions in which a portfolio of assets such as mortgages, auto loans, student loans, or credit card receivables are acquired by raising different tranches of equity and debt. These assets are used as collateral for the debt securities. The assets can span from public and private equity, to early stage preclinical investments, to new drug applications and royalty interests. Currently, there has not been a securitization method for early stage and preclinical biomedical research (Fernandez et al., 2012).

The debt that is collateralized by assets was coined "research-backed obligations" in the seminal article "Commercializing Biomedical Research Through Securitization Techniques." The RBO model attempts to cover the void in early stage securitized biomedical investments. Research backed obligations can be customized to appeal to a wide range of investors through varying maturity ranges from the short term to the long term. Effectively, this investment strategy aligns R&D developments that may take 8-15 years without pressuring biomedical projects to quickly monetize in sync with business cycles. Securitizations would typically employ debt maturities of 15 years or less that are backed by FDA approved royalty rights for biopharmaceutical products (Fernandez et al., 2012).

The principles of portfolio theory are crucial for the understanding of the megafund structure with securitization. Fernandez et al., provides in his explanation of the megafund model that within a single project, if debt were to be issued, then the default probability of that debt instrument is 95%. However, when 150 projects are pooled together under a megafund model, the default probability is

only .4% for raising $24.6 billion in zero coupon debt, which is comparable to the highest rated category of debt, Aaa rating according to Moody's. As such, portfolio theory suggests that diversification can reduce risk in biopharmaceutical investments (Fernandez et al, 2012).

Furthermore, Fernandez et al., offers the following illustrative example: in a scenario of investing in a drug with a 5% chance of success that costs 200 million dollars across a period of 10 years, the investment would not be attractive to a lot of people. After all, the drug has a 95% chance of losing 100% and a 5% chance of earning 51% (assuming 2 billion dollars in peak sales and a 10% cost of capital). However, if 150 such investments were to made under a single investment vehicle, the probability of at least one success is 1-.95^(150). Furthermore, risk is further reduced from 423% for an individual draw to only 34.6%=423%/sqrt(150) for the annualized portfolio return (Fernandez et al., 2012).

To further explain this concept we provide the formula for calculating standard deviation for two pooled assets. Sp=Sqrt(f^2Sa^2+2f(1-f)RSaSb+(1-f)^2Sc^2). The standard deviation of the two pooled assets is equal to the square root of the proportion of the first asset squared times the standard deviation of the asset squared plus two times the proportion of the first asset times the proportion of the second asset times the correlation between the two assets times the standard deviation of the first asset times the standard deviation of the second asset plus the proportion of the second asset squared times the standard deviation of the second asset squared (Perold, 2007).

Securitization with debt creates leverage that can also amplify returns. In a securitized model financed by both equity and debt, with a zero coupon bond at 3.85% with proceeds of 16.8 billion and the remaining $13.2 billion financed through equity the expected rate of return would be 21.5% and the standard deviation would be 78.9%. The values may be higher than an all equity financed scenario with an 11.9% expected rate of return and 34.6% standard deviation due to the leverage, but the risk reward profiles are still within the range of publicly traded equities. Of course, correlation can reduce the effects of diversification so it is important to take into consideration the correlation of underlying

assets. This should be intuitive from the formula Sp=Sqrt(f^2Sa^2+2f(1-f)RSaSb+(1-f)^2Sc^2) as higher correlations increase pooled standard deviations (Perold, 2007). For the cancer megafund model a correlation of 20% was used (Fernandez et al., 2012). We will apply these principles of leverage and securitization in our proposed megafund IPO model structure.

To implement theories of securitization and portfolio theory, we used a sample size of twenty projects picked out from our comprehensive list of global biotech and pharmaceutical IPOs in our ten year back test from 2003-2013 (2013 data had to be excluded because 1 year horizons could not be captured yet) and ran Monte Carlo Simulations for 1,000,000 trials using a securitized MATLAB formula to calculate the returns using leverage. The results will be shared at the end but they confirmed previous notions in theorems and past literature, that risk is reduced with increased sample size, higher correlations reduce effects of diversification, and leverage amplifies returns while increasing some risk (Fernandez et al., 2012).

Credit enhancements and triggers can also be used for further protection of researched backed obligations – credit default swaps, over-collateralization, interest and debt coverage ratios that trigger accelerated payments when breached, government guarantees, and tax incentives. Based on the special-purpose vehicle's capital structure, priority of payments, and various coverage tests and credit enhancements a "cash flow waterfall" of senior to junior tranches are formed. The economic value of the securities in various tranches can be directly related to the performance of the assets, and the risk reward profile can be measure based on the statistical properties and its securities can be potentially rated by bond rating agencies. As such, the various securities can be measured by a wide array of investors. In essence, a large portfolio of well diversified biopharma investments that spreads the risks and rewards to a wide array of investors through securitization could align the financing with the long term and large scale characteristic of biomedical innovation (Fernandez et al., 2012).

Similarly to how credit enhancement can mitigate risks, we also believe that derivative structures and long short techniques would further make our megafund IPO model more attractive in

terms of returns on a risk adjusted basis. According to Professor Phil Cooper at MIT Sloan School of Management and founder and former head of Goldman Capital Partners, long only funds on average cannot beat the market index on average and only when equipped with sophisticated hedging techniques, arbitrage or arbitrage like opportunities, and financial products can we achieve results above the mean in a normal distribution of returns for long only products. For these reasons, we propose that the megafund IPO model should be structured using principles derived from hedge funds. Furthermore, arbitrage like strategies we propose in this megafund IPO model investing in derisked IPOs does not apply within the domain of traditional stock picking that Professor Cooper was referring to and work most synergistically with hedge fund like models given the high levels of alpha. Therefore, it should be no surprise that within our empirical study that only looked at long opportunities, without the effects of hedging or other derivative strategies in IPOs, that the arbitrage like opportunity itself negated previous literature that cautions against investing in IPOs (Ritter, 1991). We will dedicate an entire section to this topic later in the thesis.

Currently the venture capital industry or biopharma does not use securitization to finance early stage and preclinical development. The industry has of course utilized the principal of diversification in their patent portfolios but has not really utilized financial engineering in their early stage investments (Fernandez et al, 2012). Indeed, if early stage investments were to be explored they would have to be primarily equity or convertible debt options (Lo & Naraharisetti, 2013). Whereas, providing simulations for private placements in equity interests of early stage investments are beyond the scope of this thesis, our stylized megafund IPO model can be applied to companies that have promising early stage drug candidates that require private placements. Nonetheless, proving in this thesis that an attractive market exists for biotech and pharmaceutical IPOs will only encourage private placements in equity and convertible debt where people can take advantage of IPO exits.

Securitization may have become a questionable capital raising technique after the subprime crisis. Nonetheless, it cannot be denied that securitization is a very effective tool for raising capital.

For instance, during the housing bubble crisis, securitization enabled homeowners to have access directly into a much larger pool of capital instead of obtaining mortgages from financial institutions. Whereas the exact source of the subprime crisis is debatable, there are important precedents set by the government that can be applied to a biomedical megafund. One is the way that governments guarantees supporting the housing market. Public funds such as the National Center for Advancing Translational Sciences can be used to guarantee debt financed private entities rather than directly investing themselves. Furthermore, the pitfalls of the subprime crisis can be used as a guideline to make sure that the biomedical megafund will operate efficiently. Fernandez et al., explains that statistical models of biomedical returns need to be based on not just historical returns but a strong understanding of the science and engineering of the projects. In addition, to avoid bubbles from bursting in the market, portfolio valuations need to reflect market realities rather than hypothetical expectations to avoid panic selling and proper credit risk analysis for investors and risk disclosures of megafund securities need to be displayed (Fernandez et al. 2012).

Cancer Megafund Model

The first simulation study using the megafund model was done on cancer. The study demonstrated how the megafund differed from the current biopharma investment models. The current trend for biopharma companies is to rely more on R&D expansion through acquisitions in later stage pipeline companies, which effectively reduces risk and increases operational efficiency. This has been partially achieved by issuing debt. For example, corporate debt has been issued by Roche in the amount of $16.5 billion for its $46.8 billion acquisition of Genentech. The industry is known to diversify across various therapeutic classes through mergers and acquisitions, licensing agreements (Fernandez et al., 2012).

However, the proposal from the megafund strives to use debt encompassing more early stages

through securitization. Securitization is not used in current investment models such as large venture capital funds, a new biopharmaceutical company, or biopharma mutual funds (Fernandez et al., 2012).

Another distinguishing factor about the biomedical megafund is that it is a single financial entity, financed through debt and equity, which invests across various stages of the pipeline. Unlike a large publicly trading pharmaceutical company that focuses on later stages, megafunds can fill the gap in early stage investments through diversification through sufficient risk reduction. Furthermore, in early stage investments the smaller investment amounts enables megafunds to pivot away from continuing to invest in companies that are not promising and allocate capital to one's that are more promising. Unlike a small biotech company whose existence in contingent on one or two drugs in the pipeline that is forced to continue operating until money runs out if it is not successful, a megafund can more objectively scan and allocate capital to projects that are more likely to be successful and terminate projects that are failing rapidly. As such, this "preclinical incubator" will offer economies of scale that reduce duplicative costs (Fernandez et al., 2012).

Finally, another difference is that the proposed megafund is not a biopharma mutual fund that solely invests in public equities. The megafund can invest in private companies, royalty streams, intellectual property, and other assets. A megafund portfolio manager will be more likely to analyze the underlying science and engineering of the portfolio assets than a mutual fund manager who is interested more in business cycles and immediate economic gains. The megafund structure that is securitized based on debt and equity also aligns the megafund fund manager's interest with a more long term view with the underlying science and engineering because the business pressures, priorities, and horizons are fundamentally different from a mutual fund manager (Fernandez et al, 2012). Within this study, we will look at a unique application of the megafund model to IPO equity investments and expand the scope of the study from just cancer to the entire biotech and pharmaceutical industry

The megafund IPO model is unique in the sense that it is neither just a hedge fund, nor a private equity fund, nor just a venture capital fund. In essence it is all of these and neither of these investment

structures. The model proposes to invest in the early stages of a company before it goes public like a venture capital fund. However, it does not offer convertible bonds and equity investments like a traditional venture capital fund. Whereas, we only mention investing in IPOs in this thesis and private placements and follow on offerings are beyond the scope of our back testing, we believe that these opportunities also would parallel the discounted alpha opportunities for IPO investments. In many ways, these private placement investments resemble private equity as well as the leverage that is being used in investments through securitization. However, this model is obviously inherently different from private equity as it is not a model that operates leveraged buyouts like a traditional private equity fund. The investment model resembles a hedge fund as it can long and short IPOs and hedge with derivative strategies such as shorting ETFs when they believe the overall market will go down but long certain alpha generating IPOs. However, it is inherently different from a traditional long short equity funds that invests in public companies and are more sensitive to quarterly earnings releases.

The cancer megafund model is a special purpose vehicle model that has startup expenses and purchases. The megafund will invest in acquiring anti-cancer economic rights by receiving an upfront payment and milestone payments in exchange for funding R&D and clinical trials. There will also be initial post-launch expenses and principal and interest: A reserve needs to be set in place to make sure that the debt obligations are being paid in a timely manner and the clinical trials can be funded because there may be some time before monetization of revenues will occur through upfront and milestone payments. There will undoubtedly also be ongoing R&D and financing expenses. The megafund's ongoing R&D expenses and financial expenses will be primarily funded by corporate transactions and sale of its assets. Management cost such as salaries to staff, fee to external servicers, and other maintenance and operating costs will be defrayed my management fees as a fixed percentage of assets under management. The special purpose vehicle will be liquidated and the proceeds will be paid out to the equity holders at the end of the fund's life (Fernandez et al., 2012).

The megafund IPO model would also follow a similar trajectory as the fund life of the original

megafund proposed by Fernandez et al. Rather than invest in anti-cancer rights, the fund will invest in IPOs. The fund will have to also have a reserve to pay off debt obligations, but will not have to worry about ongoing R&D financing costs as the offerings will hypothetically cover all R&D costs and working capital needs for the company. Management and operating fees will be taken as a percentage (generally 1-2%) of assets under management to cover salaries and support. Upon the date of maturity, the fund will be liquidated, and the proceeds will also be similarly paid to equity holders (Fernandez et al., 2012).

Challenges of a Megafund

Of course, the megafund model is not unmet with many criticisms. One of the arguments that critics make about megafunds is that operating a portfolio of highly heterogeneous biomedical projects increase with scale, and reduce the effects of diversification (Fernandez et al, 2012). Furthermore, a study found that the internal rates of returns of venture capital funds peaked between $100 million and $250 million and began to decline when assets under management exceeded $500 million (MacConail., et al). However, a megafund is designed to appeal to a wide range of investors with various levels of risk rewards appetites in order to scale the fund and attain the economies of scales for operating as a megafund. Furthermore, given the reduction in risk that a megafund structure provides, the returns should not be compared against a very high risk high return venture capital threshold. Nonetheless, the correlations between assets should be balanced against the economies of scale that diversification provides so that the scientific, operational, and financial synergies are being maximized (Fernandez et al., 2012).

There are also three main challenges in raising a biomedical megafund. First, in order for the fund to be raised, investors must understand the risk reward trade off of the investment they are making. Historical biopharma data may not be an accurate representation as a guide for the future

because the rapidly changing dynamics in translational medical research and its economic implications. However, through sophisticated financial engineering, greater risk and even unknown risk can be managed. Translational research outcomes may be hard to predict. Albeit, that does not mean that a biomedical megafund that employs sophisticated financial engineering to reduce the unpredictable nature of translational research cannot be understood by investors (Fernandez et al., 2012).

Second, there is the danger of megafund financing working too well. As the housing bubble crisis suggests, securitization can lead to a boom and bust pattern. The current trend within investment management is "socially responsible investing," and if too much capital is raised, the growing trend could turn a "niche product" into a "cottage industry." Proper checks and balances such as sales practices, disclosure requirements, corporate governance structures, and suitability criteria must be strictly enforced so that biomedical megafunds fulfill their mission without causing harm to the financial system (Fernandez et al., 2012).

Third, there is an inherent conflict between the business culture and the science and medical culture. Although the combination of social relevance and profit motive may seem incompatible, it is becoming more the norm as evident from organizations such as Gates Foundation, Robin Hood Foundation, Children's Investment Foundation, United States Government's National Center for Advancing Translational Sciences, and the Israeli Life Sciences Fund (Fernandez et al., 2012).

There are also four elements in terms of challenges to deploying capital – 1. Whether academia and the biopharmaceutical industry have sufficient physical and intellectual capacity to leverage the megafund model? 2. Whether the market for compounds, licenses, and royalties will defray the cost of megafund debt? 3. Whether any single organization can manage and operate the megafund structure? 4. Whether the political and regulatory environment (FDA, healthcare reform and policy) will support the megafund model (Fernandez et al., 2012)?

With respect to the first challenge, there are more innovative ideas, graduate students, and professionals in biomedical research than funding available. With respect to the second challenge, if a

high enough of an amount of capital such as tens of billions of dollars flow into the megafund, given the amount of scale, the megafund will be able to sustain the amount of debt through royalties, licensing agreements, and fees. In response to the third challenge, there already exists an asset manager such as Royalty Pharma, which manages $8 billion in assets with only 19 full time staff suggesting that a $30 billion dollar megafund is not beyond unreasonable. In response to the fourth challenge, given the climate of political deadlock the private sector may be the answer to relieving the burden of disease, and as such a megafund model would be something of interest of bipartisan support from politicians (Fernandez et al., 2012). Of course, all of these challenges are equally applicable to the megafund IPO model and need to be overcome.

Cancer Megafund Simulation Study

The cancer megafund simulation study consisted of two simulations: simulation A and simulation B. Simulation A consists of early stage investments in the preclinical stage; the compounds are sold when transitioning into phase II. Simulation B consists of later stage investments, in which compounds are acquired in phase II and are sold when they are FDA approved. The reason that there are two separate classes of simulations is because early stage investments are typically the domain of venture capitalists and the later stage investments are typically the domain of large biotech or pharma licensing agreements. The two inherently different types of investments obviously appeal to a different set of investors with different risk reward tolerances. Furthermore, by separating the investments into two different assets classes, the maturities of the bonds are also shortened in the megafund model than if the same megafund model were to invest in early stage and later stage investments (Fernandez et al., 2012).

The cancer megafund simulations were done in pairs – an all equity fund versus a research backed obligation (RBO) fund with debt and equity components. The securitized RBO fund for

simulation A consisted of $1.25 billion senior tranche, $1.25 billion junior tranche, and 2.5 billion equity tranche. The results showed that the megafund model for simulation A was almost always profitable and 102 compounds were successful in entering phase II. The investors in the senior tranche research based obligation received an annual coupon payment of 5% and only experienced a .1% default rate. Investors in junior tranche research backed obligations were paid an annual coupon payment of 8% and only defaulted .9% of the time. Investors in the equity tranche received on average 8.9% returns with a third of the simulated paths returning over 15% for the RBO model. These returns may not be attractive to venture capitalists, but may be appealing to pension funds, insurance companies, who are looking for conservative investments. Unlike an all equity fund where the downside risk is unlimited, the researched backed obligation debt and equity structure that offers returns on a more favorable risk adjusted basis enables biomedical megafunds to gain access to these very large conservative pools of capital. In the all equity fund 52 compounds were successfully carried to Phase II and had an expected return of 7.2% (Fernandez et al., 2012).

In simulation B, compounds were acquired in phase II with the hopes that they could be sold when they were approved in the markets. However, they could transition to the next phase or be discontinued. Simulation B consisted of a $15 billion dollar megafund invested over 7.5 years in 100 phase II compounds. The capital structure had a leverage of 2.5:1 debt to equity with a $6 billion dollar senior tranche yielding 5%, a $3 billion dollar junior tranche yielding 8%, and a $6 billion dollar equity tranche. The senior tranche was repaid in full 99.9% of the time and the junior tranche was repaid 99.4% of the time. The equity tranche investors received an average return of 11.4% for the RBO model. In the all equity fund that managed $6 billion dollars, 40 phase II compounds were acquired and six advanced to phase III and five went to market. The annualized return for the all equity fund was 7.2% (Fernandez et al., 2012).

The study demonstrates that reasonably conservative returns can be achieved on a risk adjusted basis while at the same time creating a business model that aligns maximal innovation in biomedicine.

Before we move forward with our new analysis in terms of applying the megafund model to IPO investments, which we believe can generate even greater de-risked superior returns we provide a comprehensive review of all application studies of the megafund model up to date. We provide a comparison of the megafund IPO model to other models such as cancer models and orphan drug models in the empirical study.

Applications of the Megafund – Royalty Pharma

Royalty Pharma is a privately owned alternative investment manager that has 10 billion assets under management. In essence, Royalty Pharma closely resembles the biomedical megafund model that is being proposed. However, the company is fundamentally different in one key area. The company focuses on the acquisition of later stage royalty investment entities from post approved drugs to drugs in later stage clinical trials rather than all stages of the phase line (Lo & Naraharisetti, 2013).

Royalty Pharma focuses on drugs that have blockbuster potential and sources deals through two main avenues. One is through proactively seeking investment opportunities in academic institutions, research institutions, and smaller companies. The second avenue is through self-referrals of potential sellers of royalties. Royalty Pharma then assesses the commercial viability of these opportunities based on three criteria: scientific merit, strength of its patent, and expected market share (Lo & Naraharisetti, 2013).

This due diligence closely mirrors the investment analysis that is typically done in the megafund IPO model we propose as well - market sizing, strength of patents, scientific merit, stage in clinical trials all play a key role in determining whether or not to invest in an IPO offering or not. In the last section of the thesis we provide sample deal investment analysis that was conducted by Monashee Investment Management in their allocations for biotechnology and pharmaceutical IPOs to offer insight into the decision making process for investing in the IPO process.

In order to assess the scientific value of a royalty product, Royalty Pharma consults with experts and clinicians to provide their opinions. The patent status is assessed through the legal consultation with patent lawyers. The commercial value of the patent is assessed by Royalty Pharma via interviewing key thought leaders, specialists, doctors, prescribers and projecting these findings into sales estimations. These can then be cross referenced to sales projections by other investment banks who are covering companies that hold the patent as well (Lo & Naraharisetti, 2013).

In the megafund IPO model, we propose that a team of qualified R&D doctors and scientists be hired in house rather than rely on external consultants in terms of assessing the scientific basis and a team of in house lawyers investigate the viability of patent strength. Because of the 1-2% management fee structure of assets under management in a very large scaled megafund, the megafund IPO model can attract the best talent with the large management fees. Simply without the best talent, the megafund cannot succeed into becoming the best fund that encourages innovation in the healthcare industry. The finance professionals ideally should have a background in healthcare, either previous experience in healthcare investment banking, healthcare investment management, and/or course work in not just finance but also biomedicine. As such, we believe performance will be boosted by hiring the most talented team in house rather than rely on consultants.

Because of the illiquid nature of the investments that Royalty Pharma does not apply standard portfolio optimization techniques. However, Royalty Pharma does diversify investments they make based on product, therapeutic class, and marketer. Royalty Pharma's portfolio consists of 15 different therapeutic indications and products from 25 different marketers. Furthermore, Royalty Pharma is diversified by investment style such as accelerated royalty or a synthetic royalty. An example of an accelerated royalty would be receiving 9% on 3 years as opposed to 3% over 9 years. As such, Royalty Pharma provides the seller with a cash flow from a royalty over a shorter duration than the actual royalty in exchange for receiving the remainder of the royalty. A synthetic royalty is when Royalty Pharma creates a royalty structure agreement in exchange for providing capital, where there is no

preexisting royalty on the product. For example, in the case of Sunesis Pharmaceutical's Vosaroxin, Royalty Pharma provided capital in exchange for a percentage of future net sales, where the deal was also contingent on the status of the trial. In other cases, Royalty Pharma purchases an existing royalty in a pharmaceutical product (Lo & Naraharisetti, 2013).

Similarly, in the megafund IPO model we propose that a variety of therapeutic classes be invested in. However, rather than rely on too much diversification, which may be the case in Royalty Pharma, we propose that an active investment management team proactively seek out the biggest winners in terms of therapeutic classes given a specific time frame. In 2013, Royalty Pharma consisted of a portfolio of 39 approved and marketed biopharmaceutical products, and two products in clinical trials under review by the FDA and or EMA (Lo & Naraharisetti, 2013). According to the article by Fagnan et al., "Financing Drug Discovery for Orphan Diseases," orphan drugs seem to be breaking records in terms of returns (Fagnan et al., 2013). However, these trends may not continue and eventually be replaced by another therapeutic class and hence a very talented team that can assess new industry trends in healthcare should be appointed.

The following study is the summary of returns on sub-therapeutic classes in 2013, conducted by BMO Capital Markets. A talented team would have identified Pulmonary as the best therapeutic class to invest in.

Genomics/Genomic Tools, (7.9%)

Gene/Cell Therapy, 1.7%

Hematology, 22.5%

Large Cap Pharma, 24.3%

Genitourinary, 25.8%

Metabolic, 31.0%

NASDAQ, 34.2%

Generics, 34.3%

Chemistry, 41.6%

Inflammation, 43.9%

Large Cap Specialty Pharma, 46.0%

Ophthalmic, 48.1%

Cardiovascular, 49.7%

Small Cap Life Science, 52.8%

Autoimmune, 56.2%

Mid Cap Life Science, 56.6%

Antibodies, 60.0%

Neurology, 63.0%

Drug Delivery, 65.1%

Gastrointestinal, 65.8%

Cancer, 70.1%

Regenerative Medicine, 70.9%

Large Cap Biotech, 74.0%

Orphan, 79.8%

Musculoskeletal, 80.1%

Endocrine, 85.9%

Dermatology, 89.4%

Infectious, 93.9%

Hepatic, 95.6%

Pulmonary, 98.1%

(40.0%) (20.0%) 0.0% 20.0% 40.0% 60.0% 80.0% 100.0% 120.0% 140.0%

(BMO, 2014).

The result of the diversified portfolio for Royalty Pharma is remarkable with consistent attractive risk adjusted absolute returns. Whereas the absolute returns are very impressive, what is even more impressive is the stability of equity returns in periods of unprecedented volatility and low returns from other assets classes, attesting to Royalty Pharma's superb asset selection and portfolio construction (Lo & Naraharisetti, 2013).

Whereas the returns have been impressive in Royalty Pharma, we believe that a derisked arbitrage like investment strategy investing in the megafund IPO model can generate even greater returns. Professor Jay Ritter of the University of Florida explains that a lot of money is left on the table in IPO offerings. An extreme example is the Netscape IPO, which was issued at $28.00 per share, and the first day market price closed at $58.25 per share, leaving $174 million on the table. The trend, according to Professor Ritter is a phenomenon that exists globally in all countries (Ritter, 1998). The megafund IPO model strives to capitalize on this phenomenon.

Royalty Pharma Sample Deals

Royalty Pharma collaborates with academic institutions, research institutions, and pharmaceutical/biotechnology companies to acquire royalty interests. Deal structures can be synthetic or based on a preexisting royalty stream. A sample deal where Royalty Pharma collaborated with an academic institution on a preexisting royalty was when Royalty Pharma acquired the *emtricitabine* royalty from Emory University and three inventors. The royalty was not ideal for the holders because it exposed them to single product risk, illiquidity, and a long payout schedule of 15 years. In 2005, Royalty Pharma purchased the royalty for $525 million enabling the previous holders to gain access to capital and liquidity to diversify their assets (Lo & Naraharisetti, 2013).

Another sample deal on a preexisting royalty stream was when Royalty Pharma collaborated

with a pharmaceutical/biotechnology company to purchase Cambridge Antibody Technology's (CAT's) passive royalty interests in Abott's Humira. When AstraZeneca purchased the remaining 81% of CaT for $1.3 billion dollars, they divested the noncore passive asset for upfront cash of $700 million and this along with the $300 million of CaT cash brought AstraZeneca's net acquisition cost down to $300 million (Lo & Naraharisetti, 2013).

Whereas acquisitions of royalties are one means for which capital can be deployed, we believe that this should be complemented with equity investments like the IPO investments we have recommended. By adding another layer of different deal structures from royalty investments the megafund model is further diversified from types of investments such as preexisting royalties and synthetic royalties.

Royalty Pharma also invests in royalties in drugs that have not yet been approved where a preexisting royalty does not exist. For instance, in May 2012, Royalty Pharma made a $761 million acquisition of BG-12, which is a tablet version of the multiple sclerosis drug dimethyl fumarate. Royalty Pharma had claims to an earn-out payout that was made to the former shareholders of Fumapharm by Biogen, which acquired Fumapharm in 2006. Originally, Fumapharm had a drug called *Fumaderm*, which worked against moderate to severe plaque psoriasis. Biogen then modified the fumeric acid in Fumaderm to create BG-12. In April 2012, Biogen presented promising phase III data, demonstrating a 44% to 53% reduction in annualized relapse rates compared to the placebo control group without producing any serious adverse effects. Furthermore, BG-12 was expected to be the first safe and effective oral RRMS therapy and given 15 years of strong data and efficacy from Fumaderm. There was strong expectation that BG-12 would become the golden standard for multiple sclerosis. Less than one year after Royalty Pharma made an acquisition, the drug was approved by the FDA and is now marketed as Tecfidera. Before the drug was approved in March 27, 2013 a day before the stock was trading at $177.09. As of December 13, 2013 the stock was trading at $275.32, a 55.5% return that correlates to a $23.2 billion dollar increase in the company's market cap (Lo & Naraharisetti, 2013).

The structure of the Royalty Pharma's deal with Fumapharm shareholders was such that in exchange for providing upfront cash of $761 million dollars, Royalty Pharma would receive the earn out payable to the former Fumapharm shareholders linked to sales of BG-12 and Fumaderm. The earnout payable was contingent upon hitting major milestone sales such as $500 million, $1 billion, and every subsequent $1 billion until $20 billion. The payout was not non-commensurate to exposure to risk however – the drug was still not approved and whereas there was a plethora of safety data from Fumaderm, the safety within the context of multiple sclerosis indication was left unknown. Furthermore, BG-12 could have delayed its launch due to commercial reasons (Lo & Naraharisetti, 2013).

Another example of a pre-FDA approved project in which a preexisting royalty did not exist was the "adaptive financing" for Sunesis Pharmaceuticals, which was financed using a synthetic royalty structure. Sunesis was evaluating its lead product, Vosaroxin, which was in phase III trials for patients suffering from first relapsed or refractory acute myeloid leukemia (AML). Initially, phase III studies were designed to have a 90% probability of detecting a 40% difference in overall survival for 450 patients. However, Sunesis designed to move forward with an adaptive structure where the phase III study design and analyses would be altered based on interim data results. The interim data would dictate whether or not to terminate the study, go forth with 450 patients, or expand to with an additional 225 patients. Sunesis had sufficient capital to cover 450 patients but needed an extra $25 million to fund an expansion of up to 675 patients. Royalty Pharma agreed to invest the $25 million to acquire a royalty if following the interim analysis the study was stopped for efficacy or if the sample size was increased. Royalty Pharma would receive a 3.6% participation payment on future net sales if the study was stopped due to efficacy and a 6.75% participation payment on future net sales plus two warrants if the sample size was increased. The warrant's term was as following – Royalty Pharma was entitled to 1,000,000 shares of Sunesis common stock at an exercise price of $3.48 and another 1,000,000 shares at $4.64 per share. If the trials were to continue as planned, Royalty Pharma would have the option of

making the $25 million investment after the un-blinding of the study in exchange for a 3.6% participation payment on future net sales (Lo & Naraharisetti, 2013).

Through the warrant position of their investment, Royalty Pharma was able to make back a significant portion of their investment and received a sizable royalty while de-risking a negative opportunity. Sunesis on the other hand was able to focus their attention on focusing Vosaroxin's regulatory filings and U.S. commercial launch while receiving committed funding. Upon the announcement of the agreement, Sunesis's stock price rose 15% and reached a two year high when the sample size increased (Lo & Naraharisetti, 2013).

The investments in Royalty Pharma were diversified in terms of stage of investments. In order for a successful megafund model to exist, later stage investments need to coexist with early stage investments. This way, all stages of innovation are aligned with financial returns. The challenge, however is that early stage investments are more risky than later stage investments (Fernandez et al., 2012). Within the megafund IPO model that we propose, we believe that successful companies that have drugs in late stage clinical trials will also cross apply technologies into early stage trials for new indications and therapies. By investing in IPOs that have a balance in terms of phase line stages, not only do we propose a model that encourages innovation in all stages but the later stage trials counterbalance and mitigate the risk of early stage preclinical trials.

Royalty Pharma Financing

Royalty Pharma is a modern day case in point of a biopharmaceutical megafund that utilizes an optimal amount of debt and equity. Royalty Pharma finances its acquisitions through $4.2 billion in debt and $4.0 billion in equity. Equity investors are provided with liquidity events once every four years, with the most recent event occurring in 2011. Royalty Pharma operates as one investment vehicle and recapitalizes for every liquidity event. Because of this nature, the fund is able to gain

access to a low-cost debt capital. This enables Royalty Pharma to pay higher prices for attractive royalties that generate higher returns for investors (Lo & Naraharisetti, 2013).

In terms of its debt financing, the debt is held mostly by banks and other institutions. There are two main trusts – the RPI Finance Trust that continues to invest and the RP Select Finance Trust that no longer invests and returns 100% of its cash flow after debt services to its equity holders. RPIFT consists of $3.35 billion dollars in debt across three tranches – 1. $850 million of LIBOR +2.75% notes maturing in November 2016 2. $1.9 billion of LIBOR+3.00% notes maturing in May 2018, and 3. $600 million of LIBOR+3.00% notes maturing in November 2018. RPIFT operated at a debt to EBITDA of 3.5 to 1. RPSFT contained a single tranche of $850 million of LIBOR+3.00% notes and initially had a leverage ratio of 4 to 1 (Lo & Naraharisetti, 2013).

The advantage of having two distinct debt structures was to appeal to a wide range of investors. Commercial banks purchased short term debt with more liquidity and institutional lenders were interested more in the long term debt. Royalty Pharma received investment grade ratings by Moody's, S&P, and Fitch reflecting a stable outlook given the strong diversified portfolio, healthy cash flow, and reasonable leverage of the Royalty Pharma portfolio (Lo & Naraharisetti, 2013).

In our megafund IPO model, we did not implement a bifurcation of two different types of debt offerings mainly due to the fact that we wanted to first explore the investment strategy as a standalone entity and we did not think that for this particular business model it made sense. As a standalone entity, we would legally structure the fund as a hybrid hedge fund/private equity megafund, to generate more alpha using long short and derivative techniques. Divestment of investment opportunities occur on an annual basis which is also why we made the time horizon based on only one debt maturity date. Hence, we aligned debt maturity dates with the divestment of IPOs which had holding periods of 1 year and we had one debt instrument offering a 5% coupon rate. However, we are also proposing this megafund IPO model to also be a subset of the megafund proposed by Fernandez et al., which invest in licensing agreements, public and private equity, and all other areas of biopharma. We understand that

different tranches of debt that have varying maturity dates do indeed appeal to a wider array of investors that have short term and long term interests, which can further stabilize the megafund model in terms of mitigating risk (Fernandez et al., 2012). Therefore, in the megafund model proposed by Fernandez where IPOs can be just one asset class amongst many such as licensing agreements and private equity, we propose multiple layers of debt as well as longer lock up periods of 5-12 years that are more reflective of the megafund model.

Royalty Pharma Challenges and Prospects

Royalty Pharma has been successful in creating a new segment of the investment management business. However, they face challenges given the impending patent cliff with reduced R&D productivity. Targeted therapies and personalized medicine may also raise Royalty Pharma's cost of capital. Furthermore, a shortcoming in Royalty Pharma is that they do not invest in early stage investments, which are crucial to a business model that maximizes innovation in biomedicine. Early stage investments could continue the trend of scientific breakthroughs with a lot of promise in translational research – basic sciences, bioengineering, computational screening of chemical compounds. As such, there has never been a more opportune time to invest in early stage assets. However, moving to earlier stage assets increases risks of the unknown in efficacy, toxicity, and side effects (Lo & Naraharisetti, 2013) and the Royalty Pharma business model alone cannot carry out the aspirations of the biomedical megafund proposed by Fernandez et al (Fernandez et al., 2012) and hence we propose the megafund IPO model that can complement later stage licensing investments, with other investment models that will come to fruition to solve this unmet need in the early stages.

However, the Royalty Pharma business model does demonstrate that the megafund model of using equity and debt to finance biomedical innovation is not only feasible but practical and scalable. Because of the nature of investing in less riskier later stage investments, Royalty Pharma is able to

access larger pools of investment capital than traditional biotech venture capitalists. The investment style has enabled academic centers and biomedical research organization to monetize their intellectual property, which frees up capital to be plowed back into basic and translational medicine (Lo & Naraharisetti, 2013).

Earlier stage investments are characterized by lower probability of success for drugs to be approved, a greater amount of funding that is needed to achieve the same level of diversification for portfolios of later stages. Due to this nature, most early stage preclinical research is funded through government grants, foundations, high net worth individuals, and patient-advocacy groups. The leading example is the NIH and recently the NIH launched a special program called the Bridging Interventional Developmental Gaps program, which is an initiative to support researchers seeking to take basic science into the clinic whether that is in the form of investigating new drug directed toxicology, pharmacokinetic studies, or manufacturing of clinical supplies (Lo & Naraharisetti, 2013).

Whereas the early stages are financed primarily by grants they are also financed through public and private equity. The primarily form of financing for these early stage investments will have to be convertible bonds or equity (Lo & Naraharisetti, 2013). In this thesis we will focus primarily on public equity through the megafund IPO model. In order for our megafund IPO model to be successful with early stage investments however, we need to really understand statistical properties and correlations (Lo & Naraharisetti, 2013). Hence, we explore this topic with further detail in the ensuing section by learning lessons in correlations and statistical properties through orphan drugs.

Orphan Drug Diseases

Orphan drugs may just be the answer to the right correlation and statistical properties that can make early stage RBO megafund investments a reality. In alignment with the statistical properties of the biopharmaceutical megafund model, an interesting study found that even a modest number of

orphan drugs (as few as 10) with equally modest funding (between $250 million and $500 million) can provide diversification to generate attractive risk/reward profiles for equity and debt holders. So far we have reviewed the RBO megafund structure and its application to late stage royalty investments. However, another application of the RBO megafund structure provides new insights into financing biomedicine that can create innovation. Unlike previous models we explored, Orphan drugs are unique in the sense that they are less correlated, and have a higher chance and shorter time period for approval making even early stage investments less risky. Furthermore, due to the Orphan Drug Act of 1983, orphan drug development projects can generate potential lifetime revenues that match non-orphan drugs despite their smaller target patient population (Fagnan et al., 2013).

An empirical study examining the RBO megafund structure in orphan drugs examined the investment returns on a hypothetical portfolio of orphan drug development projects. Based on realistic assumptions for revenues, costs, and probability of success for orphan drug diseases simulation results revealed that even small portfolios of 10-20 compounds requiring less than $250 million dollars in capital could be diversified to yield favorable results to investors. Even though in general risk is reduced based on portfolio size (basic tenant of portfolio theory) due to the financial leverage, orphan drugs are unique in the sense that they require a very modest threshold of assets to generate favorable returns (Fagnan et al., 2013).

As medicine becomes more personalized the medical industry will become more "orphanized," "personalized," and "targeted" (Haffner, 2006). Following this trend, correlations for medicine in aggregate will become reduced (Fagnan et al., 2013). This bodes well for our megafund IPO model, because lower correlations mean less reduction to the effects of diversification. Furthermore, the findings that less capital may be necessary to implement a megafund (Fagnan et al., 2013) is great news in the sense that scaling a megafund IPO model may require less capital and hence capital raising efforts may not be as rigorous as people may conceive. Furthermore, early stage investments may become less and less risky for the megafund IPO model.

Orphan Drug Act

The Orphan Drug Act (ODA) has been in existence for over 30 years. Since the inception of the ODA the landscape has changed drastically. Orphan diseases are defined as those that affect fewer than 200,000 individuals in the USA. Originally, there was an aversion to orphan diseases within the industry because of the small market size. However, today the category of diseases account for a market worth of US$90 billion annually, which is twice the number of all US cancer patients – an estimated 25 million Americans are afflicted with one of 7000 recognized rare diseases (Fagnan et al., 2013).

The industry dynamics were such that in 1983, confronting orphan diseases was a major challenge. 80% of rare diseases are caused by genetic defects, which can be very hard to identify, and exposures to rare and unusual toxins. Some orphan diseases are so rare that afflicted individuals might not be even correctly diagnosed for many years. In fact, there are some people who never are correctly diagnosed. Another challenge for orphan diseases is the inherent small sample size that makes it difficult to comply with rigorous FDA regulations for trials of sufficient size. The Orphan Drug Act (ODA) has been broadly acclaimed for its effectiveness in lowering these barriers for development (Fagnan et al., 2013).

The ODA was designed to catalyze development in the rare disease category and has provided economic incentives such as ODA specific research grants, tax credits for up to 50% of clinical testing costs, expedited regulatory review, and most importantly a 7 year period of marketing exclusivity that precludes FDA approval or generic drug for the same orphan indication. This exclusivity is different from a patent, and offers additional protection from competition from generics and other market entrants. The ODA coupled with the recent scientific breakthroughs in molecular biology and genome sequencing has been the main drivers behind three decades of innovative orphan drug discovery. Prior

to the ODA, only 10 drugs were approved by the FDA. Today 350 drugs have been approved and orphan drugs are at the forefront of global pharmaceutical trends – between 2001 and 2010 the CAGR for molecular entities was negative but for orphan designations returned 10%. Furthermore, orphan drugs currently account for 22% of drug sales with a CAGR of 25.8% during 2001-2010 compared to a CAGR of 20.1% for the same period for the non-orphan market (Fagnan et al., 2013; Haffner, 2006).

Orphan Drugs RBO Model

There are many reasons why orphan drugs are particularly well suited for RBO portfolio financing. One reason is the higher probability of success for orphan drugs compared to other diseases such as oncology and neurodegenerative disorders. Orphan diseases are caused by a mutation in the individual's genetic code, most commonly manifested as a function of an absence of one or more key proteins. By identifying the underlying genetic factors, it is often possible to create highly targeted and effective therapies to address malfunctions and its symptoms. Examples include notable drugs like Rituxan and Gleevec for rare cancers (Fagnan et al., 2013).

Orphan drugs have a higher chance of receiving FDA approval than those of a non-orphan counterpart. Orphan drugs entering clinical testing between 1993 and 2004 were estimated to have an overall regulatory success rate of approximately 22% compared to the non-orphan drug counterparts that had success rates of 11%. The rate for anticancer compounds was even lower at 6-7% (Hay et al., 2012; Fagnan et al., 2013).

This has implications to our megafund IPO model, in the sense that with the "orphanization" of the medical industry (Fagnan et al., 2013) there will be a higher probability of success for all biomedical IPO investments which can only mean higher returns as time elapses. Given the projected high returns already through the back testing study conducted within this thesis, this adds even more tailwinds to why a megafund IPO model should be implemented as returns are projected to become

even higher.

Independent success and failure outcomes are also less contingent on one another in orphan diseases. Orphan diseases are less correlated with one another because they generally display a monogenic pathology or act through largely unrelated mechanisms. The low correlation factor is significant given the weight it has in measuring risk based on portfolio theory - the higher the correlation factor, the less effect diversification has on reducing risk (Fagnan et al., 2013).

The scientific basis of orphan drug suggests that correlations are small compared to certain therapeutic classes like oncology. Many cancer diseases have similar pathologies such as deregulation of certain signaling pathways, mutation in crucial oncogenes – Janus kinase/signal transducers and activators of transcription (JAK/STAT) and transforming growth factor (TGF-B) pathways. By contrast, orphan drugs act against a wider variety of targets compared to tyrosine kinase inhibitors or anti-angiogenesis (Fagnan et al., 2013; Thompson Reuters 2012).

Another reason why orphan drugs are compatible with RBO financing is because of the equivalent life time revenue potential to non-orphan therapies. Despite small population sizes, orphan drugs can be expected to attain sales of $US100-500 million per year. Small patient population sizes are often counterbalanced with high per patient revenues. For instance, Soliris, a drug that treats partoxysymal nocturnal hemoglobinuria - a rare blood disease that affects less than 6000 individual in the US - is priced at more than $40,000 per patient a year. Furthermore, blockbuster drugs are not exclusive to non-orphan drugs. Compounds in the top 29% of orphan drugs are each expected to earn more than $1 billion in revenue per year over their lifetime. One example of a blockbuster orphan drug is Rituxan, which is expected to attain discounted life time sales of $US 150 billion, which is second only to Pfizer's non-orphan Lipitor (Fagnan et al., 2013, Reuters 2012).

Finally, the ODA's market exclusivity clause also provides a strong financial incentive that aligns orphan drugs with the RBO financing structure. An analysis of the 7 year exclusivity period resulted in an average-competition free marketing period of 11.7 years, elongating the normal average

period by a year. Moreover, for therapies that receive approval later in their lifespans, the increase in the exclusivity period can be even longer (Fagnan et al., 2013). Longer exclusivity periods imply higher returns as "orphanization" occurs in the biomedical industry. Hence, there is further evidence that as time elapses a biomedical megafund IPO model will generate even greater returns.

Orphan Drug Megafund Simulation

In order for the mega fund simulation analysis to be implemented there were a few assumptions. Average annual sales of US$200 million and a 10% cost of capital were used as estimates for the average present value of an orphan drug's revenue during its competition free lifespan to arrive at US$1.36 billion. The margins for COGS and marketing costs were projected at 60% resulted in a final average valuation of US$818 million. To provide a range of values sensitivity analysis was also conducted. In a more aggressive projection, annual revenues of US$400 million resulted in a final average valuation of US$1.63 billion (Fagnan et al., 2013).

As of date, Fernandez *et al.* presented a stylized example of securitization in an RBO model and Fagnan *et al*, developed a more detailed version where simulations experiments incorporate more realistic aspects – "correlated assets, stochastic transitions between clinical trial phases, the need to manage cash to pay interest and principal realistic valuations of compounds that are sold during intermediate stages of the clinical trials process, and the need to manage cash to fund new trials during the approval process (Fernandez et al, 2012; Fagnan et al., 2013)."

Following this model, an early stage model for orphan drugs was simulated. This is significant because the early stages represents the riskiest portion of the drug development process and where funding is scarcest. The simulation assumed that an equal number of preclinical and phase I compounds would be acquired with the goal of selling all drugs that successfully complete Phase I compounds. Assumptions were made for clinical trial costs and valuation and duration of each phase.

Preclinical durations were projected at the same level of non-orphan drugs. For clinical trials literature from Kaitin and Dimasi which reported that orphan drug trials take approximately 5.9 years from Phase I to NDA with an additional .8 years required for the approval process, was used (Fagnan et al., 2013; Kaitin & Dimasi, 2010).

A large molecule dataset was used to project clinical transition probabilities. These probabilities reflect the characteristic of orphan drugs with targeting specificity and biological drug development. Based on the analysis, the study projected that the success rate from preclinical to approval to be 21.8%. Valuations of each phase were based on discount rates of 30%. Upfront and milestone payments were projected to be proportional to clinical costs and hence upfront payments were gradually increased. Clinical trial costs were estimated based on number of patients per clinical trial and cost per patient. A higher cost per patient in phase I was projected to account for expenses associated with locating suitable candidates for the trial, which is more difficult for orphan drugs (Fagnan et al., 2013; Dimasi, 2010; Orfali et al., 2012; Fernandez et al., 2012).

The result of two million simulations assuming a fixed correlation of 20% revealed an optimized RBO structure to a traditional equity model. The simulation acquires ten (total capital $US373.75 million) or 16 orphan drugs ($US 575 million) depending on the total amount of capital with an equal number of compounds in preclinical and Phase I, which is the substantially less than the capital required for oncology compounds. In an equity only structure of US$373.75 million, the mean return on equity in the experiment was 10.7%, which was nearly 3% below the RBO structure for the same amount of equity capital. The probability of loss of equity was higher for the equity only structure which was 16.1% compared with the 13.1% for the RBO (Fagnan et al., 2013).

What is significant to note about this study is that a correlation of 20% was used which is the same correlation level as the cancer megafund study (Fernandez et al., 2012). However, as mentioned before, orphan drugs have a lower correlation factor (Fagnan et al., 2013), and this reveals that the estimates are very conservative and should probably reflect higher returns and lower probabilities of

default.

When the equity only model was increased to US$575 million, the probability of loss is reduced to 10.1%, and the return on equity is marginally improved to a mean value of 11.8%. The RBO structure achieves a higher return on equity with an only increase in the probability of loss. However, the RBO model had twice the probability of receiving a return on equity larger than 25%. This higher return is attributed to leverage which results in more risk to equity holders, which is reflected in the higher probability of equity being lost in the RBO (60 basis points) versus the equity only case (1 bp) (Fagnan et al., 2013).

Leverage in the RBO structure consists of two tranches – the senior tranche which has a default rate of approximately 1bp, which is equivalent to the default rates for bonds rated at the highest levels by agencies, and the mezzanine tranche which has a default rate of 56 bp and an expected loss of 15 bp. These low default rates would undoubtedly be attractive to fixed income investors given the coupon rate on the debt of 5% and 8% respectively (Fagnan et al., 2013).

Results from the all equity model and RBO model above were based on annual revenue projections of $US200 million. When more aggressive revenues of $US400 million for the equity model and RBO model were projected, expected returns ranged from 20-34% with increasing levels of debt supported by the RBO model. All equity models returned 19.6% which is commensurate to the most successful biotech VC returns. Furthermore, the impact to the fund's risk profile form acquiring significant debt was minimal. RBOs only increased the probability of default over the all equity model with the same amount of equity by only 79 bp. However, there was a tradeoff as returns from the all equity model of 19.6% increased to 33.8% in the RBO financed case with the probability of total loss for the equity holder increasing by a factor of 40. These projections should be taken with a grain of salt however, as parameter assumptions are very important in driving the results of the data and assumptions need to be constantly reevaluated (Fagnan et al., 2013).

Orphan Drug Megafund Model and Implications

The orphan drug megafund model builds on previous findings that more efficient business models for drug discovery can be developed by aligning science with financial engineering to meet the challenges of translational medicine. The megafund results mirrored the effects of leverage and securitization in the application to cancer (Fernandez et al, 2012). In scenarios where success rates are considerably low and failure is positively correlated between projects, a larger number of projects and large amount of capital is necessary to create an attractive risk reward profile through diversification. When success rates are higher and projects are less correlated, fewer projects and less capital is required as demonstrated by our analysis of the orphan drug megafund simulation. An application of the unique nature of orphan drugs – "higher probability of success, uncorrelated failures, and lower cost for conducting clinical trials" - is to solve the problem of de-risking early stage investments given the lower probability of success preclinical and early clinical trials have (Fagnan et al., 2013).

As mentioned before, the greatest implication is that as diagnostic techniques and the molecular basis of disease become more and more precise, most diseases can become "orphanized." The competitive advantage then is that the probability of success is increased, correlation is decreased, and capital requirements are lowered so that there are multiple shots at goal to create an attractive risk reward profile. Early stage investments may no longer need to be as shunned by risk-averse investors. Orphan drug development also show very promising financial returns on top of the scientific and ethical obligations to solve these complex medical issues (Fagnan et al., 2013).

However, expectations must be managed given that the scientific literature and biopharma experience behind orphan disease is still relatively young. Therefore, the simulation results should be suggestive and not conclusive. Nonetheless, the orphan drug model does suggest that certain biomedical challenges can be met with a smaller scale than proposed by Fernandez *et al* (Fagnan et al., 2013; Fernandez et al., 2012). Now that we have reviewed all of the applications of the biopharma

megafund, we will introduce new applications into the IPO markets.

IPO Performance Literature

There are three anomalies in within the IPO markets. The first is the short run underpricing phenomenon. The second is the hot issue market phenomenon referring to the short term gains on the first day of trading which Ritter estimates on average as 16.4%. Furthermore, in the long run it appears that IPOs are overpriced. The study which was conducted in the early 90s, examined IPOs in 1975-1984 period. The study found that in the 3 years after going public there firms significantly underperformed a set of comparable firms based on size and industry while examining 1,526 IPOs. The study revealed that within a 3 year holding period the IPO markets returned 34.47%, whereas investments in comparable companies returned 61.86% (Ritter, 1991). In 2002, Ritter and Welch came out with a new article with less conclusive results on IPO underperformance stating that the IPO performance returns were very sensitive to inclusion and exclusion of certain dates (Ritter & Welch, 2002). Therefore, Ritter's 2002 study obscures his previous findings and it seemed that including the most recent data in the last ten years would offer much insight into the best estimates of projecting trends moving forward.

The 1991 study by Ritter is somewhat limited since the back testing is not based on most recent data that includes the financial crisis in 2007-2009 as in our empirical study. After the subprime crisis, there were significant shifts in the markets as to market expectations in returns and the changed dynamics may not necessarily be reflected of the market realities moving forward by analyzing data in the 80's and 90's. Second, our back testing was based on more short term horizons than 3 years, because we do not believe that deal dynamics within the IPO markets support such a strategy to invest in them for 3 years and we believe in creating greater liquidity for our investors within 3 months, 6 months, and 1 year. Our empirical findings found that when there were holdings for 1 year that the alpha generated was not just reflected of the initial underpricing with attractive alpha across increasing

time horizons in the equally weighted version. Higher alphas over betas in our empirical study also suggest that the IPO investment strategy outperforms the market. Our results also negate the hot issues phenomenon since alpha was consistently produced not only on the first day of trading but consistently through our time horizons of 1 day, 1 week, to 1 year. Our back testing was also conducted through the last ten years, incorporating high and low markets, negating the hot issue hypothesis.

Empirical Study

Currently up to date a megafund model has only been proposed confined to cancer (Fernandez et al, 2012). For our application of the megafund model we incorporate biotechnology and drugs and pharmaceuticals to receive a broader section of the biomedical space. Furthermore, the megafund model has been applied at later stage licensing agreements as in the Royalty Pharma case study and early stage investments have been examined looking at orphan drugs (Fagnan et al., 2013; Lo & Naraharisetti, 2013). However, by examining equity investments that entail many stages of the preclinical and clinical phase line we can add another layer of sophistication to our securitization and diversification techniques to our megafund that diversifies away risks. Moreover, early stage investments require equity and private equity investments and by studying investments in IPOs, albeit only one special class of equity, we may be able render aforementioned inferences on other discounted early stage investments. A healthy IPO return investment strategy, will only encourage more private placement and private equity investments to take place.

Equally Weighted						
	% Change Price Offer/1 Day	% Change Price Offer/1 Week	% Change Price Offer/2 Weeks	% Change Price Offer/3 Months	% Change Price Offer/6 Months	% Change Price Offer/1 Yr
RETURNS	16.08%	17.42%	15.73%	21.76%	26.76%	25.86%
STDEV	12.31%	16.95%	16.44%	27.95%	51.77%	48.42%
S&P	0.04%	0.13%	0.27%	2.31%	4.34%	8.82%
ALPHA	16.05%	17.29%	15.46%	19.45%	22.42%	17.05%

The IPO markets globally provide an arbitrage like opportunity that is decoupled from market risk beta. By conducting a back test of 10 years from 2003-2013 (2013 data was excluded because 1 year horizons could not yet be captured), investors who participated in every biotech and pharmaceutical IPO in an equally weighted fashion globally (excluding deals that Deal Logic could not track or record properly) and held the stock for 3 months would have received 21.76% returns, whereas the S&P would have only returned 2.31% for the same period. This is an alpha of 19.45%. Similar results are shown for holding periods of 6 months. Returns of 26.76% could have been expected whereas the S&P would have only returned 4.34% for the same period, providing an alpha of 22.42%. For holding periods of 1 year, the average return was 25.86% whereas the S&P only returned 8.82%, resulting in an alpha of 17.05%. Active managers would be expected to be able to achieve even higher returns with more selective investment choices while conducting due diligence on the right investment opportunities and with better timing for the investment horizon.

What is significant about the IPO investment strategy is that the business model aligns innovation in the biotechnology industry with strong returns and mitigated risks. Because the investment strategy is not really coupled to the markets, there are significant de-risking opportunities for the investment strategy at any given period of time. Given the strong returns profile of the investment strategy on a de-risked basis, institutional investors would be incentivized to participate in IPO offerings; the use the proceeds would in return be used to finance R&D development for innovative biotech and pharmaceutical companies. Hence, a virtuous cycle is created.

Another question that was explored was whether or not this investment model could be scalable. Given that the investment strategy is global, derisked, and provides a strong return profile, in order to achieve even greater scale we applied the megafund model. Like previous studies, calculations were based on correlations of 20%. According to Professor Damodaran of NYU Stern University, biotechnology has an average correlation of 19.15% and pharmaceuticals have an average correlation of 23.42% showing that the 20% projection is reasonable (Damadoran, 2014). In the megafund model

with no debt average mean returns on an annualized basis assuming that 20 projects are held for an entire year for 3 months, 6 months, and 1 year are 19.87%, 22.17%, 23.44% respectively. The moderate decrease in returns is mitigated by significant reductions in standard deviations for 3 months, 6 months, and 1 year from 79.09% to 16.50%, 146.52% to 20.59%, and 137.04% to 26.21% respectively. As such, the trend that we see is for a small decrease in returns for a significant reduction in the standard deviation of the portfolio.

Returns			
	3 Months	6Months	1 Year
Original	21.76%	26.76%	25.86%
Megafund No Debt	19.87%	22.17%	23.44%
Megafund With Deb	47.50%	54.05%	45.97%
STDEV			
Original	79.09%	146.52%	137.04%
Megafund No Debt	16.50%	20.59%	26.21%
Megafund With Deb	47.13%	58.83%	58.25%

The 3 month and 6 month holding portfolio were able to support 65% of debt with a default rate of less than 1 basis point, whereas the 1 year holding period was able to support 55% level of debt. In the scenario for megafund with debt, whereas the riskiness of the portfolio was increased, the returns were increased as well. For a 3 month holding period the average mean was 47.50% with a standard deviation of 47.13%. For a 6 month holding period, the average return mean was 54.05% and the standard deviation was 58.83%. For a 1 year holding period the returns are 45.97% with a standard deviation of 58.25%. What is crucial to understand about standard deviations, however, is to understand this risk in the context of the de-risking from Beta and that risk needs to be analyzed holistically.

These returns are astonishing compared to the 23.2% to 34% equity only and equity and debt megafund structure returns in the most aggressive scenario for orphan drugs (Fagnan et al., 2013). Furthermore, the returns for the megafund IPO model are even greater than the 7.2%-11.4% returns for the cancer megafund returns for both equity only and equity and debt models. The returns in the megafund IPO model are achieved at high alphas with very low exposure to beta risk. Also, whereas standard deviations may be higher than desired, risk needs to be accounted for by measuring the high alphas and low exposure to beta risk. Moreover, the standard deviations are higher than what the actual IPO megafund model would be in real life given that the back testing was limited to a long only strategy, and a hedge fund like strategy with derivatives and long short techniques would reduce standard deviations significantly. Furthermore, standard deviations should be able to be lowered in a comprehensive megafund model with other investments mitigating the risk such as royalty investments, cancer investments, and orphan drug investments.

The Matlab Code that we used for the analysis is as following:

```
function [ret_equity, def ] = IPOtemp( M ,correlation)
   NSIMUS = 1000000;
   debt_array=0:0.05:1;
   params=lognfit(M+1);
   mu = params(1);
   sigma = params(2);
   t = randn(NSIMUS,20);
   market = randn(NSIMUS,1);
   for i = 1:NSIMUS
      ret = exp(mu+sigma*(market(i)*correlation+sqrt(1-correlation^2)*t(i,:)))-1;
```

```
    for j = 1:length(debt_array)
        debt = debt_array(j);
        coupon = 0.05;
        equity = 1-debt;
        ret_equity(i,j) = ((1+mean(ret))*1-debt*(1+coupon))/equity-1;
        def(i,j) = (1+mean(ret))<debt*(1+coupon);
    end
  end

end
```

Based on this Matlab Code we propose an investment management business model with a lock up period of 5-12 years to align the financial incentives with long term innovation as a subset model for the megafund Fernandez et al., proposes (Fernandez et al, 2012). Furthermore, within a year we assume that 20 projects are assumed at all times, even if certain investments are divested every 3 months or 6 months. The list of investments where 20 projects were pooled from is provided below.

12-Feb-03	IPO	600521	Zhejiang Huahai Pharmaceutical Co Ltd
19-May-03	IPO	BPRG	BioProgress plc
27-May-03	IPO	600436	Zhangzhou Pientzehuang Pharmaceutical Co Ltd
30-Jun-03	IPO	8225	Venturepharm Laboratories Ltd
8-Sep-03	IPO	2369	MediBIC Group
18-Sep-03	IPO	CRP	Cryptome Pharmaceuticals Ltd
26-Sep-03	IPO	PXS	Pharmaxis Ltd
30-Sep-03	IPO	2370	MEDINET Co Ltd
29-Oct-03	IPO	CNVX	CancerVax Corp
29-Oct-03	IPO	GTOP	Genitope Corp
29-Oct-03	IPO	MYOG	Myogen Inc
5-Nov-03	IPO	NTMD	NitroMed Inc
5-Nov-03	IPO	PHRM	Pharmion Corp

11-Nov-03	IPO	1149	Broad Intelligence International Pharmaceutical Holdings Ltd
19-Nov-03	IPO	MVP	Medical Developments International Ltd
26-Nov-03	IPO	4564	OncoTherapy Science Inc
2-Dec-03	IPO	RBY	Rockeby biomed Ltd
4-Dec-03	IPO	SPH	Sinclair Pharma plc
8-Dec-03	IPO	2385	Soiken Inc
10-Dec-03	IPO	VAPH	Vaso Active Pharmaceuticals Inc
22-Dec-03	IPO	CAU	CollTech Australia Ltd
23-Dec-03	IPO	YSPSAH	YSP Southeast Asia Holding Bhd
26-Jan-04	IPO	CST	CO2 Solution Inc
29-Jan-04	IPO	EYET	Eyetech Pharmaceuticals Inc
2-Feb-04	IPO	GTXI	GTX Inc
11-Feb-04	IPO	CGTK	Corgentech Inc
18-Feb-04	IPO	DVAX	Dynavax Technologies Corp
21-Feb-04	IPO	600479	Zhuzhou Qianjin Pharmaceutical Co Ltd
23-Feb-04	IPO	TIS	Tissue Therapies Ltd
24-Feb-04	IPO	3310	Jimos Co Ltd
26-Feb-04	IPO	2395	SNBL
3-Mar-04	IPO	600594	Guizhou Yibai Pharmaceutical Co Ltd
16-Mar-04	IPO	XCYT	Xcyte Therapies Inc
17-Mar-04	IPO	BSY	Biosyntech Inc
24-Mar-04	IPO	BSLN	Basilea Pharmaceutica AG
31-Mar-04	IPO	2399	Sogo Clinical Pharmacology Co Ltd
31-Mar-04	IPO	SNTS	Santarus Inc
14-Apr-04	IPO	CORT	Corcept Therapeutics Inc
26-Apr-04	IPO	YRK	York Pharma plc
29-Apr-04	IPO	CYTK	Cytokinetics Inc
18-May-04	IPO	600421	Wuhan Spring Biological Engineering Co Ltd
26-May-04	IPO	CRTX	Critical Therapeutics Inc
27-May-04	IPO	600420	Shanghai Modern Pharmaceutical Co Ltd
28-May-04	IPO	2001	Zhejiang NHU Co Ltd
2-Jun-04	IPO	2004	Chongqing Huapont Pharmaceutical Co Ltd
3-Jun-04	IPO	INHX	Inhibitex Inc
7-Jun-04	IPO	2007	Hualan Biological Engineering Inc
9-Jun-04	IPO	GAA	Genepharm Australasia Ltd

15-Jun-04	IPO	MBRX	Metabasis Therapeutics Inc
21-Jun-04	IPO	MNTA	Momenta Pharmaceuticals Inc
21-Jun-04	IPO	SNMX	Senomyx Inc
23-Jun-04	IPO	ZNTV	Zentiva NV
25-Jun-04	IPO	VEC_L	Vectura Group plc
29-Jun-04	IPO	MYG	Methylgene Inc
19-Jul-04	IPO	ECX	Epigenomics AG
20-Jul-04	IPO	4565	Sosei Co Ltd
21-Jul-04	IPO	IDIX	Idenix Pharmaceuticals Inc
27-Jul-04	IPO	MNKD	MannKind Corp
2-Aug-04	IPO	EVC	Evolutec Group plc
7-Sep-04	IPO	3341	Nihon Chouzai Co Ltd
4-Oct-04	IPO	THRX	Theravance Inc
11-Oct-04	IPO	SAR	Sareum Holdings plc
11-Oct-04	IPO	VOX	VASTox Ltd
15-Oct-04	IPO	CTRX	CoTherix Inc
20-Oct-04	IPO	SNG	Synairgen plc
12-Nov-04	IPO	4566	LTT Bio-Pharma Co Ltd
17-Nov-04	IPO	PRAI	PRA International Inc
25-Nov-04	IPO	SBS	SemBioSys Genetics Inc
29-Nov-04	IPO	2877	China Shineway Pharmaceutical Group Ltd
15-Dec-04	IPO	HLF	Herbalife Ltd
17-Dec-04	IPO	CTI	Chemokine Therapeutics Corp
10-Jan-05	IPO	INRM	Indoco Remedies Ltd
10-Jan-05	IPO	NLS	Narhex Life Sciences Ltd
28-Jan-05	IPO	4875	MediciNova Inc
1-Feb-05	IPO	NEU	Neuren Pharmaceuticals Ltd
2-Feb-05	IPO	FVRL	Favrille Inc
2-Feb-05	IPO	ICGN	Icagen Inc
3-Feb-05	IPO	THLD	Threshold Pharmaceuticals Inc
9-Feb-05	IPO	PA8	Paion AG
15-Feb-05	IPO	CVBT	CardioVascular BioTherapeutics
25-Feb-05	IPO	ICEL	Intercell AG
15-Mar-05	IPO	HOVI	Hovid Bhd
17-Mar-05	IPO	4567	Effector Cell Institute Inc
24-Mar-05	IPO	PLE	Plethora Solutions Holdings plc
29-Mar-05	IPO	PRX	Proximagen Neuroscience plc
5-May-05	IPO	GXE	Galapagos NV
2-Jun-05	IPO	XNPT	XenoPort Inc
6-Jun-05	IPO	DEVG	Devgen NV

9-Jun-05	IPO	TOPO	TopoTarget AS
10-Jun-05	IPO	PSK	ProStrakan Group Ltd
16-Jun-05	IPO	GNT	Gentium SpA
4-Jul-05	IPO	VVMD	Vivimed Labs Ltd
6-Jul-05	IPO	NECT	Nectar Lifesciences Ltd
15-Jul-05	IPO	78160	Medipost Co Ltd
18-Jul-05	IPO	STEM	Stem Cell Sciences plc
5-Aug-05	IPO	RENE	ReNeuron Group plc
9-Aug-05	IPO	COLY	Coley Pharmaceutical Group Inc
31-Aug-05	IPO	REPL	Reyoung Pharmaceutical Holdings Ltd
31-Aug-05	IPO	REPL	Reyoung Pharmaceutical Holdings Ltd
6-Sep-05	IPO	3385	Yakuodo Co Ltd
9-Sep-05	IPO	8329	Shenzhen Neptunus Interlong Bio-Technique Co Ltd
23-Sep-05	IPO	GIA	Giaconda Ltd
26-Sep-05	IPO	SNSS	Sunesis Pharmaceuticals Inc
5-Oct-05	IPO	COPT	C&O Pharmaceutical Technology (Holdings) Ltd
31-Oct-05	IPO	HIK	Hikma Pharmaceuticals
31-Oct-05	IPO	JI4G	Jerini AG
9-Nov-05	IPO	CRXX	CombinatoRx Inc
9-Nov-05	IPO	ORX	Orexo AB
6-Dec-05	IPO	IPN	Ipsen SA
8-Dec-05	IPO	8058	Shandong Luoxin Pharmacy Stock Co Ltd
12-Dec-05	IPO	2005	Lijun International Pharmaceutical (Holding) Co Ltd
14-Dec-05	IPO	SOMX	Somaxon Pharmaceuticals Inc
16-Dec-05	IPO	64550	Bioneer Corp
31-Jan-06	IPO	SGXP	SGX Pharmaceuticals Inc
1-Feb-06	IPO	ICX	Intercytex Group plc
1-Feb-06	IPO	IOMI	Iomai Corp
6-Feb-06	IPO	SRPT	Star Pharmaceutical Ltd
24-Feb-06	IPO	8247	Biosino Bio-Technology & Science Inc
27-Feb-06	IPO	PYN	Phynova Group plc
23-Mar-06	IPO	SYN	Syntopix Group plc
7-Apr-06	IPO	RNVO	Renovo Group
11-Apr-06	IPO	TRGT	Targacept Inc
12-Apr-06	IPO	86060	Gene Bio Tech Co Ltd
12-Apr-06	IPO	ENTL	Entelos Inc
12-Apr-06	IPO	VNDA	Vanda Pharmaceuticals Inc
20-Apr-06	IPO	OMRI	Omrix Biopharmaceuticals Inc
20-Apr-06	IPO	PLPH	Plethico Pharmaceuticals Ltd
21-Apr-06	IPO	SELEC	Selcuk Ecza Deposu

25-Apr-06	IPO	VRPH	Veropharm OAO
9-May-06	IPO	NOVC	Novacea Inc
10-May-06	IPO	HCM	Hutchison China Meditech Ltd
15-May-06	IPO	GRF	Grifols SA
15-May-06	IPO	PHRC	Pharco SA
19-May-06	IPO	PRL	Pierrel SpA
7-Jun-06	IPO	REAL	Realco
21-Jun-06	IPO	BXLN	BioXell SpA
26-Jun-06	IPO	ONCOB	OncoMethylome Sciences SA
27-Jun-06	IPO	PURI	PuriCore plc
27-Jun-06	IPO	RDYN	Replidyne Inc
4-Jul-06	IPO	CLAVIS	Clavis Pharma ASA
6-Jul-06	IPO	THR	ThromboGenics NV
21-Jul-06	IPO	CBLI	Cleveland Biolabs Inc
3-Aug-06	IPO	OSIR	Osiris Therapeutics Inc
15-Sep-06	IPO	BVT	Biovitrum AB
20-Sep-06	IPO	WCRX	Warner Chilcott Ltd
4-Oct-06	IPO	OCTO	OctoPlus NV
17-Oct-06	IPO	TRBN	Trubion Pharmaceuticals Inc
24-Oct-06	IPO	CADX	Cadence Pharmaceuticals Inc
25-Oct-06	IPO	PFRM3	Profarma Distribuicao de Produtos Farmaceuticos SA
2-Nov-06	IPO	SANN	Santhera Pharmaceuticals AG
7-Nov-06	IPO	CPRX	Catalyst Pharmaceutical Partners Inc
10-Nov-06	IPO	LCP	LifeCycle Pharma A/S
14-Nov-06	IPO	EBS	Emergent BioSolutions Inc
1-Dec-06	IPO	84110	Huons Co Ltd
8-Dec-06	IPO	2099	Zhejiang Hisoar Pharmaceutical Co Ltd
8-Dec-06	IPO	NWRN	Newron Pharmaceuticals SpA
13-Dec-06	IPO	OMPI	Obagi Medical Products Inc
14-Dec-06	IPO	TAIH	Taihua plc
2-Jan-07	IPO	39200	Oscotec Inc
21-Feb-08	IPO	EUIM	Euroimplant SA
25-Feb-08	IPO	4571	NanoCarrier Co Ltd
29-Feb-08	IPO	MLM	MolMed SpA
12-Mar-08	IPO	4572	Carna Biosciences Inc
31-Mar-08	IPO	4573	R-Tech Ueno Ltd
10-Jun-08	IPO	PCIB	PCI Biotech AS
17-Jun-08	IPO	2176	Ina Research Inc
4-Aug-08	IPO	1212	Astra Industrial Group
17-Sep-08	IPO	100700	Sewoon Medical Co Ltd

24-Sep-08	IPO	SCLP	Scancell Holdings plc
26-Sep-08	IPO	2182	Mediscience Planning Inc
6-Mar-09	IPO	2190	JCL Bioassay Corp
9-Mar-09	IPO	4574	Taiko Pharmaceutical Co Ltd
17-Mar-09	IPO	2191	tella Inc
28-Jul-09	IPO	MLQGC	Quantum Genomics SA
31-Jul-09	IPO	MLPAT	Plant Advanced Technologies SAS - PAT
10-Aug-09	IPO	CPIX	Cumberland Pharmaceuticals Inc
17-Aug-09	IPO	DPRM	D-Pharm Ltd
7-Sep-09	IPO	4575	CanBas Co Ltd
24-Sep-09	IPO	300006	Hunan Kangyuan Pharmaceutical Co Ltd
24-Sep-09	IPO	300009	Anhui Anke Biotechnology (Group) Co Ltd
30-Sep-09	IPO	TLCR	Talecris Biotherapeutics Holdings Corp
7-Oct-09	IPO	OMER	Omeros Corp
12-Oct-09	IPO	300016	Beijing Beilu Pharmaceutical Co Ltd
13-Oct-09	IPO	4576	D Western Therapeutics Institute Inc
14-Oct-09	IPO	300026	Tianjin Chase Sun Pharmaceutical Co Ltd
1-Dec-09	IPO	ISKJ	Human Stem Cell Institute OAO - HSCI
3-Dec-09	IPO	MOVE	Movetis NV
8-Dec-09	IPO	114450	KPX Life Science Co Ltd
9-Dec-09	IPO	NKBP	China Nuokang Bio-Pharmaceutical Inc
15-Dec-09	IPO	FLRY3	Fleury SA
23-Dec-09	IPO	300039	Shanghai Kaibao Pharmaceutical Co Ltd
6-Jan-10	IPO	300049	Inner Mongolia Free Han & Mongolia Pharmaceutical Co Ltd
29-Jan-10	IPO	533157	Syncom Healthcare Ltd
2-Feb-10	IPO	IRWD	Ironwood Pharmaceuticals Inc
12-Feb-10	IPO	CBZ	CBio Ltd
12-Feb-10	IPO	ONG	Oxford Nutrascience Group plc
14-Feb-10	IPO	INTP	Intec Pharma Ltd
3-Mar-10	IPO	PRTL	Proteologics Ltd
4-Mar-10	IPO	7776	Cellseed Inc
9-Mar-10	IPO	8283	Paltac Corp
10-Mar-10	IPO	PVT	Provet Holdings Ltd
15-Mar-10	IPO	4577	Daito Pharmaceutical Co Ltd
21-Apr-10	IPO	CDXS	Codexis Inc
12-May-10	IPO	300086	Hainan Honz Pharmaceutical Co Ltd
12-May-10	IPO	300087	Winall Hi-tech Seed Co Ltd
17-May-10	IPO	MAB	Mabion SA
27-May-10	IPO	102460	Reyon Pharmaceutical Co Ltd
17-Jun-10	IPO	533211	Parabolic Drugs Ltd

23-Jun-10	IPO	DIOD	Diod OAO
30-Jun-10	IPO	SCC	SCC Holdings Bhd
1-Jul-10	IPO	NEU	Neuron BioPharma SA
15-Jul-10	IPO	106190	High Tech Pharm Co Ltd
2-Aug-10	IPO	TSRX	Trius Therapeutics Inc
6-Aug-10	IPO	PATH	NuPathe Inc
10-Aug-10	IPO	300110	Qingdao Huaren Pharmaceutical Co Ltd
10-Sep-10	IPO	300122	Chongqing Zhifei Biological Products Co Ltd
28-Sep-10	IPO	CELL	CellCura ASA
28-Sep-10	IPO	GENOME	Malaysian Genomics Resource Centre Bhd
18-Oct-10	IPO	SHP	ShangPharma Corp
26-Oct-10	IPO	PACB	Pacific Biosciences of California Inc
27-Oct-10	IPO	600998	Jointown Pharmaceutical Group Co Ltd
29-Oct-10	IPO	300142	Walvax Biotechnology Co Ltd
10-Nov-10	IPO	GNOM	Complete Genomics Inc
18-Nov-10	IPO	LIFE	Pharmsynthez OAO
22-Nov-10	IPO	ZGNX	Zogenix Inc
23-Nov-10	IPO	ZEAL	Zealand Pharma A/S
30-Nov-10	IPO	IGN	Inno-Gene SA
3-Dec-10	IPO	300147	Xiangxue Pharmaceutical Co Ltd
6-Dec-10	IPO	120240	Daejung Chemicals & Metals Co Ltd
6-Dec-10	IPO	4578	Otsuka Holdings Co Ltd
6-Dec-10	IPO	533288	Claris Lifesciences Ltd
16-Dec-10	IPO	VTUS	Ventrus Biosciences Inc
24-Dec-10	IPO	300158	Shanxi Zhendong Pharmaceutical Co Ltd
21-Jan-11	IPO	300171	Shanghai Tofflon Science & Technology Co Ltd
24-Jan-11	IPO	TBET	Tibet Pharmaceuticals Inc
2-Feb-11	IPO	ICCM	IceCure Medical Ltd
2-Feb-11	IPO	PCRX	Pacira Pharmaceuticals Inc
4-Feb-11	IPO	ECYT	Endocyte Inc
9-Feb-11	IPO	300181	Zhejiang Jolly Pharmaceutical Co Ltd
17-Feb-11	IPO	RSTG	Rosetta Green Ltd
23-Feb-11	IPO	GLKM	Glycominds Ltd
11-Mar-11	IPO	300194	Chongqing Fuan Pharmaceutical (Group) Co Ltd
25-Mar-11	IPO	300199	Hybio Pharmaceutical Co Ltd
1-Apr-11	IPO	300204	Staidson (Beijing) Biopharmaceuticals Co Ltd
19-Apr-11	IPO	SGNT	Sagent Pharmaceuticals Inc
28-Apr-11	IPO	SLV	Selvita SA
5-May-11	IPO	CFR	CFR Pharmaceuticals SA
20-May-11	IPO	533412	Aanjaneya Lifecare Ltd

20-May-11	IPO	MOB	Moberg Derma AB
13-Jun-11	IPO	300233	Shandong Jincheng Pharmaceutical & Chemical Co Ltd
13-Jun-11	IPO	SCS	Stem Cells Spin SA
28-Jul-11	IPO	HZNP	Horizon Pharma Inc
5-Aug-11	IPO	300255	Hebei Changshan Biochemical Pharmaceutical Co Ltd
5-Aug-11	IPO	300255	Hebei Changshan Biochemical Pharmaceutical Co Ltd
23-Aug-11	IPO	533543	Brooks Laboratories Ltd
11-Oct-11	IPO	4582	SymBio Pharmaceuticals Ltd
14-Oct-11	IPO	7777	3D Matrix Ltd
10-Nov-11	IPO	NLNK	NewLink Genetics Corp
15-Nov-11	IPO	CLVS	Clovis Oncology Inc
9-Dec-11	IPO	4583	Chiome Bioscience Inc
9-Jan-12	IPO	140410	Dong-A Pharmtech Co Ltd
26-Jan-12	IPO	VSTM	Verastem Inc
3-Feb-12	IPO	CEMP	Cempra Inc
7-Feb-12	IPO	300289	Beijing Leadman Biochemistry Co Ltd
8-Feb-12	IPO	CCXI	ChemoCentryx Inc
28-Feb-12	IPO	300294	Jiangxi Boya Biopharmaceutical Co Ltd
29-Feb-12	IPO	KKH	K&K Herbal Poland SA
21-Mar-12	IPO	CORD	Cordlife Group Ltd
28-Mar-12	IPO	MACK	Merrimack Pharmaceuticals Inc
30-Apr-12	IPO	SUPN	Supernus Pharmaceuticals Inc
5-Jun-12	IPO	RESP	Respiratorius AB
27-Jun-12	IPO	TSRO	Tesaro Inc
18-Jul-12	IPO	DRTX	Durata Therapeutics Inc
25-Jul-12	IPO	HPTX	Hyperion Therapeutics Inc
6-Aug-12	IPO	300347	Hangzhou Tigermed Consulting Co Ltd
19-Sep-12	IPO	CLIN	Clinigen Group
4-Oct-12	IPO	RGLS	Regulus Therapeutics Inc
10-Oct-12	IPO	ICPT	Intercept Pharmaceuticals Inc
10-Oct-12	IPO	KYTH	Kythera Biopharmaceuticals Inc
24-Oct-12	IPO	NANO	Nanobiotix SA
30-Nov-12	IPO	4585	UMN Pharma Inc
12-Dec-12	IPO	2931	euglena Co Ltd
14-Dec-12	IPO	VENN	Venn Life Sciences Holdings plc

By offering debt and equity investments vehicles, the megafund can appeal to a wide arrange of investors with different risk reward appetites. Furthermore, the data also suggests that on a risk reward basis for the debt equity instruments in the megafund IPO model have a short term horizon and are divested at a maximum of 1 year. Critics may argue that short term horizons are not compatible with biotech investment models that need long term investors. However, an important distinction needs to be made. In IPO stages, unlike secondary markets, biotech companies are raising capital to use proceeds to finance R&D. After participating in an IPO, even if the institutional investor were to sell after a period of 1 day to a few weeks or 3 months, essentially liquidity is being provided to the secondary markets. Furthermore, the biotech company has already raised the capital it needs to cover their R&D expenses. In addition, whereas IPO investments are being divested for a maximum of 1 year, the schedule is annually continuous for a lock up period of 5-12 years aligning a more long term view on developing R&D.

Critical Analysis

Equally Weighted						
	% Change Price Offer/1 Day	% Change Price Offer/1 Week	% Change Price Offer/2 Weeks	% Change Price Offer/3 Months	% Change Price Offer/6 Months	% Change Price Offer/1 Yr
RETURNS	16.08%	17.42%	15.73%	21.76%	26.76%	25.86%
STDEV	12.31%	16.95%	16.44%	27.95%	51.77%	48.42%
ALPHA	16.05%	17.29%	15.46%	19.45%	22.42%	17.05%
Deal Weighted						
	% Change Price Offer/1 Day	% Change Price Offer/1 Week	% Change Price Offer/2 Weeks	% Change Price Offer/3 Months	% Change Price Offer/6 Months	% Change Price Offer/1 Yr
RETURNS	33.94%	28.71%	23.98%	22.87%	27.59%	17.34%
STDEV	61.26%	53.91%	45.99%	45.49%	45.49%	76.76%
ALPHA	34.09%	28.73%	23.73%	20.54%	21.66%	7.51%
	S&P % Offer/1 Day	S&P Offer/1 Week	S&P Offer/2 Weeks	S&P Offer/3 Months	S&P/6 Months	S&P Offer/1 Yr
Equally Weighted Returns	0.04%	0.13%	0.27%	2.31%	4.34%	8.82%
Deal Weighted Returns	-0.15%	-0.01%	0.26%	2.33%	5.93%	9.83%

Equally Weighted									
	% Change Price 1 Day-3Months	% Change Price 1 Week-3Months	% Change Price 2 Weeks-3Months	% Change Price 1 Day-6Months	% Change Price 1 Week-6Months	% Change Price 2 Weeks-6Months	% Change Price 1 Day-1Year	% Change Price 1 Week-1 Year	% Change Price 2 Weeks-1 Year
RETURNS	3.80%	3.80%	5.18%	6.31%	6.31%	7.27%	9.23%	7.70%	8.97%
STDEV									
ALPHA									
Deal Weighted									
	% Change Price 1 Day-3Months	% Change Price 1 Week-3Months	% Change Price 2 Weeks-3Months	% Change Price 1 Day-6Months	% Change Price 1 Week-6Months	% Change Price 2 Weeks-6Months	% Change Price 1 Day-1Year	% Change Price 1 Week-1 Year	% Change Price 2 Weeks-1 Year
RETURNS	-2.93%	-2.93%	-1.10%	-4.52%	-1.13%	0.51%	-11.47%	-9.42%	-4.37%
STDEV									
ALPHA									
	S&P 1 Day-3Months	S&P 1 Week-3Months	S&P 2 Weeks-3Months	S&P 1 Day-6Months	S&P 1 Week-6Months	S&P 2 Weeks-6Months	S&P 1 Day-1Year	S&P1 Week-6Months	S&P 2 Weeks-1 Year
Equally Weighted Returns	2.27%	2.17%	2.03%	4.30%	4.18%	4.04%	9.23%	2.17%	8.54%
Deal Weighted Returns	2.54%	2.34%	2.03%	0.02%	5.89%	5.53%	-11.47%	-4.54%	9.58%

Both the equally weighted and deal size weighted returns suggest initial underpricing of the IPO

in the early periods. The equally weighted model seems to be a more feasible model to support a megafund model given the longer tolerance for high returns so that a portfolio of 20 drugs can be held at the same time. The deal weighted returns suggest greater evidence towards initial underpricing trends that account for the higher returns as demonstrated through the diminishing returns across time and lower returns on intervals from 1day-3months, 1week-3months…. 2weeks-1year etc. This makes sense as the largest deals such as Twitter or Linked In will have a lot of hype that can lead to irrational exuberance. The equally weighted returns show contrary evidence against the initial underpricing hypothesis however, given that in general with increasing standard deviation and time there is higher returns. This has implications to make the megafund IPO model more sustainable because 20 projects are able to be held at one time for long periods of time and the alpha is not merely just generated from the initial underpricing of the IPO.

	% Change Price Offer/1 Day	% Change Price Offer/1 Week	% Change Price Offer/2 Weeks	% Change Price Offer/3 Months	% Change Price Offer/6 Months	% Change Price Offer/1 Yr
MAX	212.36%	369.23%	326.92%	768.82%	2179.41%	1833.82%
MIN	-60.50%	-60.00%	-67.45%	-82.95%	-80.90%	-83.50%
Positive Count	194	175	171	162	151	141
Positive Average	27.65%	34.96%	34.52%	55.06%	73.70%	88.31%
Negative Count	73	95	103	121	128	139
Negative Average	-11.13%	-12.50%	-14.10%	-22.84%	-27.79%	-36.93%
0 Count	16	13	9	0	4	3
Total Count	283	283	283	283	283	283
STDEV	34.84%	47.98%	46.52%	79.09%	146.52%	137.04%

Whereas we are proposing this passive model as a potential long only fund product to be launched we are also providing a lower bound for active investments. Looking at the maximum and minimum across various investment horizons we see proportionately greater long short opportunities which is aligned with the increase in standard deviation. This makes sense because given CAPM , as riskier asset should generate higher returns in general. This also disproves theories that a megafund model cannot exist given the incentives to participate only in short term horizon opportunities as long short opportunities become more attractive with longer time horizons as the spread between the maximum and minimum increases. As such, the long short opportunity becomes more attractive as the standard deviation increases in general with greater time providing greater opportunities on average to

long short. Also with time, the number of positive and negative returns tends to converge towards similar levels showing that risk may be becoming diversified away as time elapses. In the following section, we review an investment management firm, Monashee Investment Management that already employs active hedge fund investment strategies for IPOs, which served as the backdrop for the genesis of the megafund IPO model.

Monashee Investment Management

Monashee Investment Management was established in January 2012 by founders Gerald Coughlan and Thomas J. Wynn. Mr. Coughlan spent 11 years at Deutsche Bank, 4 years at Lehman Brothers, and 8 years at Morgan Stanley primarily as a technology coverage investment banker. Mr. Wynn, spent 4 years at Lehman brothers and co-founded the pre-eminent healthcare focused investment bank Leerink Swann and spent 16 years at the firm. Although Monashee Investment Management has an open mandate to be industry agnostic the fund due to Mr. Wynn's strong background in healthcare is heavily skewed towards the industry. Whereas Monashee does not participate in securitized megafund equity investments in IPOs, their current model closely resembles the megafund IPO model that we propose. Their investment strategy is to invest in equity capital markets in events driven IPO's, follow on offerings, and private placements in North America. In the following section we provide insight behind various investment decisions that were made by the fund. Whereas we cannot provide exact returns and metrics behind each investment decision due to confidential reasons, the firm as a whole has well outperformed the back-testing returns that we have without even the leverage of debt and securitization and has provided attractive risk adjusted returns. The investment analysis offers insight into the real life mechanics behind an active fund investing in biotechnology and pharmaceuticals and how the philosophy and thought process behind active decisions would be made.

Investment Analysis

Veracyte

Background

- Diagnostics company in the field of molecular cytology to improve patient outcomes and lower healthcare costs and enable doctors to make more informed treatment decisions earlier
- Afirma Thyroid FNA Analysis: Employs a 142-gene signature to preoperatively determine whether thyroid nodules previously classified by cytopathology as indeterminate can be reclassified as benign for cancer.

SWOT Analysis

Strengths

- Cost effective quality adjusted life years is proven for thyroid cancer and estimated savings avoiding unnecessary expensive surgeries are 2600 per test, net of costs of tests
- Procedure is minimally invasive using fine needle aspiration
- 15%-30% is indeterminate of 115,000 unknown, with highly sensitive predictability
- Partnership with Genzyme across 42 countries, guideline based CLIA approval driving volume
- No competition in pricing offering a compelling price times volume = revenue story
- Works synergistically with pathologists by administering the pathology tests in own labs, minus academic centers, and then applying molecular cytology on indeterminate cases which leaves auditing trail to make sure that unnecessary tests on benign pathologies are not being made

Weakness

- Margins for sharing sales revenue with Genzyme is not strong which was previously 50%, 40%, and currently 32% cash but projected to be 100 mm cash flow positive by 2016-2017

Opportunity

- Cross validated results were available for pulmonary as well
- Opportunity to be bought out by Genzyme potentially adding premium to stock value

Threats

- Success is based on relationship with Genzyme to co-promote Afirma unless renegotiation occurs

Porter's Five Forces

- Competition: Veracyte has a monopoly on indeterminate molecular cytology
- Substitutive Powers: Finer tests may obviate indeterminate cases but not likely
- Suppliers: Government, commercial payers, direct payers
- New Entrants: New diagnostic technology that is not likely in the near term
- Consumers: Medicare, Medicaid, commercial payer receiving patients

Valuations

Company Comp Set	
Company Name	TEV/Total Revenues LTM - Latest
Exact Sciences Corporation (NasdaqCM:EXAS)	149.1x
GenMark Diagnostics, Inc. (NasdaqGM:GNMK)	15.0x
Genomic Health Inc. (NasdaqGS:GHDX)	3.3x
Average	55.8x

Using 2012 Sales – 1H2012=2H2012($12mm –$3.9mm=$8.1mm) and 1H2013 ($9.5mm) as a proxy

for LTM we receive $17.6mm and can calculate an enterprise value of (55.8x (17.6)) = $982.1 mm.

Recommendation

The company is aligned with Obamacare with cost effective solutions using diagnostics technology. There is clear quantitative analysis in pharmacoeconomic savings along with clinical validity with high sensitivity that can be used to justify and drive higher pricings – no pricings competition along with a stable 15%-30% of approximately 115,000 unknown cases will drive revenue. The tests are strategically managed so that pathologies are done in conjunction with fine needle aspiration so that unnecessary tests for benign pathologies are not being made. Furthermore, opportunities for pulmonary offers a call option in real option analysis. Although, margins for sharing revenue with Genzyme are not the best terms, they are improving and future cash flows are projected to be positive of $100 mm by 2016-2017.

Alcobra Pharma

- **Strong product line:** MG01CI, an agent for ADHD, offers the best of both worlds as a rapid effective non-stimulant that does not have the side effective of a stimulant. The drug works on a different pathway that increases Akt activity, which leads to learning and memory cognitive regulation and improved attention, without increasing ERK activity which can lead to abuse liability. Furthermore, the same compound can be used as a different drug to potentially cure Fragile X, in which the company has filed for orphan drug designation.
- **Favorable FDA Approval Probability**: Phase II studies for ADHD have been designed based on previous competitors phase III designs and based on expert advisory board. The only difference between phase II and phase III studies are the number of enrolled patients that will

roughly double in phase III. Management projects a 95% approval rate from phase II to phase III based on therapeutic class and possible fast track designation. Based on the markers, studies on Fragile X could also shed insight into how autism is developed and address a highly unmet need on top of ADHD.

- **Attractive Market Sizing**: ADHD affects 8-10% of children and about 4-5% of the adult population. The US market is valued at US$3.8 bn and accounts for 90% of the global ADHD market. The US market is projected to grow at a CAGR of 7.3% per anum and will reach US$6.3 billion by 2018. Major growth drivers in this market are increased disease recognition and increasing adoption of pharmacotherapy for children and adolescents.

- **Discounted Valuations**: Alcobra currently trades at roughly $230mm enterprise value. Had Alcobra been revenue positive, the firm could be trading up at 3.1x of enterprise value over revenue. We project that had Alcobra undergone a commercial partnership their current revenues would have been roughly $150M and that the current enterprise value should be at least $465M.

Company Comp Set	
Company Name	TEV/Total Revenues LTM - Latest
H. Lundbeck A/S (CPSE:LUN)	1.3x
Shire plc (LSE:SHP)	5.0x
UCB SA (ENXTBR:UCB)	3.1x
Average	3.1x

Bind Therapeutics

Background

- Nanonmedicine company that targets tumors at three levels – tissue, cellular, and molecular

- Recognized by the World Economic Forum as a technology pioneer

Pros

- A paradigm shift and novel way of treating therapeutics making it a good target for strategic and financial buyers that could drive up the share price
- Technology enhances efficacy while minimizing adverse effects by offering the best of both worlds of biologics and small molecules and offers great specificity
- Partnered with many premier pharmaceutical companies already to develop this technology such as Amgen, Pfizer, and AstraZeneca
- Cancer therapy is a large and broad market particularly the subclass non-small cell lung cancer and prostate cancer from a market sizing perspective
- CEO has extensive experience in the niche market, and understands the checklists that are necessary to really monetize this opportunity
- R&D team comes from the seminal people who developed the nanontechnology from Harvard/MIT
- Accurins can deliver 1000s of molecules compared to its competitors that can only deliver a few molecules
- Management team understands the business and economics and risk rewards of developing drugs – reverse engineering drugs that are preexisted to known to work and avoiding SiRNA

Cons

- Novel technology contains risks (possibly toxicity) and may face barriers during clinical trials and there was no special designations for accelerated approval
- Clinical data as of date is positive but not a dramatic effect
- Cross applicability and optionality of therapeutics exist but nothing like a library of proteins

R&D and Science

- The nanomedical technology is based on Accurins
- Accurins are polymeric nanoparticles
- Accurins operate based on the three principles
- Prolonged circulation: Accurins are designed with a stealth and protective layer that enables them to circulate within the bloodstream for a prolonged period of time, and accumulate at the diseased site before being cleared from the circulatory system.
- Targeting. Accurins are designed with specific pharmaceutical properties intended to target tumors at three levels: tissue, cellular and molecular. Tissue targeting is achieved by engineering the physical and chemical properties—size, shape and surface properties—of the Accurin to allow it to escape through gaps in the blood vessels surrounding tumors and other disease sites.
- Controlled and timely release: Accurins are designed with specific polymers that provide for the controlled and timely release of the therapeutic payload.

Overall Recommendation

Anytime there is a paradigm shift in technology and healthcare, there is ample opportunity to become a takeover target. Moreover, positive news surrounding new technologies excites investors and will drive the share price forward. The greater efficacy and specificity of the therapy provide a lot of promise for this product. Furthermore, the management team is very cognizant of the science behind the labs that started these discoveries and have demonstrated the ability to really monetize these opportunities on a risk adjusted basis by targeting drug therapies that are preexisted to known to work.

The partnerships with reputable firms provide tangible cash flows and whereas the cross applicability of the therapy is not as strong, from an efficacy, current market sizing, and partnership standpoint with even current and pending partnerships and deals they have now there is ample room for growth from the IPO.

Xencor

- **Strong Product Line:** Transformative product line with high barriers of entry that has a Fc domain focus with scalable technologies, that is differentiated from the saturated Fv targeted antibody therapeutic pipeline. Currently there are two clinical stage partnerships, in the XmAb5871 with Amgen and XmAB5574/MOR208 with Morphosys. XmAb7195, albeit in the early stages, offer very high potential for asthma and allergies that have increasing epidemiological trends with main drivers being obesity and cockroaches. Moreover, Xolair, the leading antibody therapy for the treatment of severe refractory asthma, creates many unmet needs with low clinical efficacy and lack of applicability to the patient population with the most need. XmAb7195 offers pharmacoeconomic benefits by offering better efficacy to these patients and increasing the market sizing to a wider reachable patient population.

- **Favorable Follow on Events**: 1-3 more partnerships are expected offering stabilize cash flows and release on data for XxmAb7195 ING reduction data, as well as partnership data with Amgen for XmAb5871 are expected.

- **Attractive Market Sizing**: The clinical pipeline has an attractive market sizing in the billions for indications in rheumatoid arthritis and lupus ($9.3 billion) and Leukemia ($6.1 billion) and has good milestone and royalty payments (XmAb5871 with $11 mm in upfront payments with $400 mm in milestone payments due, with royalties in single digits and teens; XmAB5574 with $13 mm upfront payments with $300 mm in milestones due and higher single lower double

digit in royalties). What is attractive about the partnerships is that they are cost effective ways to investigate unmet needs for pharmaceutical companies and to investigate opportunities to narrowly license the IP to them.

- **Valuations**: Applying Xencor's LTM of $10.9 mm we receive a mean enterprise value of $155.4 mm and a range with a low of $31.61mm and high of $288.85mm.

Company Comp Set	
Company Name	TEV/Total Revenues LTM
Abcam Plc (AIM:ABC)	7.6x
Ablynx NV (ENXTBR:ABLX)	12.7x
BioInvent International AB (OM:BINV)	5.1x
Dyax Corp. (NasdaqGM:DYAX)	18.5x
Dynavax Technologies Corporation (NasdaqCM:DVAX)	19.9x
ImmunoGen, Inc. (NasdaqGS:IMGN)	19.2x
Immunomedics Inc. (NasdaqGM:IMMU)	26.5x
MacroGenics, Inc. (NasdaqGS:MGNX)	12.8x
Morphosys AG (XTRA:MOR)	17.5x
PDL BioPharma, Inc. (NasdaqGS:PDLI)	2.9x
Seattle Genetics Inc. (NasdaqGS:SGEN)	16.0x
XOMA Corporation (NasdaqGM:XOMA)	12.4x
High	26.5x
Low	2.9x
Mean	14.3x
Median	14.4x

Metabolon

Background

- Metabolomics company focusing on obesity and cancer
- Focuses on biomaker discovery and profiling platform diagnostics

Pros

- Gain revenue partially by finding mode of actions for drugs and provide comparative efficacy studies for clientèle who has a penchant for periodically reusing technology such as pharma and publicly traded biotech companies
- An example of this is providing a phenotypic screeen for Lilly as an anticancer drug and make sure that it is not the same class of an existing drug but a novel therapeutic
- The competitive advantage is low COGS and reimbursement options driven by the scalable technology that creates long term value for patients

- Market sizing is great targeting obesity and cancer
- Quantos product resolves an unmet need that detects type II diabetes early on which from a public health perspective is great health economics and is aligned with Obama Care's cost effective and primary care based model. This is a novel way of looking at solving health care and is aligned with government trends pushing for more accountable and coordinated care.
- There are no competing products in this area of unmet need meaning high buyout and takeover risk premium that should be built into the price of the stock
- CLEP clinical trial risk is low
- Contracted with HDL until 2015 and then can license on own.

Cons

- Competition in diagnostics space in general outside of this niche area is fierce and there are low barriers of entry to enter
- Their sequencing library seemed proprietary but not with the absolute highest levels of barriers to entry.

There is great market sizing, alignment with new government and industry trends, scalability, and reimbursements. The story fits with Obamacare and public health initiatives President Obama is raising which shows that the company is changing with the times and providing an invaluable paradigm shift that makes an attractive valuation from this standpoint.

Valuations

The average EV/Sales number for comparable trading companies is 8.3125x

Sales in millions			
Comparable Companies	Exchange	Ticker	EV/Sales (LTM)
Champions Oncology	OTCPK	CSBR	11.9
Deltagen	OTCPK	DGEN	1.5
Fluidigm Corporation	Nasdaq	FLDM	8.6
Pressure Biosciences	OTCPK	PBIO	5.3
Quick-Med Technologies	OTCPK	QMDT	5.3
Sequenom Inc	Nasdaq	SQNM	9.9
Special Diversified Opportunities	OTCPK	SDOI	0.5
Wafergen Biosystems	OTCPK	WGBS.D	23.5
Average EV/Sales			8.3125

The average EV/Sales multiplied by the $35 mm 2013 revenues of Metabalon gives us $291 mm. One caveat to this approach is that the multiple is based on the industry standard of LTM but the sales multiple is based on management projections for the year 2013. Based on limited information that was provided, 2013 projections were used as a proxy for 2013 LTM.

2013 Metabalon Sales		$35.00
Enterprise Value		$290.94

Five Prime

Background

- Biologics company focusing on protein therapies targeting oncology
- The company is named five prime because the 5" end of a gene is the hardest to make

Pros

- Five prime contains proprietary library of 5,600 human extracellular proteins, which covers all of the body's important targets for protein therapeutics
- The fact that they can generate the 5" end demonstrates that there is high barrier to entry

- There is a proprietary screening system which combines complex cell screens with a proprietary in vivo screening system to increase the speed and precision of identifying, analyzing and assessing protein drug targets and candidates. The company can produce and test thousands of extracellular proteins each week.

- The proprietary screening system offers high barriers to entry for other companies to follow suit and is confirmed by the contracts they have to license out their library to partners and annual deals they have made.

- The company is leveraging this technology to partner with other biotech and pharmaceutical companies to monetize this asset class

Cons

- A concern is that they may be morphing their business model and focusing more attention away from identifying novel protein therapies to more of a biotech consulting company that offers their proprietary technology. If this is the case, then further investigations on what provides a better revenue stream needs to be conducted. This concern has been mitigated with the experience of the CEO to make contracts with optionality and learning curve that he has demonstrated in keeping the most profitable lines intact while stabilizing cash flow with partnerships. Also as long as there is demonstration of attractive financing structures and royalty payments, partnering with Big Pharma may actually be more profitable in the long run because Big Pharma has a greater eagle eye for identifying applications of the library.

- There is no paradigm shift. Protein screening is preexisting technology that has persisted for years

R&D and Science

- Currently there are three products in the R&D pipeline

- FP-1039 which acts as a ligand trap against cancer causing protein FGF for multiple solid tumors in phase 1b which has already contracted with Glaxo Smith Klein for commercialization
- FPA008 which acts as an antibody for autoimmune diseases against CSF1R Antibody
- FPA 114 which acts as an antibody against FGFR2B for Gastric Cancer
- While FP-1039 is undoubtedly the most promising candidate as it is at the clinical stage and has already licensed with GSK, the science behind the other two products are very sound and reasonable backed by scientific literature
- Concerns are the clinical efficacy and competitors surrounding these two drugs in the pipeline and a further questions need to be asked about not only the efficacy but cost effectiveness of these drugs

Overall Recommendation

From the fund's strategy to pick up discounted investments from an IPO stage five prime makes the most sense. There are stabilized cash flows with solid products in the pipeline. Even if drugs do not reach commercialization, which is a highly unlikely, the royalty streams from partnerships guarantees cash flows. The CEO and management team is very strong and experienced and whereas other investments may be attractive in terms of providing a niche with great market sizing that may develop into an acquisition target, this company is unique in that it provides a library of products that can be generated with great cross applicability to various cancers and other therapeutic diseases. The scientific model of working on cleavage for receptors is pharmacologically sound and has broad potential in the oncology market as well as other therapeutic areas.

Acceleron

Background

- Protein therapeutics company focused for cancer and rare diseases focusing on the TGF-Beta superfamily

Pros

- Targeting large oncology market with orphan drug status diversifies risks for targeting too segmented of a market
- Greatest concern with orphan drugs is the lack of a market size, even after government benefits. However, attractive licensing agreements at mid 20 percent with Celgene mitigates this risk because on top of the attractive royalty payments, Celgene is bearing the risk of R&D costs. The seal of approval by Celgene signals to the market that NPV of unlevered free cash flows at the minimum will be positive even with orphan drug status applicability for their crown jewel drug Solatercept.
- Upside potential as a breakthrough drug
- Targeting new pathways in angiogenesis demonstrating niche as a biotech company poised for takeover. Moreover, the drugs do not compete with current anti-angiogenesis drugs because they working synergistically with existing drugs in a 8 billion dollar market for cancers at different stages and pathways. Cross sales will be expected as well as a steeper growing curve in terms of market share gains translating to profits.

Cons

- No paradigm shifts, and many similar stories within the protein therapeutics.

- Protein therapeutics is a saturated market. There is risk that epidemiology or personalized medicine may show in protein therapies a lack of transferable efficacy across different subpopulations.
- Barriers of entry are low. Anyone could potentially study this same protein family.

Overall Recommendation

Due to the niche nature of the biotech-company, and seasonal balance between orphan drugs and oncology market, and attractive financing royalty structures, there are strong reasons to invest. The affirmation by Celgene, and attractive royalty structures and tangible near term unlevered free cash flows is aligned with Monashee's investment strategy.

Good Start Genetics

Background

- Emerging player in molecular diagnostics market
- Built upon proprietary NGS platform and guideline driven genetic screening
- Conducts screening for diseases such as cystic fibrosis (CF)and other carrier genetic tests

SWOT Analysis

Strengths

- Patented proprietary technologies that are broadly applicable and based on NGS platform, with higher specificity and sensitivity than competitors due to the targeted gene capture therapy that

contains special algorithm, which layers in truncating mutations on top of automatic sequencing, signaling technology with barriers to entry

- CLIA, CAP, New York accredited opening up large market for clinical lab services and extremely cost effective platform providing more tests for the same pricing levels of other tests
- Already operating cash flow positive by year end 2013 with revenue streams coming from commercial out of network payers - majority of revenue are coming in as cash and not exposed to government payers like Medicare and Medicaid; consistent growth in accounts ordering and test ordering, guideline driven genetic screening driving up the volumes of the revenue piece
- Intervention is at the pre-Pregnancy Screening level at earliest stages providing multiple options and early detections, which is aligned with Obama primary care
- Sufficient capital beyond projected 2013 profitability and extremely cost effectively managed financial operations with $28 mm in series A and B financing including reputable venture funds such as Orbimed, SV Life Sciences, Safeguard, etc.
- Provides information to patients and doctors to help reproductive care and has the seal of approval from the American Congress of Obstetricians and Gynecologists, American College of Medical Genetics and Genomics, Jewish advocacy society signaling strong brand

<u>Weakness</u>

- Current revenues are based on out of network contract pricings and as future revenues become contracted into in network prices, pricing levels may be slammed
- Proprietary technology based on an algorithm incorporating genetic mutation factors driving diseases and truncating mutations is a differentiated strategy from competitors that may not be

easily mimicked by larger competitors with bureaucratic inefficiencies but can be a strategy followed by another smaller biotech company

- Sales turnover is not a swift process and there was no mention of differentiated sales strategy ;needs to be stronger distribution channels regardless of how good of a product may exist

Opportunity

- Advent of personalized medicine and ethnic specific diagnostics could be major factor in global market, as new products targeting the Chinese market is developed

Threats

- Barriers to sales conversions, in network downward pricing, competitors mimicking strategy

Porter's Five Forces

- Competition: Quest Diagnostics, Genzyme, and other molecular diagnostic companies exist
- Substitutive Powers: Novel genetic technologies could render current technology obsolete
- Suppliers: Commercial reimbursement could price downward driving revenues down
- New Entrants: A more powerful algorithm capturing more genetic factors may exist
- Consumers: 7 billion dollar market in reproductive endocrinology and health

Valuations

Company Comp Set			
Company Name	TEV/Total Revenues LTM - Latest	TEV/EBITDA LTM - Latest	TEV/EBIT LTM - Latest
Bio-Reference Laboratories Inc. (NasdaqGS:BRLI)	1.1x	7.9x	9.7x
Opmedic Group Inc. (TSX:OMG)	2.3x	7.7x	10.4x
Quest Diagnostics Inc. (NYSE:DGX)	1.8x	8.2x	10.0x
Averages	1.7x	7.9x	10.0x
All values in millions, except per share data and ratios.			

Company Comp Set				
Company Name	Market Capitalization Latest	LTM Net Debt	LTM Minority Interest	Total Enterprise Value Latest
Bio-Reference Laboratories Inc. (NasdaqGS:BRLI)	811.6	6.0	-	817.7
Opmedic Group Inc. (TSX:OMG)	47.6	(5.2)	-	42.4
Quest Diagnostics Inc. (NYSE:DGX)	9,371.4	3,378.7	26.61	12,776.7

$21 mm in LTM revenues for Good Start Genetics using the average multiple of 1.7x gives us $35.7 mm in Enterprise Value. For the year 2013 revenues are looking to exceed $30 mm.

Recommendation

The company offers a differentiated proprietary technology aimed at a large 7 billion dollar molecular diagnostic market that offers earlier detection that can guide physicians in reproductive health and prevent unnecessary costs moving upstream by addressing costs earlier. Proprietary technology offers a premium from a takeover perspective. The seal of approval from medical associations, advocacy groups, and reputable venture capital funds all signal strong brand. The scientific results provide a higher accuracy than any other product in the market that provides a larger range of services for the same costs. The potential the product provides for various ethnic groups, offers opportunities to go global. Although there is always the risk of downward pricing from reimbursements, competition, and disappointing sales conversions, the fact that cash flows are already positive and majority of revenues are cash, signals that unlevered free cash flows are very promising.

Mirati Therapuetics

Background

- Clinical stage biopharmaceutical company focused on developing a pipeline of oncology drugs

SWOT Analysis

Strengths

- Strong market target segment in NSCLC and squamous cell carcinoma of the head and neck, solid tumors, and hematological malignancies

- Strong management team from Big Pharma (Charles Baum, CEO, Pfizer)
- Consistent with current trends in healthcare for more targeted therapy

Weakness

- Research and development are at an early stage of development and there are currently no approved products and historically no product revenue

Opportunity

- Select patient populations that are targeted can be assessed early in clinical development creating opportunities to accelerate clinical development in the phase line

Threats

- Regulatory risk based on PPACA affecting pricing and profitability due to government control

Porter's Five Forces

- Competition: Biotech and pharmaceutical companies focusing on oncology
- Substitutive Powers: New proprietary technology that cannibalizes current technology
- Suppliers: Government, commercial payers, direct payers
- New Entrants: New companies that offer greater scalability
- Consumers: Medicare, Medicaid, commercial payer receiving patients

Comparable Valuations

Company Comp Set	
Company Name	TEV/Total Revenues LTM - Latest
ArQule Inc. (NasdaqGM:ARQL)	2.6x
Astex Pharmaceuticals, Inc.	8.4x
Exelixis, Inc. (NasdaqGS:EXEL)	22.7x
Average	11.2x

Other comparable companies that do not have revenue are AVEO Pharmaceuticals and Clovis Oncology.

Recommendation

The company has a strong management team that can execute and is aligned with current healthcare trends for more targeted therapies in a very large oncology market.

Oncothyreon

Background

- Biotechnology company focusing on oncology products that can improve the lives and develop therapeutics to target cancers in both synthetic vaccines and small molecules
- ONT-380: Selective HR2+ inhibitor small molecules that does not exhibit GI toxicities and synergistically works with chemotherapy and trastuzumab to reduce HR2+& CNR metastasis
- ONT-10: Therapeutic vaccine designed to direct an individual's immune system to identify and destroy cancer cells via T-cell immune response and antibodies
- Tecemotide: Therapeutic vaccine to stimulate an individual's immune system to recognize cancer cells and control the growth and spread of cancers by incorporating a 25 amino acid peptide sequence from the tumor associated antigen MUC-1 in a liposomal formulation

SWOT Analysis

Strengths

- Good royalty payment in mid-teens with Merk for Tecemotide and other favorable terms
- Wholly owned ONT -10 that may be improvement on Tecemotide from a selectivity and improved CNS activity standpoint
- ONT-380 has best in class potency and selectivity for HER2+ targeted small molecules
- No risky discovery and preclinical stage investments – all licensed out contracts

Weakness

- Clinical data is not as strong for the approval of Tecemotide
- There are risks with the timing of the trials for ONT-10 relative to Tecemotide which is relatively early stage

Opportunity

- Transferability of ONT-380/(Tec.) to CNS diseases adds an extra call option in real option analysis

Threats

- Going head to head with Merk may create problems with business partners depending on how the market is split and may cause downward movement of the stock price

Recommendation

Whereas there is upside potential in terms of a stable royalty payment for Tecemotide and a call option on top of that with the transferability of ONT-380 for CNR diseases, fundamentally the question is too

binary as to whether the development of ONT-10 will benefit the company or hurt it more in terms of cannibalizing not just sales from preexisting product lines but also business relationships. The investment decision will have to be based on how the wholly owned ONT -10 is structured in terms of synergistic or conflicting market sharing with Merck and without that transparency an investment decision cannot be made at this point for early stage ONT-10.

Cara Therapeutics

- **Strong Product Line:** Cara has a pipeline of clinical products that are novel treatments for pain and inflammation. The CR845 is currently undergoing clinical trials and is a best in class drug for peripherally selective molecules that interact with kappa opioid receptors that are present in peripheral pain sensing nerves. Unlike the current marketed Opioids, CR845 has best in class selectivity for kappa receptors and does not have significant affinity for any other non-opioid receptors. CR845 and other kappa agonists in the pipeline does not cross the blood brain barrier and hence decreases the likelihood of CNS mediated effects.

- **Favorable Follow On Events**: Management projects a high probability of success in phase III studies for CR845. Discussions surrounding what the FDA expects have already been made – a double blinded comparison of addictions to morphine and the CR845. Because of the kappa selectivity, and the compounds poor ability to cross the blood-brain barrier, there are high hopes that the FDA will approve the drug for phase III trials.

- **Attractive Market Sizing**: Approximately 100 million patients suffer from acute and chronic pain annually in the United States alone. Global pain and inflammation markets are growing at an average of 30% per year and are estimated to reach $60 billion by 2020. However, current treatments have adverse effects such as tolerance, dependence, respiratory depression, nausea

and vomiting, drowsiness and sedation, urinary retention, etc. This signals a great opportunity where Cara Therapeutics can solve an unmet need.

- **Valuations**: Looking at similar pain companies in the market the range of enterprise values were USD $142.1mm to $353.9mm with an average of $248mm.

Company Comp Set		
Company Name	Market Capitalization Latest	Total Enterprise Value Latest
GW Pharmaceuticals plc (AIM:GWP)	420.6	353.9
Newron Pharmaceuticals S.p.A. (SWX:NWRN)	169.4	142.1
High	420.6	353.9
Low	169.4	142.1
Mean	295.0	248.0
Median	295.0	248.0

Cancer Genetics

Background

- Molecular diagnostics company that personalizes and improves the success rate in cancer treatment through a three step process – diagnosis, prognosis, and theranosis
- Diagnosis: Using genomics to provide an accurate and definitive typing of the cancer
- Prognosis: Assisting in patients outcome and disease management
- Theranosis: Personalizing therapeutic plans and treatment options

SWOT Analysis

Strengths

- High barriers of entry with proprietary molecular diagnostics & FISH probes that are clinically validated and IP protected and large targeted market opportunities across universities and research centers, community hospitals, biotechnology companies, and emerging markets

- Strong product line with MATBA for Chronic & Small Lymphocytic Leukemia, Diffuse Large B-Cell Lymphoma, Mantle Cell Lymphoma; UroGenRA for kidney; and FHACT for cervical for launch and market entry with many other tests in the pipeline in research, discovery, clinical development

- Relationships with premier cancer research institutions (Memorial Sloan- Kettering, Stanford, etc.); and collaborations with Gilead, Roche, Mayo Clinic demonstrate strong brand and potential

- Stable Pay Mix: 60% direct bill, 27% commercial payers, and only 13% risk to government payers

- Additional news on bipharma partnerships post announcement of offering will drive stock up

Weakness

- A small number of test ordering sites account for most of the sales of test

Opportunity

- Increased collaboration with other direct payers, and reimbursement based opportunities

Threats

- Competition from other molecular diagnostics companies in cancer may steal market share

Porter's Five Forces

- Competition: Other molecular diagnostics companies in cancer
- Substitutive Powers: New proprietary technology that cannibalizes current technology
- Suppliers: Government, commercial payers, direct payers
- New Entrants: New molecular diagnostics companies that offer greater scalability
- Consumers: Medicare, Medicaid, commercial payer receiving patients

Valuations

Company Comp Set	
Company Name	TEV/Total Revenues LTM - Latest
Bio-Reference Laboratories Inc. (NasdaqGS:BRLI)	1.3x
Foundation Medicine, Inc. (NasdaqGS:FMI)	42.5x
Genomic Health Inc. (NasdaqGS:GHDX)	3.3x
Myriad Genetics Inc. (NasdaqGS:MYGN)	2.5x
Neogenomics Inc. (NasdaqCM:NEO)	2.4x
Response Genetics, Inc (NasdaqCM:RGDX)	3.2x
Average	9.2x

LTM figures of $5.4 mm multiplied the 9.2x multiple gives us an enterprise value of $41.4 mm.

Recommendation

The company is aligned with Obamacare with cost effective solutions using diagnostics technology. There is strong brand with strong relationships and partners as well as high barriers of entry based on proprietary technology

Relypsa

- **Strong Product Line:** Relypsa offers novel therapies for the drug Patiromer treating Hyperkalemia (a metabolic disease caused by an increase in potassium K+ in the blood that can become fatal) by efficiently binding and removing potassium into the colonic lumen. Patiromer

is insoluble in typical solvents and passes through the GI tract without degradation with good bulk flow properties and and does not require a laxative; unlike the current treatments using SPS, Patiromer does not cause GI tolerability problems. Furthermore, it does not cause hypertension because it does not use sodium like SPS. Furthermore, Patiromer had twice the binding capacity as SPS. Patiromer is perceived as a pharmacoeconomic solution to these adverse effects. Furthermore, cross sales are predicted with RAAS inhibitors because it works synergestically with RAAS, which delays the onset of CKD. Although, there is competition from ZS-9, Relypsa is further in development and Zirconium Silicate candidate is expected by management to suffer from more adverse effects than Patiromer.

- **Favorable Follow on Events**: Positive phase III clinical data is already available. Furthermore, we suspect that with the successful completion to phase III that contains all of the clinical end points, and the strong market sizing within a niche area that Relypsa offers, a buyout that will drive the premiums on the value of the stock will be inevitable and discussions are already on the table. The use of the proceeds is being used to generate mature growth strategies such as the expansion of a specialty sales force and as well as synergistic licensing and acquisition of additional compounds rather than risky early stage growth that makes the investment attractive.

- **Attractive Market Sizing**: High barriers of entry in an almost standalone market where there is a high unmet need; the chronic nature of the disease as well as the pharmacoeconomic solutions are major revenue drivers for pricing. If approved, Patiromer will be the first drug approved for Hyperkalemia with a tolerability profile that will enable chronic daily administration. Pricing is expected to be set at 600-650 month. 450,000 targeted patients on dialysis will be a major driver for volumes of patients in the United States with pricing and volume combined gives us conservative projections of a 3.24 billion market. Management

predicts that the drug will be well received by nephrologists given the strong clinical data and a strategic sales force will target the 70,000 nephrologists and cardiologists in major HF centers.

- **Valuations**: Given the 3.24 billion market and the fact that phase III trials have clinical data endpoints, there will be strong deal premiums for a multibillion dollar drug with a conservative estimate of a billion dollars in enterprise value.

SWOT Analysis

Strengths

- Strategic sales initiative with a target market segment of 70,000 nephrologists and cardiologists.
- Furthest candidate in pipeline to compete against SPS with phase III clinical endpoints, which suffers from adverse effects
- Best in class therapy that is twice as effective at binding potassium than SPS, and does not suffer from GI tolerability and hypertension
- IPO offers a mature entry point into an already nearly proven company that has completed phase III trials and is using the proceeds to acquire and license with other competitors, and increase sales force. Furthermore, the company offers high potential for a merger arbitrage opportunity.
- Retains global licensing rights and has not yet commercialized with a partner

Weakness

- History of operating at net losses and may not achieve profitability near term; this is mitigated by the fact that our overarching investment thesis is that the company will bought out by a company like Sanofi where many synergies in this niche area can be added

Opportunity

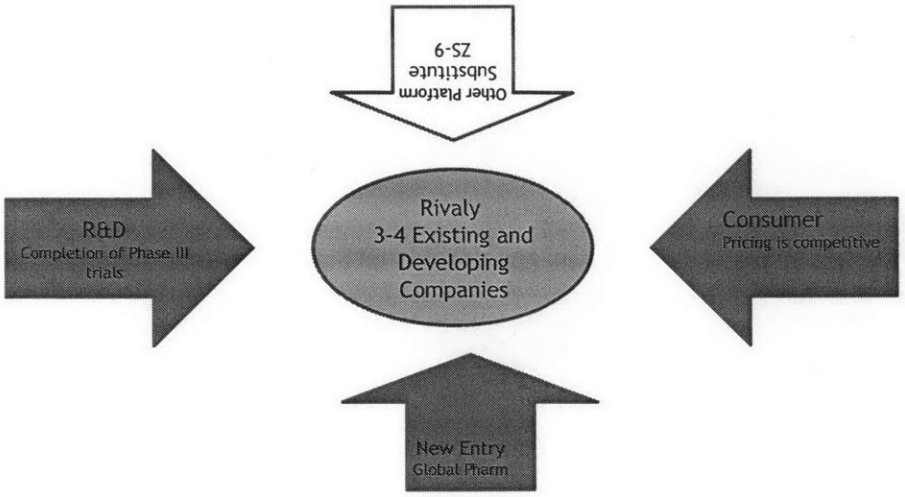
- Scalable technologies in metabolic therapeutic class for diet and exercise where polymer drug technology is being used at the preclinical stage.

Threats

- Competition from competitors such as ZS-9

Porter's Five Forces

- Competition: SPS (weak)
- Substitutive Powers: ZS-9 (weak)
- R&D: Strong completion of Phase II trials (strong)
- New Entrants: Global Pharma may acquire technology (strong)
- Consumers: Pricing is competitive with Medicare, Medicaid, commercial payers (strong)



Recommendation

The company offers the most competitive advantage and has the most potential among clinical stage development drugs for substituting SPS that suffers from adverse effects such as GI tolerability, and hypertension. The substitution would save dollars as a pharmacoeconomic substitute that is more cost effective. Pricing is projected to be competitive as the only to be approved drug for chronic daily administration. Current M&A trends in biotechnology, as demonstrated by the precedent of the Amgen Onyx deal shows that acquisitions are done on late clinical stage biotech companies and we expect Relypsa will parallel this trend given that it has completed phase III trials and has end points in clinical data. Although, there is some risk in Phase IV, we suspect that after the IPO the company will be bought by a competitor Big Pharma company such as Sanofi and that significant deal premiums will be added to the IPO.

GlycoMimetics

- **Strong Product Line:** GMI -1070 is a transformative product in sickle cell that offers many pharmacoeconomic solutions that is aligned with cost effective Obamacare and is proven to be safe and effective. The drug offers reduction in opioids and early interruption in pain that drives reduction in LOS in hospitals where the average costs in duration of stay in a hospital is estimated at $20,000 to $40,000. AML targeting E-Selectin antagonist drug GMI -1271 is also very promising by acting on a unique mechanism that not only prevents the interference of chemotherapy by stopping the binding of carbohydrates with E-Selectin but also protecting the normal cell. The technology offers high barriers of entry and is also potentially scalable to large oncology markets.

- **Favorable Follow on Events**: Oral reports are scheduled that include overall report of phase II studies, pain and opioids report, as well as an ASH release in early December. Results of inter-efficacy analysis pending approval may also accelerate the approval process.

- **Attractive Market Sizing**: Sickle cell offers an attractive market for an orphan status designation with 73,000 hospitalizations. The market for hospitals alone is projected at a billion dollars with low double digit to low teen capture of the market share. The opportunity set in emergency rooms, and self-administration also allows expansion opportunities adding a call option to the hospital market. Scalable technologies with E-Selectin offer promising candidates for a family of drug candidates, albeit in the early stages. The company offers a great product mix of potentially scalable opportunities with orphan status drugs.

- **Valuations**: Given the impending milestone payments and other forward looking revenues, a conservative estimate of $30 mm is multipled by the comps multiple to receive $459 mm in enterprise value where the company could be trading within the next year. Net debt is projected to continue to be negative in the ($10mm) - ($15mm) range, making equity value around $469

mm to $474 mm. In terms of current valuations, the company has LTM revenues of $11.5 mm, giving a valuation of $177.14 mm in enterprise value.

Company Comp Set	
Company Name	TEV/Total Revenues LTM
Five Prime Therapeutics, Inc. (NasdaqGM:FPRX)	15.1x
Threshold Pharmaceuticals Inc. (NasdaqCM:THLD)	15.4x
Average	15.3x

Celladon

- **Strong Product Line:** Mydicar, which addresses heart failure by targeting SERCA2a through genetic therapy, is a promising candidate that has been granted fast track status and special protocol consideration. The product addresses the greatest unmet need in cardiovascular drugs by improving survival rates, and potentially reducing renal and other co-morbidities.

  Favorable Follow on Events: Later stage clinical trials are similar in design to previous ones that have shown proven clinical end points in improvement in quality of life, reduction in symptoms, and increase in survival rates that have been published in peer reviewed journals and presentations are scheduled at the American Heart Association on Nov 19 leading to a great event that will drive the stock forward. The fact that the company retains all global licensing agreements signals to the market that a buyout follow on event could be feasible. Epidemiology also projects growing patient size with aging population.

- **Valuations:** Valuations of similar cardiovascular companies show a mean market cap of $556.7 mm and mean enterprise value of $450 mm.

Company Comp Set		
Company Name	Market Capitalization Latest	Total Enterprise Value Latest
Amarin Corporation plc (NasdaqGM:AMRN)	265.9	279.8
Momenta Pharmaceuticals Inc. (NasdaqGS:MNTA)	880.2	604.3
Osiris Therapeutics, Inc. (NasdaqGM:OSIR)	523.9	495.8
Summary Statistics	Market Capitalization Latest	Total Enterprise Value Latest
High	880.2	604.3
Low	265.9	279.8
Mean	556.7	460.0
Median	523.9	495.8

Moreover, based on managements' projected penetration rate of up to 50,000 patients out of 1.8 million systolic patients a year, Black Scholes Real Option Analysis for Mydicar's systolic indication alone show that at a projected $10,000 pricing point for the drug justified by the $150,000 in savings the drug provides per patient, the company will have a strong margin of safety relative to the midpoint market cap pricing based on the systolic heart failure indication alone. The patent for systolic indication alone is valued at around 1.2 billion dollar. The following figures are in thousands.

DCF	Actual	Current	Forecast										
	2012A	2013E	2014P	2015P	2016P	2017P	2018P	2019P	2020P	2021P	2022P	2023P	2024P	2025P
Mydicar Systolic Revenue	--			200,000	300,000	400,000	500,000	500,000	500,000	500,000	500,000	500,000	500,000	500,000
Probability of Success				*72%*	*72%*	*72%*	*72%*	*72%*	*72%*	*72%*	*72%*	*72%*	*72%*	*72%*
ALN-TTR02 Probability Adjusted Revenue				$144,000	$216,000	$288,000	$360,000	$360,000	$360,000	$360,000	$360,000	$360,000	$360,000	$360,000

Mydicar (Systolic)	
PV of Cash Flows	3,528,000
Drug Development Costs	813,000
Life of the Option	13.00
Variance in Expected PV	0.224
Riskless Rate	3.69%
d1	2
d2	(1)
N(d1)	0.993
N(d2)	0.981
Expected Cost of Delay	0.222
Value of the Patent	1,164,192

Given that there is an additional call option for the fact that the company is meeting the highest need for cardiovascular drugs in development by increasing survival rates, addressing renal and hypertension co-morbidities, and addressing the diastolic market, as well as developing small molecule therapies targeting SERCA2b enzymes, we believe that the company has a lot of intrinsic value that is not being manifested in these conservative projections. Moreover, the fact that pricing was intentionally set at levels that will far be exceeded given their pharmacoeonomic savings thesis we believe that this company has potential to become a moonshot IPO.

SWOT Analysis

Strengths

- Management projects 1 million heart failure hospitalizations on an annual basis and the direct and indirect costs of heart failure in the United States is estimated at $39 billion and is projected to grow by 2030 to $70 billion that leads to good market sizing

- Noninvasive genetic enzyme replacement therapy of SERCA2a deficiency with intra-coronary infusion of MYDICAR that is crucial to the calcium regulation in contraction and regulation

- Pharmacoeconomics of avoiding expensive invasive surgeries that are plagued with hospital readmissions leads to good pricing and 350,000 systolic heart failure patients in the United States alone will be eligible for MYDICAR treatment upon launch. With 280,000 heart failure related deaths annually, management projects a penetration rate of 50,000 patients a year with a range of 20,000 to 100,000 patients a year.

- Current treatments can cost in excess of $150,000 per patient for 1,500 patients per year receiving LVAD implants and 2,300 patients per year receiving transplant surgery which implies an annual projected total costs of $570 mm in invasive surgery and implant costs that can be substituted with this enzyme therapy that is minimally invasive and does not have a host of complications such as lifetime immunosuppressive therapy and risk of thrombosis and infection.

- Theoretically, pricing could be set to up to $150,000 given the savings the drug offers to patients. Very conservative pricing at even a low point of $20,000 reveals that based on market penetration rate of up to 50,000 patients predicted by management that the drug will reach sales of a billion on an annual basis.

- Fast Track Status and Special Protocol Consideration

- Clinical studies have been published in peer reviewed journals and studies have shown improved quality of life in patients leading to a pharmacoeconomic thesis. There will be favorable follow on events on Nov 19 with presentations being delivered on clinical end points at the America Heart Association

- Aligned with Obamacare by reducing hospital readmissions, which account for roughly half of the indirect and direct $39 billion dollars in costs. The Affordable Care Act has reduced hospital reimbursements for hospital readmissions and hence physicians are incentivized to utilize the drug.

Weakness

- Uncertain how the drug will compete with other substitutions and direct competitors in gene therapy for heart failure such as Carfostin, SDF-1, Vn-100, etc. The expected launch of LCZ-696, although a drug which has a target segment of preserved ejection fraction patients in heart failure, is a major drug that is expected to launch in 2015.

Opportunity

- The current heart failure market has been overtaken by generic drugs and branded drugs are looking to lose exclusivity in the next few years. The time is ripe for an opportunity to develop more efficacious treatments that could further increase survival times for heart failure patients. The highest unmet need currently is for increase in survival of heart failure patients and therapies for HF-PEF (Preserved Ejection Fraction) patients. Also, there is high unmet need for patients who have renal failures and other co-morbidities. Mydicar has shown preclinical data in support of countering heart failure with preserved ejection fraction (diastolic heart failure) and addressing co-morbidities such as hypertension and aiding AV-fistula maturation and preventing rapid proliferation of vascular smooth muscle cells in end stage renal disease patients requiring dialysis.

Threats

- Competition from competitors such as Renova Therapeutics, NanoCor Therapeutics, Juventas Therapeutics, VentriNova, and Beat BioTherapeutics.

Recommendation

Celladon is aligned with the highest unmet needs in cardiovascular drugs and has provided numerous clinical endpoints in increasing survival rates and improving quality of life. Given the crowding of generics and impending patent expiration of many brand drugs in the cardiovascular drugs in the next few years, Celladon is strategically positioned to gain strong market penetration rate of up to 50,000 patients a year and the fact that Celladon retains global rights leads to scalable commercializable volume and a buyout premium thesis. Furthermore, the pharmacoeconomic savings for reduction in hospital readmissions that Celladon provides as a noninvasive substitute can lead to favorable pricing. Celladon addresses the other highest unmet needs with promising preclinical data endpoints such as reducing renal failure co-morbidities and developing a drug that can also have diastolic applications, which the market is in dire need of. Furthermore, the fast track status and special protocol consideration will drive the valuations even higher.

Conclusion

The megafund model has been proposed as an investment vehicle to solve the broken chain of financial returns and innovation in biomedicine. Applications of the megafund model have been studied in Royalty Pharma late stage licensing deals, early stage orphan drugs, and now we propose a new application in the megafund IPO model. Case studies and theoretical simulations shed light on the fact that the megafund RBO model can be scalable and is realizable. Furthermore, evidence is supported against IPO investments not being a sound strategy through the empirical study. Implications for the megafund IPO model are that early stage investments can be derisked and balanced with later stage investments as IPO equity investments. With increasing sophistication of securitization and underlying science, the biopharma megafund business model can be constantly improved to not only fulfill social and ethical obligations but maximize financial returns.

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