Prospect patents and CRISPR; rivalry and ethical licensing in a semi-commons environment

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ABSTRACT

The prospect theory of patents views patents as a tool for the development and commercialization of inventions. Prospect patents rely on broad control of technology so that rivalry between competing products is diminished thus avoiding waste of common-pool resources. The theory has been widely criticized but in this article we argue that it does not address the realities of an economy where many innovations are created by universities. Although university patents on inventions such as new gene-editing tools fit squarely in the definition of prospect patents, they may still allow rivalry to resurface at the commercialization stage. This rivalry is not between competing firms; it is between competing visions of the prospect: ‘the university’s vision versus the licensees.’ We use as a case study the CRISPR-Cas9 technology invented by universities and commercialized by licensees. We employ patent landscape analysis showing that CRISPR-Cas9’s prospects comply with the characteristics of prospect patents and, above all, diminish rivalry at the commercialization stage. As the lack of competition leads to excessive treatment prices, tensions arise because the licensee understands CRISPR-Cas9 as a revenue-generating prospect, whereas the university views it as a technology requiring broad distribution. Such discerning visions can breed rivalry between licensor and licensee despite broad patent rights. In addressing this we turn to the literature on semi-commons, which implies an environment where private rights of exclusion such as prospect patents work with ethical licenses and a domain of resources open for reuse to foster innovation. We argue that in this environment, universities can emerge as important actors in the regulatory enterprise through additional ex post
licensing. To this end, we propose a market-based solution in the form of a license allowing for patent re-licensing if the licensee fails to address a predefined demand for the final product.

KEYWORDS: prospect patents, CRISPR-Cas9, semi-commons, university patents, rivalry

I. INTRODUCTION

In his 1977 article, *The Nature and Function of the Patent System*, Edmund Kitch argued that patents have a 'prospect' function, where a prospect implies the commercial applications of a mature technology. In contrast with the mainstream justifications of patents as either a means to reward innovators for their *ex ante* R&D investments or as a way to promote the disclosure of knowledge, Kitch's justification for the patent system was forward-looking, focusing on the *ex post* aspect of the commercialization of innovations. Central to this view of patents is the need for broad rights to be assigned to the innovator. Such broad rights allow for the unified control of the technology, minimizing rivalry between competing designs and innovators. The idea is that rivalry, by leading to a more competitive outcome, would inevitably diminish the benefits from commercialization and the corresponding incentives to develop the technology to its full potential.

Although Kitch’s prospect theory is now a standard part of the law and economics literature, it is controversial. Critics point out that broad patents allow inventors to claim more than what is invented. They also question Kitch's presumption that rivalry is resolved, or that it is in fact socially wasteful. If anything, prospect patents seem to push rivalry back in time at the discovery stage, a critique that resonates with the empirical findings of this article as well. More importantly, the *ex post* justification of patents may still create conflicts with follow-on improvements at the commercialization stage, without leading to faster technology progress.

Focusing on rivalry at the commercialization stage, we argue that Kitch’s aspiration for the elimination of rivalry between the prospect and its follow-on improvements is indeed happening in the context of our case study on CRISPR-Cas9. Feeney et al. also make the link between the prospect theory of patents and the current CRISPR patent licensing environment. The authors explain that the universities have realized that the availability of exclusive rights for products, which are expensive to develop may better promote their development. Yet, this lack of conflict does not necessarily mean that prospect patents fully curtail rivalry. Rivalry may unexpectedly resurface later, albeit between licensees and licensors. This rivalry is not between competing technological

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1 E. W. Kitch, *The Nature and Function of the Patent System*, 20 J. LAW ECON. 265–290 (1977).
2 R. P. Merges & R. R. Nelson, *On the Complex Economics of Patent Scope*, 90 Col. L. REV. 839–916 (1990).
3 D. G. McFetridge & D. A. Smith, *Patents, Prospects, and Economic Surplus: A Comment*, 23 J. LAW ECON. 197–203 (1980).
4 M. Abramowicz & J. F. Duffy, *Intellectual Property for Market Experimentation*, 83 NYUL REV. 337 (2008).
5 J. F. Duffy, *Rethinking the Prospect Theory of Patents*, 71 U. CHI. L. REV. 2, 439–510 (2004).
6 M. A. Lemley, *Ex Ante versus Ex Post Justifications for Iproperty*, 71 U. CHI. L. REV. 9, 129–149 (2004).
7 O. Feeney, et al., *Patenting Foundational Technologies: Lessons from CRISPR and Other Core Biotechnologies*, 18 Am. J. Bio. 36–48 (2018).
designs aiming at using the knowledge pool in different ways. It is between competing ‘visions’ of the same technological design.

The idea of unification of control, which is central to prospect patents, largely stems from an era when firms had an integrated value chain linking R&D and manufacturing, developing their technologies ‘in-house’. However, firms are not always cocooned within their internal R&D capabilities. In fact, manufacturers frequently incorporate R&D efforts carried ‘out-of-house’ in the so called open innovation paradigm. A prominent way of doing this is by means of licensing ideas from universities. Under the prism of this vision, the unification of control is difficult because the inventor and the agent commercializing the technology are not always the one and the same. Though such segmentation does not impede commercialization when the innovator and the licensor share similar views about the innovation’s prospects, things may be different when the innovator is a university.

Universities and their licensees often make strange bed-fellows because the two parties do not necessarily share the same vision, mission and goals. When the prospect does not abide with the university’s vision, the ensuing misalignment of aspirations can lead to tension and disagreements. Examples are cases where faculty discovered that clinical trials placed patients at risk; because of disagreements over the business direction of university spin-offs; or due to concerns that the university aligned its policy and licensing with industrial interests. A vocal example of a disagreement between ivory tower and industry involved the AIDS drug Zerit that Yale University had licensed to Bristol-Meyers Squibb, which sold the drug at very high prices to South Africa and other developing countries. In this occasion, what Yale University understood as the purposes of commercializing Zerit conflicted with the aspirations of Bristol-Meyers Squibb. The pharmaceutical company viewed Zerit under the prism of a revenue-generating product, whereas Yale understood Zerit as a product whose primary purpose was to save lives, requiring the broadest distribution possible. A more recent example of rivalry over high pricing involved the 2019 University of California, Los Angeles (UCLA) student protests over the prostate drug enzalutamide that UCLA has licensed to Pfizer.

It seems that Kitch’s implicit understanding of the relationship between licensor and licensee is incomplete and not as simple as originally envisioned. In fact, as the examples of Bristol-Meyers Squibb and Pfizer illustrate, disagreements over the purpose of the drug could emerge at the commercialization stage, forcing firms to alter their business

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8 Contemporary examples of such innovations include Apple’s development of iPod and Nintendo’s Wii.
9 H. W. Chesbrough, Open Innovation: The New Imperative for Creating and Profiting from Technology (2003).
10 J. West & M. Bogers, Leveraging External Sources of Innovation: A Review of Research on Open Innovation, 31 J. Prod. Innov. Manag. 814–831.
11 D. C. Mowery et al., Ivory Tower and Industrial Innovation: University-Industry Technology Transfer before and after the Bayh-Dole Act. (2015).
12 N. F. Olivieri, Patients’ Health or Company Profits? The Commercialisation of Academic Research, 9 Sci Eng Ethics 29–41 (2003).
13 T. Kennedy, Lavish Praise, then a Quick Ouster for Star U Scientist; University fired Doris Taylor from the board of the promising spinoff firm that she founded. Summary. STAR TRIBUNE, 2011.
14 C. Hamilton & D. Schumann, Love and Hate in University Transfer: Examining Faculty and Staff Conflicts and Ethical Issues, in The Contribution of Love, and Hate, to Organizational Ethics (2016).
strategies. Thereby, despite Kitch’s desire for unhindered commercialization, prospect patents may be unable to fulfill this role. The rivalry between universities and their licensees is the focus of this paper, which views universities patents as textbook examples of prospect patents. To illustrate our argument, we focus our attention on one of the most important university innovations of this decade: CRISPR-Cas9, a gene-editing tool adapted from a naturally occurring genome editing system in bacteria, which allows removing, altering, or adding genetic material at particular locations in the genome with great precision.

As we explain CRISP-Cas9 technology has all the characteristics of a prospect. True, many university inventions are understood to capture well the idea of a prospect as patents clearly provide incentives for commercialization and not invention. But beyond this aspect, we view CRISP-Cas9 as a prospect because, as we will describe in detail, it has an extended spectrum of possible future applications; it has witnessed acute rivalry in the form of a patent race at the discovery stage; and it is protected by broad property rights in the form of extensive patent portfolios that universities have exclusively licensed to surrogate companies.

Importantly, by reading the abstracts of the patents, the surrogate firms have licensed from the universities and the patents on improvements they are pursuing on their own, and by outlining their product pipeline, we find that the surrogate firms have largely focused their patenting and business strategies on non-conflicting technological paths. Thereby, despite sharing a common starting point, the surrogate firms have chosen to branch their strategies and focus on non-overlapping uses, precluding rivalry at the commercialization stage. To rephrase, despite the anticipation that rivalry is not subdued at the commercialization stage because follow-on patents will create conflicts due to overlapping exclusive rights, and in line with prospect theory, rivalry in the form of competition seems subdued at the commercialization stage.

Therein lays the conundrum of prospect patents: because broad patents stifle competition they inevitably lead to supracompetitive prices. In fact, the price tag of new gene therapy treatments stemming from CRISPR-Cas9 is inordinate, raising concerns about access. For example, the price of Luxturna (a gene therapy for Leber’s congenital amaurosis—an eye disease) costs $425,000 per eye. These concerns have raised eyebrows, and pressure is rising for universities to take action so that therapies are priced and structured in line with the public mission of universities. As we explain the emphasis on commercialization and wealth maximization is at the heart of a species of property such as a prospect, therefore a conflict emerges. This conflict is not between competing designs as originally envisioned by Kitch. It is between two different visions and aspirations about the prospect’s potential. The one vision encompasses ethical

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15 R. D. Nelson and R. Mazzoleni, Economic Theories about the Costs and Benefits of Patents, in INTELLECTUAL PROPERTY RIGHTS AND RESEARCH TOOLS IN MOLECULAR BIOLOGY 1–9 (1997).

16 Note that the term ‘surrogate companies’ has been introduced by Contreras and Sherkow (2017) and it refers to profit companies responsible for commercialization, development and sublicensing university IP to others. See J. L. Contreras & J. S. Sherkow, CRISPR, Surrogate Licensing, and Scientific Discovery, 355 SCIENCE 698–700 (2017).

17 See for example Lemley, supra note 6, at 129–149.

18 J. S. Sherkow, Focus: Genome Editing: CRISPR, Patents, and the Public Health, 90 YALE J. BIOL. MED. 667 (2017).
Concerns such as those concerning price, whereas the other, unhindered by the espousal of social values, does not.

Rivalry in this sense can be disruptive to commercialization despite the monopoly control of surrogate firms over specific applications of CRISPR-Cas9. This is because universities hold the essential patents needed in order to deploy this technology. The essential nature of these patents and their value was brought to light unexpectedly when the European Patent Office (EPO; in January 2020) revoked the first patent granted on CRISPR-Cas9 to the Broad Institute of MIT and Harvard (until revocation they were the owners of the first patent on CRISPR-Cas9 genome editing that specified usage for multicellular organisms), ending a long-standing dispute about patent ownership with the University of California, Berkeley. This decision led the US stock price of Editas Medicine (the main licensee of the Broad Institute) into a free fall, losing 17 percent of its value; the equivalent of about $250 million. This amount is no doubt indicative of the leverage the University of California now has on surrogate firms, as without this license commercialization is very difficult.

Indeed, the potential of disagreements between universities and the entities to which the patents are licensed is looming; rivalry may be nigh and this may be a good thing too. Public sector institutions can adopt more socially responsible patenting and licensing policies. Though prospect patents are all about bringing something to the market and as such any limits posed to commercialization are thought as interfering with market exchanges and potentially stalling innovation, ethical licenses need not produce a stalemate. We explain the specific function of ethical licensing in a competitive market using the framework of ‘semi-commons’, which implies the coexistence of private rights of exclusion, management by public authority, ethical licenses, and a domain of resources that are open for reuse. If prospect patents aspire to solve the problem of wasteful competition and use of common-pool resources via broad monopolies, a semi-commons approach is the answer to the problem of supracompetitive prices. After all, a property owner will have no incentive to reduce her price unless faced with competition from others.

We argue that when things go wrong with private rights such as patents, we can search for a solution that goes beyond proposals for governmental intervention: universities themselves have the potential to emerge as important actors in the regulatory enterprise. From this vantage point of view, we can rethink licensing for university prospect patents (for the problem of exclusive also see Contreras and Sherkow, 2017;19 Sideri, 2014;20 Lee, 2013;21 Thursby and Thursby, 200722). One way to do this would be to recognize duties we owe to others and include these in a license of a prospect patent. This way, externalities such as increased health care costs or loss of quality-of-life, despite being of secondary importance to private companies, will be taken into account. Yet, since such licensing inevitably involves the imposition of the university’s

19 Contreras & Sherkow, supra note 16, at 698–700.
20 K. Sideri, Bioproperty, Biomedicine and Deliberative Governance: Patents as Discourse on Life (2014).
21 P. Lee, Patents and the University, DUKE L.J. 1–87 (2013).
22 J. G. Thursby & M. C. Thursby, University Licensing, 23 OXF. REV. ECON. POLICY 620–639 (2007).
values on private entities, we opt for a market-based approach: market performance is the factor underpinning licensing behavior.

We propose a ‘use it or lose it’ (UoL) license for university patents that have been licensed exclusively. Under such a license, if the licensed technology has failed to be adequately commercialized, the university retains the right to license non-exclusively. Specifically, a UoL license sets a threshold for market demand. The inability of the licensee to commercialize the invention in a way that meets this threshold triggers possible non-exclusivity. As demand is contingent on price, by employing such a threshold, the university is indirectly setting an upper barrier for the price of the technology, and it is the market (not the university) that decides if this barrier has been met or not.

This type of license is essentially a diligence milestone that uses a verifiable market-based metric to decide when non-exclusivity should kick in, without undermining the ability of the prospect’s licensee to coordinate the further investments needed in maximizing the value of the technology. What it does is to contextualize the domain of usage, restricting strategies that aim at limiting commercialization. As the firms know the rules in advance, and considering that the market is the ultimate arbitrator of non-exclusivity, a UoL license is an \textit{ex ante} tool that precludes wanton usage.

We are not the first to try and address non-exclusive licensing for technologies. Kremer suggested that public bodies should auction their technologies, forcing the market to reveal the true price of an innovation, and then buy back these innovations and license them non-exclusively. This idea has been further advanced by Ayres and Ouellette, who suggest that prior to licensing the university should first try and offer a non-exclusive license for a small fee. If this does not work, then the invention should be auctioned \textit{a la} Kremer. Our suggestion reverses the order of affairs. First, the university offers an exclusive license, and if there is limited commercialization then the licensee is threatened with non-exclusivity. In doing so the UoL acts as an incentive to commercialize, contrasting Kremer and Ayres and Ouellette whose mechanisms aim at forcing perspective licensees to reveal their preferences regarding the value of the innovation.

The paper is structured as follows: in section second we provide a primer on prospect patents. We explain how prospect patents and the Bayh Dole Act, which allowed universities to patent their research, share a common \textit{ex post} purpose in pursuing the commercialization of an invention. We then outline the reasoning behind the universities’ strategy of building patent fences to achieve broad protection and explain why universities license their patents to surrogate companies. Section third starts with a brief timeline of CRISPR-Cas9, and an introduction to the main academic players. In accordance with prospect patents, we explain how the discovery of CRISPR-Cas9 has led to rivalry between academic institutions during the innovation stage. We then map the US patent landscape (reading the patent abstracts) and examine the

\begin{footnotesize}
\begin{itemize}
\item[23] C. J. Guerrini, et al., \textit{The Rise of the Ethical License}, 35 Nat. Biotechnol. 22–24 (2017).
\item[24] When the Broad Institute licensed its patents to Editas, it licensed under a diligence milestone that allowed it to retain the right to license to other firms if Editas was not adequately working on a specific gene. However, the scope of such limitations is narrow and firms can meet these requirements even if they are not planning to commercialize: Contreras & Sherkow, supra note 16, at 698, 699.
\item[25] M. Kremer, \textit{Patent Buyouts: A Mechanism for Encouraging Innovation}, 113 Q. J. Econ. 1137–1167 (1998).
\item[26] I. Ayres & L. L. Ouellette, \textit{A Market Test for Bayh-Dole Patents}, 102 Cornell L. Rev. 271 (2016).
\end{itemize}
\end{footnotesize}
existing product pipeline so as to show the lack of rivalry at the commercialization stage. This section ends with an explanation about the kind of bottlenecks that broad monopolies create for CRISPR-Cas9 users and the potential of ensuing high treatment prices. In section third, we shift our attention to ethical licensing and the basic tenets of property theory that justify this type of licenses. We use the conceptual tools of a semi-commons approach, which takes the shape of a UoL license outlined in section fourth.

II. PROSPECT PATENTS

II.A. University licensing and the reward theory of patents

Firms’ technology licensing is driven by strategic forces or emerges out of necessity. For example, firms license so as to gain freedom to operate, to collect revenue, to benefit from network externalities such as the setting of standards and the formation of alliances, to settle disputes, or to manage their technology surpluses and deficits. Equally, licensing is necessitated by the surrounding imitative environment and the innovator’s inability to protect her intellectual property (IP) from copy-cats or the lack of manufacturing capacity.

University technology licensing is not as multifaceted. It is enabled by legislative initiatives such as the Bayh-Dole Act in the USA, which granted universities the right to patent inventions funded with public money. The Bayh-Dole Act views patents as necessary in bridging the gap between academia and industry and allows them so as to ensure the commercialization of university inventions. This latter view of patents is at odds with traditional justifications of IP. Assuming

27 C. Shapiro, Navigating the Patent Thicket: Cross Licenses, Patent Pools, and Standard Setting, 1 INNOV. POLICY ECON. 119–150 (2000).
28 J. R. Green & S. Scotchmer, On the Division of Profit in Sequential Innovation, 26 RAND J. ECON. 20–33 (1995).
29 D. Kline, Sharing the Corporate Crown Jewels, 44 MIT Sloan MANAG. REV. 89–93 (2003).
30 M. L. Katz & C. Shapiro, Technology Adoption in the Presence of Network Externalities, 94 J. POLITICAL ECON. 822–841 (1986).
31 M. Ehrhardt, Network Effects, Standardisation and Competitive Strategy: How Companies Influence the Emergence of Dominant Designs, 27 INT. J. TECHNOLOG. MANAG. 272–294 (2004).
32 A. C. Inkpen & E. W. Tsang, Social Capital, Networks, and Knowledge Transfer, 30 ACAD. MANAGE. REV. 146–165 (2005).
33 B. H. Hall & R. H. Ziedonis, The Patent Paradox Revisited: An Empirical Study of Patenting in the US Semiconductor Industry, 1979–1995, 32 RAND J. ECON. 101–128 (2001).
34 Supra note 9.
35 N. T. Gallini, Deterrence by Market Sharing: A Strategic Incentive for Licensing, 74 AM. ECON. REV. 931–941 (1984).
36 E. Henry & C. J. Ponce, Waiting to Imitate: On the Dynamic Pricing of Knowledge, 119 J. POLITICAL ECON. 959–981 (2011).
37 J. J. Anton & D. A. Yao, Expropriation and Inventions: Appropriable Rents in the Absence of Property Rights, AM. ECON. REV. 190–209 (1994).
38 Supra note 11.
39 As stated in Sec. 200 (Policy and objective) of the Bayh Dole Act 35 U.S.C. §200–212 ‘It is the policy and objective of the Congress to use the patent system to promote collaboration between commercial concerns and nonprofit organizations, including universities.’
40 R. S. Eisenberg & R. Cook-Deegan, Universities: The Fallen Angels of Bayh- Dole? 147 DAEDALUS 76–89 (2018).
that a patent is not a right, it may be viewed as a ‘privilege’ bestowed to the innovator by society in a quid pro quo. In this ‘tit-for-tat’ society is willing to self-inflict itself with a monopoly in exchange for something. Under the usual economic understanding of patents, this ‘tat’ is a compensation for ex-ante R&D investments that are disclosed to the public. To rephrase, society offers the innovator the right to exclude unauthorized copying in exchange for disclosure. This viewpoint, which is referred to as the reward theory, takes the pessimistic view for that absent patents there will be no inventions. The lack of empirical evidence to back this view compromises the appeal of this otherwise intuitive understanding of patents as incentives.

The pessimistic view of reward theory (research needs pecuniary incentives) is at odds with the mission of Universities as research centers. University faculty does not need additional incentives so as to do research; academic curiosity on its own suffices for this purpose. Though pecuniary incentives may be non-essential for faculty research, this is not necessarily true for the commercialization of faculty research. Such commercialization requires a set of skills that ventures beyond academic curiosity, well into the realm of competitive markets, which are costly to access and acquire. Considering that the Bayh Dole Act views commercialization of university technologies as one of the missions of universities, the aforementioned quid pro quo must be rephrased. Society is willing to bear the costs of a monopoly (and in the process suffer a loss in social welfare) in exchange for the promise of a functional future product that increases social welfare. This barter shifts attention to the ex post investments needed to commercialize an end-product and not in the ex ante investments needed for invention.

II.B. Prospect patents and broad property rights

This forward-looking view of patents, which is not restricted to university patents, is referred to as the prospect theory of patents. Under this view, the function of the patent system is to encourage investment in a technological prospect (a particular opportunity to develop a known technological possibility) after the property right has been granted. Thus, similar to the reward theory, prospect theory is a species of utilitarianism that is concerned with the question of incentives, albeit the incentive is to encourage the production of an end-product that would not have been possible without granting exclusive rights.

Under the reward theory, it is sufficient for a university to patent a newly found idea and then the university technology transfer office will try and transfer it to a

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41 F. Machlup & E. Penrose, The Patent Controversy in the Nineteenth Century, 10 J. ECON. HIST. 1–29 (1950).
42 J. S. Sherkow, Patent Law’s Reproducibility Paradox, 66 DUKE L.J. 845 (2016).
43 R. C. Levin, et al., Appropriating the Returns from Industrial Research and Development. BROOK, 1987 PAP. ECON. ACT. 783–831 (1987).
44 W. M. Cohen, R. R. Nelson & J. P. Walsh, Protecting Their Intellectual Assets: Appropriability Conditions and Why US Manufacturing Firms Patent (or Not) (No. w7552), National Bureau of Economic Research (2000).
45 P. T. Gianiodis, G. D. Markman & A. Panagopoulos, Entrepreneurial Universities and Overt Opportunism, 47 SMALL BUS. ECON. 609–631 (2016).
46 Supra note 11.
47 Supra note 2.
suitable firm. This linear and singular process (one idea, one patent, one license) is unsuited for the commercialization of a prospect. In fact, the nature of prospect patents dictates the relevant university strategy in two ways: in erecting barriers to exclude competitors from commercializing similar technological trajectories and in the outsourcing of management.

In detail, to fulfill their purpose prospect patents need to be broad, allowing for unification of control. Broad patents would allow the patent owner to coordinate the evolution of the needed technological and market enhancements, and in doing so avoid the duplicative R&D investments that would take place when different patent holders attempt to commercialize variants of the technology. In practice though, patents are seldom broad enough so as to encompass all future uses.

As Suzan Scotchmer has noted, when a new patented technology builds on an older one the purpose of patent strength is to delineate how the first and second patentee will bargain in splitting the surplus created by the second innovation. In such an occasion the second innovator has a good bargaining position because absent her innovation there is no additional surplus to split. As a result, the first innovator cannot appropriate the full benefits of her innovation. To counter this, agents resolve in barricading their technologies from competition by building fences in the form of patent portfolios. Their aim is two-fold, to control all the assets needed, and to be able to bargain with agents threatening freedom to operate.

Textbook examples of such attempts to fence one’s technology include: firms that try to dominate a field with a broad pioneer patent, putting their eggs initially in one basket; then, such firms protect improvements inside and outside the scope of the dominant patent with follow-up patents, to put more eggs into more baskets. An alternative to having one broad, pioneering patent is to have several narrower patents fencing off the field into smaller sections. A series of narrow patents leaves gaps, but creates a maze. In other words, firms either try to create a monopoly with one broad ‘master’ patent and/or a maze of multiple narrow patents.

However, managing such portfolios to the fulfillment of a prospect lies outside university expertise. To elaborate, any entity that aims to commercialize the prospects stemming from a prototype invention must enter uncharted waters. Beyond the complexities of the race for a scientific discovery and final production, it must pursue risky market experimentation, face the challenges of clinical trials and Food and Drug Administration (FDA) approval, convince outside funders for the needed capital

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49 Supra note 2.
50 Supra note 5.
51 S. Scotchmer, Standing on the Shoulders of Giants: Cumulative Research and the Patent Law, 5 J. ECON. PERSPECT. 29–41 (1991).
52 A. Panagopoulos & I. U. Park, Patents as Negotiating Assets: Patenting versus Secrecy for Startups, 128 ECON. J. 2876–2894 (2018).
53 Supra note 6.
54 J. O. Lanjouw & M. Schankerman, Protecting Intellectual Property Rights: Are Small Firms Handicapped? J. L. ECON. 45–74 (2004).
55 Supra note 6.
56 Supra note 4.
injections,\textsuperscript{57} and market the final product. In terms of IP alone, the university must gain freedom to operate. This often involves strategic moves such as licensing and cross-licensing essential technologies. Plus, the university must protect its technology from challengers, which is not an easy task because patents are not a stable form of property.\textsuperscript{58} In the light of the above, considering that the requisite patent portfolios require complex strategies, it is not surprising that universities outsource the management of their prospects.

Unfortunately, companies that manage extensive portfolios of patents are a byword for a monopoly. Considering the fact that agents will always innovate as long as they can sell at a price higher than their costs,\textsuperscript{59} whether or not such monopolies offer the only viable way to manage a prospect is debatable\textsuperscript{60} and may depend on the availability of the substitute technologies\textsuperscript{61}--\textsuperscript{62} the said portfolios try to pre-empt.\textsuperscript{63} In the following section, we offer a genealogy of CRISPR-Cas9 with an eye on such monopolies and the way they may affect the pricing of new treatments.

\textbf{III. CRISPR}

\textbf{III.A. A timeline}

CRISPR-Cas9 is a major breakthrough technology. It is a gene-editing method that can be used in modifying the genome of living organisms, achieving precision changes in a gene, and allowing existing genes to be removed and/or new ones added. CRISPR denotes a system of bacterial immunity found within the genome of unicellular organisms. CRISPR sequences are derived from DNA fragments of bacteria that have previously infected these organisms. They act as an adaptive immune system because they are used to detect and destroy DNA from similar bacteria during new infections.

The initial discovery of CRISPR and its function is based on the basic research carried out between 1993 and 2005 by Francisco Mojica at the University of Alicante. Mojica was the first researcher to characterize what is now called a CRISPR locus and he coined the term CRISPR. To achieve its purpose this technology relies on the Cas9 protein, which uses CRISPR sequences as a guide to recognize and detach specific strands of DNA. Cas9 was discovered in 2005 by Alexander Bolotin at the French National Institute for Agricultural Research. Subsequent research carried out in many different universities (in the USA and the EU) between 2005 and 2010 by Eugene Koonin, Philippe Horvath, John van der Oost, Luciano Marraffini, Erik Sontheimer, and Sylvain Moineau, demonstrated that CRISPR is an adaptive immune system,

\textsuperscript{57} C. Long, \textit{Patent Signals}, 69 U. CHI. L. REV. 625, 636–637 (2002).
\textsuperscript{58} J. E. Bessen, J. Bessen & M. J. Meurer, \textit{Patent Failure: How Judges, Bureaucrats, and Lawyers Put Innovators at Risk} (2008).
\textsuperscript{59} M. A. Lemley, \textit{Property, Intellectual Property, and Free Riding}, 83 TEX. L. REV. 1031 (2004).
\textsuperscript{60} Lemley, supra note 6, at 129–149.
\textsuperscript{61} L. L. Ouellette, \textit{How Many Patents Does It Take to Make a Drug-Follow-On Pharmaceutical Patents and University Licensing}, 17 MICH. TELECOMM. TECH. L. REV. 299 (2010).
\textsuperscript{62} W. M. Landes & R. A. Posner, The Economic Structure of Intellectual Property Law (2009).
\textsuperscript{63} R. J. Gilbert & D. M. Newbery, \textit{Preemptive Patenting and the Persistence of Monopoly}, 72 AM. ECON. REV. 514–526 (1982).
understood the mechanism that allows CRISPR-Cas systems to interfere with the DNA of bacteria during infection, explained how CRISPR targets the DNA and not the RNA, and that it can create a break in targeted DNA at a precise position.64

The puzzle was pieced together in 2011 by Emmanuelle Charpentier (Umea University and University of Vienna) who fully explained how Cas9 is guided to its target, and Virginijus Šikšnys (Vilnius University) who showed that the function of CRISPR is not restricted to bacteria; opening up its uses to the human genome. In a concomitant set of discoveries that had all the characteristics of an R&D race, Charpentier with Jennifer Doudna (University of California, Berkeley), in June 2012, and Šikšnys, in September 201265 independently displayed that Cas9 can be reprogrammed to choose any target DNA site. The first successful adaptation of CRISPR-Cas9 for genome editing in multicellular organisms (in this case human and mouse cells) followed suit a few months after, in January 2013, by Feng Zhang (The Broad Institute of MIT and Harvard).66

Two points emerge from the above analysis. First, contrary to the commonly assumed idea of the heroic inventor,67 there were many researchers who over time contributed to CRISPR. Unfortunately, as we will shortly see, property rights were only assigned to the ones who offered the final pieces of the puzzle. Second, the inventors of CRISPR were all university researchers whose work was funded by public money.

III.B. Rivalry at the discovery stage

Undeniably, CRISPR-Cas9 has the potential to revolutionize medicine and a Nobel Prize seems likely. Sadly, part of the publicity and interest sparked by this major discovery is due to the bitter rivalry at the discovery stage between university researchers over patent rights. This rivalry is mainly between the University of California, Berkeley (henceforth UC) and The Broad Institute of MIT and Harvard.

To chronologically illustrate the issue: Šikšnys (March 20, 2012),68 the Doudna/Charpentier team of UC (May 25, 2012),69 and Zhang of The Broad Institute (December 12, 2012)70 all filed patent applications at the US Patent and Trademark Office (USPTO) claiming some variation of the CRISPR system using the Cas9 enzyme. Though the UC team had priority on its side, the patent application by Zhang claimed that, unlike the UC application, it was the only one not restricted to simple life forms. Therein lays the essence of a bitter patent battle that lasted until October 2019.

In interference proceedings before the USPTO (to determine the priority of two sets of conflicting patent applications), the USPTO ruled that the Doudna/Charpentier patent application and Zhang patents were directed to different inventions; Zhang’s

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64 For a detailed timeline, see Y. Ishino, M. Krupovic & P. Forterre, History of CRISPR-Cas from Encounter with a Mysterious Repeated Sequence to Genome Editing Technology, 200 J. BACTERIOL. (2018).
65 To be fair Šikšnys’s work was completed earlier but it was published later.
66 On these issues also see J. S Sherkow, Patent Protection for CRISPR: An ELSI Review, 4 J. L. BIOSCI. 565–576 (2017).
67 M. A. Lemley, The Myth of the Sole Inventor, MICHI. 110 L. REV. 709–760 (2012).
68 USSN 61/613,373.
69 USSN 61/652,086.
70 US Patent No. 8,697,359.
patents specified how CRISPR could be adapted for use in eukaryotic cells and Doudna/Charpentier did not. The Patent Trial and Appeal Board (PTAB) ruled against UC (February 2017), and one year later the US Court of Appeals for the Federal Circuit denied UC’s appeal. In April 2018, following a new patent filed by UC that highlighted its invention’s utility in eukaryotic cells, the PTAB ruled that the two parties’ claims now create an interference issue that needs to be examined in a hearing. Finally, on October 1, 2019, the USPTO granted a new CRISPR-Cas9 patent (No. 10428352) to UC, the University of Vienna and Emmanuelle Charpentier, covering new methods of gene editing for targeting, binding, and cleaving a target DNA cell using Cas9 protein and single-molecule DNA targeting RNAs.

This dispute was not restricted to the USPTO. The Chinese Patent Office in 2017 sided with the Charpentier/Doudna team and granted a patent to edit genes in that country. In 2017, the EPO announced its intention to grant a first patent recognizing as inventors the team led by Doudna and Charpentier for the use of CRISPR across all organisms. In February 2018, the EPO granted the Doudna/Charpentier team a second patent for CRISPR-Cas9 applications with very broad claims covering the use of the technology and is directed to applications that use a modified version of the Cas9 protein. Going beyond gene editing, this second patent addresses applications of the CRISPR technology in drug discovery. Plus, in 2018, the EPO revoked one of The Broad Institute’s patents relating to a fundamental aspect of CRISPR technology. The opposition board upheld the EPO’s preliminary opinion that the claims were invalid in view of an invalid priority claim.

Finally, on January 16, 2020, the EPO’s board of appeals revoked the CRISPR-Cas9 patent of the Broad Institute. The EPO’s decision was not unexpected, given the long-standing approach of the EPO to priority (the right to claim priority from an earlier application is afforded to the applicant of the earlier application, or his successor in title). This decision led the US stock price of Editas Medicine (the main licensee of the Broad Institute—see below) into a free fall, losing 17 percent of its value until the end of the month; the equivalent of about $250 million.

Overall, as Duffy anticipated, in a prospect patent setting there exists rivalry at the discovery stage. In this case, it was rivalry between the competing teams of Doudna/Charpentier and Zhang. However, when the dust has settled down and the main players have reached an equilibrium in which everybody understands who owns what, the sensible choice for each player is to focus on the individual market segments that they control, minimizing rivalry at the commercialization stage. To further understand

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71 Organisms that have eukaryotic cells include protozoa, fungi, plants, and animals. Unlike archaea and bacteria (the other two life forms), eukaryotic cells have cellular nuclei in which the genetic material is packed.
72 J. Cohen, CRISPR Patent Fight Revived, 365 SCIENCE 15 (2019).
73 https://register.epo.org/epfwservlet?apn=CN.201380038920.A&lng=en.
74 EP2800811 (A4), Inventors EMMANUELLE CHARPENTIER [DE]; JAMES HARRISON DOUDNA CATE [US]; JENNIFER A DOUDNA [US]; KRZYSZTOF CHYLINSKI [AT]; LEI QI [US]; MARTIN JINEK [US]; WENDELL LIM [US].
75 DK3241902 (T3)—2018-05-07
76 http://www.ersgenomics.com/news-press-release-20180228.php
77 Supra note 5.
III.C. Rivalry at the commercialization stage

The firms

Considering that the universities awarded the patents lacked the expertise in developing marketable applications they licensed their rights to surrogate companies that spun-off from the universities. The Broad Institute licensed to Editas Medicine, UC licensed to Intellia Therapeutics and Caribou Biosciences. Emmanuelle Charpentier on the other hand, who was not under obligation to assign her inventor rights to either university, licensed her rights to ERS Genomics and Casebia Therapeutics.

Editas is a publicly traded company that describes itself as a clinical stage genome editing company. Intellia Therapeutics is also a publicly listed genome editing company. Intellia was founded by Caribou, which, unlike Intellia, is still a private firm. Casebia Therapeutics, on the other hand, is affiliated to Bayer via a 50–50 joint venture with CRISPR Therapeutics and has now been absorbed by the latter. The smallest of these firms is ERS Genomics, which is a private firm co-founded by Emmanuelle Charpentier.

Despite being endowed with many of the fundamental patents on CRISPR-Cas9, these surrogate firms continued research on the subject and applied for many more patents on their own. They are not alone: Private entities that were not players at the discovery stage are now also patenting heavily in this scientific domain.

The CRISPR patent landscape

Against this background, we now try to come to grips with the relevant US patent landscape by identifying which patents the firms, universities, and individuals involved hold. The aim is to try and understand the technological aspirations and the adjacent long terms strategies of the firms. In order to map the patent landscape we start with pending patent applications.

We accessed the USPTO database in December 2019 and searched for US patent applications that list as applicants or assignees the surrogate firms, and included the words CRISPR or Cas9 in their front page description. We find that Editas has applied for 59 patents, Caribou Biosciences for 49 patents, Intellia Therapeutics for 8, Casebia (before being absorbed by CRISPR Therapeutics) for 4, whereas ERS Genomics has no US patent applications. From a patent application viewpoint, it seems that Editas and Caribou have a clear lead in terms of technologies in the developing stage.

We next shift attention to patents granted. To this end, the World Intellectual Property Organizations (WIPO) database was accessed in December 2019. We aimed at identifying US patents granted after 2013 listing as inventors the main scientists whose patents are credited with fuelling the aforementioned rivalry. Accordingly, we searched for US patents that list Doudna, Charpentier, or Zhang as inventors and included the words CRISPR or Cas9 in their front-page description. We found that Doudna is credited as the inventor in 100 patents, Charpentier in 58, and Zhang in 101 patents.

The next step is to identify the patents held by the surrogate firms. We again followed the same search strategy, focusing on US patents that list as applicants the surrogate
firms and included the words CRISPR or Cas9 in their front-page description. Starting with Editas, we identified 53 US patents that list the firm as an applicant. In fact, Editas’s portfolio should be even bigger because it must include some of the related patents currently assigned to The Broad Institute. The patent portfolio of Editas is diversified. In fact, out of the 53 patents, 36 are on uses of CRISPR-Cas9, six are on further uses of Cas9, 78 six are on guide RNA with emphasis on one-shot RNA, 79 and three in genome editing. 80 The remaining two are on ophthalmological diseases, Leber’s Congenital Amaurosis (a form of retinitis pigmentosa) and CEP290 Retinal dystrophy. 81

Caribou Biosciences has 55 US patents. Out of these 55 US patents, 23 are on CRISPR and Cas9 uses. The remaining 32 patents focus on the mechanism that allows an engineered nucleic acid to target another nucleic acid, ie, on the DNA cut and paste method. 82 By reading the patents’ abstracts, it seems that, compared to Editas’s patents, Caribou’s patents are of broader nature and focus on different aspects of gene editing. The emerging picture is of two firms whose expertise lays strongly in CRISPR-related technologies, but have pursued different research paths focusing on different parts of the DNA cut and paste process. Such diversification forms a recurrent theme and applies to the other firms as well, albeit these firms focus even more on practical applications.

Intellia Therapeutics, for example, holds 10 US patents, two of which with Novartis. With the exception of three patents (two on CRISPR and one on guide RNA) all remaining patents are on compositions and methods for immunology and the remaining on specific diseases, eg, hemoglobinopathies. CRISPR Therapeutics’s US patent portfolio is even more focused on practical applications. Its portfolio includes three US CRISPR-Cas9 patents that it acquired from Casebia Therapeutics (one is on hemophilia and two on retinitis pigmentosa) and two CRISPR-Cas9 patents it developed on its own. The remaining portfolio of CRISPR Therapeutics includes 29 patents that mainly focus on hemoglobinopathies and haemachromatosis (12 patents), and immuno-oncology and immuno-deficiencies (6 patents).

Lastly, the WIPO search did not reveal any patents held by ERS Genomics in their first page. This does not mean that this company has no patents. In fact, as mentioned earlier, both ERS Genomics and Casebia Therapeutics have been assigned the CRISPR and Cas9 patents of Charpentier.

Trying to look at the big picture, we broadened our search criteria. We searched for all granted US patents that list the word CRISPR or Cas9 both in their front page and in their claims and description. After finding 7560 US patents, we identified the applicants of these patents. Pioneer Hi-Bred International Inc. (a producer of seeds for agriculture) is first in the list with 728 patents (almost 10 percent of all patents), followed by Monsanto Co. with 502 patents. DowDuPont was the applicant for 61

78 20190201550, 20180135109, 20180250424, 20190136210, 20180355332, 2017027126.
79 2017027150, 2016029252, 20190062734, 20180210956, 20180251792, 09963719.
80 20190345490, 2015055002, 2017031464.
81 20180155789, 20190169652.
82 20160046949, 2018011920, 20150089681, 20160319349, 20160312280, 20170204388, 20180201913, 20170159073, 09816081, 20170327820, 20160024568, 20190112587, 20160251640, 20180251788, 20160076020, 20160046963, 20180237770, 20180171359, 20180346894, 20190040373, 20180155720, 20140315985, 20160046978, 20180119173, 20160068887, 20170114369, 09816093, 20160046962, 20160108470, 20170051276, 20180312827, WO/2014/150624.
patents through its affiliate Dow Agroscience LLC. The Broad Institute is listed as one of the applicants in 166 patents, Harvard University and MIT for 231 and 251 patents respectively, whereas the Regents of the University of California for 249 patents.

Our finding of the prevalence of big chemical firms and their focus on agricultural uses is not unexpected. What is unexpected is the absence of a significant portfolio by big pharmaceutical firms, with Bayer being the exception, because Casebia Therapeutics (now part of CRISPR therapeutics) was controlled by Bayer. A closer look at these firms highlights the role of DowDuPont. Even though it may directly hold a modest patent portfolio, it has been aggressive in its licensing and cross-licensing activity, aimed at agricultural applications. In detail, in June 2015, it negotiated an exclusive license for commercial use in agriculture with Vilnius University; in October 2015, it cross-licensed this exclusive license, together with its own patent assets, to Caribou BioSciences; in June 2017, it entered into an exclusive licensing agreement for all agricultural applications with ERS Genomics; and in October 2017, it entered into a joint non-exclusive licensing agreement with The Broad Institute for use of the CRISPR-Cas9 in commercial agricultural research and product development, except gene-drive and tobacco for human use. Plus, DowDuPont has access to the patents of one of its spin-off companies, Cortevia, which has of late incorporated Pioneer Hi-Bred International as one of its subsidiaries, which in turn has a 2015 cross-licensing agreement with Caribou.

The product pipeline

To be able to translate patent holdings into business strategy, one needs to take a look at the products the firms are commercializing in the near future. For brevity, we do not focus on the products that are still at the designing stage through various collaborations. Plus, we do not outline the products developed by DowDuPont, Monsanto, or Cortevia, because they clearly do not overlap with the ones that the surrogate firms focus upon.

Starting with Editas, its main pipeline product is EDIT-101 that treats Leber Congenital Amaurosis type 10, a genetic form of vision loss that leads to blindness. Editas seem to be specializing in therapies for eye diseases, focusing also on retinitis pigmentosa (a progressive form of retinal degeneration), Usher Syndrome 2A (a form of retinitis pigmentosa that also includes hearing loss) and Herpes Simplex Virus 1 (the cause of infections leading to both ocular and oral disease). In addition, the company develops hematopoietic stem cells for treating sickle cell disease and beta thalassemia.

Caribou develops anti-bacterial therapies to modulate or eliminate specific strains of bacteria. It also works on industrial fermentation by creating large-scale cell cultures that can find applications in creating recombinant therapeutic proteins, vaccines, or gene therapy vectors. Intellia develops in vivo programs focused on liver diseases,

83 On this point also see Adam Houldsworth, Who owns the most CRISPR patents worldwide? Surprisingly, it is agrochemical giant DowDuPont published online at Genetic Literacy Project (February 16, 2018), https://geneticliteracyproject.org/2018/02/16/owns-crispr-patents-worldwide-surprisingly-agrochemical-giant-dowdupont/ (accessed on Aug. 21, 2020).
84 https://www.ipstudies.ch/2018/02/myths-and-realities-on-dupont-crispr-assets/ (accessed Aug. 21, 2020).
including transthyretin amyloidosis, alpha-1 antitrypsin deficiency, and primary hyperoxaluria. CRISPR therapeutics’ lead programs (despite being endowed with Casebia’s patents on hemophilia and retinitis pigmentosa) are in hemoglobinopathies, immunology cell therapies, and regenerative medicine with a focus on diabetes. Lastly, ERS’s business model rests in licensing the key CRISPR-Cas9 patents it inherited from Charpentier. It is the only firm that has licensed its portfolio to a non-profit firm, the Danish research services firm Bioneer.

The only firm that holds patents in areas that may possibly overlap with the interests of others is CRISPR therapeutics, which holds patents on hemoglobinopathies and retinitis pigmentosa. However, in contrast with Editas, which actively works on Retinitis, CRISPR therapeutics has no pipeline products in this field. Plus, although CRISPR therapeutics has pipeline products on hemoglobinopathies, the only other firm with patents in this area, Intelia has no related pipeline products. Consequently, the overall picture emerging from this analysis is not of firms competing over the same markets. Instead, it seems that the main surrogate firms have focused on separate uses of this novel technology. This result has been anticipated by Contreras who explains that private surrogate companies may have incentives to license technology to others and in doing so avoid competitors pursuing research on similar market uses. The above analysis has proven empirically that this is the case. Plus, we have shown that the large chemical firms have directed their attention to agricultural uses.

III.D. Bottlenecks and high drug prices

No doubt the patent portfolios, we described serve the purpose of fencing off the foundational patents so as to block competitors, forcing rivals to enter into licensing and cross-licensing agreements, which would allow the firms to access the needed technologies. Yet, such a broad scope of protection also means that even the most basic use of the CRISPR-Cas9 system needs a license. To make an analogy with rDNA, the Cohen/Boyer patent granted by the USPTO in 1980, which sprang from the University of Stanford and University of California, was similarly very broad and could be used in ways that could potentially raise ethical concerns. Back then, the technology transfer offices of Stanford/California decided to license non-exclusively after extensive consultation with key stakeholders and allowed a large number of companies to push the technology forward in diverse ways simultaneously.

Additionally, with different owners claiming different aspects of the technology, companies that wish to utilize CRISPR to develop new therapies need to license from various institutions. This could bottleneck the use of CRISPR technology to discover and develop useful human therapeutics. Notwithstanding the above, the main criticism afforded to the decision of the universities involved to license exclusively to their surrogate firms involves the pricing of gene therapies.

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85 J.L. Contreras, Is CRISPR Different? Considering Exclusivity for Research Tools, Therapeutics, and Everything In Between, 18 Am. J. Bioet. 59–61 (2018).
86 Sherkow, supra note 66, at 565–576.
87 P. Berg, et al., Summary Statement of the Asilomar Conference on Recombinant DNA Molecules. 72 Proc. Natl. Acad. Sci. U.S.A. 1981 (1975).
88 R. Dana Ono, Business of Biotechnology: From the Bench to the Street (1991).
89 Supra note 19.
When a gene therapy was approved for a rare form of blindness in December 2017, the debate on price echoed these concerns. Luxturna, a gene therapy for Leber’s congenital amaurosis that was developed by Spark Therapeutics, costs $425,000 per eye. Equally, Kymriah, a treatment approved recently that delivers an engineered immune system protein, is a one-time treatment for a form of leukemia, costing $475,000. Glybera, the first gene therapy approved in Europe for lipoprotein lipase deficiency, was administered in only two patients before being pulled off the market. It costs more than $1 million-plus, a cost deemed excessive (in view of the costs of clinical trials and small number of patients and one dose). The second gene therapy approved in Europe, Strimvelis, to treat an inherited immune deficiency, is a one-off therapy, which costs $697,750. The National Institute for Health and Care Excellence (NICE) in the UK approved the drug (which means that the National Health System must fund it) as cost effective. Despite the price, NICE approved the drug as it helps more children to survive the disease than the current standard stem cell transplant treatment.  

IV. ETHICAL LICENSES IN A SEMI-COMMONS ENVIRONMENT

Despite the promise of prospect patents to limit rivalry at the discovery stage, the developments discussed invite us to rethink the licensing role of universities. As university technology transfer activities are predominately focused on securing patents with a focus on generating licensing income and obtaining reimbursement for legal expenses, various commentators urge public sector institutions to adopt more socially responsible patenting and licensing policies in promoting access. It is argued that although the right to exclude is a core right, patents allow their owners to dictate the terms of use of a resource. where the claimed technology raises ethical or social concerns, patent holders could dictate terms that make licensees behave ethically and provide access to downstream inventions. Examples include the license that Editas Medicine, Inc., the surrogate licensee of Broad Institute, granted to Monsanto, which requires that specific applications of the technology are expressly prohibited, such as the creation of sterile ‘terminator’ seeds or doing research for tobacco products. Another example is Kevin Esvelt’s proposal to use gene drive patents as a way to exercise more broad control over the conduct of licensees’ use of a contested technology by means
of requiring them to disclose their research plans and accompanying safety and ethical issues.\textsuperscript{99}

Justifying patents on the basis of prospect theory seemingly makes it difficult to reconcile patents with ethical concerns. \textit{Ex post} justifications stress the need for incentives to develop or improve the claimed invention. From this vantage point of view, a patent is nothing more than an asset to be exchanged in markets and prospect patents are all about increasing prosperity and wealth. Carol Rose’s idea of property functioning as a ‘luxury good’ captures this function of prospect patents having mere economic features and facilitating transactions to build wealth.\textsuperscript{100} Yet, we can justify ethical licensing if we view patent law as a policy tool open to calibration as we do with any form of market regulation.

Ethical licensing then fits well within a regulatory theory of patents. Ghosh explains that IP law serves to regulate the activities associated with marketing, creating, and inventing new products and services. Once IP is understood as regulation then it is possible to address a set of institutional and policy issues,\textsuperscript{101} rather than merely wealth maximization. For example, a regulatory view of IP allows the reconciliation of the exclusive rights of various forms of IP with the public benefit promoted by doctrines such as fair use and experimental use. IP occupies a space between the proprietary and the public; it can be both a means for commercial development of the technology and it may promote ethical demands.

The regulatory angle allows us to take a broader perspective, a bird’s eye view of the political institution of IP. Prospect patents (with their narrow economic focus) are an integral part of a broader institutional setting, built to regulate the use of a resource, in our case knowledge. IP, in turn, is part of various initiatives in law and policy to construct the broader information environment. Madison, Frischmann and Strandburg’s\textsuperscript{102} work on the information commons will help illustrate this point. The authors explain that we can divide the information environment into three domains: first, the domain of exclusion, where producers use IP rights to exclude competitors and prevent unlicensed sharing of the technology. Second, there is the domain of government or public subsidy, where government directly or indirectly is actively engaged in creating knowledge, for example through grants, tax credits, prizes and

\begin{itemize}
\item \textsuperscript{99} Id.
\item \textsuperscript{100} Rose explains that the ‘luxury good’ role of property is based on the simple idea of liberties being luxury goods in that they can be secured only in a wealthy society. In fact, wealth generated as a result of holding property provides the ground for the stability required to secure a system of rights. Accordingly, property and the wealth it generates are necessary for a system of liberties and takes priority. Without property and the ensued wealth liberty is unstable. Examples are wars due to scarcity of resources and poverty. Rose concludes that ‘\textit{thus of all the arguments for property’s keystone role, the Luxury-Good Argument most directly builds on property’s ‘merely economic’ features}’ Current examples can be found in argument stressing the role of patents in fueling much needed medical innovation that will benefit society. Wealth creation comes first and future patients will benefit when prices drop. This is the core of the economic argument for property: property and commerce create wealth and help create an environment where there are equal opportunities to all. The (hyper)optimistic view is criticized as failing to address the question of inequality and corruption; see C. M. Rose, \textit{Property as the Keystone Right}, 71 Notre Dame L. Rev. 329 (1995).
\item \textsuperscript{101} S. Ghosh, \textit{Decoding and Recoding Natural Monopoly, Deregulation, and Intellectual Property}, U. ILL. L. REV. 1125 (2008).
\item \textsuperscript{102} M. J. Madison, B. M. Frischmann & K. J. Strandburg, \textit{Constructing Commons in the Cultural Environment}, 95 Cornell L. Rev. 657 (2009).
\end{itemize}
purchasing and distributing private research. The third domain, which is of interest to the present discussion, is referred to as a ‘semi-commons’, which comprises of a combination of private rights of exclusion, management by public authority, and a domain of resources that are open for reuse. As knowledge is cumulative and combinatorial, IP incorporates exclusions and limitations, which help construct an open commons as well as a variety of semi-commons or limited commons of resources, which are partly open and partly closed. Others can use these resources but access is not always completely free. In a semi-commons, the exclusionary rules of IP may be combined with licenses and contracts, with social norms and institutions to construct a semi-commons. ‘These cultural commons, depend on but are built alongside and on top of the basic forms of knowledge and culture, on the one hand, and intellectual property rules, on the other hand.’

Importantly, the idea of semi-commons can more realistically describe how the institution of property functions on the ground, going beyond the more stylized depictions presented in the debate between proponents of the ‘tragedy of the commons’ and the ‘tragedy of the anti-commons’. On the one hand, Hardin famously coined the phrase ‘tragedy of the commons’ to argue that commons spaces, such as pastures, would be overgrazed and polluted and people will have no incentive to invest in a communal activity. On the other hand, Heller’s and Eisenberg’s work famously popularized the term ‘tragedy if the anticommons’ in biomedical research to argue that it is excessive privatization and parcelization of resources that hinders the productive use of assets. The idea of semi-commons goes beyond these polarities pointing to the possibility of a smart mix of private and public elements in property arrangements, which will need to be adjusted to the specific social context and needs.

Going back to the theory of prospect patents, it implies that property rights function merely to generate wealth. From the perspective of a prospect patent, the price tag of treatments is an externality, and economic thinking suggests that only if the costs of changing harmful behavior (transaction costs) are less than the costs created by harmful behavior (an externality) will, for example, government consider to intervene. But these ideas are highly problematic in the case of university patenting. Even if university patents are prospect patents serving commercialization, these patents present a more complicated case given the public mission of universities, a point made clear by the ‘Nine Points to Consider in Licensing University’ published by the Association of University Technology Managers.

To further flesh out this idea, let us take the textbook example of ‘neighborly’ relations: Social norms prescribe that you do not erect a wall obstructing your neighbor’s

103 Id. at 667
104 H. E. Smith, Governing Water: The Semicommons of Fluid Property Rights, 50 ARIZ. L. REV. 445 (2008).
105 Id. at 669.
106 G. Hardin, The Tragedy of the Commons, 1 J. NAT. RESOUR. POLICY RES. 243–253 (2009).
107 M. A. Heller & R. S. Eisenberg, Can Patents Deter Innovation? The Anticommons in Biomedical Research, 280 SCIENCE 698–701 (1998).
108 M. Heller, Gridlock Economy: How Too Much Ownership Wrecks Markets, Stops Innovation, and Costs Lives (2010).
109 F. M. Scherer, The Economics of Human Gene Patents, 77 ACAD. MED. 1348–1367 (2002).
110 L. A. Fennell, Commons, Anticommons, Semicommons, in RESEARCH HANDBOOK ON THE ECONOMICS OF PROPERTY LAW 35–56 (2011).
sea view. It is always possible for property holders to grant specific privileges, for example access rights. Such licenses (we call these servitudes in property law) remind us that there is the possibility of numerous limits on exclusive control in service of ‘neighbors’ and the ‘neighborhood’ and they make sense if viewed as part of the larger moral picture about how we use resources and how we value them. What is more, servitudes in property law tie rights and obligations to possession of land and run with the land to successive owners and occupiers. We could think in similar terms for patent licenses: they run with the patent even when this is, for example, assigned (a subsequent owner could not terminate them).

The suggestion here is that universities may essentially seek to regulate harmful behavior for the benefit of society and for this reason licensing reflects more than the will of parties entering an agreement. In other words, going beyond proposals for governmental intervention, universities themselves have the potential to emerge as important actors in the regulatory enterprise. We explained that rather than recognize labor, reward effort, or incentivize invention, the relationship between the university and the technology it produces is captured by the prospect patent. Yet, a university prospect patent is seemingly only focused on commercialization. It ought to be also concerned with harms created by the ‘thing’, that is the object of the transaction, in our case a piece of technology. Commercialization of university technology invites an ethical response.

Indeed, licensing is very important in the CRISPR patent landscape and universities are key players constructing a space of semi-commons with both closed and open features. The patent owners (UC and The Broad Institute) broadly licensed CRISPR for research purposes to non-profits, universities, and commercial entities. UC, The Broad Institute, and hundreds of institutions have all agreed to make their CRISPR IP available through AddGene, a non-profit repository and patent licensor of CRISPR technologies for academic organizations. Some institutions, such as the Montreal Neurological Institute, have refused to patent altogether, and there is discussion to set up a CRISPR licensing facility to ensure broad licensing to firms.

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111 Michaels (2016) mentions that this interpretation goes against the dominant theory of bundle of sticks, according to which a license binds those who signed the licensing agreement. Moreover, Michaels (p. 7) explains that ‘this “encumbrance” theory is also in some tension with the principle that covenants cannot run with personal property, given that by statute, “patents shall have the attributes of personal property”’; also see Henry Smith-‘Institutions and Indirectness in IP’ explaining the hostility of courts towards servitudes running with personal property. On the other hand, as Michaels explains if these benefits do not run with the patent, then there would be nothing stopping a subsequent patent owner from exercising the right to terminate. Thus if termination power runs with the patent, this could effectively eviscerate the general rule that patent assignees must respect pre-existing licenses. See A. Michaels, Patent Transfer and the Bundle of Sticks (2016).

112 Van Houweling (2008) notes that the hostility towards servitudes on personal property is due to information burdens (property rights need to be known by an indefinite number of people). She suggests that the distinction made in earlier Supreme Court cases between commercial producing entities and individual consumers (the latter of which may have more of an everyday expectation of permission to use a physical article) is potentially a good rule of thumb. There is less reason for the law to worry about the processing costs of expert duty holders, who are given notice. See M. S. Van Houweling, The New Servitudes, 96 GEO. L.J. 885 (2007).

113 https://www.addgene.org/crispr/.

114 http://www.mpelga.com/main/pid/CRISPR/Terms.aspx.
Another example of ethical licensing is the use of CRISPR in ‘gene-drives’. As mentioned earlier, researchers proposed patenting the use of CRISPR-based gene-drives so as to license only the researchers that intend to use rigorous scientific and ethical controls. A different example is The Broad Institute’s license to Monsanto covering the use of CRISPR-Cas9 for a variety of agricultural purposes. The license requires Monsanto to allow farmers to save and re-sew seed from one season to the next. As we argue, we can think in similar terms in the context of therapeutics. License terms of use can be used to require price controls to allow for affordable novel treatments and restrict controversial germline therapies until society is given the chance to deliberate on relevant questions.

In this framework, prospect patents with their limited economic justification coexist with licenses incorporating norms of proper use that may advance distributive justice concerns. An interesting comparison with IP can be found in licenses such as those accompanying Microsoft’s Vista operating system (End User License Agreement). The license allows installation and use of the software, but serial transfers of the user’s copy of the software and reverse engineering of the software code that would otherwise be forbidden under copyright law. The General Public License promulgated by the Free Software Foundation is also attached to software programs and purports to govern certain aspects of their use (Van Houweling and Shaffer, 2008). Creative commons licenses present another example. University licensing can be thought of in similar terms.

V. LICENSING UNIVERSITY PROSPECT PATENTS

In view of the above, we now focus on how to ameliorate the issue of high drug pricing and ethical issues. The obvious solution must involve some realignment of property rights. The question we try to address in this section is how extensive such a realignment should be, what form it should take and where it should focus. As to its focal point, viewing university patents under the prism of prospect theory dictates that any policy suggestion must focus on the final product and not on a set of patents, essential or not. A realignment of the property rights of some technologies is bound to set in motion an R&D race, which prospect theory tries hard to avoid. The policy proposal that follows seeks to avoid setting a race in motion.

We propose the following license: if universities should aim at fully materializing the expected benefits of a technology, then they should license under the condition that, if the licensed technology has not been embodied in a product for which there is demand within a certain period, then the university retains the right to comprehensively license its portfolio of patents non-exclusively. To offer an example of such a UoL license, if after years the exclusive licensee has yet to generate demand for the technology covered by the patent, and another prospective licensee requests an extra license to use the patent, it should be in the university’s power to issue such an additional license. The provision of years allows the licensee a head start in order to embody the licensed technology into a final product and accounts for the need for possible FDA approval. Therefore, years

115 Supra note 86.
116 Id.
117 M. S. Van Houweling, The New Servitudes, 96 GEO. L.J. 885 (2007).
cannot be too small nor, on the other hand, can it be close to the statutory patent term of 20 years; for this, it would nullify the purpose of the UoL.

It should be stressed that this policy does not affect licensing revenue, on the contrary. To start with, in this instance the university does not forego any lost royalties because the technology has not been used at all as to generate income from royalties. Equally, it does not sacrifice lost fixed-fees from licensing because such fees are paid upon licensing the technology. Furthermore, if the university issues more licenses it stands to further increase its licensing revenue.

Moving beyond an understanding of patents as prospects, we have envisioned the university as a social actor whose utility does not simply rest on the full materialization of a technology's prospects. The main issue we have touched upon is affordability and the inequality created by overpriced university-licensed technologies that beg for a redistribution policy. To this end, in what follows we aim to extend the simple UoL license by noting that the price of a treatment, and its demand are essentially two faces of the same coin.

To an economist, every price projects a specific demand, and every quantity demanded is the result of one particular price. Furthermore, there is a negative relationship between price and demand. In simple terms, when a therapy is priced high its demand is low, when it is inexpensively priced its demand increases. By the same logic, if one aims for a therapy that will be of high demand the product cannot be overpriced.

The logic linking quantity to price can be used to extent the UoL license as follows: if after $t$ years the exclusive licensee has yet to generate an $x$ demand for the technology described by the patent, and another prospective licensee requests an extra license to use the patent, it is the university's prerogative to issue such an additional license. Since every demand $x$ rests on one price $p$, this contractual agreement basically implies that unless the licensee is committed to a price $p$ that is sufficiently low as to generate demand $x$ she is facing potential competition from future licensees.

It is important to note that this extended UoL policy has its limitations. Basically, it is not a priori guaranteed to maximize university licensing revenue. To do this, it needs fine tuning. For example, if $x$ is set at a very high level the price required to achieve such demand may be less than the price needed to maximize profits. This in turn suggests that there may be no interest in licensing the patent. If on the other hand it is set at a low level, it is inconsequential.

To offer an example of UoL, consider a drug that is targeted to a sub-population within a broad disease category with high-unmet need. This could be a personalized drug or even an orphan drug for which total demand is by definition small. As the UoL license does not involve an absolute threshold $x$ below, which non-exclusivity is possible, it is up to the university to set the bar. In short, the bar is relative to the drug population in question. Moreover, if this $x$ is not met, then it is up to the university to consider the benefits of licensing non-exclusively. If the university has reason to believe that non-exclusivity will not solve the problem, the university is not obliged to follow suit.

Effectively, this type of licensing is a diligence milestone whose enforceability resides on market performance. It is the market that triggers this threat. All the university has to do is to choose the appropriate threshold.
VI. BROADER ISSUES

Kitch’s argument in favor of justifying patents as prospects may be understood as a way to address the ‘tragedy of the commons’ dilemma: since anyone can innovate using the resources in the common pool, we can avoid waste of resources and solve the common-pool problem ‘by awarding exclusive and publicly recorded ownership of a [technological] prospect shortly after its discovery’.\textsuperscript{118} Indeed, in the previous analysis we found that surrogate firms have largely focused their patenting and business strategies on different technological paths, focusing on non-overlapping uses of the technology, precluding rivalry at the commercialization stage. Therefore, despite critique on prospect patents by authors like Lemley who predicted conflicts during the commercialization stage between the prospect and follow-on innovations,\textsuperscript{119} we found that in accordance with prospect theory, rivalry in the form of competition seems subdued at the commercialization stage. Therefore, we see no issues that relate to the parcelization of resources envisaged in the notion of anticommons.\textsuperscript{120} Yet, a different problem emerges: the price tag of new gene therapy treatments stemming from CRISPR-Cas9 is enormous, raising concerns about access.

To address concerns over price, we argued in favor of ethical licensing as a way out of the conundrum. For one thing, we argued that prospect theory opens the way to justify patents as a form of market regulation. We can easily justify ethical licensing if we view patent law as a policy tool open to calibration as we do with any form of market regulation. For another, our analysis goes beyond the concepts of commons and anti-commons to frame the policy response in terms of a calibrated semi-commons. A semi-commons envisages resource systems as a combination of private and common property which impact significantly on each other.\textsuperscript{121} Ethical licensing is one way in which actors such as universities and other public institutions can seek to alter this interface given their public mission. From this vantage point, policy makers could also focus on tuning the interface between private and common ownership at any given point in time. That interface can be altered either by privatizing more or bringing under common control more of what is private property.\textsuperscript{122} As Fennell explains the notion of semi-commons can accommodate the idea that property arrangements can be reconfigured in a variety of different ways depending on the particular circumstances including the need to defeat strategic behavior by private parties.\textsuperscript{123}

The article discussed ethical licensing as a way to think about universities and other public institutions role in the regulatory exercise but there is a wealth of other initiatives promoting ethical licensing. IP pooling, clearing houses and open sources initiatives are examples of private ordering mechanisms that differ from solutions that aim at changing or harmonizing the legislative framework in that they are generated by the users themselves.\textsuperscript{124} A particularly development with respect to CRISPR is the attempt by MPEG LA to create a patent pool that leads to a one stop licensing

\textsuperscript{118} For a discussion see Duffy, supra note 5, at 439–510, 441 citing Kitch, supra note 1, at 265–290.
\textsuperscript{119} M. A. Lemley, Economics of Improvement in Intellectual Property Law, 75 Tex. L. Rev. 989 (1996).
\textsuperscript{120} Supra note 107.
\textsuperscript{121} H. E. Smith, Semicommon Property Rights and Scattering in the Open Fields, 29 J. Legal Stud. 131–169 (2000).
\textsuperscript{122} Fennell, supra note 110, at 35–56.
\textsuperscript{123} Id.
\textsuperscript{124} A. Nordberg et al., Cutting Edges and Weaving Threads in the Gene Editing (R) Evolution: Reconciling Scientific Progress with Legal, Ethical, and Social Concerns, 5 J. L. Biosc. 35–83 (2018).
point for CRISPR patents. A patent pool forms when multiple patentees combine their patents and use a single administrative entity to license the package of patents to third-parties non-exclusively. MPEG LA, an independent licensing agent, has been a key player in the past in creating patent pools in the consumer electronics and telecommunications sectors. The same body has attempted to create pools and similar management structures such as clearing houses in the biotechnology field albeit with little success, but in 2017 it announced its intention to create a patent pool for CRISPR. The hope is that non-exclusive licenses granted by the pool can ensure affordability and freedom to operate while giving licensors adequate royalty returns.

In this way, a voluntary pool or a similar structure such as a clearinghouse model may foster commercialization and could include provisions for royalty-free research use by public institutions, alleviating the uncertainty of the current national research exemptions, and at the same time, it could address ethical concerns regarding particular CRISPR applications. MPEG LA’s CRISPR patent pool is a promising approach but it remains to be seen whether it will be successful as it depends on whether enough IP holders will join the pool. These are wider issues, which fall outside the scope of the article, yet their relevance is of increasing importance in light of the COVID-19 crisis and the need for a clearer international framework for research exemptions.

**VII. CONCLUSIONS**

The function of patents is not independent of the external innovation environment. The holders of prospect patents wish to control invention and innovation but the case of university patenting reveals a picture where the innovator and the entity commercializing the idea are not the one and the same. In such an occasion differences in what the aims of a technology are may offer drastically different views of the technology’s prospect, generating rivalry at the commercialization stage. For university technologies, such rivalry may also encompass ethical dimensions, as in the case of the CRISPR-Cas9 technology. True as it may be that ethical forms of licensing can present solutions to the difficulties described, there is a deficit in our economic understanding of how to frame such solutions. Embodied within the framework of semi-commons, we propose an intuitive and easy to implement solution that allows for purposeful reuse of resources in the form of a UoL license for university patents.

In this way, we adopt a broader view of IP as a political institution that serves important social goods and individual development. Redistribution is built in the semi-commons guided by pre-legal socnorderial norms concerning the limits of the right to exclude and the proper uses of a resource. Open licenses for research purposes and licenses imposing specific duties are examples to this direction and universities emerge as important actors in the regulatory enterprise.

125 P. Neville, MPEG LA’s Use of a Patent Pool to Solve the CRISPR Industry’s Licensing Problems, 2020 Utah L. Rev. (2020).
126 G. Van Overwalle et al., Models for Facilitating Access to Patents on Genetic Inventions. 7 Nat. Rev. Genet. 143–148 (2006).
127 Supra note 27.
128 https://www.mpegla.com/.
129 T. Minssen, E. Van Zimmeren & J. Wested, Clearing a Way through the CRISPR Patent Jungle, 8/5 L. Sci. Intell. Property Rev. (2018).