Business Models for Information Commons in the Pharmaceutical Industry

By

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The pharmaceutical industry needs new modes of innovation. The industry’s innovation system - based on massive investments in R&D protected by intellectual property rights - has worked well for many years, providing incentives for pharmaceutical firms to invest in developing drugs across a wide variety of major medical needs. However, this traditional drug development process is subject to decreasing productivity and increasing costs. In addition, it encourages pharmaceutical firms to focus on “blockbuster” drugs, and to neglect meeting needs in small potential markets such as “orphan” diseases and diseases primarily found in third world countries.

This thesis focuses on new modes of innovation, specifically the sharing of safety information prior to clinical trials. To inform this analysis, I first discuss the data that informs why the industry is in need of new modes of innovation. I then proceed to outline the potential promise of some new modes of pharmaceutical development that are emerging. I then explore a specific novel innovation mode in more detail: the sharing of non-competitive safety information prior to clinical trials, leading to significant reductions in both costs and chances of failure in drug discovery and development. I propose that this new innovation mode offers the potential of significant benefit to both drug developers and medical patients.

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# Table of Contents

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABSTRACT</td>
<td>2</td>
</tr>
<tr>
<td>CHAPTER 1. Introduction</td>
<td>4</td>
</tr>
<tr>
<td>CHAPTER 2. New Modes of Innovation are Needed in Drug Discovery</td>
<td>8</td>
</tr>
<tr>
<td>Orphan Diseases</td>
<td>8</td>
</tr>
<tr>
<td>Neglected Diseases</td>
<td>9</td>
</tr>
<tr>
<td>Minority groups of patients who experience side effects</td>
<td>9</td>
</tr>
<tr>
<td>Economically disadvantaged patients who need cheaper cures</td>
<td>10</td>
</tr>
<tr>
<td>Drug discovery is expensive and failure prone</td>
<td>12</td>
</tr>
<tr>
<td>Why is the drug discovery process so expensive and long?</td>
<td>14</td>
</tr>
<tr>
<td>Effects of the Patent System on firm-innovation</td>
<td>23</td>
</tr>
<tr>
<td>Newer modes of innovation could be complementary and could even help the pharmaceutical firms</td>
<td>25</td>
</tr>
<tr>
<td>CHAPTER 3. Potential value of increased information sharing in drug discovery</td>
<td>27</td>
</tr>
<tr>
<td>The current state of information sharing in drug discovery</td>
<td>28</td>
</tr>
<tr>
<td>Need for increased data sharing on preclinical research</td>
<td>29</td>
</tr>
<tr>
<td>Target Identification and Validation</td>
<td>29</td>
</tr>
<tr>
<td>Need for increased information sharing in Lead Identification and Optimization</td>
<td>30</td>
</tr>
<tr>
<td>Need for increased Data sharing on Clinical Trial Failures &amp; Successes</td>
<td>33</td>
</tr>
<tr>
<td>Does information sharing yield additional innovation?</td>
<td>36</td>
</tr>
<tr>
<td>CHAPTER 4. Increased patient involvement in Drug Discovery</td>
<td>38</td>
</tr>
<tr>
<td>PatientsLikeMe</td>
<td>39</td>
</tr>
<tr>
<td>CHAPTER 5. Prediction Markets: A Novel Way to Increase Information-Sharing and potentially reduce Drug Failures in clinical testing and associated costs</td>
<td>46</td>
</tr>
<tr>
<td>Some reasons for Phase I failure</td>
<td>47</td>
</tr>
<tr>
<td>Our Hypothesis</td>
<td>48</td>
</tr>
<tr>
<td>Prediction Markets</td>
<td>49</td>
</tr>
<tr>
<td>How we plan to test our hypothesis</td>
<td>50</td>
</tr>
<tr>
<td>What we hope to get from the market’s results:</td>
<td>54</td>
</tr>
<tr>
<td>Possible problems</td>
<td>55</td>
</tr>
<tr>
<td>REFERENCES</td>
<td>57</td>
</tr>
</tbody>
</table>
CHAPTER 1

Introduction

Drug discovery and development, as practiced by pharmaceutical firms since the end of WWII has been undertaken inside large, in-house corporate research facilities. Discovery guided towards large-scale patients’ needs and new drugs are developed that are then protected by patents to keep imitators from free-riding. Pharma firms also invest heavily in manufacturing assets as well as expertise in clinical trials and marketing with the aim of taking their innovations all the way from discovery to physicians through a proprietary, in-house value chain.

Firm-based innovation in drug discovery has engendered valuable life-enhancing innovations which have helped increase life expectancy in the Unites States from 47 years in 1900 to 77 years in 2003[4]. However, the current drug development process as practiced by major pharmaceutical firms requires specialized know-how, project management and large investments.

Genetics, Cellular and Molecular Biology and Biochemistry are used to develop the rational basis of a cure, and simplified models of a disease. Chemistry is used to screen molecules and develop leads for its treatment, using the simplified models. Materials science, toxicology, pharmacokinetics, pharmaco-dynamics and scale-up chemistry are important during preclinical development, to yield a preclinical
candidate that is hoped to be bioavailable, non-toxic and metabolized efficiently from the human body. In addition to being complex, these processes are very long and expensive, as currently performed in most pharmaceutical firms.

![Diagram of the Drug Discovery and Development Process]

Figure 1. The Drug Discovery and Development Process

Clinical trials, as mandated by the FDA, are randomized, and double-blinded. They typically involve multiple trial centers, doctors, participating patients, healthy volunteers, trials with both current and proposed treatments and are therefore expensive, with costs ranging in the hundreds of millions of dollars. Around 60% of failures in drug development take place during the later phases of clinical trials [2]. Research and development for most of the medicines available today has required 12-24 years for each medicine from starting a project to the launch of a drug product [3]. Clinical trials alone can take 3-5 years of this time. Together these factors have made it quite difficult, until recently for users, be they patients, doctors or practitioners from the pharmaceutical industry, to succeed at user-innovation efforts in drug discovery. Put together, the complexity, costs and time
involved in drug discovery have inhibited non-firm innovation in drug discovery.

![Figure 2. Factors inhibiting non-firm innovation in drug discovery](image)

As a consequence this system has failed to meet all needs and the industry is in need of new modes of innovation. To underscore the importance of the unmet needs, we consider a patient of a typical orphan disease, such as Cystic Fibrosis, a condition affecting about 250,000 people in the United States. The disease is genetically inherited. The disease has multiple variants with one dominant strain. It manifests as a defective chloride channel protein in the lung, causing large mucus buildup in the lungs and breathing passages. Most patients live up to their early thirties, at which time the mucus buildup increases to a point where they can either not breathe any more or they succumb to bacterial infections which grow on the accumulated mucus. There are no known cures to the disease and death in the prime of life, between 30 and 34, is certain. With such a small patient population, it
is unlikely that a pharmaceutical firm will, without external funding, ever be interested in developing a cure. The most effective palliative treatments today, include thumping the patient on his or her back, in an attempt to dislodge the mucus stuck in the lungs. Or a patient of Lou Gehrig's disease, an equally fatal condition. There is absolutely nothing that a patient can do, to affect firm-based innovation in a timeframe that will address his or her condition. About 90% of pharmaceutical innovation addresses 10% of the world’s medical needs[8]. The current patent based system fails to incentivize firm-based drug discovery innovation for the remaining 90% of medical need.

Recently, the growth in internet-based social networking has spawned new user-innovation among patients of orphan diseases, in the face of death and suboptimal palliative treatments. Newer modes of innovation that are emerging can potentially offer a good complement to current patent-based innovation as practiced by pharmaceutical firms. In the following chapters I first review some of the unmet needs in drug discovery along with some of the reasons underlying why the current innovation system has failed with meeting those needs. I then explain why establishing an information commons may be helpful to increasing progress in drug discovery. Finally, I examine an evolving example of patient-led user-innovation. I conclude with a way to increase information-sharing for safety data between pharmaceutical firms.
CHAPTER 2

New Modes of Innovation are Needed in Drug Discovery

Pharmaceutical firms, like any business, are motivated by profits. The patent system governing their profits has worked well for certain categories of diseases by sparking innovation. The business model for pharmaceutical firms is straightforward. Newly launched drugs are protected by the patent system so as to allow for monopolistic or oligopolistic pricing for 10-12 years. After the patents expire, generic versions of the drug emerge to take over the market, wiping out profits in weeks. The high costs of drug development and its high chances of failure, discussed in the previous chapter, can be made up for, only by the extraordinarily high profits possible as a result of the patent system.

Pharmaceutical firms have little incentive to develop treatments for diseases or conditions where anticipated profits are not high. This has led to multiple categories of diseases where patent-based firm innovation is clearly insufficient to address all user-needs. Below we examine some of these categories in some more detail.

**Orphan Diseases**

These are diseases for which there isn't a sufficiently large market due to small numbers of patients. An orphan disease is defined as one affecting fewer than 200,000 in the United States[5]. Examples of such diseases are Cystic Fibrosis, Huntington's disease, and Lou Gehrig's syndrome (ALS). These diseases are often
genetic conditions, which do not spread but are transmitted either along genetic lineages, such as Cystic Fibrosis, or occur with extremely rare genetic mutations spontaneously. Eurordis, the European Organization for Rare Diseases, estimates that there are between 5000 and 8000 rare diseases afflicting between 6-8% of the population.

Neglected Diseases

These are diseases for which there aren't sufficient numbers of patients in developed nations. These diseases are often endemic in low-income populations in developing regions of Asia, Africa and South America. Examples of neglected diseases include malaria, tuberculosis, Buruli ulcer, leishmaniasis, Chagas disease, dengue, African sleeping sickness (trypanosomiasis), diarrheal diseases among others. Few patients can afford to pay patented prices for drugs. Hence private firms cannot sell enough patented products to cover their R&D costs, let alone capture profits. Some of these diseases can also make more prominent diseases like HIV/AIDS more deadly. It has been estimated that less than 1% of newly developed drugs are for tropical diseases such as leishmaniasis, sleeping sickness or dengue[6].

Small groups of patients who experience side effects

Under the current system, drugs launched from pharmaceutical firms are tailored to be effective for the largest subpopulation of patients in a disease. Almost always, such drugs either do not work well with or produce numerous side-effects for certain subsections of the patients. Commonly prescribed drugs work in only 40-60% of patients and serious side effects are still quite common, resulting in
about 100,000 deaths in the US alone, each year[7]. For example, interferon, a
treatment for Hepatitis C, a potentially fatal liver disease, works on only less than
75% of the patients it is administered to[9]. In a large subpopulation of its patients,
debilitating flu-like symptoms are a side-effect. Given the extraordinary profits
from the population it successfully treats, and the expensive costs of clinical trials,
there is little incentive for the drug manufacturer to develop incrementally better
drugs which reduce side-effects for a small subsection of the patient population.
Such drug development efforts therefore go largely unmet.

**Economically disadvantaged patients who need cheaper cures**

While commercially developed drugs are easily accessible to the more affluent folk
in developed nations, those who can't afford the high costs, are greatly in need of
cheaper versions. Pharmaceutical firms and governments in underdeveloped
nations deal with this, primarily through charitable contributions and exceptions to
the patent system[]. However, this does not meet the needs of those in developed
countries, who still need to take on expensive loans to get access to these drugs.
Such patients either experiment with alternative and less effective forms of
healthcare such as acupuncture or travel to underdeveloped nations for cheaper
access to their medication.

Patients in the above categories lack access to effective drugs as a result of the high
costs and high risks of the traditional drug development model. This has produced
considerable frustration - especially amongst the patients and families afflicted by
orphan diseases. Many of these individuals are financially well-off, but have in the
main been unable to affect their situation. However, some have attempted to address the costs and times to a cure using several means. Multiple foundations like the CFFT, the Huntington’s Disease Foundation, and the ALS Foundation fund orphan drug research in multiple drug companies. Alternatively, philanthropic entities such as the Gates Foundation incentivize research in neglected diseases by funding pharmaceutical research programs for third world diseases such as leishmaniasis, malaria and tuberculosis. Such foundations have funded research to the tune of around 1.15 billion dollars in 2005 and have committed upto 3.5 billion dollars for the future[8]. To reduce development times, political activism by patients and their families, have encouraged regulatory bodies such as the FDA, to provide fast reviews and special incentives to trials aimed at orphan diseases, along with tax breaks for the participating pharmaceutical companies.

Figure 3. User-efforts at Drug Discovery
Innovation outside of the firm-led model, can serve to fill in part of this requirement. As mentioned before, drug discovery is an extremely long, expensive and risky process. To understand why let us try and understand the currently practiced drug development process better.

**Drug discovery is expensive and failure prone**

Shown below in Figure 4 is the average cost of developing a drug plotted over time. In 2007, the average cost to develop a drug rose up to 1.2 billion dollars, up 400 million dollars from the previous year[10].

![Figure 4. The increasing cost of drug discovery and development](image)

Large incentives in the form of extraordinary rents, made possible via the patent system, are needed to meet costs and continue funding research. Failure rates are
also very high in drug development. Figure 5 below shows the percentage of failures during clinical trials[11]. In aggregate, only 1 in 9 compounds entering clinical trials, makes it successfully either in the US or in Europe. A vast majority of the attrition occurs during later phases of the clinical trials typically after well over 500 million dollars has been spent on drug development efforts. Approximately 62% of all compounds entering Phase II trials undergo attrition and 45% of all compounds entering Phase III clinical trials fail. 23% of compounds that pass all clinical trials fail during registration with the FDA thereby incurring full costs of discovery and development and opportunity costs which are as high as 10-15 years.

Figure 5. Failure rates for drugs in clinical trials

With such large and increasing costs and high chances of failure, pharmaceutical
firms have evolved to play it very safe. They have tended to develop “blockbuster” drugs, drugs which they can sell for large profits to large populations (referred to hereinafter as the blockbuster model). What this means is that the disease or condition they are targeting must affect a large population capable of paying well for a cure and without access to a good treatment currently. This strategy has worked remarkably well for them. Blockbuster drugs like Gleevec have literally worked wonders for certain cancer patients and have raked in huge profits for their creators Novartis, AstraZeneca and GlaxoSmithKline. However the blockbuster model is not without its flaws.

When it succeeds, the blockbuster model typically rakes in sales of between 1-5 billion dollars per year per drug. Once a drug comes to market, its patents last 10-15 years. By using patent extensions and various other mechanisms, firms may extend this time by a few more years, where possible. Success via a blockbuster therefore buys a pharmaceutical firm 10-15 years of time to bring the next drug to market. This is also the time that a typical drug expects to take, to develop a new drug. All its organization, and processes have evolved to deal with this timeline. To give an idea of the extent by which the blockbuster approach skews drug research, about 90% of the money spent on drug discovery goes towards discovering cures for about 10% of diseases and conditions[8].

**Why is the drug discovery process so expensive and long?**

Since the mid-1980's until the 2000's, based on profits from blockbusters, pharmaceutical firms have regularly delivered double-digit growth in sales year after year[]. Shareholders, as a result, have come to expect a high level of profits as
a result of the blockbuster model. This has resulted in some unique organizational issues with pharmaceutical firms, some of which contribute to the length and costs for drug discovery. We delve into some of these issues below.

As mentioned in the previous chapter, drug discovery and development are complicated, and long processes involving multiple sciences, each of which has progressed quite deeply over the last few decades. Based on the fact that the sciences were advancing quickly and on a product clockspeed (the time to develop a new product) of 10-15 years, pharmaceutical firms have chosen to organize by function, instead of by project.

![Figure 6. Functional organization and its lack of alignment to Market](image)
While this organizational structure has enabled new technology to be adopted very quickly within the departments, it has hindered the application of process improvements to the drug discovery process.

Interdepartmental communication in most big pharmaceutical firms is almost always quite poor and has led to the creation of information silos within companies. While matrix structures have emerged as an attempt to solve this issue, this structure has almost always led to resource struggles between the multiple projects.
As the sciences within the functions have always advanced while the product clockspeed for the drug has remained unchanged, these power struggles have typically resolved in favor of the functions.
Using Allen's organizational theory[13], the industry chose to substitute increased time to market for a product versus increased coordination between functions. Given the long product clockspeeds this has not made much difference. However as a result, processes in the pharmaceutical drug discovery and development are highly inefficient. As an example, Lead Optimization is a process that usually takes between 2-4 years in drug discovery.
Figure 10. The drug discovery and development process

Lead optimization is a very iterative process involving Design, Build, Test cycles wherein lead molecules are designed to be more efficacious while attaining desired biological properties such as metabolic stability, bioavailability, and target selectivity.
It usually takes about 50-100 cycles of lead optimization to develop a reasonable candidate for further preclinical development. The most uncertain part in each cycle is synthesis. Once a compound is synthesized, all the remaining steps can usually be completed within hours to 1 week. However, because of the functional
organization of pharmaceutical firms, these processes typically take between 2-8 weeks per cycle. Given that at each cycle we are designing molecules based on information that we have from previous cycles, faster cycle times can have multiple reinforcing effects on costs and times. Faster cycle times will greatly reduce the length of the lead optimization phase itself and reduce costs as operational overheads are lowered, all else remaining equal. It will also increase the quality of design in each cycle, since for the design phase of any cycle, due to faster previous cycles, more information is available and hence better molecules can be designed. Better molecules could also mean faster progress towards to project parameters, and therefore fewer cycles. Fewer cycles would mean fewer molecules implying lower material costs and lower operational costs. While all of these points are quite clear and have been repeatedly published in literature[, efforts to apply process improvements such as Lean or Lean Six Sigma have been highly confounded due to the organizational structure and culture within the pharmaceutical firms. Most big pharmaceutical companies still have cycle times of at least 1-2 weeks[14] when going from synthesized compound to gating results. Based on several recent publications[15,16,17,18] and the author's own experience, it is clear that process innovations can greatly help lower costs, cycle times and improve quality in the drug discovery.

The blockbuster philosophy has guided pharmaceutical organization, research, timescales, shareholder expectations and, via successful lobbying, public policy incentivizing their innovation via tools such as patents and other protections. In the absence of an effective model for innovation for non-blockbuster categories, such patients have few options other than a user-centric innovation model. On the other hand, the blockbuster approach has also led to a wasteful allocation of
research from a social viewpoint. Because the numbers of blockbuster therapies and conditions are limited, multiple pharmaceutical firms are often researching to develop “me-too” cures for the same exact condition. While the effects of competition is generally good, this usually lowers the potential window in which the pharmaceutical firm can charge extraordinary rent for its drug (the competition’s newly developed drug will soon take half the pie), thereby causing the drug costs to be even larger in the window before the entry of price-lowering competition. For example, DiMasi et al. found that the period of marketing exclusivity for a breakthrough drug in a new class has fallen dramatically from an average of 8.2 years in the 1970s to 1.8 years in the 1990s[12].

Figure 12. Years to competitive entry for a blockbuster drug
Effects of the Patent System on firm-innovation

The chemical patent system grants patents via entire chemical scaffold families, called Markushes. A pharmaceutical firm can patent not just the molecules explicitly mentioned in the patent, but also all molecules related to the molecules specified, by a few changes. For example, in the Markush structure mentioned below

```
R^1
R^2
R^3
```

```
X-Z
```

Figure 13. A Markush structure

the firm is granted ownership of any molecule which contains the show core structure where R1, R2, R3 and Z are large lists of groups. Firms, overeager to protect their chemical space from rivals, often include very hard to define definitions for these groups such as

"R1 can be a six membered heterocycle attached by a carbon linker group. A carbon linker group is defined as any group of carbon atoms containing upto 15 carbon atoms."

Such practices have often made it very hard for rivals to innovate and effectively
block out entire areas of druggable chemical space from innovation, due to doubtful ownership issues.

Sometimes, making a new drug that effectively deals with the side effect issue from an existing drug, will involve a small modification to one of the side chains of the existing drug. Without such broad ownership enabled by the patent system, a rival drug developer might be willing to perform a clinical trial to test the modified drug. However with such broad ownership, the rival will have to research in an entire new patentable chemical scaffold family, using either a process known as scaffold hopping, or via an entirely new lead identification project. All of this greatly increase the costs, time and risk associated with drug discovery, often causing promising new treatments with good therapeutic potential but low profit potential to be abandoned.

Given the various economic and scientific factors guiding drug discovery, firms routinely abandon patented scaffolds, even when they look promising for a disease, for example, when they lack the resources to proceed with development or when there are more pressing targets to be developed. Such patented scaffolds are often unattractive to the firm when visited later, because of the lapsed time on the patent. They are also unattractive to competitors because of the lack of patentability for the competitors. Because many of these patents are claimed very early on in the process, it is also tough to lay an exact value to a patent. Unlike other technology areas, where there exist marketplaces such as OceanTomo where intellectual property and patents are regularly traded, there is no marketplace for patents in drug discovery. Hence the only way to trade patents between companies
has been through laborious business development-led negotiations, involving contingent contracts. The agency costs for such trades are quite high, therefore causing many firms to forgo even considering such trades unless they discover very promising leads late in a project, which fall in a rival firm’s patent space. Firms also have no incentive to seek out cures in already patented portions of chemical space even if the patents have expired. Chemical space with expired patents, therefore lies largely unexploited for drug development. A large number of potential cures therefore, go unexplored due to such problems.

**Newer modes of innovation could be complementary and could even help the pharmaceutical firms**

Newer models for innovation could prove valuable to exploit such cures and bring about increased social welfare in healthcare. For example, by focusing on unmet needs and eliminating agency issues, user-innovation by patients can provide a very necessary complement for manufacturer innovation by pharmaceutical firms and thereby create tremendous social value. While the framework for this has not yet clearly emerged, there appear to be multiple efforts underway to build it. We will discuss some of these efforts in future chapters. As we will see later, when coupled with the right policy changes, some of this innovation could even provide the pharmaceutical firms with a secondary source of income based on users’ efforts in their patented chemical space. This secondary source of income would have a very high Return On Equity as much of the costs of clinical trials are offloaded onto the user-innovators.

Such open, distributed innovation by patients can appear to be “attacking” to the
medical and pharmaceutical establishment. Regulators, doctors and pharmaceutical firms may need to make fundamental changes to their existing business models to adapt. However, despite the difficulties, such innovation appears to be well worth striving for.
CHAPTER 3

Potential value of increased information sharing in drug discovery

With the advent of genomics and associated biological sciences such as proteomics and structural biology, modern biology is increasingly becoming an information-oriented science. The explosion of information from these sciences has led to increasingly granularity of information in drug discovery. Previously where the pharmacology of a drug might be measured by a single measurement in an animal, now, in addition its correlation with five other enzyme levels in the animal are also measured. And when it is known that the correlation is good to the point of reasonable predictability, the five other measurements are converted to cheaper in vitro tests, which are instead measured, as a proxy for the more expensive single measurement. As a result discovery efforts for a drug now accumulate far more information than for previous drugs. Also, with the advent of lab robotics in enzymology and high throughput chemistry, this increased amount of information is being measured on many more molecules. There are valuable mountains of information associated with drug discovery, being accumulated in pharma firms.

Drucker (1985): “Pharmaceuticals are a knowledge business. The value of a medicine is embodied in the knowledge needed to create and use it”[19]

A large part of the high costs of drug discovery arise from the effort required to generate some of this information leading to knowledge that creates it. Given the inherent importance of information-sharing for innovation, we discuss the current state of information sharing in drug discovery.
The current state of information sharing in drug discovery

As discussed in the previous chapter, pharmaceutical firms often are characterized by “information silos:” firm departments often do not share information they know widely within individual firms. The long time-scale of pharmaceutical research (10-15 years to develop a drug) has also led to over-competitive attitudes to sharing of information between similar functions in different firms. Since a blockbuster is launched much after the discovery process, there is often a great amount of uncertainty in determining the competitive value of any information that could be shared. Rival firms are often competing to develop a blockbuster cures for the same therapeutic area. Between the firms, this has led to a fixed pie mentality, where any and all information is often considered competitive, in the absence of guidance and any supporting logic. Below we examine the state of data sharing in each part of the drug discovery chain, shown below.

Figure 14. The drug discovery and development process
Need for increased data sharing on preclinical research

Target Identification and Validation

Open source R&D has made inroads into bioinformatics and research tools for drug hunters. Multiple open-source efforts have spawned tools such as BioPerl, BioJava, BioPython, Simple Molecular Mechanics for Proteins, and also inspired other open information initiatives such as the Human Genome Project, the SNP Consortium, and the Alliance for Cellular Signaling. About 30% of drugs that fail clinical trials fail due to efficacy reasons i.e. they affect the wrong target. Hence information about targets is often quite valuable from a competitive perspective. While there are a lot of open information and tools available, it usually takes more experiments and work based on this information, to decide on the correct protein target to develop a drug against, to treat a condition. When dealing with new unvalidated targets, information about the correct target is often guarded by drug discovery firms. To continue hiding the target, firms, in chemical patent documents, often try to be unclear about the specific target they are going after, in the treatment of a disease. However given the extent of academia’s involvement in bioinformatics and target validation efforts, such information hiding buys an increasingly smaller amount of exclusivity time for the firm.

Research on valid targets gets hindered when the tragedy of the anticommons affects target selection. As opposed to the tragedy of the commons, where commons based resources are depleted by free-riders, or inconsiderate users, the tragedy of the anticommons occurs when a resource is broken up into too many small pieces, so that the agency costs in accumulating the resource
dominates the development cost of a product, based on the resource[20]. In his book, Heller[20] describes a classic anticommons situation where the drugmaker Bristol-Meyers Squibb is not able to consider about 50 proteins possibly involved in cancer, due to the anticommons tragedy. Any of these targets could possibly lead to a cure, but cannot be investigated due to agency problems.

Firms used to tend to hide information about the right kinds of assays and animal models to use. However this is increasingly tending to not be the case as third party suppliers often develop and sell animal models or perform assay services specifically for diseases. Given that the third party wants to sell more of their product or service, it is in their interest to publish more about their assay or animal model.

**Need for increased information sharing in Lead Identification and Optimization**

Lead identification often begins with a hit screening project where hundreds of thousands of molecules are screened or assayed against the target for activity. Pharmaceutical firms, each have their own screening decks of these compounds and keep them secret from everyone else. The results of the screening are also kept secret from the world. While these results only point out micromolar hits and might be considered to be of low value, especially during later stages of the project, the fact that institutional knowledge is embedded in the screening molecules, has often kept firms from disclosing the results of screening projects.
There is currently an open source initiative called PubChem from the NIH, which is developing its own screens of molecules, based on public suggestions and publishing screening results online[43]. PubChem is a noteworthy initiative and is now beginning to develop a collection of information, valuable even to firms.

Molecule structures are a paramount secret in lead optimization. They largely codify both the intellectual property and the state of knowledge about lead optimization. When they are published, it is usually either well after they are patented and in preclinical development, or when their chemical scaffold has been abandoned, perhaps due to insurmountable toxicity problems. Despite being discouraged from publishing by the firms lawyers, scientists publish mainly due to private benefits they obtain from publishing.

Since the structure of the compound must appear in a patent and the patent becomes accessible to rivals, the most effective compound is often downplayed in the patent filing. Since patents are filed on Markushes, fuzzy Markushes are specified, which lay claim to larger chemical space than required. Alternatively some very clever patent filings, lay claim to chemical space with prominent gaps, where molecules with perhaps unsuitable toxicological or metabolic properties are known to be present, in the hope that they can lead rivals down the wrong alley.

The net effect of all of the above, is that lead optimization becomes more expensive and incorrect information often gets published. Given how much
information is generated in a program, and the limited capacity of a human being to retain such information, after a program ends, much of the knowledge, gleaned during the lead optimization project remains unavailable for the general public.

Patenting is itself expensive and when done aggressively, excludes vast portions of chemical space from patent-based drug innovation. In fact, so endemic are competitive considerations during patenting, that the tragedy of the anticommons[20] is a problem here. For example, Heller[20] points out how a potential cure for Alzheimer’s disease was prevented by agency problems emanating from patents. When a firm researches a chemical scaffold for a promising lead, only to uncover nothing of use, after much effort, they usually abandon the chemical scaffold. However not before “killing the goat and throwing it in the well”. This commonly used term refers to the practice of using patents defensively to foil a rival’s chances. At some additional cost, they patent the scaffold very extensively so as to prevent rivals from exploring the chemical scaffold successfully where they themselves failed. In addition to increasing operating costs for the pharmaceutical firm (this patenting action entails at least the cost of filing the patent, not a small sum nowadays, given the data required), this also removes any incentive and any chance for a rival to develop a cure within that chemical scaffold.

5000-15000 molecules made and assayed during the lead optimization phase. Due to resource and time constraints, and talent limitations, not all followed through, even when they look promising. This information is a treasure trove
for future generations attempting to get better at drug discovery. However it can also spawn rival innovations. Firms have absolutely no incentive to release assay data from lead development and optimization to the general public. As a result, there is a large amount of duplication of effort and slower learning throughout the industry. Information that is published in journal articles only contains very small nuggets of this information and is often filtered by the views of the publishing scientists.

**Need for increased Data sharing on Clinical Trial Failures & Successes**

Over 30% of drug failures happen in Phase 1 clinical trials, where safety studies are done on healthy volunteers[30]. Drug developing firms would benefit greatly and the whole industry would become more efficient from sharing such data for all Phase 1 failures, as the shared knowledgebase would eliminate multiple preclinical candidates[22]. At a minimum, one would expect that Phase 1 safety data should be available to patients considering enrolling in clinical trials for Phase 2 to base their decisions on. Nausea, vomiting, and painful immune reactions are common side effects when taking some of these drugs, most of which fail. Some trials such as the TGN1412 trial in the UK[21], can even result in extremely violent death. Given the nature of some of the adverse side effects of drugs in clinical trials, it would seem that revealing Phase 1 trial data information should be mandatory, in the interest of protecting patient rights.
However, clinical trial information is considered private and owned by the firm conducting the trial. This is despite the fact that the trial is conducted on participants from the general public. Firms only reveal trial information which they deem necessary for the world to know about, in order to say, convince doctors about the benefits of prescribing their medicines. This is mainly a general precaution against lawsuits. So worried are the lawyers about possible incriminations that even the people within the firm itself are generally not allowed access to the clinical trial information. This behavior promulgates selective feedback for learning and inadvertently ensures that the firms will never get better at learning about certain issues such as safety and toxicology.

Despite several attempts to mandate public sharing of clinical trial results information, such sharing has yet to occur in a uniform standard manner. While the Enzi-Kennedy bill tried to mandate sharing trial results information, due to lobbying and opposition from the pharmaceutical industry, it had to stop short and could not attain this[22]. While there are some dispersed efforts to enable sharing of such Phase 1 trial data, overall the firms claim that they will be revealing too much competitive information at this stage and the efforts themselves seem to be merely burying the public with a lot of statistics. Some of these databases are listed in the table below. Almost all of them publish only data from Phase 2 trials and beyond. The most valuable data, from Phase 1 trials is largely unavailable.
Database | Description
---|---
ClinicalTrials.gov http://clinicaltrials.gov/ | Mandatory trial registration for serious or life-threatening diseases
Clinical Study Results http://www.clinicalstudyresults.org/ | Voluntary results database for trials regardless of outcome
Search Clinical Trials http://www.searchclinicaltrials.org/ | Metasite providing access to multiple registries
Eli Lilly Trial Registry http://www.lillytrials.com/ | Trial results for marketed products
Roche Trials Database http://www.roche-trials.com/ | Registers all ongoing non-phase 1 clinical trials and data from ‘confirmatory’ non-phase 1 trials
AstraZeneca Trials http://www.astrazenecaclinicaltrials.com/ | Registers ‘hypothesis testing’ trials and results of these trials

Table 1. Various clinical trial registries

Currently much of the information for designing safe molecules, is captured as tacit knowledge, within the firms. This is essentially tacit information generated over time by firms. Since multiple firms often learn about different pieces of information with respect to safety, sharing of this information could be vital and help the industry as a whole, by preventing a lot of Phase 1 failures and by improving the quality of preclinical candidates[22]. Given the large number of drugs that fail in Phase 1 trials, its positive effects to the industry and to society, in terms of lowered drug development costs and higher success rates are unquestionable.
Does information sharing yield additional innovation?

To test if information about drug safety is indeed dispersed among multiple firms, the authors tried out an experiment where they obtained the structures of 10 current clinical candidates and showed it to a safety expert in a large pharmaceutical company. The expert, after running all his firms’ models, based on its institutional data, gave reasons for 5 of the drugs to fail in clinical candidates. While this is just one isolated example and therefore has no statistical value, when taken together with Bouchie’s comments[20], it makes one wonder about a mechanism to more rigorously test the validity in a rigorous, non-gameable setting. The potential savings to the industry from reducing Phase 1 attrition run in the billions of dollars.

As the pharmaceutical industry undergoes change in the form of mergers and acquisitions and layoffs due to financial uncertainties, and technological capabilities move outside the US, much of this tacit information may be getting lost. Capturing this information for learning, in a commons, could be key to avoid repeating mistakes. We will, in the concluding chapter, talk about an experiment we are conducting to verify if our experience in the previous paragraph is common and generalizable.

Of late, the pharmaceutical industry has witnessed a great decline in productivity of new molecule entities (NMEs). An NME is defined as a drug which is essentially new and not an extension of an already existing drug[25].
There is a tremendous amount of information and knowledge that has been generated about drug discovery and we need to harness it for future generations. In their relentless pursuit of shareholder interests pharmaceutical firms are, understandably, not very interested in sharing this information. An information commons for this kind of information, would definitely spur innovation efforts and progress in drug discovery. Some efforts have begun to effect this. We briefly discuss them in next chapters.
CHAPTER 4

Increased patient involvement in Drug Discovery – and implications for increased information sharing

The rise of social networking on the web has engendered several startups addressing networking amongst patients of chronic diseases and conditions. As part of the Health 2.0 social movement, they all strive to lower the role of physicians and firms while increasing the role of the patients. The table below lists some of them along with their main strategies.

<table>
<thead>
<tr>
<th>Company</th>
<th>URL</th>
<th>Activities</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medhelp</td>
<td><a href="http://www.medhelp.com">http://www.medhelp.com</a></td>
<td></td>
</tr>
<tr>
<td>PatientsLikeMe</td>
<td><a href="http://www.patientslikeme.com">http://www.patientslikeme.com</a></td>
<td></td>
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<tr>
<td>Trusera</td>
<td><a href="http://www.trusera.com">http://www.trusera.com</a></td>
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<tr>
<td>Eurordis</td>
<td><a href="http://www.eurordis.org">http://www.eurordis.org</a></td>
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</tr>
<tr>
<td>SugarStats</td>
<td><a href="http://www.sugarstats.com">http://www.sugarstats.com</a></td>
<td>Online tools for diabetes monitoring and management</td>
</tr>
<tr>
<td>CollabRx</td>
<td><a href="http://www.collabrx.com">http://www.collabrx.com</a></td>
<td></td>
</tr>
<tr>
<td>Vitals</td>
<td><a href="http://www.vitals.com">http://www.vitals.com</a></td>
<td>Free doctor reviews and ratings. Patients rate physicians for other patients.</td>
</tr>
</tbody>
</table>

Table 2. Some Health 2.0 startups and their offerings

These startups primarily evolved as informational services providing detailed information to patients about diseases, doctors, therapies existing and upcoming. They later helped form support-groups to patients with like diseases or conditions.
With easy-to-use tools and services for disease or condition management they allow patients to network with each other and help assess their disease progression.

With the capability to form user groups and access to specific disease information, some of the user communities have, of late, begun multiple user-centered innovation efforts for access to better cures. PatientsLikeMe (hereafter referred to as PLM) and CollabRx offer case studies of such user-innovation in drug discovery. User communities of fatal rare disorders in PLM, are experimenting with new therapies in the form of user-led trials. We discuss this phenomenon in greater detail below. CollabRx is part of a general phenomenon dubbed “Virtual Pharmas”. It functions as a virtual pharmaceutical by contracting research to contract organizations and acting as the maestro for the discovery process for orphan diseases. Below we discuss a recent effort of user-innovation involving patient-led trials at PLM in greater detail.

**PatientsLikeMe**

PatientsLikeMe (PLM) was founded with the primary mission of providing a data sharing platform for patients of rare diseases to enable information-sharing so as to improve their lives. To this end, PLM cultivates communities of patients for multiple diseases and conditions and helps them network with each other. It also offers patients easy-to-use, friendly disease management tools. The pictures below attempt to highlight some of these tools for a Multiple Sclerosis patient.
Figure 16. Some of the disease management tools at PatientsLikeMe
This combination of networking, information and disease management has enabled patients to conduct research outside the healthcare system in the form of patient-led clinical trials. If successfully adapted and adopted into the regulatory system, this could potentially lower clinical trial costs in some areas.

ALS (Amyotrophic Lateral Sclerosis) also known as Lou Gehrig’s Disease is a fatal neurogenerative disease where the patient progressively loses voluntary motor function. This culminates in the ability to initiate and control all voluntary muscular movement except for the eyes, thereby leading to death[27]. While no cure has been found for ALS, the FDA has approved treatments which are believed to slow disease progress and increase survival by a few months or relieve symptoms such as fatigue, muscle cramps and spasticity and increase their quality of life[]. Opinion is somewhat divided about the benefits of these palliative treatments as historical evidence shows that some of these treatments have caused more harm than good[]. As it strikes only about 8 people in every 100,000 there is little incentive for drug developers to invest much in researching possible cures for ALS. PLM was founded to develop data and find a cure for this disease. It hosts communities for the disease. PLM’s erstwhile CEO, Stephen Heywood died of ALS recently. PLM currently hosts 5% of the US ALS population on its site and has the largest ALS patient collection.

In March 2007, Humberto Macedo, a systems analyst from Brasilia City, Brazil was diagnosed with ALS[1,27]. Confined to a wheelchair, and unable to speak, he researched his condition on the internet and found information about a small Italian study on Lithium which indicated a beneficial effect for ALS patients[28].
The patent on Lithium has expired a long while ago. The medicine itself is not expensive and is used for other conditions. There seemed little that a drug development firm can do to extract a large profit from selling it to ALS patients. Hence there is no incentive for the firm to run expensive clinical trials to prove its utility. This is a classic example of an imperfect agency problem. ALS patients, the users, desperately seek a cure. They would die without one. The manufacturers see potential for a cure, but cannot perceive a way to justify its expense. A few drug developers are still researching for cures to ALS, however using molecules that they can patent and justify their costs. The lead users then took charge.

Realizing the lack of manufacturer incentives, and having access to a user-community within PLM, Humberto Macedo along with Karen Helzer, an ALS caregiver, initiated a trial of their own by proposing to the community that they test it themselves. Over 250 patients signed up and began testing Lithium by taking Lithium Carbonate everyday and documenting their results. The ALS patients participated in this rough trial, despite its lack of rigor or adherence to FDA trial protocols. In the absence of a cure, the patients with a limited life expectancy would try and know, rather than have a lingering doubt about an untried potential cure. As well put in a respectable editorial by the journal Nature Biotechnology[1]:

“For patients with limited life expectancy, the ability to participate in a very rough, low-level clinical study on a new treatment is far more appealing and timely than waiting for clinical data to be published in peer reviewed literature.”

To ease trial management, PLM, placed a plethora of data recording and information management tools for its patients. Some of these tools are shown in
the figure below. With these tools, and with trial participants as passionate, it was possible for the first time, to view the results of the trial, as it proceeded, in real-time. Motivated by their own needs, using these tools, the patients reported outcomes to generate a body of evidence at a level of detail never collected before. The patients in the trial essentially articulated their role, not only as users, but also as treatment subjects, reporters, analysts and both producers and evaluators of knowledge.

Figure 17. Trial management tools at PatientsLikeMe. Obtained from Ref. 31

Patient-experimentation with novel, off-label and alternative treatments (sometimes without the approval of their doctors) has been happening for a while now. Except for a few experiences which were published, these efforts have largely gone unnoticed and uncoordinated. With a platform like PLM, this work can go on, systematically along with the data being collected for analysis. Based on the
publicity from this trial, PLM’s platform has become a launchpad supporting similar trials in other areas too. Interestingly, its web site is also becoming an information commons for the data generated during these patient-led trials. For example, anyone can query and obtain, in an unparalleled level of detail, all collected data about the ALS trials.

Like with ALS, the PLM platform is currently also hosting multiple other trials in other disease areas (Low-dose Naltrexone and Stem Cell Transplants for ALS, 4-aminopyridine and botox injections to manage excess saliva and others). Given the
sensitive nature of regulation for doctors (who often have to prescribe these drugs, with off-label justifications), there is some secrecy for some of these trials.

Patient-led trials do have to prove their credibility and as such present a novel set of challenges to medicine. Risks include patient optimism, the placebo effect and many other such variables which compromise data quality. However, despite these risks such trials have the potential to create much value if used appropriately. If adapted to the current clinical regulatory system, they can offer a channel for low-cost trials for certain categories of drugs and therapies. For example, it is known that a large percentage of drugs that make it through Phase 2 trials have their development terminated mainly due to economic reasons. These drugs will either not make enough profits to the firm for the indication tested, or rank lower in potential profits than other drugs in the pipeline, which therefore consume all the fixed resources of the firm. A patient-led trial adapted to the FDA’s needs could rescue such potential cures, by offering them to patient communities in need of the cure proposed by the drug. In the event of success, both patients and firms could win, as the trials would be inexpensive, much like the drug treatment extensions enabled by physicians with off-label uses currently[]. In the area of orphan diseases where the only research to cures are externally funded either via foundations or the government, such trials could serve to reduce clinical trial costs, which are often both, the most expensive and least “creative” portion of drug discovery and development. The collected data, if publicly available, in the form, that the ALS Lithium trial is, could also serve to educate firms about successes and failures and therefore, eventually improve drug quality.
CHAPTER 5

Prediction Markets: A Novel Way to Increase Information-Sharing and potentially reduce Drug Failures in clinical testing and associated costs

Around 30% of drugs entering clinical trials fail during phase 1 due to safety issues[30]. The per-phase failure rates from 2003 are as shown below.

Figure 19. Drug development failure rates by trial

Costs for Phase II and III trials are far larger than Phase I trials. While, much work has been done in trying to fail early and quickly, as mentioned earlier in
Chapter 3, due to the lack of information sharing, there is potentially more improvement possible in predicting failure prior to Phase I trials. Below we explain why and explore how a mechanism using prediction markets may help us in the process.

**Some reasons for Phase I failure**

Phase 1 trials test for the safety of drugs. Drug safety is largely determined by metabolic processes. As the drug enters the body, it is cleared or metabolized into other products, in the liver. Sometimes a side group is cleaved, at other times, a group may be attached. Given the dozens of enzymes in the liver, each operating with its own unique sets of rules, predicting what metabolic events occur, is a very difficult process. Sometimes a drug could be metabolized into a dangerous reactive entity which could prove fatal. At other times, it could bind too strongly to an enzyme such as CYP3A4 and prevent other drugs from being cleared. While a molecule’s structure is sometimes indicative of its metabolic profile, this is not always true. In the absence of a perfect way, harmless to humans, to test a drug’s safety profile, firms end up testing on model animals such as dogs or monkeys. While such animals have metabolisms quite similar to human metabolism, they only serve as faulty surrogates at best. Given the costs and ethical considerations, there is not much data on such studies within each firm. Even the data that is available is often not of high quality. Repeat measurements and triplicates in such models can be very expensive and take time. When drugs prove fatal in these models, they do not make it to Phase I trials. But when they do, there aren’t many good ways to predict failure in humans.
Our Hypothesis

Based on the low-level of information sharing from publications, experts in firms have managed to piece together fragmented sets of rules, often augmented with private information within the firm. Based on personal communications with toxicity experts in some firms and on publications[22], it appears that toxicity data and knowledge for improving the prediction power are currently distributed in a number of firms. The tests to generate some of the data itself are quite expensive and carry ethical considerations. This has restricted the amount of data in the datasets used to generate the knowledge within the firms. The collective data if accessible would be useful. As explained before in Chapter 3, there are several inter-firm problems such as gaming, and doubt of rivalry which increase moral hazard during the sharing of such safety information. Together with these competitive problems, the possibilities of future legal problems have further contributed to a lack of high quality channels for experts to exchange high value safety information on Phase 1 drug candidates, when they can save the most money, which is before they enter trials. In the absence of this sharing, the collective wisdom of the individual experts within the firms, if accessible by any other means, would be powerful. We would like to convince the pharmaceutical industry of the value of sharing safety information. To do so, we would first like to test and see if there is, as our limited research suggests, valuable safety information available across firms, that individual firms could tap into. We would like to do so by using a prediction market for drugs in clinical trials.
Prediction Markets

A prediction market[31, 32] is an online marketplace where participants can buy and sell futures on the possibility of occurrence or non-occurrence of an event. Prediction markets, have shown value in the aggregation of wisdom from crowds. They have proven themselves in multiple circumstances, the most notable of which are Iowa Electronic Markets[33] for the US presidential elections and the Hollywood Stock Exchange[34]. The Iowa Electronic Markets regularly hosts prediction markets to predict the winners of US elections. In forty-nine elections between 1988 and 2000, it has generally outperformed the major national polls and has been more accurate than those polls, even months in advance of the actual elections[32]. Prediction markets are a mechanism for harnessing wisdom from crowds. For crowds to be wise, three attributes need to be fulfilled[32]:

1. The participants of the market, must be diverse. The market must have both experts and non-experts about the event being traded.

2. The market participants must be independent. This avoids information cascades or ‘groupthink’ where people tend to follow the crowds. Through independent purchase or sale of stocks of the probability of events, prediction markets offer such a mechanism.

3. There must be a mechanism to aggregate the information from the crowds. Prediction markets offer such a mechanism via their dynamic pricing.

Prediction Markets are being used, with reasonable success, within multiple companies. For example, Hewlett-Packard has experimented with and found that internal prediction markets are often a better predictor of product sales, than their
experts alone[36]. Google, likewise, regularly uses 300 prediction markets consisting of panels of employees to assess customer demand for new products[35]. Other companies which have experimented with them include GE, Intel and Microsoft[36].

How We Plan to Test Our Hypothesis
Toxicity information is present distributed among a lot of different players in multiple firms, independent agents and retired folk. However this information is not shared when required, due to information ‘stickiness’ and ‘repulsion’(we explain this ahead). Firms view information as competitively important, and hence have a disincentive to comment on any other firm's clinical candidate. Information is, therefore sticky from the perspective of the firm that has the information. Also, due to the competitive conceptions in the industry, when firm A comments on possible toxicity problems in firm B's clinical candidates, firm B assumes high degree of moral hazard on part of firm A, thereby causing firm B to have low reason to believe it. Hence information from firm A is ‘repelled’ or may not be considered seriously.

There is no real venue for independent or unbiased experts, such as retired personnel, to air their concerns, before a drug enters clinical trials. Even if they did so, firm B may not listen to them, as by doing so, this adds legal complications in case firm B does proceeds ahead despite listening to the problems, and post-launch problems surface with the drug if successful.
Our prediction market will work as follows. 20 drugs in Phase 1 clinical trials in the therapeutic area of cancer will be available as stocks to buy and sell. We have selected the therapeutic area of cancer, based on the fact that there is more information available for trial drugs on this class than any other class. Cancer is a terminal disease and has multiple firms working on it. So there is more experience in drugs in this class. Trials are required to be registered at the NCI clinical trials database. There are a lot of patients and newgroups abound with their chatter. Hence there is a larger possibility of obtaining information about the trial and the drug itself, during the trial. Shown below is an example of how a stock for such a trial would look, in our marketplace.
JNJ-26481585 - Bet On Will Phase 2 Clinical Trials will be announced by January 30 2010?

JNJ-26481585 is a Phase 1 trial cancer drug from Johnson & Johnson and Jannsen.

- **NCI ID:** NCT00677105
- **Other IDs:** CR013924
- **Indication:** Lymphoma neoplasms
- **Mechanism of Action:** a pan-Histone Deacetylase (HDAC) inhibitor - theorized to interfere with expression of genes that control cancer cell proliferation, angiogenesis and metastasis

The crowd forecasts the probability at: 49%

- I forecast it will be higher than 49%
- I forecast it will be lower than 49%

I have $10,000 of cash to invest.

I bet: $0 $10,000

The new forecast will be: 49.01%

The information gleaned from a clinical trial is considered the private information of the firm conducting the trial. With no reason for a firm to declare the failure (or success) of a trial, that event by itself could be impossible to adjudicate as it may not occur. However firms are mandated to declare the next phase trial of that stock at the NCI trials web site, in the case of cancer. Given the cost losses associated with late recruitment[38], it is also in their interest to declare their trial on this site. Since prediction markets need an event to adjudicate (this determines the winners of the stock when the event
concludes), we have decided to use for adjudication of success or failure, the
date when the next phase trial will be declared for a drug. The expected date
for conclusion of a trial is usually mentioned on the trials recruitment page.
Hence, with some additional padding, the date for declaration of the Phase II
trial is estimated and placed. While economic reasons are often stated for not
moving a drug to Phase III trials, such reasons rarely prevent a drug successful
in Phase I trials from moving to Phase II trials. Hence it is expected that the
adjudicated event can represent success or failure during Phase I trials fairly
well. In the event that it doesn’t, the participants are still betting on the
adjudicated event, and having access to all public information about it, are
hoped to predict correctly. Their prediction on the adjudicated event, if
correct, can still be of value to firms. Associated with every stock is also, a
discussion group, where participants may leave comments. If the prediction
market works well, it is expected that some useful information may emerge
from the discussion groups.

As seen in the figure, along with each trial are associated information, such as
the structure of the drug being tested in the trial, links to the trial page and any
publications associated with the drug. Links to patient discussion groups will
also be placed, if available.

Stakeholders in the clinical trials process, who are believed to have
information, explicit or tacit, about drug safety, will be invited to participate.
Their accounts are credited with an initial sum of pretend money (real money
cannot be used due to legal restrictions in the US). And they will be
encouraged to engage in purchasing and selling shares. A participant has a high
confidence in the successful endpoint of a clinical trial being reached, can purchase stocks for the next phase II trial of that trial drug. Conversely a participant with low confidence in the success of a clinical trial, can sell stocks for that trial. Within due time, we hope that the experts will emerge and be identifiable, via their larger cash balances.

Given the lengths of these trials, we expect that it will be at least a year before we can begin collecting statistically significant information. We plan to include members via an invite-only basis, as this will permit us to identify and perhaps correct any gaming situations which might occur. While we are still researching into correcting gaming situations, (this is a relatively new and unresearched area in prediction marketplaces[39]), we expect that the gamers will go down in relevance as the winning experts emerge.

**What we hope to get from the market’s results:**

On average drugs fail Phase I trials, 30% of the time. If the participating crowds, identify successes and failures with statistical significance most of the time, this will prove that there is wisdom in the crowds that the firms could benefit from. If this is so, our next analysis will look at how much time prior to an event, can the crowds forecast the event with accuracy. The earlier the crowds are able to forecast the event correctly, the more the value of the forecasts for the firms. If the probability of failure could, for example, be predicted just on the basis of simple rules based on the chemical structure of the drug, known to expert traders(as identified by historical successes) but not to the firm, then the firm could save
considerable cost and time by including this forecast in their decision making process. We also expect value to emerge from the blogs for each trial candidate, where firms can glean information from comments placed, about possible issues that they overlooked or were not aware of. Alternatively, firms may use this mechanism to identify experts, who can be further tapped as free agents or via mechanisms such as Innocentive.

**Possible problems**

The proposed prediction market can fail to prove our hypothesis due to several reasons highlighted below.

**Lack of liquidity:** From the experience of experts who run prediction markets regularly within companies, it usually takes a minimum of 20 involved traders to get value for success. Below this critical amount, prediction markets may not work well. With a reasonable amount of marketing amongst doctors participating in clinical trials, medicinal chemists from problem-solving venues like Innocentive, participants from industry meetings on clinical oncology and toxicology, we should be able to attain this target participation.

**Our assumption is wrong:** Perhaps drug safety is really not a crowdsourcing problem in the sense that we are considering. We assume that toxicological information is distributed amongst the targeted masses. Could it be that, while this is true, the knowledge space involved is really so large, that only a part of the information is really known? If so, the prediction market would help in some cases, and not help in others, possibly behaving like a black or grey swan[]. And the prediction market would be a failure.

**Participants don't reveal information:** The incentives are not enough or traders
feel bound to their firms, so as to keep information hidden. This can occur if the private benefits of peer-recognition are not enough to enable information revealing.

**The system is gamed successfully**: Should the prediction market prove popular, there is a chance that the system will be gamed by firms whose drugs are represented. Something similar has happened, for example, at Intrade[41], a prediction market, while holding a futures market to predict the 2008 US presidential election winner[42]. In our case, the driving reason for such gaming, would be, for example, if a firm felt that the prediction market forecasts had effects on activities, such as its potential to raise capital, or its stock price. While we cannot do much to prevent such gaming, we will be making our site, an invite site. This will enable some traceback, and eventual removal of offending members.

Despite the above problems, we feel that, given the potential benefits accruing from success, and the interest such a market could generate, it is worth pursuing further. The prediction market will start in February 2009. Those interested are welcome to email PharmersMarket@gmail.com for more information.
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