Market Exclusivity Period Extensions as a Means to Increase the Pace of Useful Drug Development

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Market Exclusivity Period Extensions as a Means to Increase the Pace of Useful Drug Development

by Javed Qadrud-Din
Abstract

Many have recognized that the pharmaceutical industry produces too few useful innovations and too many minor or incremental innovations. Many of the new drugs produced yield only slight improvements in patient welfare and public health.\(^1\) New therapies for serious diseases often serve only to extend life by a few months, cause painful or dangerous side effects, and carry high costs.\(^2\) Moreover, the rate of innovation may actually be slowing.\(^3\) Many factors may contribute to the observed paucity of useful innovation, but one important factor is an incentive misalignment. The incentives pharmaceutical companies receive do not encourage the kind of high-risk research that is likely to lead to groundbreaking new drugs. A firm must respond appropriately to the incentives that exist in its market if it is to be competitive. Consequently, firms tend to direct more funds toward research projects likely to yield incremental improvements instead of those that are more likely to yield therapeutic breakthroughs.

The current market exclusivity and patent regimes contribute substantially to the incentive misalignment. Under the current system, a breakthrough new drug for a serious illness and a drug that is an incremental improvement are awarded the same period of market exclusivity and patent protection. As a result, breakthrough drugs do not earn a premium over their incremental counterparts sufficient to incentivize their development at the rate we would want. The United States Government Accountability Office’s

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\(^1\) For example, there is controversy over whether the drug Crestor® produced any benefit over the existing therapy for high cholesterol, Lipitor® (see Wolfe, Sidney M. “Should rosuvastatin be withdrawn from the market.” *The Lancet*, vol. 364, issue 9445. (October, 2004); Editorial “The statin wars: why AstraZeneca must retreat.” *The Lancet*, vol. 362, issue 9393. (October, 2003))

\(^2\) For example, the new chemotherapy drug, Folotyn® has not been proven to extend life at all, only to reduce tumor size temporarily. It will cost $30,000 per month. (Andrew Pollack, “Questioning a $30,00-a-Month Cancer Drug.” *The New York Times*. (December 4, 2009)).

suggestion that patent protection for truly useful new drugs should be extended is sound.\textsuperscript{4} This paper will argue that a market exclusivity period extension should be awarded for new drugs that have therapeutic values great enough to be considered breakthroughs in their fields. First, the paper will show that, currently, there is a paucity of useful innovation. Second, it will discuss the current system of incentives and the reasons why they help to create a paucity of useful innovation. Third, it will explain why market exclusivity period extensions will help correct the problem, and, fourth, it will address potential counter-arguments.

I. There is a Paucity of Therapeutic Breakthroughs

The United States Government Accountability Office reported to Congress in 2006 that returns to research and development investment in the pharmaceutical industry have declined since 1993 and show signs of continuing decline.\textsuperscript{5} The report noted that pharmaceutical research and development spending increased by 147\% between 1993 and 2004, but the number of new drug applications (NDAs) submitted to the Food and Drug Administration (FDA) increased by only 38\% during the same period, and actually declined between 1999 and 2004.\textsuperscript{6} Moreover, the number of new molecular entities (NMEs) submitted to the FDA declined significantly between 1996 and 2003.\textsuperscript{7} The number of NMEs is indicative of the quantity of innovation occurring because most innovative drug products are newly discovered or newly synthesized molecules.\textsuperscript{8}

\textsuperscript{4} Id at 36.
\textsuperscript{5} Id at 15.
\textsuperscript{6} Id.
\textsuperscript{7} Id.
\textsuperscript{8} Id at 2.
FDA also noted a decline in applications for "truly innovative products" in a 2003 report on improving innovation in medical technology.\(^9\)

In 2004, only about 30% of drugs approved by the FDA were NMEs and only 14% were priority NMEs.\(^10\) Priority NDAs are classified as such by the FDA because they are likely to provide "significant improvement" over already-available therapies.\(^11\)

Between 1989 and 2000, only 24% of NDAs (NMEs and non-NMEs) were given priority status, meaning that, in the FDA's estimation, over three quarters of the drugs approved during that time had no significant therapeutic benefit over existing therapies.\(^12\)

Moreover, even priority drugs for serious diseases often do not extend life by more than a few months. A "significant" advance over existing therapies does not mean that the advance greatly improves patient outcomes or quality of life. For example, Avastin™ was given priority approval by the FDA in 2004.\(^13\) In clinical trials it was found to extend median survival time by only 4.7 months.\(^14\) The drug was also found to cause gastrointestinal perforation in 2% of patients. Gastrointestinal perforation is a serious condition in which the lining of the intestinal tract tears. The condition can result in death. The trials also found that Avastin caused serious or fatal hemorrhages in 31% of patients with a certain type of non-small cell lung cancer and 4% of patients with adenocarcinoma.\(^15\) It seems that, even though Avastin is a significant improvement over

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\(^9\) Id citing FDA, Improving Innovation in Medical Technology: Beyond 2002 (Jan. 31, 2003)

\(^10\) Id at 18-19.


\(^14\) Avastin Labeling Text, Table 1, available at http://www.accessdata.fda.gov/drugsatfda_docs/label/2004/125085sbl.pdf (last visited April 3, 2010).

\(^15\) Id. at 1.
previously available therapies, it cannot reasonably be considered a therapeutic breakthrough. Thus, the number of true breakthroughs being produced by pharmaceutical research and development is even smaller than the already small number of priority NDAs might suggest.

Some argue that the present situation is actually a good one because incremental improvements to drugs, and the production of so-called "me-too" compounds (compounds that are similar to existing drugs in mode of action and effect\textsuperscript{16}), are beneficial for patients.\textsuperscript{17} They argue that incremental improvements to existing drugs, like placing existing drugs in time-release capsules, or creating oral formulations of previously intravenous drugs help patients. Indeed, patients tend to stick to medication regimens more strictly when it is more convenient for them to take their medications.\textsuperscript{18} Proper adherence to medication regimens does result in better outcomes for patients.\textsuperscript{19} Some argue that "me-too" drugs are beneficial for patients because, though they are similar to existing drugs, they are not identical and consequently they offer additional options when one drug does not have the desired effect or is not well-tolerated.\textsuperscript{20}

It is certainly true that incremental advances provide some benefit, but, while incremental advances may be useful, they are not necessarily desirable when they come at the expense of innovations that could save additional lives or greatly improve patient

\textsuperscript{17} GAO Report at 29.
quality of life. There is a certain optimal mix of incremental and breakthrough advances that we should strive to reach.²¹ Many people knowledgeable in the field agree that the present balance results in too few breakthroughs,²² and, intuitively, it seems something has gone wrong when more than three quarters of newly approved drugs confer no significant therapeutic benefit.

II. An Incentive Misalignment is at Least Partly Responsible for the Observed Paucity of Therapeutic Breakthroughs

The fact that so few innovative and useful therapies are being developed out of the research funds spent means that something in the system of incentives for the pharmaceutical industry must be broken. It is a fundamental principle of economics that people and firms respond to incentives.²³ For some reason, firms are not being incentivized to engage in high-risk research that could lead to more breakthrough therapies. There may be many problems with the system of incentives that firms face, but one of them is that the market exclusivity regime currently in place offers little reward for breakthrough products compared to the rewards for incremental innovations. Moreover, some elements of the current system actually create disincentives for the drugs that are most desirable—i.e. cures for diseases. Firms are not intentionally holding back on creating cures for serious diseases, but the incentives do not encourage the kind of research most likely to produce outright cures. If incentives were re-aligned, more

²² Supra notes 9 and 12
investment would go to high-risk research projects that are more likely to yield products of high therapeutic value, and breakthroughs, or cures, might be developed sooner.

A. Under the current system, monopoly protection periods are the same for incremental improvements and for breakthroughs

At present, new drug developers have a period of time during which they are the sole entities that can legally market their new drugs. During that time period, they can charge a high price for the drug and recoup their research and development investments. After this period, generic producers enter the market. Generic producers can charge a much lower price for the drug because they did not need to invest in research and development, and because they did not need to pay for the expensive clinical trials that were required to approve the drug initially. Generic producers need show the FDA only that their product is bioequivalent to the original drug by filing an abbreviated NDA.\textsuperscript{24} Once generic makers enter the market, the original innovator makes little profit from the drug.\textsuperscript{25}

The period during which the innovator is the only seller in the market is derived from two legal sources: patent law and the Hatch-Waxman Act. A patent gives the owner the sole right to sell the drug for 20 years from the date the patent was issued.\textsuperscript{26} If anyone else attempts to sell or use the drug during that period, the patent owner can file a patent infringement suit to enjoin the offending activity or recover damages.\textsuperscript{27} A pharmaceutical company will usually file a patent on a compound as soon as it shows

\textsuperscript{24} Peter Barton Hutt, \textit{Landmark Pharmaceutical Law Enacted.} 1 Health Scan, No. 3, p. 11 (1984)
\textsuperscript{26} 35 U.S.C.A. §156(a) (West 2010).
\textsuperscript{27} 35 U.S.C.A. §271(e)(4) (West 2010).
some promise of therapeutic benefit. \textsuperscript{28} The compound will then have to go through the various stages of testing and the FDA approval process before it can be marketed. On average, an innovative new compound will have about 11.7 years of patent protection remaining by the time it is approved to be marketed. \textsuperscript{29}

The Hatch-Waxman Act grants the innovator firm 5 years of market exclusivity after it is approved by the FDA. \textsuperscript{30} During this period, the FDA cannot approve another product for sale that relies on the same clinical trial data as the original drug, effectively blocking generics from entering the market during the period. \textsuperscript{31} The market exclusivity period gives the firm two major advantages. First, even if the patent runs out, or is found invalid, the innovator firm will still enjoy a monopoly during the market exclusivity period. Second, during the market exclusivity period, the innovator firm will not face the threat of infringement because a potential infringer will never be permitted to market its product in the first place. If some entity other than the innovator attempted to market the same drug during the Hatch-Waxman market exclusivity period, it would be doing so without FDA approval. FDA approval is required in order to market new drugs and generics alike. \textsuperscript{32} Thus, the innovator firm does not need to spend its own legal resources to protect its product during the Hatch-Waxman market exclusivity period because the FDA takes care of the protection during that period.

The Act grants the innovator firm two additional benefits. First, it grants additional market exclusivity time if the innovator firm improves the drug in certain

\textsuperscript{28} Barton and Emanuel \textit{supra} note 26
\textsuperscript{29} Henry Grabowski, \textit{Longer Patents for Increased Generic Competition in the US: The Waxman-Hatch Act after One Decade}, \textsc{PharmacoEconomics}, Vol. 10 Suppl 2, 1996.
\textsuperscript{30} Henry Grabowski, \textit{Are the Economics of Pharmaceutical Research and Development Changing?} 22 \textsc{PharmacoEconomics} Suppl. 2 (2004) at 19.
\textsuperscript{31} \textit{Id.}
ways. Second, it gives a patent term extension equal to about half the time that the drug spent in human testing and the regulatory approval process. The patent term extension is, however, capped such that the total term will not exceed 14 years from the date of approval for marketing.

The reality of current policy is that pharmaceutical firms have about 11 to 12 years of effective monopoly protection. They cannot expect to make much profit from a new drug after that period expires. As a result, they must recoup their research and development investment and make a return on that investment within this time period. The protection periods are the same for all drugs, no matter the size of the initial research and development investment, and regardless of the magnitude of therapeutic benefit the drug confers.

**B. Incentives under the current system do not encourage high-risk research most likely to lead to therapeutic breakthroughs**

In general, incremental improvements over existing drugs are cheaper and easier to develop than breakthrough drugs. While incremental advances can often be achieved by delivering an existing drug in a new way, or by starting with a known therapeutic compound and tweaking its structure so as to change its properties, a new therapy that

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34 Id. citing 35 U.S.C. §156(c) (2006).
will offer significant therapeutic benefits often, though not always, requires discovery or synthesis of an entirely new compound. Discovering or synthesizing a new compound is costly. In order to find or create a new chemical entity that has a therapeutic effect, thousands of compounds must be screened. On average, ten thousand compounds are screened for every one compound that is ultimately approved for sale by the FDA. Incremental re-packagings of existing drugs are cheaper and less risky to develop because they often face much lower regulatory hurdles. Structural changes to known compounds that yield slightly different new compounds are also cheaper and less risky to develop, because creating those compounds requires screening fewer compounds and less complicated processes.

There are provisions in the patent statutes that are meant to prevent easy-to-develop products from receiving patent protection. The non-obviousness standard prevents patenting of advances that require little risk to invent. But it follows logically that some research projects are just risky enough to satisfy the non-obviousness standard, while other research projects, that may have higher rewards, are more risky. Moreover, even if incremental research projects and breakthrough research projects had the same chances of failure, breakthrough research is usually more expensive, and the non-obviousness standard does not take expense of an innovation into account. Thus, the

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37 See GAO Report supra note 3 at 17 (showing that one third of NMEs obtain priority status, meaning that FDA expects them to offer significant benefits over existing therapies, while only about 13% of non-NMEs obtain priority status).
non-obviousness standard is not sufficient to encourage high-risk projects that are more likely to yield therapeutic breakthroughs.

One might argue that, even though breakthroughs and incremental advances have the same monopoly period, the breakthrough drug will sell so much better than an incremental advance that there will be sufficient incentive to invest in high-risk research. Indeed, breakthrough drugs often sell well, but, particularly in the context of serious diseases, the sales premium a breakthrough will command over the sales of an incremental drug is not so large. People with serious medical conditions will want to take the best drug available. Pharmaceutical companies with monopolies created by their patents and market exclusivity periods can adopt monopoly pricing strategies and charge high prices for those drugs. As long as a pharmaceutical company has the best drug currently available for a serious condition, or a drug that is part of the best available drug cocktail, it will find a ready market for that drug and be able to charge high prices as long as its monopoly lasts. The fact that the drug is only slightly better than the second best drug on the market will not stop that drug from earning massive revenues and achieving blockbuster status. That being so, if a firm sees an opportunity to make a small improvement over existing drugs with a relatively small research and development

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42 For example, Pfizer's Sutent®, a kidney and gastrointestinal stromal tumor drug approved by the FDA in January, 2006, is one of a number of therapies available for kidney cancer and one of a few available for gastrointestinal stromal tumors. It has not been proven to cure either kidney cancer or gastrointestinal stromal tumors, but merely delays their progression (see Center for Drug Evaluation and Research Approval Package for: Application Number NDA 21-938 (GIST) NDA 21-968 (MRCC) Approval Letter(s), Department of Health and Human Services, Public Health Service, Food and Drug Administration). Despite the fact that it is not much better than other available drugs, Sutent earned over $1 billion in revenues for Pfizer in 2009 (Pfizer 2009 Financial Report at 21), enough to qualify it for "blockbuster" status. Sutent was a priority NME, but, even though it was a "significant" advance, it was not much better than other available therapies, and could not be considered a therapeutic breakthrough. It was still able to bring in over $1 billion in revenues. Thus, Sutent stands for the proposition that, in the context of life-threatening conditions, a drug need not be a large improvement over existing therapies in order to earn large amounts; it need only be a small, yet significant, improvement.
investment, there is little incentive for the firm to invest more to research and develop a
drug that is a large improvement over existing therapies.

Even if a drug that is a large improvement over its predecessors sells better than
one that is an incremental improvement, it would take a very large increase in sales to
offset a relatively small increase in development costs. This is because the drug
development and approval process is lengthy,\textsuperscript{43} and, as a result, the payoff from
investment in research and development conducted today comes many years in the future.
When firms make decisions about the projects in which they should invest, they apply a
discount rate to cash flows that will come in the future. The further in the future a cash
flow is expected, the less value it will be given in the firm's calculation. An extra dollar
earned six years in the future is worth less than an extra dollar spent in research and
development today.\textsuperscript{44} As a result, if project A costs \$1 more today than project B, then
project A will need to produce significantly more than \$1 more in future revenues in
order for the firm to prefer project A.

To better understand the decision that pharmaceutical firms face when making
research and development investment allocation decisions, it is helpful to construct rough
financial models similar to those the firm might construct. The models constructed for
this paper use rough assumptions that are reasonable for the pharmaceutical industry.\textsuperscript{45}
The assumptions are not precise, so the models do not yield precise numbers on which
policy should be based, but they do serve to illustrate the general state of the incentives

\textsuperscript{44} Stephen A. Ross et al., \textit{Fundamentals of Corporate Finance}, Chapter 5 (Irwin 1993).
that drive pharmaceutical investment decisions. The model used in Figure 1 assumes $1 billion in development costs for an incremental advance and $2 billion for high-risk research aimed at developing a breakthrough drug. Net present values were calculated using a simple model of drug development projects similar to the models used by companies when making investment decisions. The model makes the following assumptions for both projects: a 10% discount rate, an even distribution of research and development costs over 6 years of development, a constant rate ramp-up to peak sales for five years after release to the market, 100% of revenues spent on marketing in the first year of sales then ramping down to 20% of revenues by the fifth year after product introduction and continuing at 20% thereafter, 11.1% of revenues spent on general and administrative expenses during each year of sales, and a 35% tax rate. These are reasonable assumptions for pharmaceutical industry projects.\textsuperscript{46} The model subtracts the expenses from the revenues for each year, extending 20 years into the future (the length of patent protection), and applies a discount rate to the resulting cash flows. Cash flows earned in later years are worth less because of the discount rate applied to them. The model then adds the discounted cash flows for each year together to yield a net present value for each project. When making an investment decision, a firm will select the project with the higher net present value.\textsuperscript{47}

Given reasonable assumptions for the pharmaceutical industry,\textsuperscript{48} it would take a 65% increase in peak sales to justify a 100% increase in research and development costs. This is a conservative estimate, because the simplifications made in the model strongly favor the incremental drug. The model uses a single discount rate for both drugs. In

\textsuperscript{46} Id.
\textsuperscript{47} See supra note 41 (explaining that firms usually choose projects with the highest net present value).
\textsuperscript{48} Supra note 42.
reality, a higher discount rate would be used for the breakthrough drug because research with the goal of developing a breakthrough often has a higher failure rate than research to tweak an existing compound. The cash flows from the riskier project should be adjusted for the lower probability of earning them, either through an increased discount rate, or through probability-adjusted cash flows. The model also assumes that development time for both drugs will be the same, whereas it is likely that the incremental drug can be developed faster and start earning positive cash flows sooner. The model does not adjust for breakthrough project’s higher risk and longer development time and the breakthrough drug still needs to earn 65% greater peak sales in order for it and the incremental drug to be equally attractive investments. See Figure 1.

Figure 1: The graph compares net present values of a potential research project aimed at producing a breakthrough drug to the net present value of a project aimed at producing an incremental advance. The graph shows the net present value of the breakthrough drug project given a range of expected peak annual sales values that the breakthrough drug might produce. The net present value of the incremental project is shown assuming peak annual sales of $1 billion per year. The graph shows that, in order to match the incremental project’s net present value, the breakthrough product must earn $1.65 billion per year.
It is reasonable to believe that a drug that is a large improvement over its predecessors will sell better than a drug that is an incremental improvement, but, in the context of serious diseases, it is unlikely to sell so much better that it will offset a substantial increase in the initial research and development investment. Consequently, the current system of incentives for drugs that treat serious medical conditions does not incentivize extra research and development spending that could lead to drugs that are a large improvement over existing ones.

Ideally, we would want drugs that are not just large improvements over existing therapies for serious conditions, but are actually cures for those conditions with minimal side effects. Cures should be the holy grails of drug development. Intuitively, and from a social welfare standpoint, cures are the most desirable products of pharmaceutical research and development. The current system, however, actually creates a disincentive for developing drugs that are cures for diseases. At present, a pharmaceutical company that produces such a drug will turn a good profit for 11 to 12 years, as it would with any drug that is better than its predecessors. With a curative drug, however, the company will make no more significant profits after the monopoly expires. If it had, instead, produced a non-cure drug, it would be able to then produce another, incrementally better drug for that condition, and enjoy another 11 to 12 years of profitable sales. Consequently, the drug we desire most from a social welfare perspective has a far smaller financial value for its creator than a non-cure drug. A series of incrementally improved drugs can earn profits in perpetuity, but a cure can earn substantial profits only until its monopoly expires. In the real world, firms are not given the direct choice between curing a disease
and creating a series of incrementally better drugs, but, if there were such a choice, management would be remiss in its duty to maximize shareholder value if it chose to develop the cure. If the breakthrough drug in the previous example (Figure 1) were a cure, it would have to earn an even greater premium in order to be as attractive an investment as the incremental drug. In the following model, the breakthrough cure had to earn peak sales 85% greater than the stream of incremental improvement drugs in order for the two to be equally attractive investments. (See Figure 2). The perpetual stream of incremental improvements was modeled using the present value of a single incremental drug project, applied to the perpetuity formula, and discounted back from the end of the first drug’s 20-year product life.

![Net Present Value of a Breakthrough Cure at Various Peak Sales Levels compared to the Net Present Value of a Perpetual Stream of Incrementally Improved Drugs](image)

**Figure 2:** This model uses the same assumptions as the model in Figure 1. The present value of a stream of incrementally improved drugs is greater than the present value of just one incrementally improved drug. As a result, peak sales of a breakthrough cure project would have to be even higher in order to be as attractive an investment as an incremental drug project. In the model, the breakthrough cure would have to have peak sales 85% greater than the incremental drug’s peak sales in order to be an equally attractive investment.
It would be a mistake to say that the pharmaceutical industry is intentionally dragging its heels on development of cures because it can maximize investor value better by developing a series of incremental improvements. Firms are not intentionally holding back cures that can be developed, but they are responding to incentives when they make investment decisions. More investment would flow to high-risk research projects that are more likely to yield a breakthrough or cure if the incentives were different. As a result, breakthroughs and cures might be developed sooner if the incentives were improved.

At present, it makes more sense to develop incremental improvements rather than great advances because both carry the same rewards, while incremental improvements are less costly and less risky to develop. The current market exclusivity regime creates this system of bad incentives and is, most likely, a major factor behind the observed paucity of therapeutic breakthroughs.

III. Granting extended market exclusivity for breakthrough products is a possible remedy for the problem

One could imagine a number of ways to re-align incentives in order to accelerate breakthrough drug development. The list of possible responses to the problem is endless, but one way that promises to be particularly effective is to selectively extend the market exclusivity period for drugs that greatly improve the standard of care for certain serious diseases. Pharmaceutical companies would thereby be encouraged to develop therapies meeting those specifications because such therapies would offer a higher return on

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49 Shitlerman supra notes 40, 41.
investment than other potential projects. The US Government Accountability Office listed this approach as one way to help solve the pharmaceutical innovation problem.\textsuperscript{50}

Economists recognize that longer market exclusivity periods result in "larger" innovations.\textsuperscript{51} Andrew Horowitz and Edwin Lai wrote in their 1996 article, Patent Length and the Rate of Innovation, that there is some point on the spectrum between zero market exclusivity and infinite market exclusivity that results in the socially optimal innovation "size." Given the recognized problems with the relative lack of innovation in the pharmaceutical industry, and the paucity of breakthroughs,\textsuperscript{52} it seems clear that we are at a sub-optimal point on the spectrum. At our present point on the spectrum, innovations in the pharmaceutical sector are too "small." In order to increase the size of innovations, we should extend the length of market exclusivity. We can further increase the benefit of lengthening market exclusivity periods by rewarding only those innovations that we consider the most worthwhile.

\textbf{A. Extending the market exclusivity period would increase return on investment for groundbreaking new drugs enough to offset their greater research and development costs}

Creating a new drug that is a substantial improvement over existing therapies often requires a greater research and development investment than would an incremental improvement.\textsuperscript{53} That being so, the earning potential for new and groundbreaking drugs should be increased such that the returns from them will offset their additional research and development costs. Extending the market exclusivity period for drugs meeting the criteria for truly groundbreaking therapies will do just that. See Figure

\textsuperscript{50} GAO Report \textit{supra} note 3
\textsuperscript{52} See GAO Report \textit{supra} note 3.
\textsuperscript{53} Shitlerman \textit{supra} notes 40, 41.
Figure 3: This model relies on the same assumptions as the models detailed in Figures 1 and 2. The graph shows the effect of longer market exclusivity periods for breakthrough drugs. The longer the market exclusivity period, the smaller the difference in peak sales required to make the breakthrough drug project have the same net present value as the incremental project. The curve crosses the x-axis at 18 years, meaning that, in this model, the two investments are equally attractive if the breakthrough product earns the same peak sales as the incremental product and is given a market exclusivity extension of 18 years past the current 20-year monopoly protection period.

According to the model in Figure 3, extending the market exclusivity period by 10 years—resulting in a period of 27 years from the date of patent filing, and about 20 years from the date of FDA approval—would reduce the premium in peak sales required for a breakthrough research project that is twice as expensive as an incremental research project to about 10%. An 18-year extension would make the two projects equally attractive even if the firm expects both drugs to have the same peak sales levels. The assumptions in the model are rough, so the model does not suggest the precise length that the extension should be. The model does illustrate the fact that, with a long enough extension, a more-costly-to-develop breakthrough drug will be just as valuable from the
firm's perspective as an incremental drug, even if the two drugs have the same peak sales.

Extending the market exclusivity period can also mitigate the disincentive that currently exists for creating outright cures. (See Figure 4). It should be noted that the curve is asymptotic. Even granting a perpetual market exclusivity period would not permit the cure to have the same net present value as the stream of incremental drugs given the same peak sales. We can safely assume however, that a cure would sell at least a bit better than an incrementally improved drug and so a market exclusivity period extension could sufficiently mitigate the disincentive that otherwise exists for creating a cure.

![Peak Sales Percentage Increase Required for a Breakthrough Cure to have the Same NPV as an Incremental Drug vs. Market Exclusivity Extension Period](image)

**Figure 4:** This model relies on the same assumptions as the models detailed in Figures 1-3. The graph shows the effect of longer market exclusivity extension periods on a breakthrough cure. The curve represents the percentage premiums in peak sales needed for the cure drug to have the same net present value as a perpetual stream of incrementally improved drugs.

The models in this paper are, of course, simplified, and are included merely to illustrate principles. The precise length of the market exclusivity extension would have to be determined through much more detailed analysis aimed at finding an extension
length that would give a return on investment for groundbreaking therapies sufficient to encourage pharmaceutical companies to invest more in researching and developing them. The return on investment for a groundbreaking therapy should be made at least on a par with the return on investment for the average incremental improvement.

The definition of what level of efficacy a drug would need in order to earn a market exclusivity period extension would be a thorny issue. Any useful definition would, of course, be difficult to draft and difficult to apply. Policymakers would have to be very cautious not to make the definition so over-inclusive that marginal improvements over existing therapies would qualify for the reward, and not so under-inclusive that it would be too difficult to attain and thus be ineffective. The definition of “breakthrough” should be less inclusive than the definition of a drug that qualifies for priority review by the FDA. Drugs that qualify for priority review are significant improvements over existing therapies, but many of them do not rise to the level of a “breakthrough,” because they are small yet significant improvements over existing therapies. There are already sufficient incentives for small yet significant advances over existing therapies. The drugs that represent substantial improvements over existing therapies are the drugs that need additional incentives, therefore, only they should qualify as “breakthroughs,” and receive the market exclusivity extension.

The process for determining which drugs meet the definition will also need to be considered. Any pharmaceutical company that believes it has developed a drug that has a chance to get the extension will apply for it. An appropriate agency or body will need to determine whether a drug qualifies for the extension. The judgment could be made by

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54 See Sutent® supra note 43.
55 See Sutent® supra note 43 and Crestor® supra note 1, which both achieved blockbuster status even though they were, at best, small but significant improvements over their predecessors.
the FDA at the same time that it determines whether to approve the drug for sale. The 
FDA could examine the clinical trial data, to which it would already have access in the 
New Drug Application (NDA), and determine from those data whether the drug meets the 
extension criteria. During the review process, the FDA already classifies some drugs for 
priority review and others for standard review. In order to make the determination, the 
FDA decides whether the new drug would be a “significant improvement” over existing 
therapies. “Significant improvement” can be demonstrated by (1) increased effectiveness 
in treating, diagnosing or preventing a disease, (2) eliminating some “treatment-limiting” 
side effect, (3) enhancing patient compliance or (4) effectiveness in a new 
subpopulation. The determinations necessary to decide whether a drug is a 
“breakthrough” would be similar, except the standard would be stricter. Instead of 
simply a significant improvement, the drug would need to be a vast improvement in one 
or more of the four areas. If the FDA has the experience to make the priority versus 
standard review decision, it also has the experience required to make the breakthrough 
determination, because the two decisions are quite similar.

The determination would not necessarily have to be made at the same time as the 
approval for marketing. Policymakers could decide to award the extension at some point 
after the drug is released to the market. After a few years of sales on the market, more 
data on the drug would be available and perhaps its efficacy and usefulness could be 
better assessed. The FDA could still be the agency to make the determination, as it has 
the requisite expertise.

BARTON HUTT, RICHARD A. MERRILL AND LEWIS A. GROSSMAN, FOOD AND DRUG LAW 709 (Robert C. 
57 Id.
The FDA, of course, has finite resources. It would take additional resources to analyze the effects of a new drug to determine if it is a breakthrough therapy. The resources could be provided either through additional funding for the FDA from Congress or by creating a user fee that companies applying for the extension would have to pay. The charging of a user fee for FDA review of drugs has already been implemented. The user fee allows the burden of the need for additional resources to fall on the people using those resources, namely the pharmaceutical company that developed the drug, and, when the costs are passed on, the patients who benefit from the drug. A user fee will help to prevent companies from attempting to get extension for drugs that they know are not really breakthroughs. Without a user fee, a company would have an incentive to apply for an extension for drugs that do not qualify, on the off-chance that they might get an extension anyway. With a user fee, companies will not risk the resources unless they are fairly confident that their claims are meritorious.

IV. The extension should be a market exclusivity period based on the Hatch-Waxman model, rather than a patent term extension

A pharmaceutical company's monopoly can be maintained through either or both of two legal mechanisms. A monopoly can be maintained with a patent on the drug, and it can be maintained by preventing the FDA from approving any other drug based on the compound in question. The Hatch-Waxman Act created a market exclusivity period using the latter method. Creating a market exclusivity period based on the Hatch-Waxman method would be a better way to incentivize increased investment in

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59 See supra p. 6.
researching and developing drugs that are potential medical breakthroughs for two reasons. Exclusivity periods would be better, first, because it decreases the risk that the pharmaceutical company will be taking when making that investment, and second, because it will incentivize development of breakthrough drugs from compounds that are not patentable.

First, patents are not absolute protections for a pharmaceutical company’s intellectual property. A patent owner must actively defend its patent from challenges and infringements.\(^{60}\) In the 73% of pharmaceutical patent infringement or patent invalidation cases that go to trial, the infringer or patent challenger wins.\(^{61}\) Many cases never go to trial and instead result in settlements\(^{62}\) in which the pharmaceutical company may have to pay a substantial sum to stop the infringing party from carrying on its activities. When a pharmaceutical company loses an infringement suit or has its patent rendered invalid, it loses the benefits of its monopoly. Consequently, it is much more difficult for the company to earn an adequate return on its investment in research and development. As a result of the looming specter of litigation, patent protection is fraught with risk. Risk is taken into account when pharmaceutical companies make decisions about where to invest. Additional risk lowers the present value of a potential project and makes the firm less likely to invest in it. Thus, a patent term extension would be a weaker incentive than an incentive method that did not carry those risks.

\(^{60}\) The patent owner must bring a suit to stop an infringer from carrying on infringing activities (see 35 U.S.C.A. §271)


\(^{62}\) Id. (of the suits studied that were brought by firms to defend their patents 38% of them ended in settlement).
With a market exclusivity period on the Hatch-Waxman model, the risks and expenses associated with litigation are minimized. The FDA cannot approve another drug containing the company’s compound during the exclusivity period.\(^{63}\) As a result, an infringing drug cannot be marketed legally.\(^{64}\) If an infringing drug were marketed, the FDA would enforce the exclusivity period by using its resources to stop the illegal marketing of an unapproved drug.\(^{65}\)

Second, granting an extended market exclusivity period for breakthrough drugs would encourage the development of breakthrough compounds that are not patentable. Many compounds that could have therapeutic value are not pursued by pharmaceutical companies because they cannot be patented. These compounds often cannot be patented, either because they are already widely known, and not novel, and therefore unpatentable,\(^ {66}\) or because their use is obvious, and therefore they are unpatentable.\(^ {67}\) Unlike other fields, in the pharmaceutical industry, even a well-known or obvious product takes considerable resources to develop because drugs must go through the expensive clinical trial process.\(^ {68}\) Consequently, many promising compounds, which could lead to therapeutic breakthroughs, never make it to market, or are delayed unnecessarily.\(^ {69}\) If pharmaceutical companies could count on a long market exclusivity

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\(^{63}\) Grabowski supra note 27.
\(^{64}\) 21 U.S.C.A. § 355 (West, 2010)
\(^{66}\) Benjamin Roin, Unpatentable Drugs and the Standards of Patentability, 87 Tex. L. Rev. 503, 517 (2009).
\(^{67}\) Id. at 532.
\(^{68}\) Id. at 511.
\(^{69}\) Id. at 555.
period overseen by the FDA, they would not need patent protection in order to develop the most promising unpatentable compounds.\textsuperscript{70}

Given that the goal is to incentivize more research into potential medical breakthroughs, a market exclusivity period extension for breakthrough new drugs based on the Hatch-Waxman model would be preferable to a patent extension. The market exclusivity period extension offers a stronger incentive than a patent period extension because it has less risk of being infringed or invalidated. With less risk, pharmaceutical companies will assign higher value to the extension when making their investment allocation decisions. Market exclusivity period extensions have the added benefit that they can mitigate a serious problem with the patent system that hampers development of many promising compounds that are obvious or not novel.

V. Responses to counter-arguments and alternative systems

There are a number of objections that can be leveled against the proposal in this paper. Many believe that drug prices are too high. They claim that pharmaceutical companies already make excessive profits, and do not require additional incentives. Also, even if one accepts that altered incentives are needed, there are alternative ways in which incentives could be re-aligned. I will argue that a re-alignment of incentives is necessary if we hope to speed up the pace of useful medical innovation, and that speeding useful medical innovation should be one of our goals. I will also argue that, while other methods of re-aligning incentives could be useful, the market exclusivity period extension is one of the best methods for reaching the goal.

\textsuperscript{70} \textit{Id.} at 564
A. Market exclusivity extension would not give undue rewards to pharmaceuticals at consumers’ expense

Some people argue that pharmaceutical companies already make enormous profits and charge too much for drugs. They argue that further incentives for pharmaceutical companies are unnecessary, and that monopoly periods for drugs should be, or that price controls should be established.\textsuperscript{71} They point out that access to medication would be improved by ending monopolies sooner, allowing generics to enter the market, and bring prices down to a universally affordable level sooner. There is certainly a difficult balance to be struck between providing drugs at a low price and paying for research into new drugs. However, the issue of high drug prices is gradually becoming less significant for individual consumers in light of recent health reforms that will lead to almost universal insurance coverage.\textsuperscript{72} Previously, high drug prices meant that some people could not afford necessary medications. Now, society as a whole will bear the cost of medications, and the access problem is no longer as serious an issue.

The remaining question is: how much we are willing to spend as a society on drugs? Since monopoly prices encourage firms to invest more in research and development, and the exclusivity extensions would encourage firms to allocate more funds toward socially desirable research projects, it seems that it would be desirable to implement the extensions. Some might argue, however, that, even if we would benefit from increased research into the types of drugs that are most desirable, we do not want society to spend more on drugs than it already does.

\textsuperscript{72} HR 3590 §1401
We currently spend about 16% of GDP on healthcare,\textsuperscript{73} and some believe that that is too much. There are a few arguments that oppose such a view. First, increasing market exclusivity periods as proposed will improve the return society gets from the money spent, because it will incentivize research into more useful products. Second, healthcare is one of the best sectors in which to spend society’s resources. There can be no better use of money than to keep people alive and healthy. The list of things that matter more than life and health is a short one. Medical research yields a very high return on investment from the perspective of enhancing human wellbeing. Third, even if expenditure on pharmaceutical research and development in the US were sub-optimally high, excess spending by the US helps the global research and development spending level come closer to the optimal level, because other countries’ spending is sub-optimally low.\textsuperscript{74} Moreover, it will enable the US to continue to lead the world in the field of pharmaceutical research and production.

**B. Many potential abuses of the market exclusivity extension could easily be combated by threatening to revoke the extension if a firm engages in such abuses**

One potential abuse of the market exclusivity extension system would be for firms to wait until the end of their extended market exclusivity period before making some easy incremental improvement to their drug, and gaining patent protection for that improvement. For example, the firm could wait until the end of the extended period to place the same molecule in a time-release capsule, and then enjoy an additional period of


patent protection. One response to this potential abuse would be to require firms taking advantage of the extension to make all obvious and easy re-formulations available as soon as practicable. The FDA could use its expertise to come up with a list of such improvements and require that the firm make those improvements available, or risk losing the extension. No firm would want to risk losing the extension, so it is likely that there would be high compliance.

C. Market exclusivity period extensions would not slow innovation by allowing pharmaceutical companies to sell a monopoly product for a long period without innovating further

Some might argue that granting a lengthy monopoly would allow pharmaceutical companies to, essentially, “rest on their laurels” and fail to make additional advances. Actually, under a market exclusivity regime, a pharmaceutical company would still have an incentive to make further advances, even within the same field as the drug on which they have the market exclusivity. A pharmaceutical company would enjoy a monopoly with its market exclusivity period only as long as its drug was the best one on the market. If another company created a better drug, be it a breakthrough drug, or mere incremental improvement, the company with the market exclusivity period would quickly lose market share. As a result, even the company that holds the extended monopoly has an incentive to continue to innovate in order to stay ahead of the competition.

D. Market exclusivity periods allow for use of a protected compound for research as soon as the patent period expires

It might be problematic if extended protections for breakthrough drugs allowed the developer of a breakthrough compound to monopolize the compound’s use for further
research. With a market exclusivity period, the compound could be used for further
research as soon as the patent on that compound expired. Patents allow their owners to
stop others from using the protected product at all.\textsuperscript{75} Consequently, patents allow their
owners to stop others from using the innovation for further research. A market
exclusivity period does not allow the developer of the drug to stop others from using it
for further research because it only blocks others from selling the drug.\textsuperscript{76} Other uses are
not prohibited. As a result, extending market exclusivity periods would not hamper the
pace of research by limiting access to breakthrough compounds for research purposes.
As under the current system, others can begin research with a breakthrough compound as
soon as the patent on the compound expires.

\textbf{E. Extending market exclusivity in the US would cause US consumers to pay
an unfair percentage of the drug research bill for the rest of the world,
but the US consumer would still be better off under the proposed regime
than under the current one}

American consumers already pay higher prices for drugs than anyone else in the
world.\textsuperscript{77} Pharmaceutical companies derive nearly half of their revenues from the United
States.\textsuperscript{78} Other developed countries that are capable of paying high prices for drugs have
socialized healthcare systems. Since the government is the only purchaser of
pharmaceutical products in socialized healthcare systems, the governments are able to
bargain down pharmaceutical prices.\textsuperscript{79} As a result, pharmaceutical companies recoup a

\textsuperscript{75} See Ann Weilbaecher, Diseases Endemic in Developing Countries: How to Incentivize Innovation, 18
ANNALS HEALTH L. 281, 285 (2009). (Stating that patent rights often create “patent thickets” which retard
further research).
\textsuperscript{76} 35 U.S.C.A. §156(a) (West 2010).
\textsuperscript{77} See Chu supra note 71.
Available at http://129.3.20.41/eps/get/papers/0405/0405002.pdf
\textsuperscript{79} See Chu supra note 71.
lot of their research and development investments from US sales. Thus, American consumers subsidize drug research and development for the rest of the world.

If the US were to extend market exclusivity periods for certain drugs, it is unlikely that other developed countries would voluntarily follow suit. Their incentive would be to free ride, as they already do, off of US expenditure on drug research. Treaties currently allow patents to be filed internationally, and international patents are generally enforced in developed countries.\textsuperscript{80} Once a drug is off patent, other developed countries will begin to buy or produce generics. As a result, they will not just be paying a negotiated lower price for the new drugs while they are on patent, they will actually be paying practically nothing for the same drugs once they are off patent, while American consumers will have to pay monopoly prices created by the market exclusivity extension. American consumers will be providing an even larger subsidy for research from which the rest of the world benefits.

This is a strong argument against extending market exclusivity periods. There are, however, two counter arguments. First, even if only US consumers are paying monopoly prices, and the rest of the world is not, US consumers will still benefit from the re-alignment of incentives. The US market is the largest healthcare market in the world, making up nearly 50\% of global healthcare spending.\textsuperscript{81} As a result, even if just the US market offers the extended market exclusivity period, it will provide a strong incentive to which pharmaceutical companies are likely to respond. Second it would be ideal if an international agreement could be reached to respect the market exclusivity period just as

\textsuperscript{81} Supra note 79
an agreement has been reached over patent protections.\textsuperscript{82} It is not altogether unrealistic to think that such an agreement might be possible, at least among developed countries. A number of other developed countries have large pharmaceutical industries, notably the United Kingdom,\textsuperscript{83} France,\textsuperscript{84} Switzerland,\textsuperscript{85} Israel,\textsuperscript{86} Germany,\textsuperscript{87} and Japan.\textsuperscript{88} Those countries would also benefit if extended market exclusivity periods were honored across the developed world. The United States could encourage those countries to cooperate by only granting market exclusivity extensions to American firms and to firms from countries that reciprocate by granting market exclusivity extensions to American firms.

**F. Extending market exclusivity periods for all drugs would not be as beneficial as extending them only for breakthrough drugs**

Extending market exclusivity periods for all drugs might be somewhat helpful in spurring more rapid innovation. Longer exclusivity periods would incentivize “larger” innovations even if the extensions were not directed solely at breakthrough drugs.\textsuperscript{89} The disincentive problem for cures would be mitigated.\textsuperscript{90} A drug for a serious illness that is much better than its predecessors will likely sell slightly better than an incremental improvement.\textsuperscript{91} With a longer market exclusivity period, this slight price advantage that the large improvement has over the incremental improvement will weigh more heavily on corporate decisions because both drugs will have more time at peak sales levels. During

\textsuperscript{82} See supra note 77
\textsuperscript{83} GlaxoSmithKline is based in the United Kingdom.
\textsuperscript{84} Sanofi-Aventis is based in France.
\textsuperscript{85} Hoffman-La Roche and Novartis are based in Switzerland.
\textsuperscript{86} Teva Pharmaceuticals is based in Israel.
\textsuperscript{87} Boehringer Ingelheim, Bayer, and Merck are based in Germany.
\textsuperscript{88} Astellas Pharma, Daiichi Sankyo and Eisai are based in Japan.
\textsuperscript{89} Horowitz supra note 47.
\textsuperscript{90} Figure 4 supra.
\textsuperscript{91} See supra note 39.
that extended time, the slightly better price that the company can get from the large improvement drug will accumulate. Even though additional dollars earned in the future are worth less than additional dollars spent today, if you earn enough additional dollars in the future, they will eventually add up to offset dollars spent today.

While extending market exclusivity periods across the board would be helpful, targeting breakthrough drugs for extensions would be better for two reasons. First, if all drugs received a longer market exclusivity period, incremental advances would have the same market exclusivity period as breakthrough drugs, as is the case today. As a result, the incentive to create breakthrough drugs would be improved under the across-the-board market exclusivity extension regime, but would not be as strong as the incentives would be if only breakthrough drugs received the extension. According to the model in Figure 3, if only breakthrough drugs receive the extension, an 18-year extension will offset a 100% increase in research and development costs, assuming the same peak sales figures. With an across-the-board extension, the extension could be as long as 21 years, and it still would not come close to offsetting a 100% increase in research and development costs.

G. Direct payments from the government would not be as beneficial as market exclusivity extensions

Many have advocated a system in which direct payments from the government could be used to incentivize pharmaceutical research and development. Direct payments from the government as rewards for producing breakthrough therapies would create a strong incentive for pharmaceutical companies to invest more money in research that would be likely to yield such breakthroughs. There are, however, a few significant

92 See e.g. Sara E. Crager and Matt Price. Prizes and Parasites: Incentive Models for Addressing Chagas Disease. 37 J.L. MED. & ETHICS 292, 295.
drawbacks to that approach. First, the market is often better at assigning an efficient value to a certain drug than individuals or government bodies are. With an extended market exclusivity period, a drug will still only earn as much in the market as its usefulness warrants. If, hypothetically, a company were able to qualify its drug as a "breakthrough" even though it was not particularly useful or beneficial, the government would still have to pay the reward money. If, on the other hand, a company did the same thing under a market exclusivity extension regime, the company would not receive an undue reward because few people would buy the drug. The company would have a long exclusivity period, but would be unable to profit from the drug.

Second, market-based incentives are generally preferable to direct government payments because direct government payments have to be raised from taxes. Taxes cause society to incur a "dead-weight loss." Market-based incentives would incur no such dead-weight loss and would therefore be preferable whenever a viable market-based alternative exists, as it does in this case.

It is important to note, however, that a viable market-based incentive does not exist for drugs for diseases that primarily affect people in the developing world. For breakthroughs in treatment of these diseases, a market exclusivity period extension would be ineffective because, even with a long market exclusivity period, people in the developing world cannot afford to pay enough for pharmaceutical companies to earn a sufficient return on their investments. This is why so few treatments for diseases that

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93 Mankiw, Gregory. *Principles of Economics.* 5th ed., South-Western Cengage Learning, Mason, OH. (2009), Chapter 8 (Explaining that a dead-weight loss occurs when taxation moves a market away from its natural equilibrium of supply and demand. When a tax is imposed, some people who would have bought a good at the pre-tax price no longer demand the good, and, accordingly, that amount the good is no longer supplied. Society has thus lost that amount of value).
predominantly affect developing countries have been devised. To incentivize investment in developing treatments for diseases that primarily affect people in developing countries, direct government subsidies probably are the most effective incentives.

**H. Market exclusivity period extensions are better than increasing funding for research**

The government already provides funding for research that might lead to medical breakthroughs. Increasing the amount of funding the government provides would help increase the pace of medical development. Government research funds have, traditionally, gone to basic science rather than directly to drug development, but, even if funding were made available for drug development, it would not be as effective as extending market exclusivity periods for breakthrough drugs. First, the government would have to provide a huge amount of money to match the expenditures made on drug research and development by the private sector. The pharmaceutical industry in the United States spent $40 billion per year on research and development as of 2004. The US government spent $28.5 billion to fund research in fields related to medicine as of 2004. The government would need to significantly increase its spending in order to increase the pace of medical breakthroughs. Perhaps the government should spend more on funding medical research, but there is no reason why we should not also attempt to

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94 Crager *supra* note 89 at 292; Weilbaecher *supra* note 72 at 281.
96 GAO Report *supra* note 3 at 4; Congressional Budget Office Study *supra* note 33 at 7.
97 Congressional Budget Office Study *supra* note 33 at 28.
align incentives so that the vast amounts spent by the private sector are channeled towards the most desirable projects.

I. Regulatory hurdles could be decreased, but that would not be as desirable as extending market exclusivity periods

Some have proposed decreasing the regulatory hurdles that all new drugs face, or decreasing regulatory hurdles only for the most promising new drugs. Regulatory hurdles have already been decreased, to some extent, for the most promising new drugs through the priority review process. Regulatory delays and requirements certainly impose very significant costs on pharmaceutical companies. Reducing them for certain types of drugs would make investment in the projects that might yield those drugs more appealing; however, we must be cautious when reducing regulatory requirements. The requirements that exist were put in place in order to promote the public health. Streamlining the process might expose the public to greater danger from drugs that turn out to be harmful. As it is, the process does not catch every potentially harmful drug. If the process can be streamlined in some way that does not put the public at greater risk, then it should be streamlined, however, it is unclear what savings could be made in this way before the risk would become too great. As a result, extending market exclusivity

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98 RICHARD A. EPSSTEIN, OVERDOSE: HOW EXCESSIVE GOVERNMENT REGULATION STIFLES PHARMACEUTICAL INNOVATION (Yale University Press 2006).
99 GAO Report supra note 3 at 36.
101 Food Drug and Cosmetics Act §903(b)(1) (stating that FDA’s mission is to promote the public health by reviewing clinical research and taking appropriate action on the marketing of regulated products).
periods would probably be preferable, though some safe regulatory streamlining should certainly be undertaken where possible.

VI. Conclusion

The drug development process does not seem to be yielding as many useful breakthroughs as it could be. This paper does not argue that pharmaceutical companies are not currently trying to develop breakthrough products. Pharmaceutical companies and biotechnology companies certainly are trying to develop breakthroughs. This paper argues that the pace at which those breakthroughs are developed can be increased by incentivizing investment in high-risk research. Under the current system, incremental improvements and major breakthroughs yield similar rewards for their creators, but breakthroughs are far more difficult, costly, and risky to develop. If breakthrough therapies for certain diseases were rewarded with a longer market exclusivity period, then the system of incentives that pharmaceutical firms face would be significantly improved. There would be an incentive to produce breakthrough drugs and, therefore, research projects likely to yield breakthroughs would be undertaken more often. As a result, it is likely that the pace at which medical breakthroughs are achieved would increase. There are a number of other ways in which research likely to yield breakthroughs might be incentivized, and a combination of these approaches should probably be adopted. Increasing market exclusivity periods for breakthrough drugs is one of the strongest incentives that can be offered, and it has fewer drawbacks than many of the other possible methods.