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Abstract

The biotechnology and pharmaceutical industries are facing significant challenges to their existing business models because of expiring drug patents, declining risk tolerance of venture capitalists and other investors, and increasing complexity in translational medicine. In response to these challenges, new alternative investment companies have emerged to bridge the biopharma funding gap by purchasing economic interests in drug royalty streams. Such purchases allow universities and biopharma companies to monetize their intellectual property, creating greater financial flexibility for them while giving investors an opportunity to participate in the life sciences industry at lower risk. Royalty Pharma is the largest of these drug royalty investment companies, and in this case study, we profile its business model and show how its unique financing structure greatly enhances the impact it has had on the biopharma industry and biomedical innovation.

Keywords: Biotech, Pharmaceutical, Translational Medicine, Drug Royalty Investment Company, Intellectual Property, Royalties, Corporate Finance

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1 Introduction

Although the pharmaceutical industry has historically been a leader in financial performance, it is now facing serious challenges to its business model. With blockbuster-drug sales slowing,¹ the industry has seen losses in the equity markets coupled with decreasing drug development productivity. From 2001 to 2007, the average annual return for the pharmaceutical industry fell to $-0.7\%$ from its 1985–2000 average of $20.3\%$. By 2008, the industry had seen an erosion of roughly $850$ billion in shareholder value, despite rising gross margins (8). Furthermore, the “patent cliff,”—the expiration of patents to highly profitable drugs of several major pharmaceutical companies—is expected to put $209$ billion in annual drug sales at risk between 2010 and 2014 (12). For example, in 2011, Pfizer lost patent protection on Lipitor, its most profitable product which accounted for $27\%$ of its total revenues in 2006 (13).

The main challenge of the patent cliff is the difficulty in replacing these expiring drugs—it has been estimated that large manufacturers will only be able to replace each dollar of expiring-patent revenue with $26$ cents of new product revenue. Of the new drugs approved in 2009—part of a five-year stretch where major regulatory bodies approved $50\%$ fewer new molecular entities than in the previous five-year period—only $17\%$ are considered blockbuster medicines (12). Meanwhile drug-development costs have ballooned from an estimated $802$ million to $1.2$ billion per drug from 2003 to 2009 (4, 1).

These factors have potentially devastating effects on the ability of the biotechnology and pharmaceutical industries to “translate” scientific discoveries into useful therapeutics, which directly impacts patient health and life-expectancy. In a 2005 study, Lichtenberg found that $40\%$ of the two-year increase in life expectancy from 1986 to 2000 can be attributed to new drug innovation (10). With more than $60\%$ of all worldwide deaths caused by heart disease, stroke, cancer, chronic respiratory diseases, and diabetes according to the World Health Organization, the need for medical innovation has never been greater. The combination of reduced R&D productivity, increased economic risks, capital outflows, and loss of revenues due to loss of patent protection and generic competition have created an urgency for innovative financing approaches that can support more productive drug development.

Recently, a new approach to commercializing biomedical research based on financial engineering techniques such as portfolio theory and securitization has been proposed (6). In contrast to existing business models such as venture capital, private equity, and public equity (via publicly traded pharma companies), this new alternative—called a “megafund”—

¹A “blockbuster” in the pharmaceutical industry is a drug that generates more than $1$ billion in annual revenues.
involves the use of securitized debt, i.e., bonds that pay a fixed rate of interest and where repayment is secured by collateral in the form of various biomedical projects that are funded by the proceeds of the bonds. Because the bond market is considerably larger than venture capital and public equity markets, and because debt can be structured to have longer maturities which are better suited to drug development, such financing vehicles offer several advantages to traditional sources of funding in the biopharma industry. However, these new vehicles require new business models, and in this article we provide a detailed examination of one structure—the drug royalty investment company—that offers a “proof of concept” for certain aspects of the megafund model.

In this case study, we profile the business model of Royalty Pharma, Inc., the largest of a new breed of investment companies that acquires ownership interests in drug royalties. Founded in 1996 by Pablo Legorreta, an investment banker who successfully established a proof-of-concept for investing in drug royalty streams several years earlier, Royalty Pharma now manages $10 billion in assets, consisting of 39 approved and marketed biopharma products and two products in clinical trials and/or under review with the United States Food and Drug Administration (FDA) and/or the European Medicines Agency (EMA). By focusing on approved drugs, drug royalty investment companies are able to accurately estimate the current market value of the drugs’ future royalty streams, allowing them to invest responsibly and achieve an attractive risk/reward profile for their investors. From the perspective of the patent-holders—typically universities, hospitals, and biomedical research centers—selling a portion of their future royalty streams is often a welcome prospect because it provides these institutions with much-needed cash to fund new research initiatives, as well as a concrete lower bound for the value of the intellectual property.

However, perhaps the most interesting aspect of Royalty Pharma is the fact that it has made use of debt financing since 2003 and raised new debt totaling $4 billion. This is significant because the traditional sources of financing for the biopharma industry are private and public equity; debt financing is feasible only for large pharmaceutical companies with relatively stable cashflows, which is precisely what a portfolio of royalties on approved drugs provides.

Debt financing is particularly important for biomedical R&D for at least two reasons. First, debt maturities can range from a few months to 100 years, allowing the issuer to customize the pattern of obligations to match their cashflows. Given that the drug-approval process can often take a decade or more from beginning to end, long-term debt financing may provide greater flexibility than traditional models such as venture capital or public eq-

\(^2\)For example, in May 2011 the Massachusetts Institute of Technology issued $750 million in 100-year bonds at the historically low rate of 5.623%.
uity. Of course, equity capital is often preferred to debt financing by entrepreneurs because the former is more “permanent” than the latter. However, permanent capital requires relinquishing certain control rights and, in the case of public equity, subjects the company to quarterly earnings targets, daily stock price fluctuations, and a degree of transparency and public scrutiny that discourages high-risk but truly transformative translational medical research. In this respect, equity financing can lead to greater “short-termism” than long-term debt. However, because of the highly predictable nature of Royalty Pharma’s cashflows, the company is able to issue debt with relatively short maturities.

The second reason debt financing is important is the fact that the pool of potential bond investors is much larger. For example, in 2012 the total amount of bonds issued in the U.S. was $1.3 trillion, compared to $253 billion of public equity issued, and $126 billion of capital committed to private equity (of which only $20 billion was venture capital, and only $6.8 was invested in medical/health/life sciences companies). However, while the pool of capital is larger, the risk appetite of bond investors is considerably lower than that of equity investors. Therefore, the ability to tap into this larger pool of capital is to be able to reduce the risk of the underlying assets to the point where debt financing is feasible. Royalty Pharma has accomplished this feat by focusing only on approved drugs and, most recently, Phase III compounds. This raises the possibility that other methods of de-risking a portfolio of assets—such as the megafund proposed by Fernandez et al. (6)—might also be possible. In any case, Royalty Pharma provides compelling proof that new financial methods and models can play a pivotal role in helping the biopharma industry address its pressing short-term funding needs and longer-term productivity challenges.

2 Industry Background

The challenges facing the biopharma industry and the need for new business models to finance drug discovery are motivated by the lengthy, expensive, and risky nature of the drug discovery process.

Before entering the market, a drug must pass through many levels of research and then clinical trials, incurring varying costs at each stage. The new drug development process starts in the so-called “preclinical” phase, which includes the search for certain chemical compounds with potential medicinal value, testing the properties of candidate compounds such as chemical stability, toxicity, and efficacy and side-effects in animals such as mice.

Once a compound demonstrates sufficient promise in the preclinical phase, the next step is to begin testing it with human subjects which consists of three successive phases. In Phase
I, general qualities such as safe dosages and metabolic effects are evaluated in a small number of volunteers. Subsequently, preliminary efficacy and safety data are obtained in patients with the target disease or condition during Phase II trials. Phase III consists of large-scale trials and is the final clinical phase before approval. Upon successful completion of Phase III trials, the drug developer can then submit a new drug application (NDA) to the FDA for review and marketing approval.

Typically, the majority of drug discovery and preclinical data collection occurs outside of pharmaceutical companies in academic institutions, as evidenced by the fact that only 12% of active preclinical assets currently reside in large pharmaceutical companies (11). Phase I and Phase II human trials are then typically conducted at small and mid-cap biotech companies with the drug then being passed on to the main marketers—large-cap pharmaceutical and biotech companies. Each stage has infrastructure and expertise suited for its role in the development cycle. Recent trends indicate increasing collaboration between various institutions in the drug development cycle. As the complexity of drugs continues to increase, more alliances between academic institutions, biotechnology companies, and pharmaceutical companies have been launched (16). Just as pharmaceutical companies have reached back to academic institutions to aid in the innovation gap, biotech companies are starting to do so as well (12, 9).

Moreover, every four-year period between 1995 and 2009 has seen a 30% increase in licensing deals between biotech companies and large-cap pharmaceutical companies. From 1995 to 1999, there were 180 reported licensing deals between biotech and the top 20 pharmaceutical companies; this number grew to 238 between 2000 and 2004, and to 306 between 2005 and 2009 (11). This is a reflection of both the increasing complexity of new pharmaceutical products and the exponentially increasing costs of the successive phases of clinical trials. Cost sharing is a fundamental driver of these licensing deals which, in turn, are facilitated by intellectual property that is protected by patents.

Pharmaceutical products are granted patent protection for a period of 20 years from the date of the patent application, which is particularly important for this industry since most drugs, once developed, can be imitated easily (15). This protection is designed to promote innovation by allowing manufacturers to achieve above-average returns for a limited period. With the 1984 introduction of the Hatch-Waxman Act, which significantly lowered the barrier for generic market entry, most manufacturers aim to realize a majority of their returns on a given product before patent expiry. From 1984 to 2010, the overall generic market share grew from 19% to 78% (2, 7). However, a significant risk to the returns on a product is presented when generic competitors believe they can break a patent before expiry. This risk, combined with the growing complexity of the science behind new medicines, presents
the need to develop a strong patent before entering the market and motivates collaboration between biotech and pharma.

Because it is simpler and less expensive for smaller biotech companies to conduct early trials that do not require large infrastructure and large patient populations, big pharma has relied on its smaller counterparts to conduct Phase I and Phase II trials. At the same time, most small and mid-cap biotech companies have experienced difficulty in securing financing in both equity and debt markets. To pay for the expenses of collaborations, therefore, such companies have supplemented the traditional cash or work-for-hire payments by issuing royalty-based licenses that do not immediately affect their bottom line. A royalty payment is a percentage of sales or a fixed amount per unit sold that is derived from the use of a proprietary asset. A royalty interest is a financial contract that allows an entity to collect a future stream of royalty payments for a predetermined timeframe, typically in exchange for an up-front cash payment. Upon patent expiration, the asset underlying the royalty is no longer proprietary and the royalty payments cease.

Royalties play a significant role in the biopharmaceutical industry, where multiple licensing agreements may be attached to a product as it passes through the various stages of the drug-development cycle. Payments based on future earnings allow smaller companies to work with more established firms and academia without affecting their already difficult financing situation. Licensing royalties can be substantial to a manufacturer, with rates ranging from 10% to 30% of revenues (2).

The larger role of academic institutions in commercial drug development calls for a better funding mechanism for rewarding academic contributions and a more efficient collaboration between industry and academia. While this process is complicated by the fact that academic and commercial interests are not always aligned, the evolving drug discovery model can be useful in mitigating risks by sharing resources. Due to the high risk of early-stage R&D, investors are reluctant to bear the full cost of this phase, which is often referred to as the “Valley of Death,” because of the dearth of funding for such projects. Accordingly, government funding bodies and charitable institutions play a larger role in this stage—at the 20 most research-focused medical schools, an average of 80–85% of total research dollars comes from federal research grants (3).

However, there are several significant public-private collaborations in funding academic research. For instance, the Broad Institute in Cambridge, MA is a partnership between the Massachusetts Institute of Technology, Harvard University and its hospitals, and the Whitehead Institute for Biomedical Research, and has been funded by charitable donations, the Novartis Diabetes Initiative, and the RNAi consortium (14). Such partnerships are still early in their life cycle and will require continued effort to become an efficient method of
bringing new medicines to market. The growing complexity of collaborations with academia has significant implications for the royalties attached to a product by the time it reaches the market.

3 Brief Company History

Royalty Pharma is a privately owned alternative investment company that focuses on the acquisition of pharmaceutical royalty interests. With a portfolio valued above $10 billion, it is the global leader in dedicated royalty investment entities. Royalty Pharma, though founded in 1996, has been through two distinct stages before becoming the company it is today. In the 1980s, certain members of Royalty Pharma’s management team and investment committee established Research & Development Partnerships to fund clinical development of pharmaceutical products via royalty interests. In 1993 and 1994, Royalty Pharma founder Pablo Legorreta developed two acquisition vehicles to acquire royalty interests in Neupogen and ReoPro, two leading biotechnology products. Prior to creating the investment vehicles, Mr. Legorreta provided cross-border merger and acquisition and corporate finance advisory services at Lazard Frères. In 1996, the predecessors of Royalty Pharma were founded and in 2003, the predecessors were consolidated to form Royalty Pharma as it currently operates. Figure 1 contains a size comparison between Royalty Pharma and other leading drug royalty investment companies.

4 Investment Process

Royalty Pharma invests in products after regulatory approval and, more recently, also in the late stages of clinical trials. Its current portfolio consists of royalty interests in 39 approved and marketed biopharmaceutical products, and in two products in clinical trials and/or under review with the FDA and/or EMA. Furthermore, it focuses on drugs with blockbuster potential that are marketed by leading pharmaceutical and biotech companies. The management team manages everything, such as research and due diligence, except the final investment decision, which is subject to the approval of a separate investment committee.

Once the management team conducts its due diligence and decides to pursue a potential project, the executive board must present the project to the investment committee for approval before continuing. No investment can be made without approval from the investment committee. The seven-person investment committee is comprised of representatives of several major investor groups and two independent directors from a variety of backgrounds,
Figure 1: Size comparison of Royalty Pharma and other drug royalty investment companies, based on consolidated RPI and RPS financials for the period ending March 30, 2012; pro forma inclusion of the BG12 royalty asset and the $650 million RPIFT Term Loan Debt (May 2012). (1) Cash and royalty receivables.
with the CEO, Pablo Legorreta, being the only member of both the investment committee and management team. This unique feature of Royalty Pharma’s investment committee provides a degree of objectivity and investor representation that has served the company well over the years.

Royalty Pharma identifies investment opportunities through two main methods. First, it proactively searches for holders of royalties such as academic institutions, research institutions, and smaller companies. Second, as the largest royalty investment company, Royalty Pharma is often contacted by potential sellers of royalties with new opportunities. After identifying a potential investment, Royalty Pharma conducts research to determine the commercial viability of the product in question. The product must be evaluated in three separate parts to provide an accurate sales estimate from which Royalty Pharma obtains its potential revenue stream. The pharmaceutical is measured by its scientific merit, the strength of its patent, and its expected market share.

To establish the scientific value of the product, Royalty Pharma brings in opinion leaders and clinicians to provide their opinions. The patent status of the product is established by engaging patent attorneys who can attest to the strength of the patents. Finally, the commercial value research is conducted by the Royalty Pharma management team by interviewing key opinion leaders, specialists, community practice doctors, and other prescribers, and compiling the resulting data into sales projections. In addition, because the products are typically blockbuster drugs from large-cap marketers, many investment banks provide sales projections for upcoming years. This increases visibility for future market share and provides more data to which the in-house projections can be compared.

Due to the illiquid nature of the market in which it invests, Royalty Pharma does not apply standard portfolio optimization techniques. It does, however, diversify its portfolio in terms of product, therapeutic class, and marketer, and this diversification is achieved in several ways. With respect to therapeutic class, Royalty Pharma’s portfolio consists of products for over 15 indications, and with respect to exposure to marketers, the portfolio covers products from 25 different marketers.

In addition, Royalty Pharma is diversified in terms of the type of investment it makes, some of which go well beyond the standard royalty investment. Depending on the seller’s desired cash flows, Royalty Pharma can provide many types of royalty investments, such as an accelerated royalty or a synthetic royalty. In an accelerated royalty investment, Royalty Pharma provides the seller with the cash flow from a royalty over a shorter duration than the

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3An “indication” is an approved use for a drug, e.g., Humira for rheumatoid arthritis and beta-blockers for high blood pressure. Indications are listed on the label of a drug, which is regulated by a government regulatory body such as the U.S. Food and Drug Administration.
actual royalty in exchange for receiving the remainder of the royalty. For example, the seller receives its 9% royalty in three years instead of 3% over the course of nine years. In some cases, a synthetic royalty is created when Royalty Pharma provides capital to a company in exchange for a royalty where there is no existing royalty in the product. For instance, in the case of Sunesis Pharmaceuticals’s Vosaroxin, Royalty Pharma agreed to provide capital to finance a Phase III clinical trial in exchange for various percentages of future net sales, depending on the status of the trial (see below for a more detailed discussion of this deal). In this case, Royalty Pharma created a royalty instead of purchasing one. In other cases, Royalty Pharma purchases an existing royalty in a pharmaceutical product outright. Therefore, its portfolio is diversified in terms of type of royalties and products owned.

This stratified diversification approach seems to have paid off—Royalty Pharma’s portfolio has delivered attractive risk-adjusted absolute returns with a remarkable level of consistency. With the addition of conservative leverage, the returns to equity holders have been increased without duly increasing the risk. While the absolute returns are impressive, the stability of the equity returns through a period of unprecedented equity-market volatility and notably poor performance across other asset classes support Royalty Pharma’s approach to asset selection and portfolio construction.

5 Sample Deals

Royalty Pharma works closely and collaboratively with academic institutions, research institutions, and pharmaceutical/biotechnology companies to acquire royalty interests. In 2005, Royalty Pharma acquired the *emtricitabine* royalty from Emory University and three inventors. The royalty was 40% owned by three inventors and 60% owned by the Emory University Medical School. The royalty, which represented a significant portion of the respective parties’ net worth, was not ideal for the holders because it exposed them to single-product risk, illiquidity, and a long payout schedule (15 years). Royalty Pharma purchased the royalty for $525 million, providing the holders with the capital and liquidity with which to diversify their assets.

Similarly, in 2006, Royalty Pharma purchased Cambridge Antibody Technology’s (CaT) passive royalty interest in Abbott’s *Humira*. This occurred as part of AstraZeneca’s $1.3 billion purchase of the remaining 81% of CaT it did not already own. Since the non-core passive asset was not as useful as upfront capital for AstraZeneca, it sold the royalty interest to Royalty Pharma for $700 million. This, along with $300 million of CaT cash, brought AstraZeneca’s net acquisition cost down to $300 million. Since the purpose of the collaboration
between CaT and AstraZeneca was to develop antibody products and add to AstraZeneca’s pipeline, the sale of a passive royalty interest did not undercut the main objective of the acquisition.

While these examples involve approved products, Royalty Pharma also acquires royalties in drugs that have yet to be approved such as the $761 million acquisition in May 2012 of an interest in BG-12, a tablet version of the multiple sclerosis drug dimethyl fumarate. Royalty Pharma’s interest represents a portion of an earn-out payable to the former shareholders of Fumapharm by Biogen Idec, which acquired Fumapharm in 2006. The acquisition gave Biogen Idec Fumaderm, a therapeutic approved in Germany for moderate to severe plaque psoriasis. Biogen Idec adapted the base ingredient in Fumaderm, fumaric acid, into BG-12. In April 2012, Biogen Idec presented its second set of promising Phase III data, bringing the total to two global, placebo-controlled studies involving more than 2,600 relapsing-remitting multiple sclerosis (RRMS) patients, further supporting BG-12’s NDA. The studies showed a 44% to 53% reduction in annualized relapse rate when compared to the placebo. Furthermore, BG-12 has not been associated with any increased risk for serious adverse effect compared to the placebo. In addition, BG-12 was expected to be the first safe and effective oral RRMS therapy and there was over 15 years of psoriasis safety data from Fumaderm. Given the strong data for the efficacy and safety of BG-12 at the time of Royalty Pharma’s acquisition, it was expected to become the standard of care for multiple sclerosis. Less than one year after Royalty Pharma’s acquisition, this drug was approved by the FDA on March 27, 2013 and is now marketed as Tecfidera, and will be approved in Europe shortly. Biogen Idec’s stock price, which was $177.09 on March 26, 2013—the day before the FDA approval—has grown to $275.32 as of December 13, 2013, a 55.5% return that amounts to a remarkable $23.2 billion increase in Biogen Idec’s market capitalization since BG-12 was approved.

Royalty Pharma’s purchase provided the former Fumapharm shareholders with $761 million in exchange for a portion of the earn-out payable to the former Fumapharm shareholders linked to sales of BG-12 and Fumaderm. The structure of Fumapharm’s royalty with Biogen Idec requires payments when net sales equal $500 million, $1 billion, and every subsequent $1 billion up to $20 billion. To evaluate the expected revenue from this investment, Royalty Pharma interviewed 105 U.S. and European neurologists. As is the case with any investment, there were risks involved with BG-12, primarily due to the drug’s unapproved status.

4The current standard of care involves a group of drugs called the ABCRs (Avonex, Betaseron, Copaxone, Rebif), which require painful daily to weekly injections for a lower efficacy (30% reduction). The other group of treatments includes two drugs called Tysabri and Gilenya, which provide a higher efficacy but have severe potential adverse effects including cancer and death.
at the time of acquisition. Although the clinical trial data was strong and there was an abundance of safety data from Fumaderm, the limited data with respect to multiple sclerosis did leave some room for doubt. Furthermore, BG-12 had not yet launched and Biogen Idec could, therefore, have delayed market entry for commercial reasons, though this was unlikely. Finally, the upside is capped when net sales reach $20 billion due to the terms of the royalty. Despite these risks, BG-12 was a viable investment due to the highly promising nature of the product itself, sales projections, and visibility in the context of potential competitors, both in-market and currently in-trials.

Another example of pre-FDA-approval financing is Royalty Pharma’s “adaptive financing” for Sunesis Pharmaceuticals using a creative synthetic royalty structure. At that time, Sunesis was evaluating its lead product candidate, Vosaroxin, in a Phase-III, randomized, double-blind, placebo-controlled trial—the VALOR trial—among patients with first relapsed or refractory acute myeloid leukemia (AML). Initially designed to have a 90% probability of detecting a 40% difference in overall survival among 450 patients, this trial employed an “adaptive” structure that would allow for changes in design or analyses based on the examination of data at an interim point in the trial. Using the Access Control Execution System (ACES) developed by Cytel—the leader in the design and implementation of adaptive clinical trials—the Vosaroxin interim analysis was to be conducted by an independent data safety monitoring board (DSMB) once 50% of the events were reached, i.e., 187 deaths. This was expected to occur at approximately 300 patients enrolled, and based on this interim analysis, the DSMB would then decide whether to stop the study early, continue the study as planned with 450 patients, or implement a one-time increase in sample size with an additional 225 patients. By designing the study this way, Sunesis could avoid conducting an unnecessarily large trial in certain cases, potentially reducing the overall cost and risk of their study.

While Sunesis had sufficient capital to fund the original Phase-III design of 450 patients, the company was seeking an additional $25 million to fund the potential expansion to 675 patients at the interim analysis. Given Royalty Pharma’s interest in AML, the positive role the company thought Vosaroxin could play in treating the disease, and the possibility of expanding Vosaroxin’s use into additional blood cancers and solid tumors, discussions with Sunesis were initiated in the Fall of 2011. After conducting its due diligence, in March 2012, Royalty Pharma conditionally agreed to pay Sunesis the $25 million to acquire a royalty on the future net sales of Vosaroxin. However, under the terms of the agreement, Royalty Pharma would only invest the $25 million if, following the interim analysis, the study was stopped early for efficacy or if the sample-size increase was implemented. In return, Royalty Pharma would get a 3.6% participation payment on future net sales of the drug if the study was stopped early for efficacy, or a 6.75% participation payment on future net sales plus two
warrants if the sample size was increased. Each warrant would entitle Royalty Pharma to purchase 1,000,000 shares of Sunesis common stock at an exercise price of $3.48 and $4.64 per share, respectively. If the DSMB decided that the trial should continue as planned, Royalty Pharma would have the option of making the $25 million investment upon the un-blinding of the study in exchange for a 3.6% participation payment on future net sales.

This adaptive trial design enabled Royalty Pharma to invest in Vosaroxin on terms that were a win-win for both parties. Sunesis received committed funding, greatly reducing their risk and allowing them to focus on preparing Vosaroxin’s regulatory filings and U.S. commercial launch and to expand their development program. Accordingly, upon the announcement of this agreement, Sunesis’s stock price rose 15% and reached a two-year high when the DSMB recommended the sample-size increase in September 2012. Royalty Pharma was able to significantly limit its exposure to the risk of a negative outcome of the clinical trial and, at the same time, position itself to receive a sizable royalty in the event that Vosaroxin is approved. In addition, through the warrant portion of their investment, they stood to earn back a significant portion of their initial investment upon the positive completion of the trial. This type of “adaptive financing” is a potentially transformative technique for commercializing biomedical research.

6 Financing

Royalty Pharma finances its acquisitions by an even mixture of debt and equity: $4.2 billion and $4.0 billion, respectively. Equity investors are provided liquidity events once every four years, with the most recent event occurring in 2011. The liquidity event in 2003 effectively marked the start of Royalty Pharma’s current structure. By maintaining Royalty Pharma as one investment vehicle and recapitalizing for each liquidity event, the fund is able to gain access to low-cost debt capital. The reduced cost of capital allows Royalty Pharma to pay higher prices for royalties while providing attractive returns to investors. Possible liquidity options for 2015 include continuing the process of leveraged recapitalization or taking Royalty Pharma public.

Over time, Royalty Pharma’s investor base has grown more institutional. In some cases, royalty sellers are given the opportunity to reinvest a portion of the cash received in the sale of the royalty and acquire equity in Royalty Pharma’s diversified portfolio. This occurs as a separate process from the royalty acquisition, since the acquisition is paid for in full and the seller then chooses to reinvest at the portfolio’s current net asset value. However, the reinvestment, despite operating as a separate process, decreases the effective net acqui-
sition cost to Royalty Pharma while providing diversification benefits to the royalty seller. Furthermore, the seller can also receive the upside benefits of Royalty Pharma’s diversified portfolio, including the royalty it sold.

The debt is held primarily by banks and other institutions, and is split into two main trusts: RPI Finance Trust (RPIFT), a trust that continues to invest, and RP Select Finance Trust (RPSFT), a trust that no longer invests and thus distributes 100% of its cash flow after debt service to its equity investors. RPIFT, has approximately $3.35 billion of debt outstanding across three tranches: $850 million of LIBOR+2.75% notes maturing in November 2016, $1.9 billion of LIBOR+3.00% notes maturing in May 2018, and $600 million of LIBOR+3.00% notes maturing in November 2018. Based on total debt to EBIDTA, RPIFT operates with a leverage ratio of 3.5-to-1. RPSFT consists of a single tranche of $850 million notes at LIBOR+2.25% maturing in November 2016; this trust had an initial leverage ratio of 4.0-to-1.

By creating two distinct vehicles, Royalty Pharma broadened the types of investors that could purchase its debt, i.e., commercial banks purchased the short-term amortizing debt while institutional lenders and funds purchased the longer-dated “bullet” debt. Furthermore, Royalty Pharma debt has received investment grade ratings by the three major rating agencies (Moody’s, S&P, and Fitch), with ratings of Baa2, BBB−, and BBB−, respectively. The rating agencies affirmed a stable outlook given the strong diversified portfolio, healthy cash flow, and reasonable leverage of the Royalty Pharma portfolio.

Except for the $600 million tranche of RPIFT, which was raised in 2012, the remaining $3.6 billion was refinanced in 2011 as part of the required liquidity event. In this event, Royalty Pharma’s overall portfolio was split into a 20% run-off portfolio with the remaining 80% operating as a continuing investment vehicle. Royalty Pharma then refinanced its existing $2.75 billion in outstanding debt and borrowed the additional $850 million on its passive portfolio to distribute cash to shareholders.

7 Challenges and Future Prospects

Royalty Pharma has clearly been successful in creating a new segment of the investment management industry, a particularly important one given the recent decline in investment capital in the biopharma industry. However, the challenges facing that industry also have implications for Royalty Pharma’s business model. The patent cliff will necessarily reduce royalty streams for all the affected drugs and the combination of reduced R&D productivity, increasing complexity and economic risks, changes in the regulatory approval process,
and targeted therapies and personalized medicine may have the effect of increasing Royalty Pharma’s cost of capital.

At the same time, the number of scientific breakthroughs in translational medical research has been growing, thanks to a confluence of innovations in basic science, bioengineering, and computational advances such as high-throughput screening of chemical compounds, in silico drug discovery, and faster and cheaper gene-sequencing techniques. Therefore, new investment opportunities have never seemed greater, particularly at the earlier stages of the drug development process. However, as investors move into earlier-stage assets, the economic risk becomes greater since less is known about these assets’ efficacy, toxicity, and side effects. Therefore, from a purely financial perspective, a larger amount of capital is required for these earlier stage investments to bring down the risk to a more investor-friendly level.

Furthermore, while Royalty Pharma’s revolving equity structure has been successful to date, with demand outstripping supply at each liquidity event, the size of its business would be better served by permanent and more liquid capital, i.e., public equity. However, under current law, drug royalty investment companies would become subject to entity-level tax if they went public, which would render their cost of capital uncompetitive with their private competitors. Royalty Pharma has advocated a change in the tax law that would enable it to go public without becoming subject to entity-level tax, as is the case for real estate investment trusts (REITs) and other publicly-traded partnerships.

Even without this change, Royalty Pharma is likely to continue its growth in the near term given its track record and the demand for its services from both investors and patent holders. The emergence of intellectual property exchanges such as IPXI also bodes well for Royalty Pharma’s business model by creating greater liquidity and transparency into otherwise hard-to-value royalty streams. But perhaps the most promising indication of Royalty Pharma’s future is the current low-yield environment facing fixed-income investors and the opportunity to issue large amounts of long-term debt securitized by royalty streams.

8 The Megafund Business Model

The Royalty Pharma business model clearly demonstrates that the megafund concept of using both debt and equity to finance biomedical innovation is not only feasible but practical and scalable. By focusing on approved and late-stage therapeutics which have less risky financial returns, drug royalty investment companies can access a much larger pool of investment capital than traditional biotech venture capitalists. These financing vehicles allow universities and biomedical research organizations to monetize their intellectual prop-

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erty, freeing up much-needed financial resources to be plowed back into basic research and translational medicine.

However, the focus on late-stage assets does little to address the Valley of Death of funding for preclinical and early-stage assets. While it is true that, by definition, drug royalty investment companies currently focus only on assets for which royalties are imminent, they highlight a key issue with respect to financing drug discovery: as we move from later-stage to earlier-stage assets, the risks become greater, the likelihood of success is correspondingly lower, and more projects and funding are needed to yield the same level of diversification as that of portfolios of later-stage assets.

In fact, as we move to the very earliest stages of the drug discovery process—basic scientific research—the practical relevance is so speculative that for-profit private-sector funding is virtually non-existent for such activities. This stage can only be supported by the government and not-for-profit organizations such as foundations, endowments, high net worth individuals, and patient-advocacy groups. The leading example is, of course, the National Institutes of Health (NIH). A recent innovation of the NIH is the Bridging Interventional Development Gaps (BriDGs) program, a non-profit initiative of the NIH’s National Center for Advancing Translational Sciences that provides support—including investigational new drug (IND)-directed toxicology, pharmacokinetic studies, and manufacturing of clinical trial supplies—for researchers seeking to take basic research into the clinic.5

This spectrum of drug-discovery risk has a corresponding spectrum of possible financing methods and natural investors, depicted in Figure 2. As drug discovery progresses from early to late stages, and as the risk decreases along the way, the available sources of financing progresses from grants and donations, which carry no expectation of any economic return, to private and public equity, for which the returns are highly volatile but with unlimited upside, to debt, for which the returns have very little volatility but very little upside.

This financing spectrum implies that the megafund proposed by Fernandez et al. (6) will likely require a hybrid capital structure if it is to invest across the full spectrum of drug discovery: securitized debt can finance the later-stage assets and various forms of convertible bonds, and equity will be needed to finance earlier-stage assets. However, the specific components of this hybrid capital structure will be highly dependent on the statistical properties of the projects in the portfolio. For example, if the early-stage projects consist primarily of therapeutics for rare diseases, i.e., “orphan drugs,” it can be shown that even a relatively modest number of them (as few as 10) and equally modest funding (between $250 to $500 million) can provide sufficient diversification to yield attractive risk/reward profiles

5For more information, see http://www.ncats.nih.gov/research/reengineering/bridgs/bridgs.html.
### Stages of Drug Discovery

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Natural Investors</th>
<th>Financing Method</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low cost per project; many projects; top/down selection; high failure rate</td>
<td>Non-profits, hedge funds, VCs</td>
<td>Grants, gifts, private equity</td>
</tr>
<tr>
<td>Medium cost per project; medium # of projects; medium failure rate</td>
<td>Hedge funds, VCs, pharma</td>
<td>Private and public equity, high-yield debt</td>
</tr>
<tr>
<td>High cost per project; few projects; low failure rate</td>
<td>Pharma, retail and institutional investors</td>
<td>Public equity, investment-grade debt</td>
</tr>
</tbody>
</table>

Figure 2: Relationship between the stages of drug discovery, their financial characteristics, the natural investors for each stage, and the type of financing method most appropriate. Earlier-stage assets are more risky hence their financing vehicles naturally reflect investors with those risk preferences.

for both debt and equity holders (5).

These considerations underscore the many new possibilities for financing biomedical innovation, and the opportunity for the biopharma industry to reinvent itself in light of these new financing structures.
A Appendix

In this appendix, we provide more detailed information about Royalty Pharma. We present some basic facts and figures for the organization in Appendix A.1, include the biographies of senior management in Appendix A.2, and provide an example of a typical term sheet for a royalty acquisition deal in Appendix A.3.

A.1 Royalty Pharma Facts and Figures

Founded: 1996
Ownership: Privately Held
Employees: 21
Investment Focus: Biopharmaceutical royalty interests
Assets: Royalty interests in thirty-seven approved and marketed products and five products in clinical trials and/or under review with the United States Food and Drug Administration (FDA) and/or the European Medicines Agency (EMA).
Main Office: 110 East 59th Street 33rd Floor
New York, NY 10022
Contact Information: ir@royaltypharma.com
(212) 883–0200 (tel)

A.2 Biographies of Senior Management

Pablo Legorreta, Founder and Chief Executive Officer

Mr. Legorreta founded Royalty Pharma in 1996, after creating and managing two “proof of principle” investment vehicles in 1993 and 1994 that invested in royalty interests in two leading biotechnology products. Prior to founding these investment vehicles, Mr. Legorreta spent ten years at Lazard Frères where he provided cross-border merger and acquisition and corporate finance advisory services to U.S. and European corporations. Mr. Legorreta currently serves as a Director of Giuliani SpA and is a founding member of Boston Children’s Hospital Medical Research Council, as well as a member of the Board of Trustees of The Allen-Stevenson School. He received a degree in industrial engineering from Universidad Iberoamericana.
Susannah Gray, Executive Vice President and Chief Financial Officer

Ms. Gray joined Royalty Pharma in January 2005 after a fourteen year career in investment banking. Prior to joining Royalty Pharma, Ms. Gray was a managing director and the senior analyst covering the healthcare sector for CIBC World Markets (now Oppenheimer & Co.). Prior to that, Ms. Gray worked at Merrill Lynch and Chase Securities (a predecessor of JP Morgan), working in various capacities within the healthcare, high yield, and structured finance groups. Ms. Gray received a BA with honors from Wesleyan University and holds an MBA degree from Columbia University.

Alexander Kwit, Executive Vice President

Mr. Kwit joined Royalty Pharma in 2001 after practicing law for five years. Prior to joining Royalty Pharma, Mr. Kwit served as Vice President of Business Affairs and General Counsel for a New York based digital media entertainment company. Prior to that, Mr. Kwit was an Associate at Davis, Polk & Wardwell, where he specialized in mergers & acquisitions and securities laws. Mr. Kwit received a BA from Duke University, where he was elected to Phi Beta Kappa, and holds a JD degree from Columbia University Law School, where he was a Harlan Fiske Stone Scholar. He has been a member of the New York State Bar Association since 1997.

Jim Reddoch, PhD, Executive Vice President, Head of Research & Investments

Dr. Reddoch joined Royalty Pharma in July 2008 after twelve years on Wall Street as a biotechnology analyst. Prior to joining Royalty Pharma, Dr. Reddoch was Managing Director and Head of Healthcare Equity Research at Friedman Billings Ramsey. Prior to that, Mr. Reddoch worked at Banc of America Securities and CIBC World Markets (now Oppenheimer & Co.). Dr. Reddoch holds a BA from Furman University and a PhD in biochemistry and molecular genetics from the University of Alabama at Birmingham. He was a postdoctoral fellow at the Yale University School of Medicine.

George Lloyd, Executive Vice President, Investments

Mr. Lloyd joined Royalty Pharma in 2011 after practicing law for 25 years. Prior to joining Royalty Pharma, Mr. Lloyd was a partner in Goodwin Procter LLP’s Private Equity Group. Prior to that, Mr. Lloyd was a partner at Testa Hurwitz & Thibeault LLP and an associate at Davis Polk & Wardwell LLP. Mr. Lloyd received an AB from Princeton University and a JD degree from New York University Law School, where he was on the Law Review.
Molly Chiaramonte, PhD, Vice President, Research & Investments

Dr. Chiaramonte joined Royalty Pharma in January 2008. Prior to joining Royalty Pharma, Dr. Chiaramonte worked as a biotechnology equity research associate at Jefferies & Company. Prior to that, she was a postdoctoral fellow in the Department of Biochemistry and Molecular Genetics at the University of Colorado Health Sciences Center. Dr. Chiaramonte received a BA in mathematics, summa cum laude, from Providence College; an MA in mathematics from the University of Colorado; and a PhD in chemistry (Biochemistry Program) from the University of Colorado.

Terrance Coyne, Vice President, Research & Investments

Mr. Coyne joined Royalty Pharma in 2010. Prior to joining Royalty Pharma, Mr. Coyne worked as a senior biotechnology equity research analyst at JP Morgan. Prior to that, he worked at Rodman & Renshaw and Wyeth Pharmaceuticals. Mr. Coyne received a BS in business administration from La Salle University and an MBA from La Salle University.

James S. Rielly, Vice President, Finance

Mr. Rielly joined Royalty Pharma in 1999. Prior to joining Royalty Pharma, Mr. Rielly was the Vice President of Finance, Treasurer and Secretary of Cadus Pharmaceutical Corporation, a publicly traded biotechnology company. Prior to that, Mr. Rielly was the Controller and Treasurer for Baring Brothers & Company Ltd, an investment banking firm. Mr. Rielly is a certified public accountant and holds a BSBA from Bucknell University.

Alexander von Perfall, Vice President, Investor Relations

Mr. von Perfall joined Royalty Pharma in 2009. Prior to joining Royalty Pharma, Mr. von Perfall was the Co-Founder and Chief Network Officer of XTF, a start-up exchange traded fund ratings agency. Prior to joining Royalty Pharma, Mr. von Perfall worked at Bertelsmann AG’s BMG Entertainment division and the International Finance Corporation/World Bank Group. Mr. von Perfall attended the Hochschule St. Gallen in Switzerland and holds a BA in politics from the University of San Francisco and an MBA from the Stern School of Business at New York University.
A.3 Sample Term Sheet

**Royalty Opportunity Summary**

- **Product:** Humira (subcutaneous injection)
- **Compound:** Adalimumab (biologic, monoclonal antibody)
- **Product Type:** TNF Inhibitor
- **Indications:**
  - Rheumatoid Arthritis (RA), Psoriatic Arthritis (PsA), Early RA
- **Marketers:**
  - Japan: Eisai
- **Launch Dates:**
  - US: January 2003 (RA)
  - EU: September 2003 (RA)
- **Royalty Holder:**
  - Cambridge Antibody Technology (CAT)
  - AstraZeneca (AZ) expected to close the acquisition of CAT in June 2006
- **Royalty Terms:**
  - CAT receives 2.688% on worldwide sales
- **Duration:** June 2018 (US) and December 2017 (Non-US)
- **Frequency:** Semi-annually
- **Expected Peak Sales:** $7.5bn per year
- **Expected Peak Royalties:** $203m per year
- **Approximate Value:** $715m, assuming royalties on sales from H1 06

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**Deal Status**

- CAT and Abbott settled a dispute relating to the Humira payments in October 2005, resulting in a fixed 2.688% royalty from Abbott to CAT
- On May 15, 2006 AZ announced $1.3bn acquisition of CAT, expected to close in June
- RP submitted an unsolicited bid of $715m for the Humira royalty to AZ through Goldman Sachs, AZ’s advisor
- Goldman Sachs stated that AZ may be interested in selling the royalty after the transaction closes
- RP to meet with Goldman/AZ in London in June

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Figure 3: Sample term sheet for Humira royalty acquisition opportunity.
B Bibliography


