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Financial Innovations Lab Report

Financial Innovations for Accelerating Medical Solutions

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Milken Institute

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Financial Innovations Labs bring together researchers, policy-makers, and business, financial, and professional practitioners for a series of meetings to create market-based solutions to business and public-policy challenges. Using real and simulated case studies, Lab participants consider and design alternative capital structures and then apply appropriate financial technologies to them.

Acknowledgments

This "Financial Innovations Lab Report for Accelerating Medical Solutions" was prepared by Glenn Yago, Martha Amram, and Teresa Magula. We are grateful to all lab participants for their contributions to the ideas summarized in this report. We give special thanks to Margaret Anderson, Dr. Nir Kossovsky, Joel Kurtzman, Dr. Howard Soule and Lee Cole, founder of Inflect Technologies, for their editorial comments and support.

The Milken Institute is an independent economic think tank whose mission is to improve the lives and economic conditions of diverse populations in the U.S. and around the world by helping business and public-policy leaders identify and implement innovative ideas for creating broad-based prosperity. We put research to work with the goal of revitalizing regions and finding new ways to generate capital for people with original ideas.

We do this by focusing on *human capital* – the talent, knowledge and experience of people, and their value to organizations, economies and society; *financial capital* – innovations that allocate financial resources efficiently, especially to those who ordinarily would not have access to it, but who can best use it to build companies, create jobs and solve long-standing social and economic problems; and *social capital* – the bonds of society, including schools, health care, cultural institutions and government services, that underlie economic advancement.

By creating ways to spread the benefits of human, financial and social capital to as many people as possible – *the democratization of capital* – we hope to contribute to prosperity and freedom in all corners of the globe.

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Less than 10 percent of global investment in pharmaceutical R&D targets the diseases that may affect up to 90 percent of the world's population.

Introduction

In the fall of 2005, the Milken Institute held two Financial Innovations Labs, one in Santa Monica, Calif., and the other in New York City, to address the crisis of diminished funding for biomedical research and development, and to explore new channels for attracting capital to drug development. The rationale for the labs grew from several concerns:

- Large drug companies have seen their stock values drop and business models crumble, and have withdrawn from risky early-stage drug discovery and development.
- R&D "output" — as measured by pharmaceutical applications to the FDA, both to initiate clinical trials and market new drugs — has plummeted.
- The shortage of investment capital remains most acute at the very early stage in drug discovery R&D through Phase II clinical trials — where it is needed most and when scientific risk begins to escalate.
- Less than 10 percent of global investment in pharmaceutical R&D targets the diseases that may affect up to 90 percent of the world's population.
- In the current financial environment, good ideas with the potential to cure disease are nearly impossible to fund.

In particular, the Financial Innovation Labs hoped to identify market vehicles that could leverage private foundation resources and donations to reduce credit risk, attract investors, and accelerate commercialization in a broad range of disease areas.

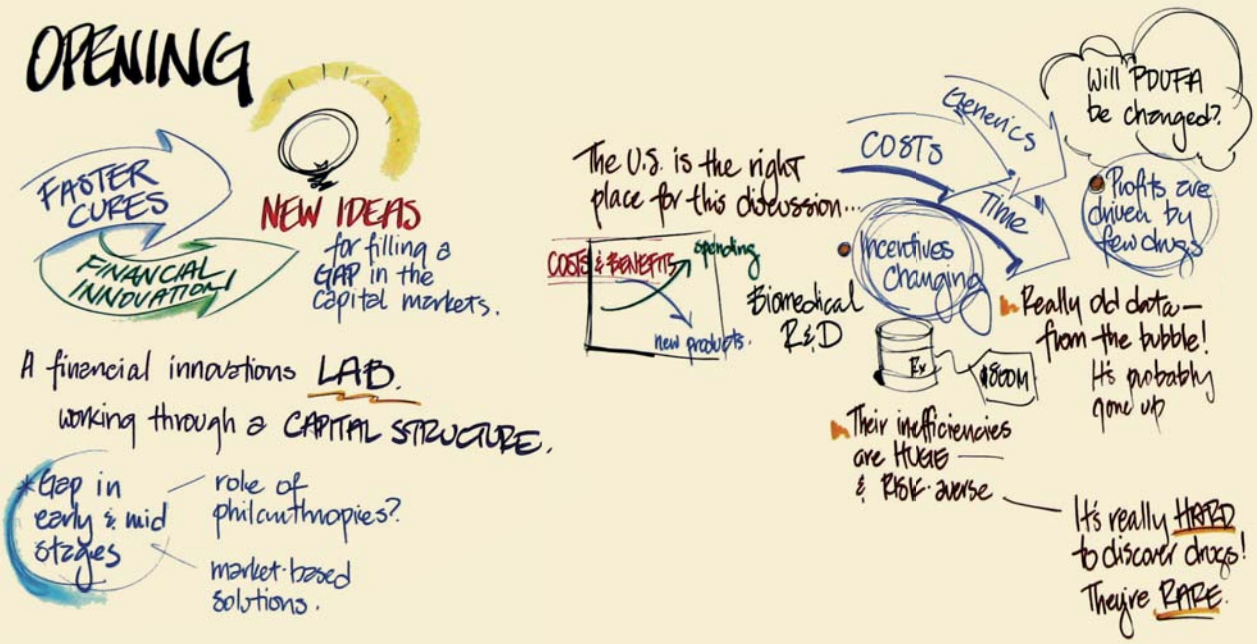
Lab participants, who attended day-long workshops and breakout panels, were representative of stakeholders in the solutions: members of foundations, patent brokers and intellectual property lawyers, private equity investors and analysts, insurance consultants, valuation and strategy consultants, biotech entrepreneurs, and academics who specialize in finance, entrepreneurship, and risk. A number of those with experience in the financial markets had no previous exposure to drug discovery issues and came away with a sense that this might be an emerging market of interest. Further, all the participants were touched by the size of the funding problem, its human consequences, and the opportunity to contribute their expertise to the solution. A list of participants can be found in Appendix 1.

The group produced innovative recommendations:

- ***Reduce scientific risk through the diversification (pooling) of intellectual property.*** This sounds like an obvious solution, but its implementation in the financial markets requires new investment vehicles. Precedent exists, for example, in the film industry, where investor syndicates finance pools of films (intellectual property). Similar vehicles could be used in the biotech industry.

- ***Use foundation funds to enhance credit quality and attract potential investors.*** A diversified pool of drugs under development for Alzheimer's disease may have only moderate scientific risk, but nonetheless too much financial risk to qualify as an investment-grade vehicle. Instead, a foundation focused on Alzheimer's could provide the financial guarantees that raise the credit quality of the pool, opening up the investment to a significantly larger group.

- ***Use directors and officers (D&O) liability insurance to enhance credit quality.*** D&O insurance covers the actions of corporate senior management and boards of directors, including actions pertaining to intellectual property and product development. For a premium increase, coverage could be expanded to cover the scientific and commercial risks of biotech product development.



Graphic recordings by Tom Benthin

- ***Tap into the emerging market for intellectual property (IP)- backed securities.*** Recent years have seen an increasing number of loans and securitization transactions for copyrights and brands. The Labs explored how these structures can be applied to patents and early-stage drug development programs.

- ***Use IP equity derivatives.*** The rise of captive intellectual property holding companies and private investment in public equity (PIPES) suggests that it would be possible to create instruments indexed to IP value, much of which is captured in enterprise value.

- ***Use donor bonds to underwrite medical research and drug delivery to under-funded patient groups.*** Just as credit card companies use future customer repayments as the collateral for borrowing, donors could sell bonds whose payments are met by future gifts. As of May 2006, eight European governments had already signed on to this promising securitization approach, issuing bonds worth $4 billion for massive immunization programs in Africa and Asia, and offering future donor pledges as collateral.

- ***Fund drug development through advanced (customer-financed) purchases.*** The industry has been moving toward this innovation in the monetization of future sales. In effect, it is the trade of upfront R&D funding in exchange for a share of future royalties. In June 2005, Great Britain took the concept further, with the announcement of plans to purchase 200 to 300 million doses of a malaria vaccine, thus ensuring a market if a vaccine is developed.

- ***Fund drug development through an equity investment by a strategic or down-stream value-chain partner.*** This is a common practice of later-stage biotech firms that partner with large pharmaceutical companies, and involves the trade of upfront R&D funding in exchange for a share of future royalties or other economic interest.

The Financial Innovations Lab generated three action plan proposals.

Proposal No. 1

Develop a case study around one or more of the recommendations. Participants would identify specific incentives and problems, and design an implementation plan. The case study would conclude with a one-day session for potential "transaction partners," who would determine funding feasibility.

Proposal No. 2

Create a simulated diversified pool of patents and/or early-stage drugs under development for a single disease area. Analysts and experts from ratings agencies, as well as representatives from interested foundations, would provide a detailed review of risks and opportunities.

Proposal No. 3

Use a real, rather than simulated, pool of patents and/or early-stage drugs for which there exist both market need and philanthropic foundation support. Lab participants representing pharmaceutical and biotechnology companies, institution-al investors, medical foundations, rating agencies, and government health agencies would then utilize one or more of the recommended financing solutions to earn the patent portfolio an investment-grade rating through the mitigation of credit, basis, and performance risk.

"We should expect to see new markets develop between large pharma and smaller biotechs. But the emergence of these markets has been stubbornly slow."

Jerry Cacciotti

Managing Director, Strategic Decisions Group

PART I:

ISSUES & PERSPECTIVE

The Funding Challenge: Across the Spectrum

It is a sad irony of our time that while immense potential exists to cure disease, customize treatment, and improve global health standards, both public and private funding for biomedical research are in decline.

As figure 1 on the following page illustrates, for the period 1993 through 2003, research funding by the National Institutes of Health (NIH), and research and development (R&D) spending by large pharmaceutical companies, rose dramatically. The annual rate of patenting for medical discoveries rose even faster. But during the same period, applications to the FDA to initiate clinical trials plunged, as did key output: the number of applications for FDA marketing approval.

Since 2004, NIH research funding has remained static or decreased, based on adjusted dollars. In fact, the most recent budget cut of 2006 is steep enough to bring NIH R&D below the 2003 funding level in real terms, erasing the increases of previous years.[1] And our most productive engines of innovation to date, the large pharmaceutical companies, have come under increasing competitive and financial pressures, and have pulled back from early-stage discovery and development.

As shown in figure 2, a decade or more ago, the pharmaceutical giants worked within fully integrated business models (i.e., from development to final product commercialization) that led to significant value creation. Between 1985 and 2000, for example, their market value increased 85-fold, far outpacing the stock market as a whole. Yet since 2000, despite still impressive profit margins, pharmaceutical companies have generated much less value and have seen their integrated business models fall into disarray.

Promising discoveries in cancer and other human disease areas languish for lack of capital resources and development expertise, and developed products fail as a result of inadequate access to marketing platforms. Industry trends, however, may not favor easy solutions. The average cost of bringing a new drug through development, clinical trials, and market launch has risen sharply, more than 7 percent per year for the past 15 years, and is reportedly more than $800 million today. And market launch is no guarantee of success: of products that reach the market, 70 percent fail to recoup their R&D investments.

Generic drugs, a major source of competition, hold an increasing share of the market — currently around half — and continue to draw profits away from large pharmaceuticals, despite laws providing limited extension of patent life. The high-profile drugs launched in 1965 could expect to thrive in the marketplace for ten to twelve years without competition. By 1985, this had shrunk to five years, and the high-profile drugs launched after 1995 have faced immediate competition, sometimes within the same year. When a high-profile drug debuts against another high-profile drug, large pharmaceutical companies cannot recoup their investments. With these discouraging trends, it is no surprise that a solution that accelerates medical innovation has not emerged from the industry.

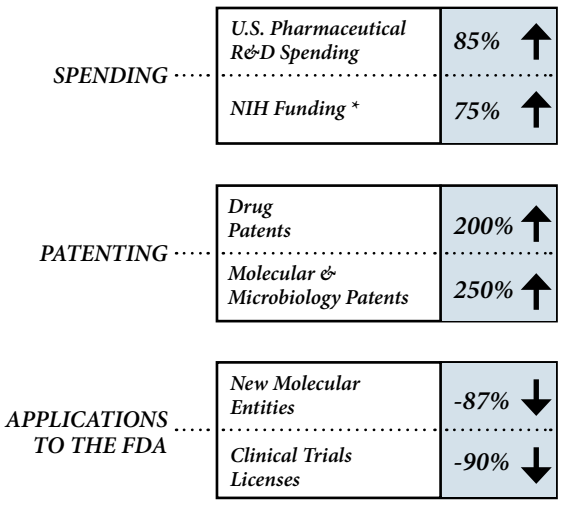
In addition, financing for the biotech industry in general has diminished for early, innovative projects. There is nearly no venture capital available for innovative ideas that lack significant clinical data. This risk capital seeks to mitigate risk at all stages, especially at the very early stages that could represent blockbuster ideas. One of the Financial Innovation Lab participants, Joe Daniele, Chief Operating Officer of Acorn Technologies, has completed more than 350 patent and intellectual

"The mission of FasterCures is to clear the path between an idea for treatment and getting a treatment to the patient."

Greg Simon
President
FasterCures

FIGURE 1

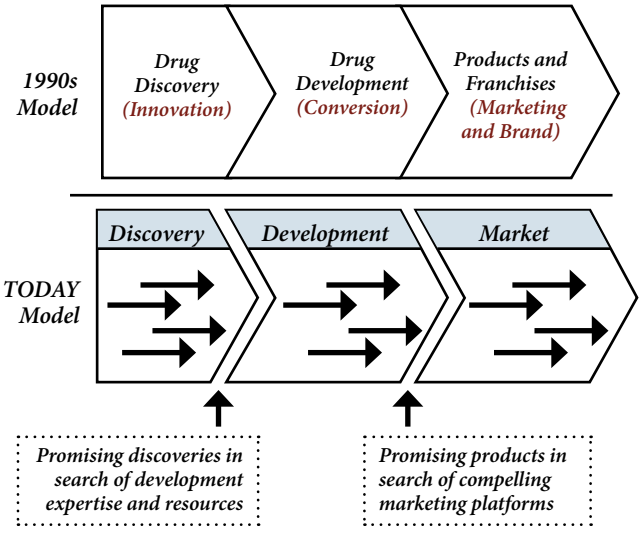
Drug Development, 1993-2003: Increased Spending and Patenting, But Fewer New Drugs



*Since 2004, NIH research funding has remained static or decreased, based on adjusted dollars.
Source: Compiled from Yago/Phillipson presentation

FIGURE 2

The Integrated Business Model of Large Pharma Is Under Pressure



Source: Jerry Cacciotti, SDG

property deals during his career. He currently has rights to key discoveries for epilepsy, complete with positive early-stage results. "But finding a buyer for these discoveries has been nearly impossible," he said. "The pharmaceutical industry is the most difficult I've faced."

Finally, looking more broadly across the negative trend, many are dismayed with the current allocations of health care investment: less than 10 percent of global investment in pharmaceutical R&D is devoted to diseases of poverty, such as malaria, AIDS, and tuberculosis, which may affect up to 90 percent of the world. Instead, pressure to turn a profit means that pharmaceutical companies turn to drug development for "lifestyle" and "Western" diseases.

From the small startup in a VC squeeze to the corporate behemoth under pressure from shareholders and regulators, the biotech industry is undergoing a painful shakeup that could impede, if not derail, the advancement of treatments and cures. This is what the Labs sought to explore, asking such questions as:

- What issues confront corporations acquiring the key output of risky early-stage discovery and development — the number of applications to the FDA to market new drugs?
- How does the widespread dissemination of IP rights increase the risk associated with early-stage discovery and development?
- How can IP be grouped, mobilized, and protected to advance medical solutions to chronic and infectious diseases?
- Can we identify infectious and chronic disease groups for which there are promising therapies and technologies (biologics, pharmaceuticals, devices, and health care) that have not yet produced clinically acceptable results?
- What are the risks going forward in these therapeutic areas, and how do they vary (by frequency, incidence, duration, costs of disease and clinical trials)?
- How can these risks be mitigated using structured finance tools that enable those risks to be valued, priced, and sold?
- Are there dynamics in research, discovery, development, and commercialization that allow the value chain to be financed in separate stages?

The R&D Process

Phase I

Phase I is the first time the drug is tested on humans. Usually between 20 and 80 normal, healthy human volunteers take the drug to test it for toxicity (negative side effects) and its effect on people of different races.

Phase II

Phase II is still a pilot stage. But the volunteers this time are people who suffer from the disease the drug aims to help. About 100 to 300 patients are involved, and the trial can last up to two years. This phase is used to determine the drug's therapeutic effects and the dosage required. It provides the preliminary data needed to prepare for the larger, Phase III trials.

Phase III

Phase III is the main clinical trial, usually involving between 1,000 and 3,000 patients. The trial tests for both therapeutic effects and adverse reactions. If there are established drugs for the disease, the new drug is tested against the best on the market. If there is no existing drug, the new drug is tested against a placebo. One group of patients will be given the new drug; another will get either a placebo or an established drug.

Phase IV

Phase IV is carried out after the drug has been registered with the FDA. The trial is conducted to allow local doctors to become familiar with the drug and to gain their trust.

The Financial Innovation Labs

The vision that financial incentives and resources can accelerate medical research was demonstrated by the Prostate Cancer Foundation (formerly CaPCure), founded by Michael Milken in 1993 to fund the discovery of better treatments and a cure for advanced prostate cancer. The foundation's investments in laboratory and clinical science have accelerated research, raised awareness of the disease, and helped to bring commercial and NIH interest to the area. Based on the success of this first effort for prostate cancer, the Milken Institute founded *FasterCures*, a nonprofit organization focused on facilitating medical R&D for all major human diseases.

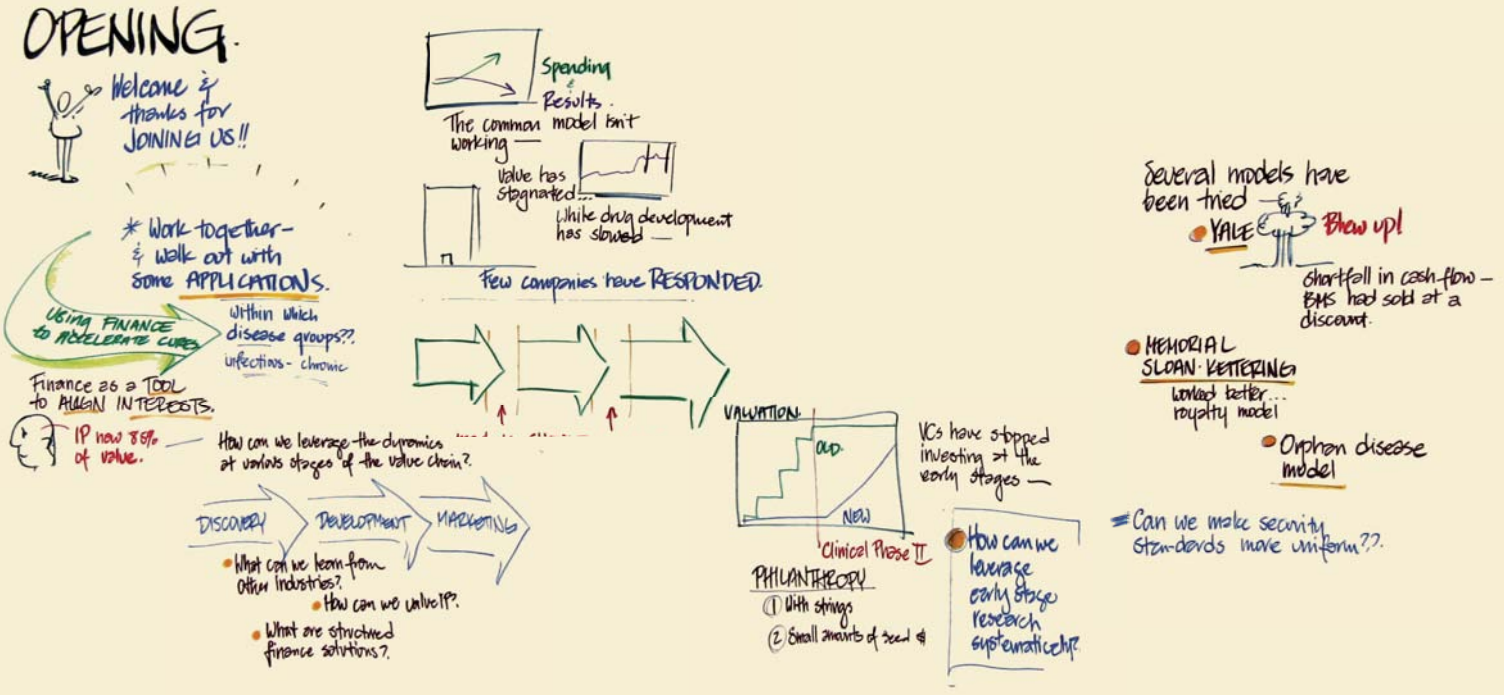
Many participants hoped to leverage the resources of nonprofit foundations. The Bill and Melinda Gates Foundation, for example, has demonstrated that private resources can catalyze public funds to better address the diseases of poverty, such as work in AIDS, tuberculosis, and malaria. And organizations like the Prostate Cancer Foundation have shown that foundations focused on a single disease can make a big difference in the lives of many Americans who suffer from that disease.

Over the course of the two labs, the groups found answers to the following questions:

- Where are the funding inadequacies in the drug development industry?
- How can foundation investments be leveraged?
- What are examples of successes and failures?
- What are some lessons from other industries?
- What types of financial innovations might help close the funding gap?

"Is there a way to take the interest of various foundations and mix it up with financial structures that might generate interest in capital markets?"

Glenn Yago
Director of Capital Studies
Milken Institute

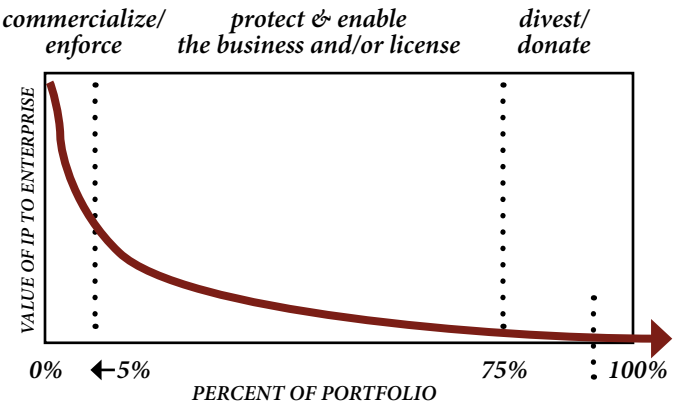


Risks, Valuation and Markets

Potential solutions to the problems of drug development and funding can be coupled to the process of IP protection. Several Lab sessions presented context and facts for the value and management of IP.

FIGURE 3

Only a Few Items Are Valuable in an Intellectual Property Portfolio

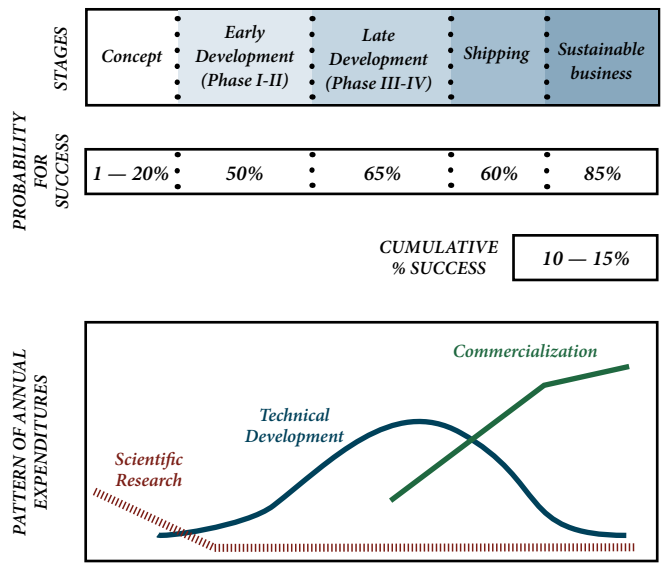


Source: Joe Daniele, Acorn Technology

Figure 3 illustrates a typical risk pattern of biotech patent portfolios. In general, only about 5 percent of the innovations hold commercialization value. And many types of intellectual property — e.g., copyright royalties, the value of patents, the value of drug compounds — have a log-normal distribution of returns, according to a number of studies (these are addressed in more detail in the literature review in Appendix 2, which notes findings from recent pertinent recent studies). Thus, it is fair to conclude that a large portfolio of early-stage opportunities will increase confidence that any single project may yield commercial value.

FIGURE 4

Innovation: After the Science Is Completed, Large Risks Remain



Source: Martha Amram, Growth Options Insights

Risks remain throughout the development and commercialization process. The top panel of figure 4 depicts the probability for success at each stage of development and commercialization. As presented in this figure, the probability is perhaps 15 percent that an innovation will translate into a commercially successful product. With the escalating price tag of drug development, it is not difficult to understand the origins of risk-aversion.

The bottom panel of figure 4 charts the cost estimates for development and commercialization of a new pharmaceutical product. As the proof-of-concept stage is completed and scientific research is concluded, the cost of discovery escalates during development. At the shipping stage, when the product approaches market, the cost is great and risk is never completely mitigated. Because risks are not successfully mitigated, small companies with innovative science have little chance to succeed if their objective is to integrate functionality from discovery research to commercialization. There is little chance of funding in the later stages.

And there is a ripple effect: Why would investors put money in the early stages of development if they believe there is no chance of funding in the later stages? The risks of investing in the early development stages are too large due to unmitigated risks. As

such, the availability of early-stage capital (Phases I and II) depends on the risk of funding late development (Phases III and IV).

As depicted in figure 5, after an 85-fold increase in the pharmaceutical industry's market cap between 1986 and 2000, there has been essentially no net value creation in five years. Regulatory safety scrutiny will continue as a result of recent, highly publicized problems (e.g., Prozac, BioVex, Vioxx), as will pricing pressures from generic competition and tougher negotiations from federal, state, and private entities on group drug plans. Though industry investment has increased, it is being channeled into fewer products and their associated intellectual assets, with diminished prospects for return.

Figure 6 shows company valuations at different stages of the drug discovery process and illustrates the significant differences that have emerged from the traditional financing model that has dominated since 2000. Under the traditional model, depicted by the solid blue line, investment in pharmaceutical R&D occurred over the life-cycle of drug development. Investments, mainly in the form of venture capital, propelled new technology and business savvy. Slow, often negative returns, however, discouraged investment often until after Clinical Phase II.

The ability to source risk capital from private equity, corporate, and later, public markets has declined markedly under the new model of drug development funding, noted by the dotted line. Additionally, pressures on returns include the cost of starting new research processes, which some large pharmaceuticals bypass with mergers and acquisitions, by funding early-stage research in smaller companies, or funding research at universities and other scientific research institutes.

FIGURE 5

Conventional Pharmaceutical Model Coming Under Pressure

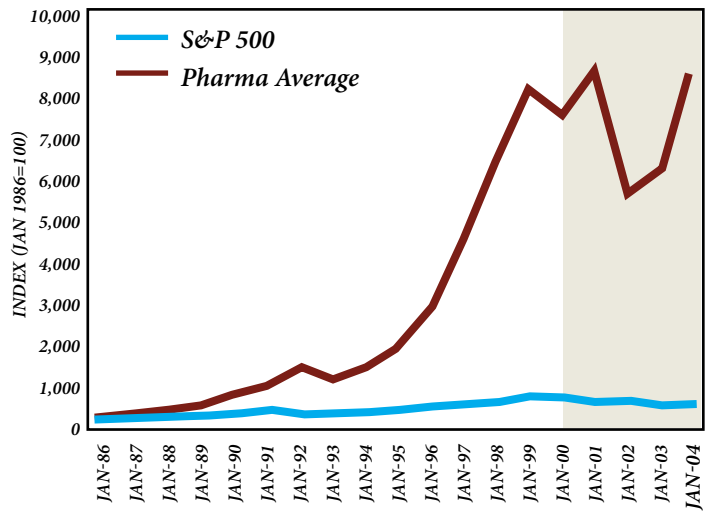
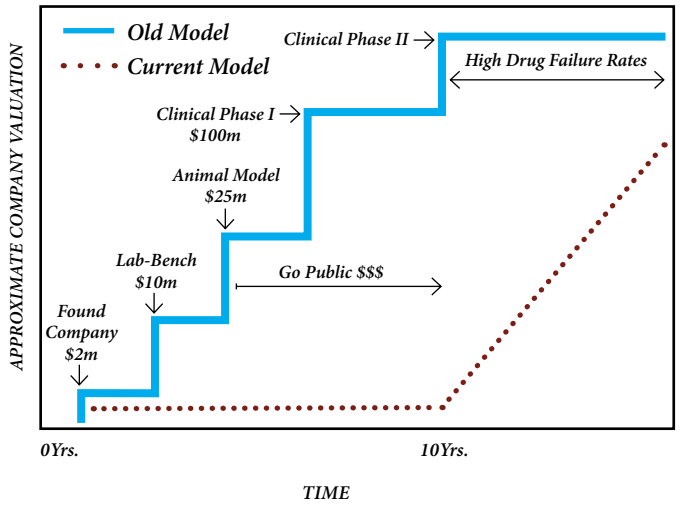


FIGURE 6

Approximate Valuations at Key Milestones in Drug Discovery Timeline Model



The cost and risk associated with developing a new medication escalate dramatically as soon as the drug candidate reaches clinical trial phase. The cost varies according to scientific complexity, but a general cost structure follows.

Stage of Product Development	Approximate Cost (millions)
Discovery - preclinical validation	$5 - $25
Phase I	$2 - $12
Phase II	$8 - $30
Phase III	$75 - $250+

"In the California model, you take great work from UC Berkeley, form a company, get venture capital, do an IPO, and grow up to be Genentech. That model is dead."

Martha Amram
Founder/Managing Partner
Growth Options Insights

The funding crisis occurs at the point of transition from preclinical to clinical stage development. Very few sources of funding are available to support early-stage work. In fact, most will not invest until the drug candidate has been exposed to humans in Phase I safety trials. Others will wait until the results of rigorous Phase II trials demonstrate efficacy. While this strategy has been fairly effective in mitigation of risk, it has had a stifling effect on innovation.

Lab participants shared examples of this funding gap in their own industries, and Martha Amram, Co-founder of Growth Options Insights, detailed some recent examples of alternative financing: [2]

- A number of private and private/university collaborations have emerged to fund preclinical and Phase I trials. These entities are designed to take projects out of the university lab and begin early commercialization. They put in on average about $2 million in equity for each venture they fund. But the problem with their business model is that they need to attract outside investors or partners for the more expensive Phase II funding.

- Symphony Capital is a hands-on private equity firm in New York City that not only funds biotech research but also, through partnership with RRD International, manages the development process, from preclinical and regulatory phases through manufacturing.

The most natural analogy with past innovations in the financial markets comes from the corporate bond market and later variations in other segments of corporate capital structure. At one time, no one would invest in below-investment-grade debt. But given a transparent valuation model (where the attributes of value and risk became clear to all) and market liquidity, investors were willing to take on the risk and flocked to the new market segment. The odds hadn't suddenly changed, but transparency made those odds understandable, while increased liquidity enabled investors to share the risk with others.

Similarly, the options markets soared after the introduction of the Black-Scholes option-pricing model, which allows investors to calculate risks and returns. Once investors could identify risks and returns, they could calibrate option prices against other traded securities. Another example is described by the author Michael Lewis in *Moneyball*: a systematic approach to valuing a ballplayer's talents relative to his contribution to the team provided the Oakland A's with repeated success. The idea now affects the pricing of player contracts in the national market.

In each example, a market gap was closed by the combination of transparent valuation models and market liquidity. In the pharmaceutical industry, transparent valuation models should be able to play an important role in closing the Phase II funding gap for drug discovery, particularly as those models could help attract new sources of funding.

Lessons from the Film Industry

Film production and drug development are both expensive, high-risk endeavors that rely on innovation. Amram and Laura Martin, a media analyst with Soleil/Media Metrics, presented the Lab with a breakdown of a film's value as it passes through various stages of production. The film industry, they said, has had to address similar questions: How and why did large film studios, once full-service providers, come to focus on the value-chain terminus? And what financial structures have evolved to finance risky early-stage projects?

The transparent valuation model makes it easy to see similarities between drug development and film production, both of which comprise multiple-stage processes.

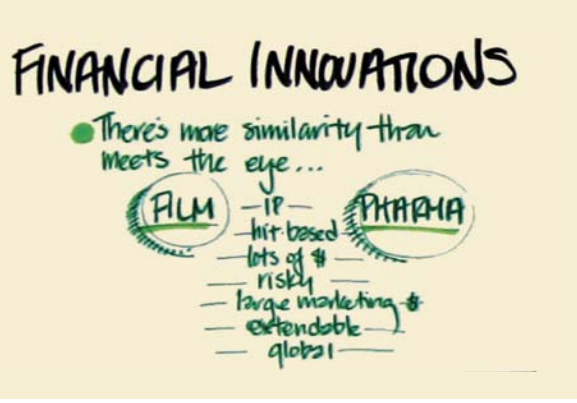


Figure 7 shows the costs and value of film production. The process begins with script development, which takes about $2 million and two years. Only 10 percent of scripts actually enter production; most are abandoned. Production costs are the major expense, running more than $55 million over 1.5 years. During that period, a studio will likely receive no new information about market size or consumer tastes. Thus, with no bad news to prevent development, most films complete production.

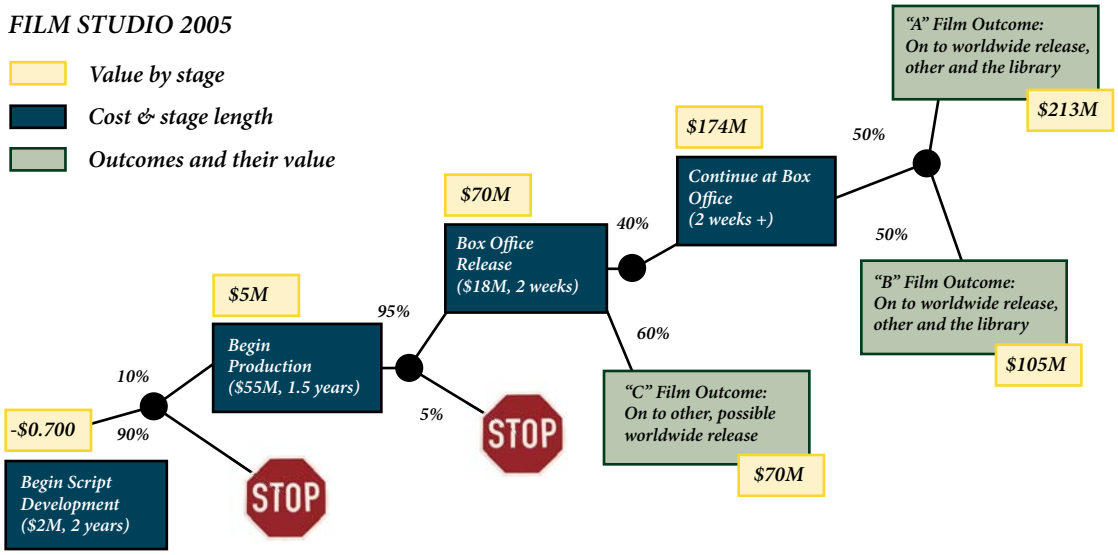
The initial advertising budget is spent in a one- to two-week window prior to a film's release nationwide. Based on the box-office results, studio executives will then either take the film out of release or spend more advertising dollars.

The yellow boxes at each stage in figure 7 indicate the changing value of the film. These amounts are found by folding back the value from the end outcomes, adjusting for risk, and discounting for time. Early in the production process, the value is low because the film is years away from distribution and faces major risks. The value rises over time as risks are resolved and the release date nears. While 2005 was considered a strong year — more films than usual recovered their costs — the valuation model shows that film production is typically a break-even project at best. Similar results are also seen in the rise of the independent and lower-budget films, such as *Brokeback Mountain*, *Capote*, and others that did well at the 2005 Academy Awards.

Both drug development and film production use the same "stage-gate" (expected value) valuation model, in which value increases as risk is resolved and the film is closer to returning revenues. In addition, both industries have a skewed value distribution, with a few immensely valuable outcomes and many outcomes of small or no value. More than 40 percent of films did not recover their costs at the box office in 2004, a success rate that is similar to biotechnology's.

FIGURE 7

Films: Valuation by Stage



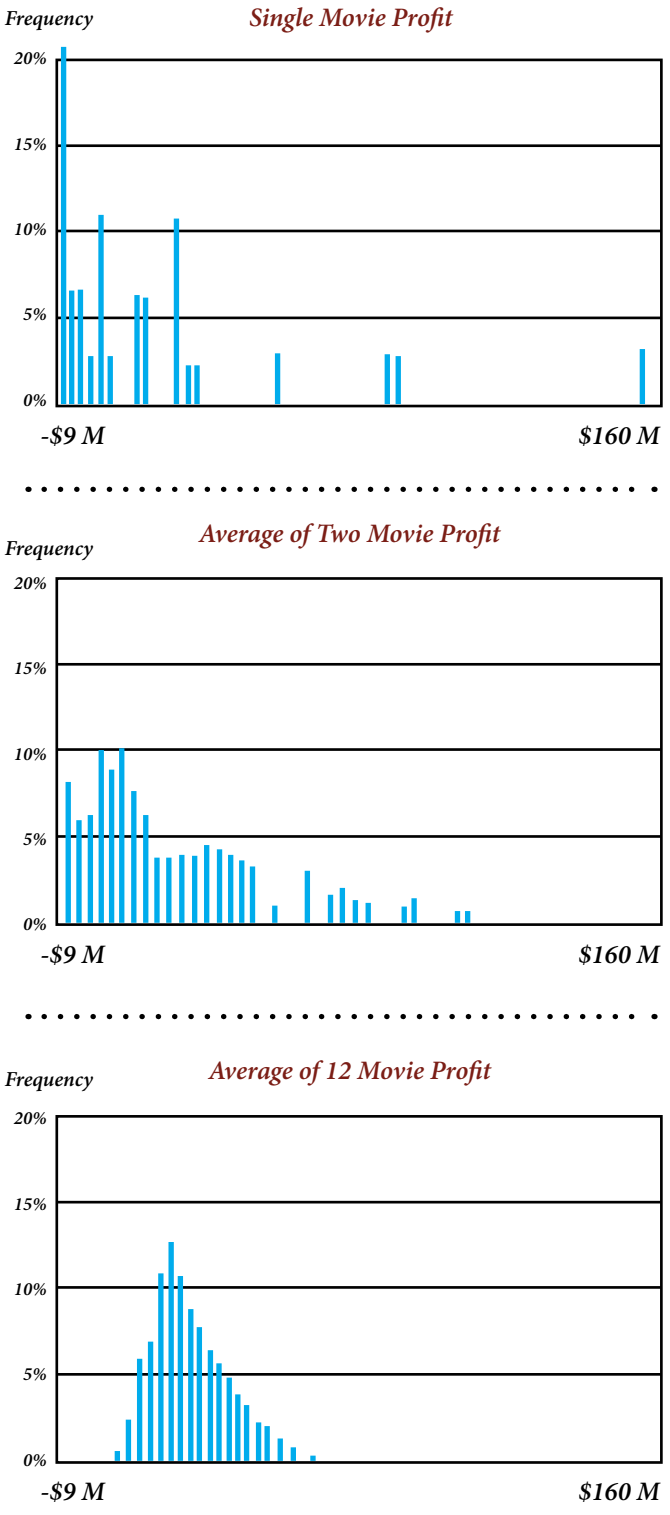
The analogy continues to the portfolio level. Work by the Los Angeles-based media consulting firm Cineval and Sam Savage, a professor at Stanford University, shows that as the studio's portfolio grows, the returns become more predictable.[3] This is illustrated in figure 8. With only a few films, the portfolio carries greater risk, as individual films may prove to be huge hits or dismal failures. More films in the portfolio mean a smoother distribution of returns, creating increased confidence among investors. Lab participants, particularly those from the asset-backed securities industry and credit-rating agencies, saw the portfolio's risk-reward trade-off as more attractive than that of individual drug prospects.

Martin also discussed the financing of films through risk-sharing mechanisms. Two current methods feature subsidization across the operating divisions of a media conglomerate (such as Disney/ABC/ESPN); and syndication across studios (for example, the Paramount and Dreamworks split of *War of the Worlds*).

A third method is for outside financiers to securitize a portfolio of films, as did Silver Screen Partners, which operated in the mid-1980s. The first Silver Screen partnership, a $100 million fund marketed by EF Hutton to retail investors, was introduced in 1983 and underwrote films shown on HBO. A second fund, raised less than two years later, invested $75 million in such Disney films as *The Color of Money* and *Down and Out in Beverly Hills*, and gave investors a 10 percent return. A third fund soon followed, with a 12.3 percent return on *Good Morning Vietnam* and other notable films. The fourth Silver Screen Partners fund raised $400 million in 1988 for Disney and funded *Pretty Woman*, *The Little Mermaid* and others, but returned only 3 percent to investors. There was no fifth Silver Screen fund: With such low returns, no one wanted to invest. Individual investors were in part attracted by the glamour of investing in films, said Martin, but ultimately, they were investors and required competitive returns.

FIGURE 8

A Larger Pool of Films Provides Greater Confidence



Source: Cineval, LLC and Dr. Sam Savage, Stanford University

"Does biotech have the same cachet as the Academy Awards? Well, you're saving lives, so you can go to a cocktail party and chat up your investment. But in terms of glamour to the retail investor, [biotech] still needs work."

Laura Martin
Media equity analyst
Soleil/Media Metrics

Today JP Morgan is the lead investment banker for film syndication, reportedly holding 80 percent of the market.[4] John Miller, head of the firm's entertainment group, has twenty-five years' experience with this kind of financing, said Martin. Instead of financing a single film, he backs studio slates, packages of five to fifteen films, because his quantitative models predict that only three out of ten films will do well, and that one out of ten will hit the jackpot — results that are very similar to those of drug development. JP Morgan places most of the film financings with a syndicate of banks and currently has $7.5 billion in loan commitments outstanding, $1.3 billion of which it is financing.

Martin noted that Silver Screen Partners fell victim to a common pattern in new and fragmented markets: as long as its funds delivered satisfactory returns, successive funds were created. But as soon as the experiment floundered, investor dollars dried up. If the initial financial innovation doesn't work, she warned, there won't be a second chance. And success for the financial innovation will need to be earned profit by profit — there is no quick fix that provides a robust solution.

Innovative Financing

Much of the focus for financial solutions was on securitization, a financial instrument strongly supported by Milken Institute research and defined as the pooling of assets that can be sold as a security (or some other means of structured finance). If there is a way, for example, to estimate the value of royalties over time from a portfolio of patents relevant to a particular disease group or medical problem, then the portfolio could be turned into a marketable security, which would in turn provide capital to accelerate research.

Participants also discussed how insurance companies and foundations might help bridge the financing gap. Providing loan-loss guarantees would require a fundamental shift in the thinking of foundations, many agreed. Designing capital structures with credit enhancement, advanced sales, and other financial, marketing, or business strategies that align interests of foundations, investors, patients, governments, and businesses would also close the early-stage funding gap. Six possible solutions, as well as an examination of past successes and failures, will be discussed in Part Two.

During the second Lab, held in New York, Peter Walsh, a Managing Director and co-head of origination and structuring at Harris Nesbitt's securitization group, listed the range of professional expertise necessary to issue a security, backed by intellectual property:

- investment bankers to provide underwriting, security placement, and funding
- securities lawyers
- valuation experts
- rating agencies
- credit enhancers such as insurance companies
- investors

The investors themselves constitute a diverse group:

- insurance companies
- pension funds
- hedge funds
- private equity
- investment banks

Those involved in transactions related to the drug discovery process would also include:

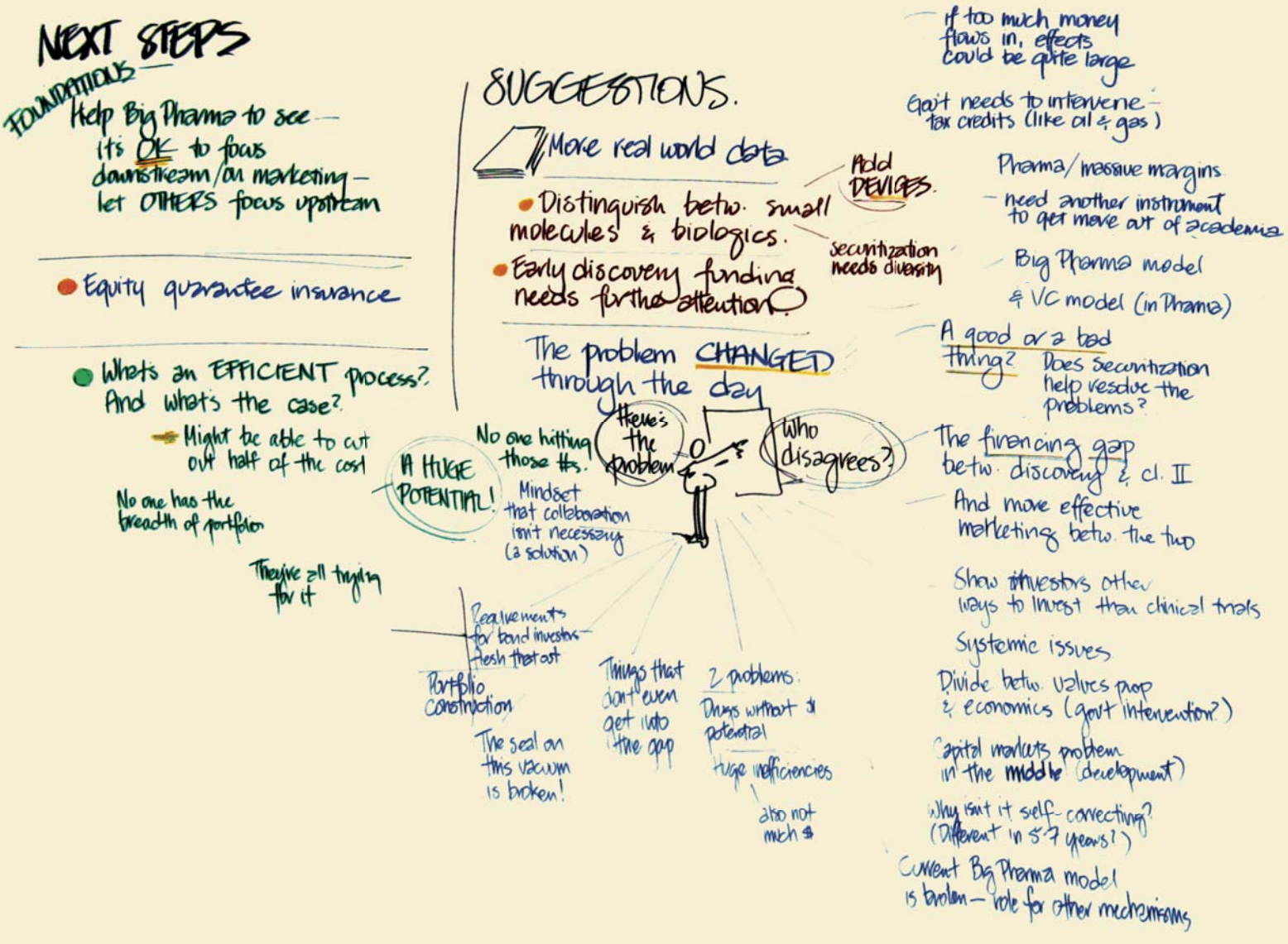
- patent attorneys with expertise in the life sciences
- medical experts to assess scientific methods, risks, and implications
- pharmaceutical industry experts to assess the prospects for commercialization and expected royalties
- foundations with an interest in providing funding and/or credit guarantees

Getting the necessary and interested parties into the same room would no doubt prove challenging, even daunting. Yet face-to-face contact among such a large and diverse group would likely accelerate a transaction.

One plan would bring together four types of participants: the party holding intellectual property or early-stage prospects; one or more interested foundations; potential investors; and an experienced attorney or business intermediary. In a day long session they would explore a potential transaction. The attorney or business intermediary would provide some structure and a set of norms for those pursuing a deal. A study of the process would explore such questions as: What are the stumbling blocks? Where are the points of contention? Who is not in the room that should be? Can the transaction structure be replicated? Will the transaction structure provide an acceleration to cure, and how can this benefit be measured?

A second plan calls for the preparation of a simulated, diversified pool of patents and/or early-stage drugs for a single disease area. Participants would be taken through a detailed review with a ratings agency and an interested foundation(s). The ratings agency would be able to pinpoint credit weaknesses, and the parties could restructure the original transaction in real time to eliminate the problems. Again, the goal is to provide potential players with the ability to identify incentives and stumbling blocks.

A third, and arguably the most aggressive alternative, is to try to incorporate a plurality of solutions (listed in the following section) to an actual pool of patents. Once basis, performance, and credit risk have been mitigated, the Lab participants would present the package to the rating agencies and, if successful, to investment bankers for placement.


NEXT STEPS
FOUNDATIONS
Help Big Pharma to see — it's OK to focus downstream/on marketing — let OTHERS focus upstream
Equity guarantee insurance
What's an EFFICIENT process? And what's the case?
Might be able to cut out half of the cost
No one has the breadth of portfolio
They're all trying for it
SUGGESTIONS.
More real world data
Distinguish betw. small molecules & biologics.
Early discovery funding needs further attention
Add DEVICES.
securitization needs diversity
The problem CHANGED through the day
There's the problem
Who disagrees?
A HUGE POTENTIAL!
No one hitting those #s.
Mindset that collaboration isn't necessary (a solution)
Realignments for bond investors — flesh that out
Portfolio construction
The seal on this vacuum is broken!
Things that don't even get into the gap
2 problems
Drugs without a potential
huge inefficiencies
also not much $
If too much money flows in, effects could be quite large
Gov't needs to intervene — tax credits (like oil & gas)
Pharma/massive margins
need another instrument to get more out of academia
Big Pharma model & VC model (in Pharma)
A good or a bad thing?
Does securitization help resolve the problems?
The financing gap betw. discovery & cl. II
And more effective marketing betw. the two
Show investors other ways to invest than clinical trials
Systemic issues
Divide betw. values prop & economics (gov't intervention?)
Capital markets problem in the middle (development)
Why isn't it self-correcting? (Different in 5-7 years?)
Current Big Pharma model is broken — role for other mechanisms

Foundations tend to limit their financial participation in drug development to funding initial research or giving reimbursable grants with the expectation of a return from royalties on potential sales.

PART II:

FINANCIAL INNOVATIONS FOR ACCELERATING MEDICAL SOLUTIONS

Possible Solutions

SOLUTION 1 — *Reduce the scientific risk through the diversification (pooling) of intellectual property*

The notion of bundling patents or early-stage drug prospects to remove risk through diversification has been cited in numerous academic studies (see Appendix 2). Early attempts were made to monetize drug development opportunities by exchanging future royalties from the patent pool for an up-front sum. But as with many complex and pioneering efforts, the details matter, and not all the early transactions were successful.

Peter Walsh of Harris Nesbitt identified four early transactions that pooled two to twenty-three medical solutions:

- **BioPharma Royalty Trust (2000):** In conjunction with Royalty Pharma AG and BancBoston Capital, Yale University agreed to pay royalties on an HIV-AIDS drug discovered at Yale to Bristol-Meyers Squibb in exchange for $79 million.

- **Royalty Pharma (2003):** Memorial Sloan-Kettering Cancer Center in New York City agreed to pay royalties to Royalty Pharma AG on two drugs used during chemotherapy treatments in exchange for $225 million.

- **Royalty Securitization Trust I (2004):** Royalties from twenty-three biopharmaceutical products, medical devices, and diagnostics from nineteen companies were securitized for $228 million. The Paul Royalty Fund had invested in the young companies and then exchanged a portion of its royalty rights for an up-front payment.

- **Drug Royalty LLC (2005):** The royalties from eight drugs that had been in the market an average of seven years were collateralized for $68.5 million. The drugs were owned by a subsidiary of Drug Royalty LLC.

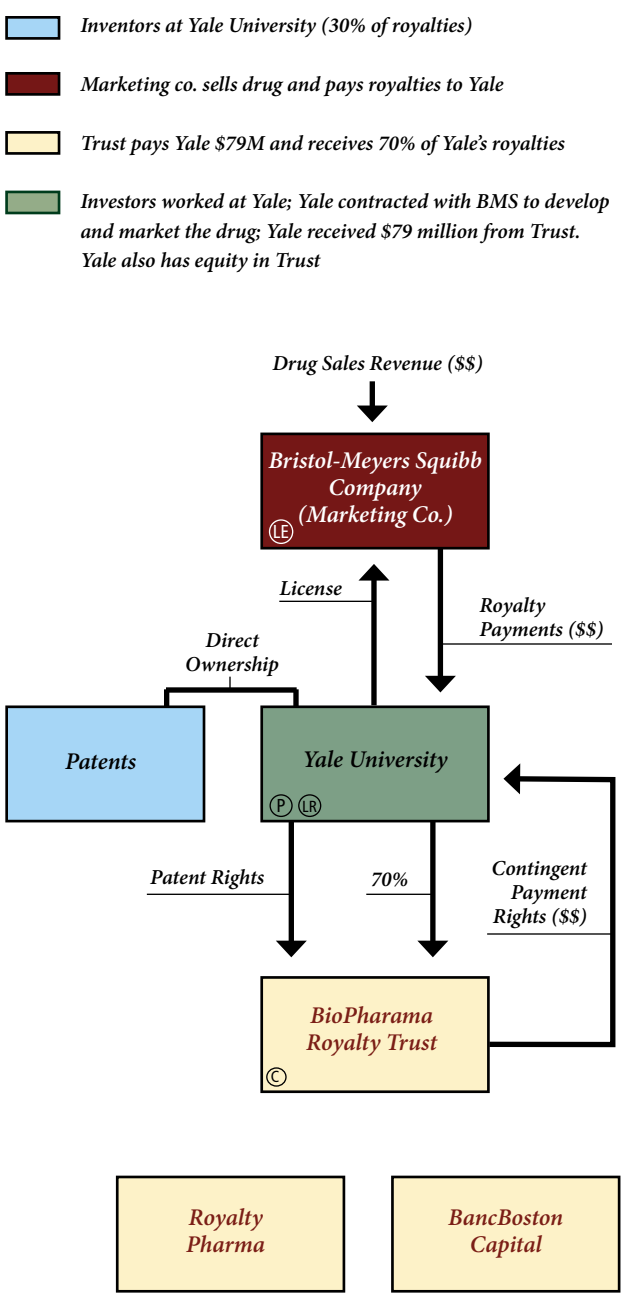
Each transaction required a rating by Standard & Poor's and/or Moody's; the ratings ranged from AAA to BB. Two of the deals also had credit insurance.

To better understand the delicate balance of the risk-reward trade-off, it useful to walk through the Yale University deal. Figure 9 depicts the transaction structure. In 1985, Yale University received a patent for a novel discovery for the treatment of HIV-AIDS. The university then granted an exclusive license to Bristol-Meyers Squibb to develop the drug Zerit. In 1994, Zerit received FDA approval. In 2000, a private company, BioPharma Royalty Trust, agreed to purchase Yale's royalty stream for Zerit. A trust was created to fund the purchase payment. Yale University, Royalty Pharma, and BancBoston participated in the trust. When the deal closed, Yale received a cash payment and equity in the trust.

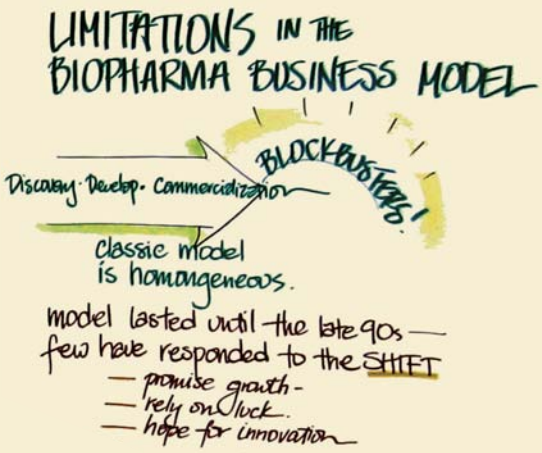
Each quarter, the trust was to receive a payment from Bristol-Meyers Squibb and, in turn, to redirect 30 percent of the payment to the inventors, per university policy. The remainder was to be used to service the loan payments, and the surplus distributed to the equity partners.

Yale University received $79 million from the trust and used the funds to finance a new classroom and research complex at Yale Medical School. The senior debt in the transaction was rated A by Standard & Poor's, and subordinated debt was rated AA, after a credit enhancement by a reinsurance company.

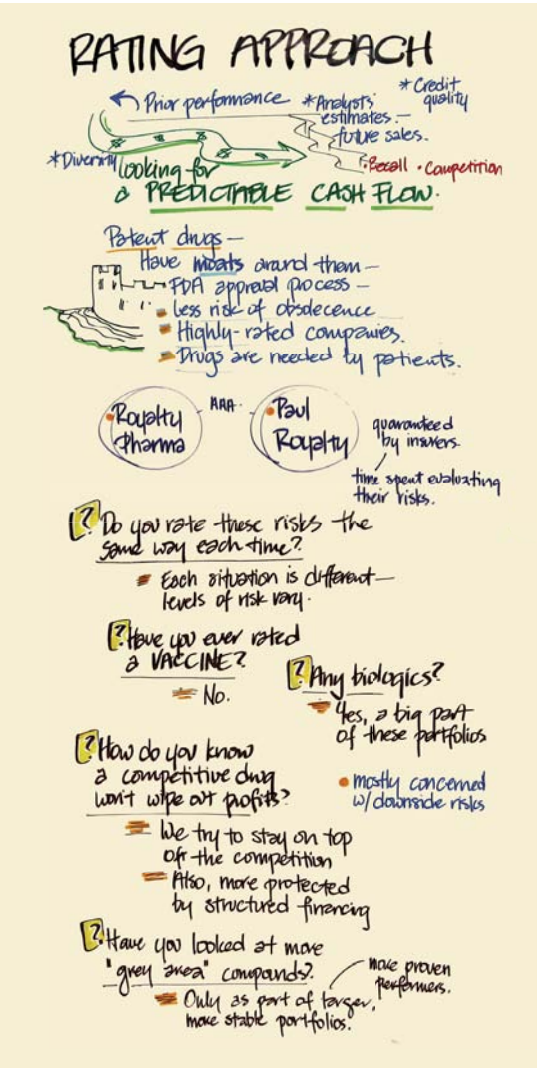
FIGURE 9 *Transaction Structure of Yale University's Royalty Monetization*



Source: Royalty Pharma



Only two years later, in 2002, the trust began an early write-down, or amortization. The trust had breached its loan covenants due to lower than expected sales for Zerit. Payment to Yale University continued however, as there was a $22 million line of insurance on the trust.



In retrospect, those close to the deal believed that three significant issues weakened the transaction structure. First was over-reliance on a single drug for the trust's revenues. Second were over-inflated estimates for sales of Zerit. While Wall Street analysts had forecast Zerit sales to within 2 percent of actual sales in 1999 and 2000, they were overly optimistic thereafter, with forecasts that exceeded actual sales by 50 percent to 200 percent. Many believe that Royalty Pharma relied too heavily on the analysts' estimates. Finally, during the second half of 2001, Bristol Meyers-Squibb sold its entire inventory of Zerit at a discount to wholesalers, possibly to meet corporate financial goals. Sales of Zerit stalled thereafter. The trust's language did not distinguish between shipments to wholesalers and sales in the market, and thus the trust was surprised by the turn of events.

The Yale transaction was the earliest of the four, and the least diversified. But the financial players quickly became more sophisticated in their scrutiny of such transactions.

In 2003, Royalty Pharma closed another transaction, with New York's Memorial Sloan-Kettering Cancer Center that monetized drug royalties; in its press release, Royalty Pharma listed the strengths of the transaction structure, clearly demonstrating what it had learned from the Yale experience: royalties from nine proven drugs were included in the transaction, as were four additional drugs in the late stages of the FDA approval process. }It also detailed the historically strong sales for each drug and the financial enhancements in the trust framework, and noted that the legal structure of the agreement had been strengthened.

Further, Royalty Pharma described its revenue projections in explicit detail: "Modeling future royalty revenues involved an examination of the current patient populations and penetrations rates, related growth and mortality rates, current and expected future dosage levels, and current and future cost per dosage expectations over the term of the transaction. Future royalty revenues were stressed based on each of the above factors and then discounted to determine a net present value for each royalty asset." Valuations were further constrained to limit borrowings in the transaction.

Moody's rated this transaction AAA, which is not surprising, given the rating criteria. According to Jay Eisbruck, the Team Managing Director for Moody's Asset-Backed Finance Group, the criteria include:

- sales performance history of the drugs in the pool
- diversity in product application
- credit quality of the royalty licensees
- the risk of an FDA recall

Solution 2

Use foundation funds to enhance credit quality and attract potential investors

Foundations tend to limit their financial participation in drug development either to providing some funding (though small amounts) to initial research or to giving reimbursable grants with the expectation of a return from royalties on potential sales. In either case, the foundations hope their early commitment will spur follow-on funding from other investors.

Glenn Yago, the Director of Capital Studies at the Milken Institute, suggested two alternative roles for foundations: playing the role of credit enhancers, so that debt and equity capital are raised more cheaply; and facilitating the sharing of research for a specific disease.

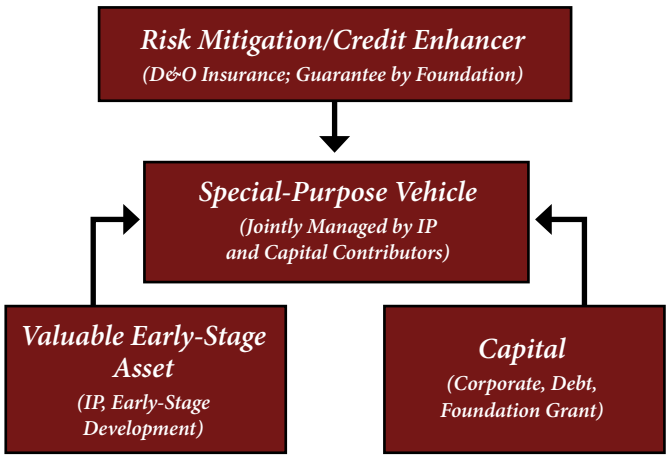
In a discussion of credit enhancement, Nir Kossovsky, founder and CEO of Technology Option Capital, said it is not enough for two parties — IP holders and capital providers — to simply join forces. They need a legal structure to capture the governance, obligations, and payouts of their collaboration. Figure 10 illustrates the four requisite elements of a transaction: the IP assets; the provider of capital; the structured entity (private company) through which the transaction would be handled and the technology developed; and credit enhancers, e.g., guarantees and insurance.

The capital provider could be an experienced pharmaceutical industry player whose know-how would reduce development and commercialization risk and help create an environment culturally aligned with the practices of the working scientists. The capital provider might also be a foundation wishing to contribute capital (for a share of the returns) or a guarantee to other capital providers and/or its industry partner.

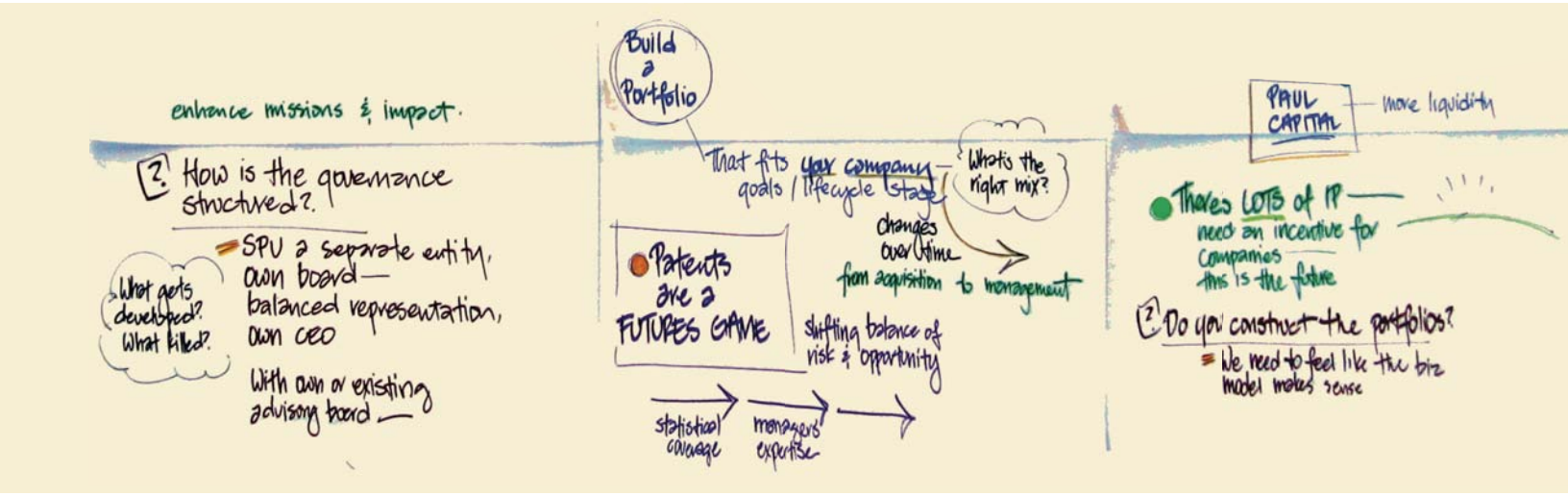
The assets could consist of a diversified patent pool (with IP rights obtained from universities or pharmaceutical or biotech firms) and the human capital involved in early-stage development.

In this case, a special-purpose vehicle (SPV), a private company, would be comprised of the assets — intellectual property and capital — provided in exchange for equity, and would be jointly managed by the IP holder and capital contributors. The goal of the SPV, and therefore the trigger for the financial incentives, would be to develop the technology, increase its value, and reduce the commercial risk to large pharmaceuticals. (Under this scenario, the IP suppliers would become minority investors with certain protections that assure them a reasonable return on their equity.)

FIGURE 10 *Leveraging Foundations to Accelerate Cures*



Source: Technology Option Capital, LLC.
Note: This is a simplified representation of a patent-pending business process.



The SPV could be adapted to the interests of a foundation focused on specific disease research. A foundation focused on Alzheimer's, for example, might assemble a diversified pool of drugs under development for the disease. While this would reduce scientific risk, significant commercialization risks would remain, preventing the SPV from qualifying as an issuer of investment-grade debt. The foundation could provide the financial guarantee, that is, a credit enhancement that raises the credit quality of the pool, opening it up to the larger market of investors. If the guarantee is actually used, it could become a grant, though the diversification of scientific approaches should help to mitigate this risk.

However, several foundation participants argued that their charters required smooth spending on projects so as to conform to the budgets arising from returns on the endowment and thus could not support the intermittent calls on their capital from a guarantee. Three modified scenarios were suggested:

Foundations are risk averse, but drug development is inherently risky — develop structures to draw in those who can TOLERATE risk.

1) After a ratings agency reviewed the deal structure to help raise it to investment-grade, the foundation could invest 10 percent to 15 percent of the funding and place a smaller guarantee, enough to raise the credit quality;

2) The foundation could work with insurance companies to structure a credit enhancement that better fit its budgetary needs;

3) A disease-focused foundation could collaborate with larger foundations, again providing just enough capital and guarantee to bring the transaction structure to investment grade.

The SPV's equity capital — which could be structured as the purchase price of a call option on control of the SPV — could come from a major pharmaceutical player (much as large pharmaceuticals invest in later-stage biotechnology firms today). To reduce investor risk, the equity capital could be leveraged 3:1 with debt capital, which in turn would be supported by credit enhancements to mitigate risk, such as D&O liability insurance, R&D tax credits, or foundation credit enhancements.

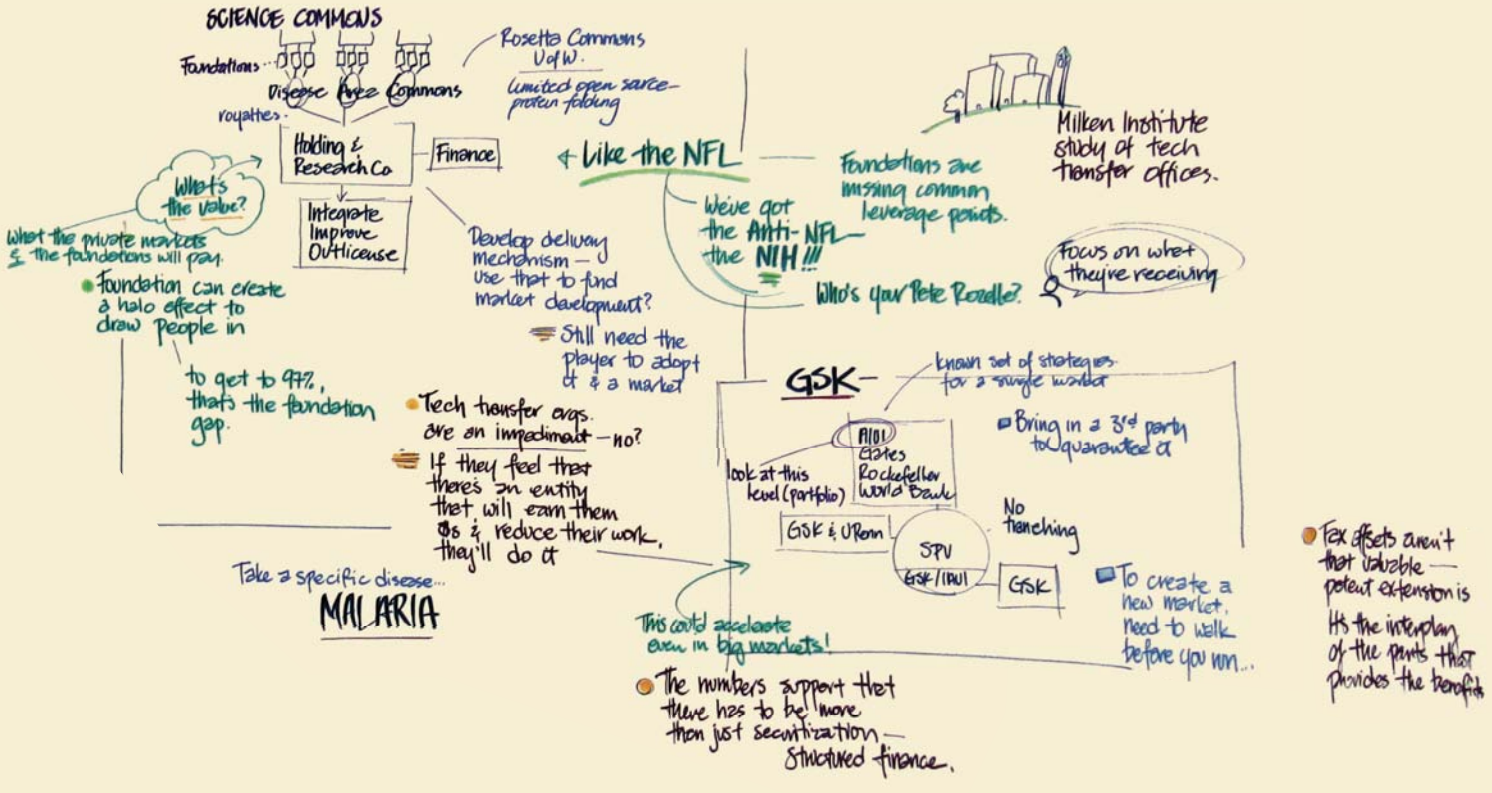
The venture would be successful once the large pharmaceutical exercised its call option (and with that payment, retired the debt). Other scenarios exist for the exercise of the option, Kossovksy said, such as through a sales/license-back transaction of the IP rights with a private equity investor. He also noted an alternative to the call option, in which the principal on the bonds is settled with cash raised through the patent investment entity's exercise of a put option to the insurer.

These financially engineered models address the problems that had prevented a natural market solution — the high risk of failure and potentially small returns — through risk mitigation and credit enhancement.

As for the role of foundations as facilitators of information sharing, John Wilbanks, the Executive Director of Science Commons, said they could design and define funding agreements to "create a commons for a single rare disease foundation." For example, he said, the Huntington Disease Society of America, which currently funds a number of universities at $25 million a year, finds that it must negotiate with each university's technology transfer office if professors from different universities want to work on the same stem cell lines and reagents. The Commons is a mechanism comprising contracts, definitions, and funding agreements that allow funded researchers direct access to the research materials of other researchers funded by the foundation. The nonprofit Science Commons, based in Cambridge, Mass., has six rare neurological disease foundations ready to adopt its legal and contractual tools, said Wilbanks.

"Risk mitigation using a market-based analysis allows risk apportionment to the different parts of the capital markets — including foundations —with varying appetites for it."

Nir Kossovsky
Founder, President & CEO
Technology Option Capital



Following up on Kossovsky's transaction structure, Wilbanks argued that the next step may be to create a holding and research company that would out-license intellectual property funded by the foundation. The holding company, a specialized SPV, could then create a royalty stream used to entice university technology transfer offices into the commons.

Solution 3 — *Use directors and officers (D&O) liability insurance to enhance credit quality*

Directors and officers (D&O) insurance covers the actions of senior corporate management and board members, and includes actions pertaining to intellectual property and product development. For a premium increase, suggested Robert Block, the Managing Director of Technology Option Capital, this coverage could be expanded to the scientific and commercial risks of biotech product development.

"The insurers can reduce the exposure of the board and their own exposure by asserting more control over the research system — including moral control and more transparency."

Robert Block
Managing Director
Technology Option Capital

As a commercial entity, the SPV in figure 10 could carry D&O insurance, which would serve as an additional credit enhancement. Block pointed to a recent court ruling where members of the Abbott Laboratories board of directors were obligated to acquaint themselves with the manufacturing process pertaining to technology development. The D&O policy was used to settle the matter out of court. Thus, Block argued, the D&O policy already insures against actions the board may take that could harm the value of the firm, including technology management in general and drug development failure, in particular. Insurers, he said, are already exposed to technology risk, and because the proposed SPV governance structure increases transparency, they should be willing to provide extra coverage for extra premium.

While some Lab participants found Blocks' proposal intriguing, others argued that D&O insurers could find the increased exposure too risky, due to the intrinsically uncertain nature of drug development. It was observed that removing the penalty for risk often increases risk-taking behavior, and that a company with enhanced D&O coverage might find its board more willing to take on high-risk drug development efforts, to the detriment of other stakeholders.

Solution 4 — *Tap into the emerging market for IP-backed securities*

Several Lab presenters were active participants in the emerging market for intellectual property-based lending. This is a growing segment of the asset-backed securitization market. Although the intellectual property in drug development is protected by patents, intellectual property protected by copyrights and trademarks has dominated the market to date.

Robert D'Loren, the President and CEO of New York-based UCC Capital Corp., spoke of the large share of corporate value created by intangible assets, particularly branding. UCC Capital works to understand the complete business model, and qualifies companies, based on their operational excellence, as well as the specifics surrounding their intellectual property. UCC's due diligence for intellectual property securitization includes addressing the strategic risks, such as competitor moves and bankruptcy risks that could disrupt the value of the company.

Many companies are eager to monetize their IP, said Keith Bergelt, President and CEO of IP Innovations, based in Charlotte, N.C. Recent data from Ocean Tomo, a merchant bank specializing in intellectual property, shows that, on average, 87 percent of corporate value comes from intangible assets.

Bergelt's firm however, does not lend solely on the value of intellectual property. The company addresses the market with two complementary transactions: it provides financial guarantees for revenue streams attached to IP, so as to remove some of the risk for traditional commercial bank and asset-financing lenders; and it makes direct loans to IP-rich companies with unused debt capacity.

Figure 11 illustrates how IP Innovations closes the finance gaps for intellectual property-based lending. The "before" panel shows the market gap in which a growing company with substantial intellectual property holdings cannot obtain a sizable loan under standard tangible asset terms. The commercial lender is unfamiliar with the valuation and risks of the cash-flow streams arising from intellectual property, and is uninterested in lending.

IP Innovations closes that market gap by searching out companies rich in IP that have positive cash flow and perhaps some unused debt capacity. After analyzing the intellectual property holdings, IP Innovations brings the potential transaction to a commercial bank, complete with its own financial guarantee. The client company pays a slightly higher closing fee on the loan to cover the guarantee and transactions costs.

Companies may hope they can monetize their IP separately from their tangible asset business, but both UCC Capital and IP Innovations perform analyses of the entire company. Both maintain a 10 percent to 40 percent loan-to-value ratio on their transactions and require strong cash flow from the IP. In addition, IP Innovations requires surplus debt capacity, such as 3X interest coverage. The result is a loan that is larger than would been written without the IP collateralization, not a loan that is separable from the ongoing business.

While IP Innovations and UCC Capital were hesitant about lending to the pre-revenue drug discovery market, IP Innovations' Bergelt said his company was evaluating a loan transaction for a company with a set of medical device patents and a history of obtaining significant licensing revenues from large industry players.

"You're going to get into trouble on a pharmaceutical deal if you don't capture all the intangibles drivers—the copyrights and patents—that support the brand."

Robert D'Loren
President and CEO
UCC Capital Corp.

"Securitization in the film markets is successful because there are specialists who can help structure the transactions."

Lee Cole
Founder
Inflect Technologies

Several Lab participants wondered if asset-backed or IP-secured financing actually could play a role in funding drug discovery, given industry practices. It seemed that lenders were willing to make loans for successful drugs, but not for drugs that faced significant scientific and commercial risks. One participant suggested that if the loan-to-value ratio was 25 percent and an early-stage drug prospect is worth $3 million to $4 million, then a loan of $1 million or less might be possible. This does not reduce the need to raise significant equity capital; nor would the debt funding be sufficient to close the Phase II funding gap.

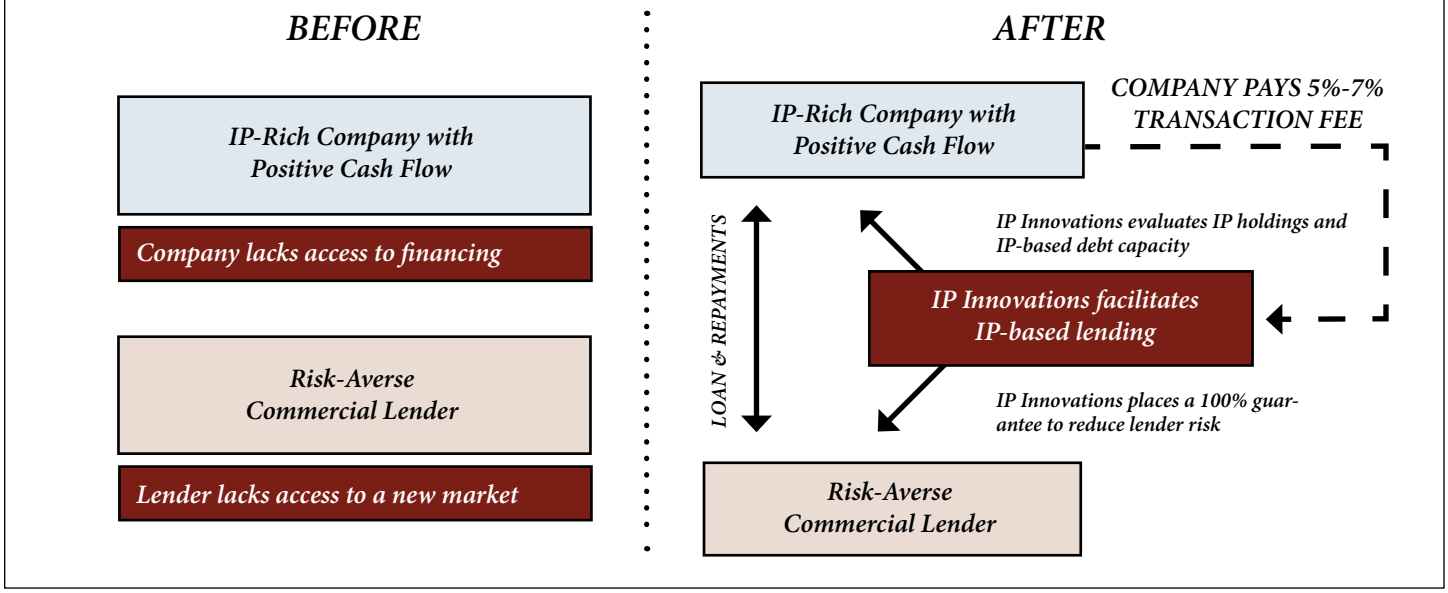
SOLUTION 5

Use advanced purchases to underwrite medical research and drug delivery to under-funded patient groups

The Lab reviewed two recent public/private partnerships for drug development to explore the economics and conflicting incentives that arise when serving under-funded patient groups.

The partnership between Bayer Healthcare AG and the Global Alliance for TB Drug Development (the TB Alliance) helps to illustrate why there has not been a private-market solution to the fight against tuberculosis. The TB Alliance estimates that the tuberculosis drug market is currently about $600 million per year and expected to increase to $700 million by 2010. The cost of developing a single anti-TB drug is estimated to be near $100 million, according to the TB Alliance. The relatively small size of the market, plus the economic and geographic considerations of this disease, have made this effort unattractive for any single drug company. The TB Alliance, a nonprofit organization, has emerged to catalyze and orchestrate a global solution that depends on public-private partnerships.

FIGURE 11 *How a Private Company (IP Innovations) Closes the Market Gap for Lending, Based on Intellectual Property*



The Alliance pursues intellectual property rights in the area of TB research, as well as coordinating drug trials and research efforts. It is funded through country donations (primarily Europe and the United States), as well as the Bill & Melinda Gates Foundation and the Rockefeller Foundation.

The Bayer/TB Alliance partnership is illustrated in Figure 12. The goal of the partnership, announced in October 2005, is to coordinate global clinical trials to study the potential of an existing antibiotic, moxifloxacin, in the treatment of TB. In an animal study, moxifloxacin shortened the standard six-month clinical treatment of TB by two months.

The TB Alliance will coordinate and help cover the cost of the trials, leveraging substantial support from several U.S. and European government agencies. As figure 12 shows, the partnership's goal is to make an anti-TB drug available at a not-for-profit price. With its costs covered, Bayer could sustain supply. Furthermore, if the drug development process is successful, Bayer will receive approval from the FDA for an additional prescriptive use for moxifloxacin.

The second public-private partnership was that between GlaxoSmithKline Biologicals (GSK) and the International AIDS Vaccine Initiative (IAVI). Similar to the partnership illustrated in figure 12, GSK and IAVI will collaborate to try to develop an AIDS vaccine. IAVI, which will contribute funding, is in turn funded by donations from countries (primarily Europe and the United States), as well as the Gates and Rockefeller foundations. And again, the goal is to make a sustained supply of an AIDS vaccine available at a not-for-profit price by GSK.

In June 2005, before the G8 Summit, GSK and Bayer joined with other large pharmaceuticals and disease-focused nonprofits to sign a letter to the G8 ministers, asking for help. The letter argued that development costs remained high, yet the bulk of the contributions were from just a handful of sources, notably the Bill & Melinda Gates Foundation and pharmaceutical and biotech companies that had the

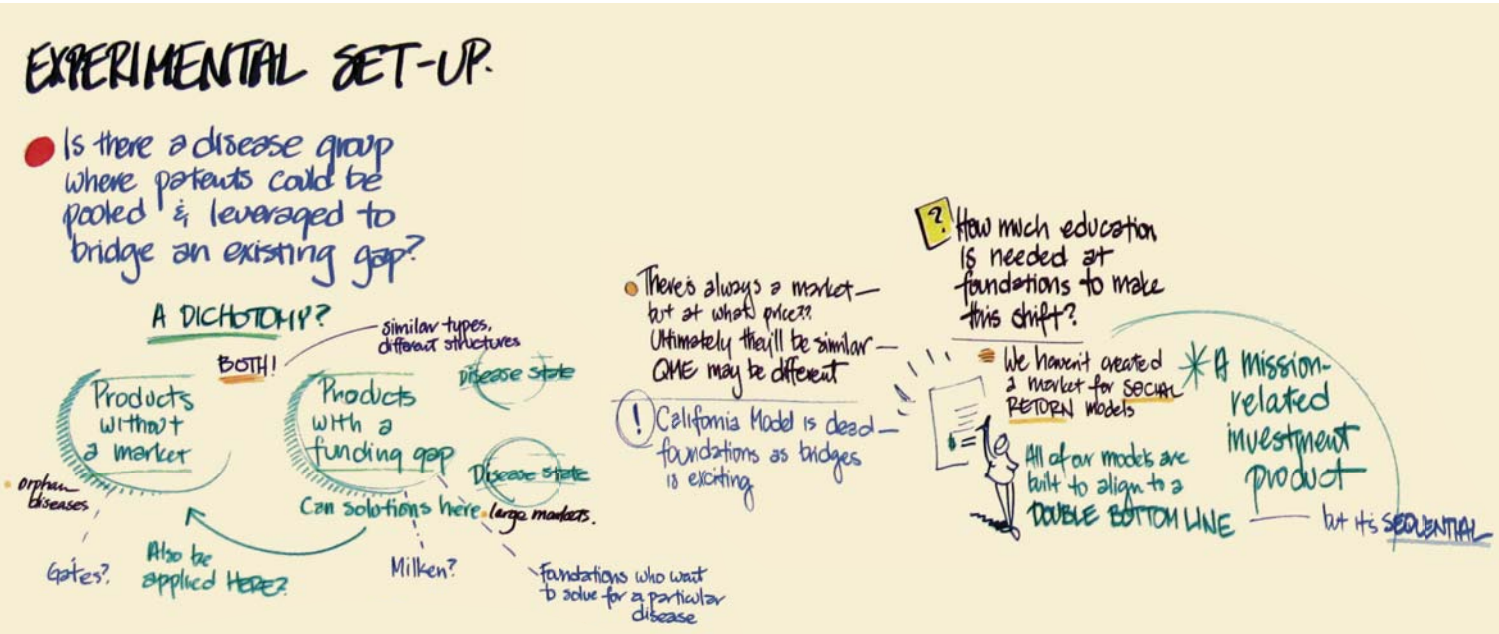
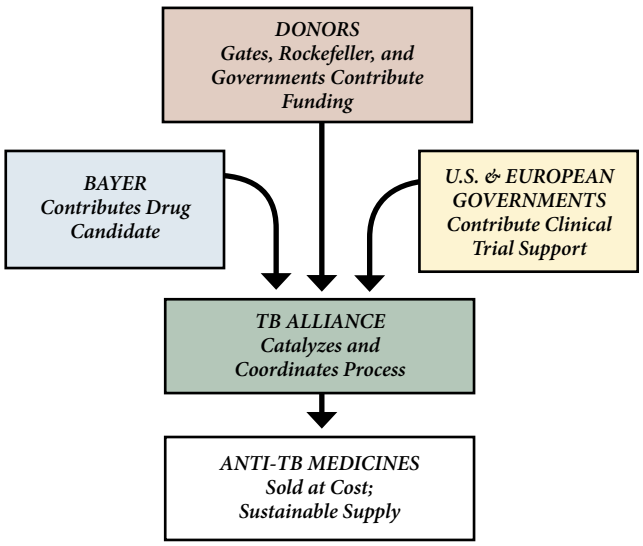


FIGURE 12 *Transaction Structure of the Bayer-TB Alliance Public/Private Partnership*



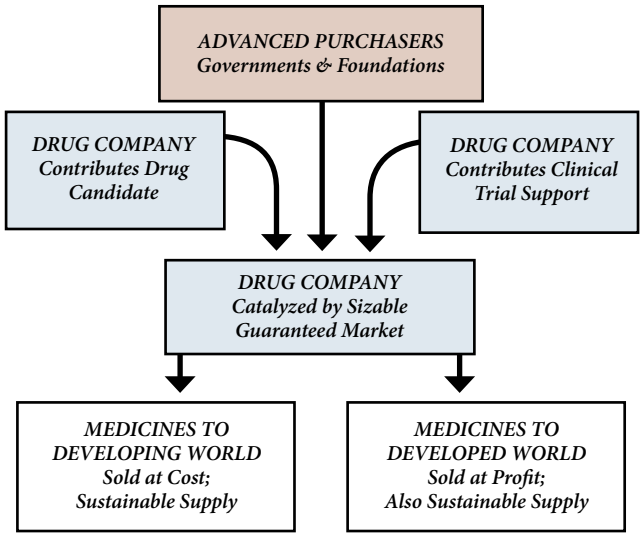
skills and compounds needed. The public-private partnership model was working, the letter stated, but most drugs will remain in research and development without greater financial support.

In recognition of the challenge, Britain's Chancellor of the Exchequer, Gordon Brown, announced at the G8 Summit that his government, working with other agencies, had agreed to purchase 200-300 million doses of the AIDS vaccine, if and when it was developed. He announced a similar commitment to a malaria vaccine.

Figure 13 highlights how this innovative financing could change the economics of the public-private partnership by creating a market that will pay fair-market price for the therapy. Note the privatization effect the advanced purchase creates, eliminating the need for complex coordination between multiple government agencies, foundations and the nonprofit catalyst.

Health economics experts have argued that advanced purchases can create a market as robust as that for pharmaceutical products in developed countries. This "pull mechanism," whereby products are delivered on a demand basis, is likely to be a cost-effective use of public funds.

FIGURE 13 *Transaction Structure of Advanced Purchase Agreements*



In a recent study, economists at the National Bureau of Economic Research calibrated the public-private market aspects of potential advanced purchase agreements.[5] Estimates show that biotech and pharmaceutical companies are motivated to pursue drug prospects for markets of $3 billion in revenue or larger. At $15 per dose for the first 200 million vaccines purchased, and $1 per dose thereafter, a $3 billion market could be created by advanced purchases. The economists found that the $15 per-dose cost of this financial mechanism is several orders of magnitude more cost effective than current treatments in underfunded countries.

A critic of the advanced purchase commitment, Andrew Farlow of Oxford University, has argued that the program design will not lead to the most effective cure for malaria because it rewards the first pharmaceutical solution to market.[6] What if the second vaccine to market is the better cure? Program supporters say that not all funds will be spent at once, so there will be purchasing power left for the second to market. Farlow also argues that the program design is rife with potential corruption, as the host government is asked to

contribute $1 per vaccine, while the foundations pay $14. An unscrupulous firm could potentially bribe government officials to allocate millions of dollars in revenue.

While these are substantive criticisms, they must be weighed against the apparent preference of the foundations and country donors for advanced purchase commitments—the parties trying to accelerate the delivery of malaria treatments in order to save more lives now, rather than some future date.[7] Economic research shows that malaria and other pervasive diseases are core contributors to poverty. Thus, a near-term reduction in disease could jump-start local economies.[8]

Solution 6

Use donor bonds to underwrite medical research and drug delivery to under-funded patient groups

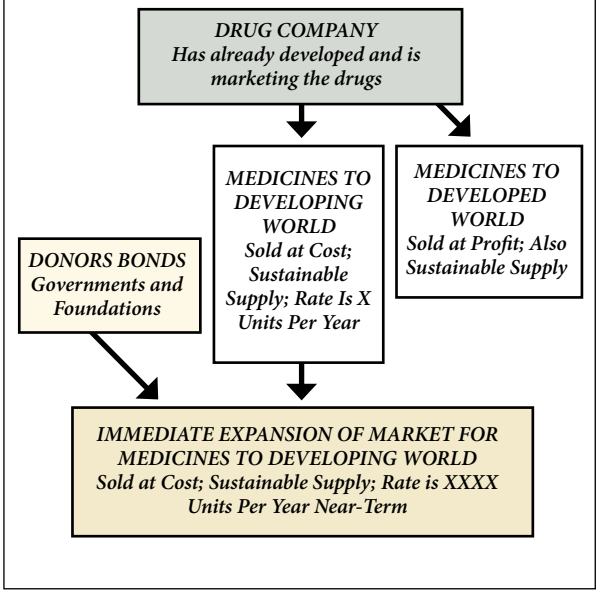
In March 2005, six European governments announced a financial innovation, donor bonds, designed to accelerate the delivery of medicines to Africa.[9] The bond offerings, expected to total $4 billion over several years, will provide governments with more to spend on immunization in Africa than is now the case.

The structure of donor bonds imitates the practice of credit card companies that use future customer repayments as the collateral for borrowing. With donor bonds, future gifts are the collateral for borrowing. The future stream of payments is transformed into an immediate lump sum.

Figure 14 shows how donor bonds enlarge the existing supply of medicines to developing countries. The drug company has already developed the drug and is now marketing it in the developed world at a profit and selling it in the developing world at cost. The donor bonds infuse the developing market with demand in the near-term. As the drug company is already in production, the mechanics of challenge are simple ones of production and supply-chain expansion.

The first donor bonds were issued in April 2006, backed by a stream of future donations from the United Kingdom, France, Italy, Norway, Sweden, South Africa and Spain. The U.S. government has declined to participate, saying that the federal budget process does not allow for the long-term commitments required by this securitization structure. The bonds will be issued by an SPV known as the International Finance Facility for Immunization. The programs financed by the bonds will be managed by the Global Alliance for Vaccines and Immunization (GAVI), which has received a pledge of $750 million over ten years from the Bill & Melinda Gates Foundation. GAVI expects that the acceleration of immunizations through donor bonds will "save the lives of five million children and protect another five million as adults." The importance of this public health improvement is seen in other studies that show how poor public health care drags down the GDP growth of under-funded nations.

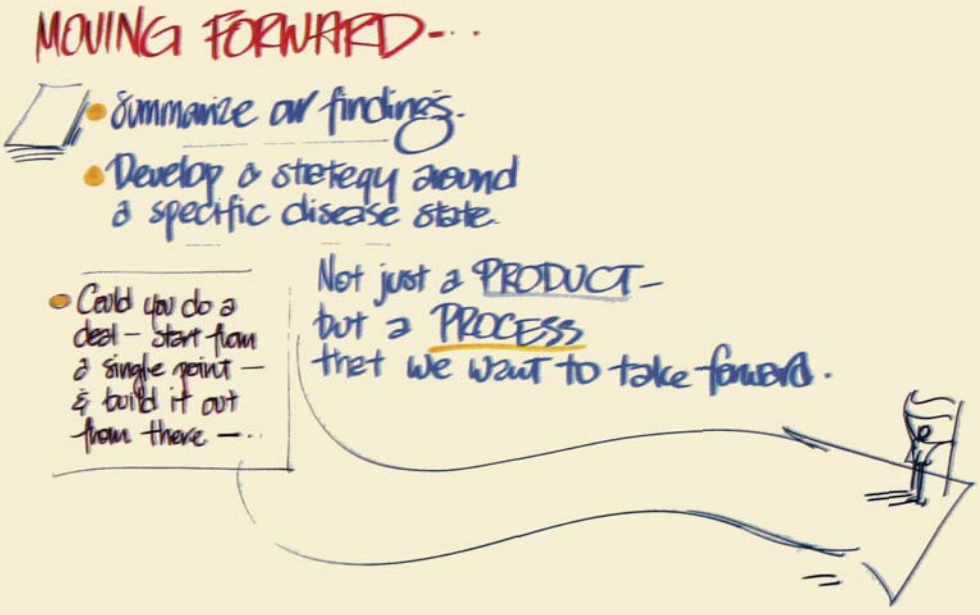
FIGURE 14 *Transaction Stucture of Donor Bonds*



Conclusion

The experts and stakeholders who gathered at the Milken Institute's Financial Innovations Lab in late 2005 provided several innovative strategies to "cure" the financing gap and offer new supplies of capital to drug development. One recommendation was to perform a case study that brings together a set of transaction partners to facilitate a potential deal and help identify the incentives and challenges. Another proposal called for the creation of a simulated pool of patents and/or early-stage drugs for review by a ratings agency and interested foundations so that the potential players would learn to identify incentives and stumbling blocks.

Whether the solution is diversification and pooling, the use of foundations, enhanced D&O insurance, advanced purchases, donor bonds, or a combination of strategies discussed in this report, one thing remains clear: the current shortage of capital in the development of drug, medical device, and health care technology can be resolved through public-private partnerships. Financial technologies, innovative securitization, and structured finance can address capital needs in the realm of global health, human capital development, and broader economic growth.



Appendix I

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Session 1

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Appendix II

Literature Review

Author(s)	Title	Purpose	Results
Amram (2005)	*The Challenge of Valuing Patents and Early-Stage Technologies*	Review several approaches to building relevant valuation models for patents and early-stage technologies.	There is no single best valuation model; instead, one must select and customize a model to match the salient features of the application. While quantitative models of real options are likely to be of limited use, real options thinking has a major role to play in framing the valuation of patents and early-stage technologies.
The Boston Consulting Group (2005)	*Market Assessment of Malaria Vaccines*	Collect more complete information about the need for a malaria vaccine to inform decision-making through identifying constraints and evaluating risks and uncertainties.	Substantial need/potential demand exists across four markets evaluated, but specific requirements for product profile exist and vary significantly by country and recipient. Third parties, such as the donor and global scientific communities, can play a role in stimulating early markets and enabling purchase of vaccine by less wealthy nations, thereby increasing demand for vaccine.
Cockburn (2005)	*Blurred Boundaries: Tensions Between Open Scientific Resources andCommercial Exploitation of Knowledge in Biomedical Research*	Examine the evolution of biomedical research as an industry.	The extension of exclusionary intellectual property rights into basic research has unleashed a surge of entrepreneurial energy and risk-taking in commercial science, bringing large potential social benefits but also possible misallocation of resources. Reforms to patent law and practice may be necessary to allow for collaborative pre-competitive research.
Czarnitzki, Hall and Oriani (2005)	*The Market Valuation of Knowledge Assets in US and European Firms*	Measure the market value of the knowledge assets owned by a firm using a hedonic regression approach. Applies the method to firm data on market, capital, and R&D.	Measures based on R&D, patents and citation-weighted patents are each highly significant in a market value regression, although patent-based measures tend to be somewhat less significant in the presence of R&D measures.
DiMasi, Hansen, and Grabowski (2003)	*The Price of Innovation: New Estimates of Drug Development Costs*	Examine the R&D costs for new drugs in the pharmaceutical industry.	Costs of compounds abandoned during testing were linked to the costs of compounds that obtained marketing approval. The estimated average out-of-pocket cost per new drug is US$403 million (2000 dollars). When comparing to previous studies, costs were shown to have increased at an annual rate of 7.4 percent above general price inflation.
Hillery (2004)	*Securitization of Intellectual Property: Recent Trends from the United States*	Review the development of the market for intellectual property (IP) securitization.	Key trends in the U.S. IP securitization market include: improvements in valuation tools; pooling of assets for securitization; idiosyncrasy of IP as cash-flow-generating assets; expansion into new types of IP (film, trademark, and patent); and wider availability of highly specialized advisers in the field.
Hsu and Schwartz (2003)	*A Model of R&D Valuation and the Design of Research Incentives*	Develop a real options model that takes into account the uncertainty in the quality of research output, time, and cost to completion, and the market demand for the R&D output.	In general, purchase commitment plans (pull subsidies) are more effective than cost subsidy plans (push subsidies), while extending patent protection is completely ineffective. Hybrid subsidy constructed from a purchase commitment combined with a sponsor co-payment feature produces the best results in all four dimensions of the effectiveness measure.

Author(s)	Title	Purpose	Results
Kortum and Lerner (2000)	*Assessing the Contribution of Venture Capital to Innovation*	Examine the influence of venture capital on patented inventions in the United States.	Increases in venture capital activity in an industry are associated with significantly higher patenting rates. While the ratio of venture capital to R&D averaged less than 3 percent from 1983 to 1992, the authors' estimates suggest that venture capital may have accounted for 8 percent of industrial innovations in that period.
Lerner (1994)	*The Importance of Patent Scope: An Empirical Analysis*	Examine the impact of patent scope on firm value.	Using a patent scope based on the International Patent Classification scheme, the breadth of patent protection significantly affects valuations. A one standard deviation increase in average patent scope is associated with a 21 percent increase in the firm's value. Broad patents are more valuable when substitutes in the same product class are plentiful, a finding consistent with theoretical suggestions.
Lichtenberg and Waldfogel (2003)	*Does Misery Love Company? Evidence from Pharmaceutical Markets Before and After the Orphan Drug Act*	Ask how market size -- measured by condition prevalence -- affects development and consumption of pharmaceutical products and individual longevity.	More prevalent conditions have substantially more products available, larger affected populations are much more likely to take a drug, and mortality rates are lower for people with more common conditions. Nevertheless, the Orphan Drug Act has successfully induced increased development of drugs targeted at small populations by reducing large fixed costs to pharmaceutical companies.
Moran et al. (2005)	*The Landscape of Neglected Disease Drug Development*	Focusing on policy, aims to improve health outcomes for developing-country neglected-disease patients by increasing the quality and number of drug treatments available to meet their needs.	Policies should match incentives to motives (financial or non-financial), be tailored to align stakeholder behavior with desired public outcomes, and include removing existing obstacles rather than providing additional funds to compensate for them. Two approaches are: public-private partnerships (relatively cheap and effective) and small-company, market-driven activity (scale more compatible with neglected disease markets).
Pitkethly (1997)	*The Valuation of Patents: A Review of Patent Valuation Methods with Consideration of Option-based Methods and the Potential for Further Research*	Consider the case of patents whose values constantly need assessing during the application process, on renewal and for licensing, purchase and sale negotiations.	Option-based valuation approaches are proposed as a useful and potentially powerful framework in which to consider management of a company's patent portfolio and other IPR assets.
Schwartz (2003)	*Patents and R&D as Real Options*	Develop and implement a simulation approach to value patents and patent-protected R&D projects, based on the Real Options approach.	The model takes into account uncertainty in the cost to completion of the project and the possibility of catastrophic events that could put an end to the effort before it is completed. It also allows for the possibility of abandoning the project. The article takes the private point of view, but it has public policy implications. It can be used to analyze the trade-offs between promoting innovation and securing competitive market outcomes.
Shockley et al. (2003)	*The Option Value of Early-Stage Biotechnology Investment*	Show how option pricing (or real options analysis) can be used to value an early-stage R&D investment.	The real options valuation of an R&D program with multiple stages of investment, as demonstrated in the article, can be used as a framework for analysis in a variety of applications. The quality of the valuation will be driven by the assumptions that go into it.

Endnotes

1. American Association for the Advancement of Science, R&D Funding Update on R&D in FY 2006 NIH Final Appropriations.

2. See also "The List: Innovative Models on Which to Build Biotech," by Cynthia Robbins-Roth, BioWorld Today, August, 2005; "Biotech Research Focus: Funding," by Arlene Weintraub, Businessweek Online, June 17, 2005; "Is Biotechnology Losing Its Nerve?" by Andrew Pollack, *New York Times*, February 29, 2004.

3. See also Sam L. Savage, "Beat the Odds: Understand Uncertainty," *Optimize*, December 2001:2.

4. See also "Multimillion Dollar Baby: JP Morgan's John Miller is holding the hottest hand at the Oscars," *BusinessWeek Online*, March 7, 2005.

5. See also "Advanced Purchase Commitments for a Malaria Vaccine: Estimating Costs and Effectiveness" (NBER Working Paper 11288), by Ernst Berndt, Rachel Glennerster, Michael Kremer, Jean Lee, Ruth Levine, Georg Weizsäcker, and Heidi Williams.

6. See also "Push and Pull: Should the G8 promise to buy vaccines that have yet to be invented?" *The Economist*, March 23, 2006; more of Prof. Farlow's critiques can be found at www.economics.ox.ac.uk/members/andrew.farlow.

7. For similar work, see also the orphan drug model developed by Dr. Victoria Hale and the Institute for One World Health. Information available at http://www.oneworldhealth.org.

8. "Cause, consequence and correlation: assessing the relationship between malaria and poverty," Gallup. J.L.; Sachs, J.D./Commission on Macroeconomics and Health, WHO, 2001. Available at http://www.eldis.org/static/DOC6010.htm.

9. "Funding Tools to Fight Disease: Six European Nations to Float Bond Deals to Stretch Aid Budgets," by Andrew Peaple and Tom Marshall, *Wall Street Journal*, March 3, 2006."

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