Process innovation in the pharmaceutical industry

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Problem definition: Process innovation is commonly claimed to be a major source of competitive advantage for firms. Despite this perceived influence it has received substantially less attention than product innovation and much uncertainty remains about its true association with firm performance. We investigate the relationship between a pharmaceutical manufacturing firm's process-innovation portfolio and its economic performance.

Academic/Practical relevance: Our study uniquely conducts a multi-dimensional evaluation of a firm's portfolio of process innovations at the product level. This allows a quantitative evaluation of both the relative benefit of the different dimensions of a portfolio as well as the potential complementarities between these.

Methodology: Through a collaboration with expert patent attorneys we develop a unique longitudinal dataset that combines secondary data and evaluations of a firm's portfolio of process patents along three key dimensions: novelty, scope, and locus. We conduct econometric analyses for a large-scale sample of drugs open to competition from generics, for which process innovation is the main source of competitive advantage.

Results: We find a positive association between overall process innovation and firm performance. When differentiating between dimensions of process innovation, results further suggest that high novelty is beneficial, and complemented by a broad scope, but only for patents applying to the later phase of the pharmaceutical manufacturing process.

Managerial Implications: Our results provide important practical insights that can inform process-related R&D investments across many industries. In particular, it may not always be economically beneficial to invest in high-novelty process innovations in production stages where there are many opportunities to innovate and payoffs are potentially higher but less predictable. On the other hand, in production stages where the opportunities to innovate are less numerous with potentially lower but more predictable economic payoffs, portfolios that are jointly characterized by high novelty and high scope could be more valuable.

1. Introduction

In manufacturing settings, process innovation can be broadly defined as the development of new or significantly improved *methods* for producing and delivering products (OECD 2005, Khazanchi et al. 2007). As such, it involves the introduction of novel elements into an organization's operations (e.g., input materials, task specifications, work and information flow mechanisms, and equipment; Damanpour 2008) so as to reduce production or delivery costs (OECD 2005), improve production yields (Tushman and Nadler 1986) and broader measures of productivity (Utterback and Aber-

nathy 1975, Ettlie and Reza 1992), and enable the manufacturing of products characterized by improved quality and reliability (Gopalakrishnan et al. 1999, OECD 2005). Process innovation is thus commonly claimed to be a major source of competitive advantage for firms (Pisano 1997) and is the dominant form of innovation in a product's life-cycle once product design has matured (Utterback and Abernathy 1975).

Despite its perceived influence over a firm's economic performance, process innovation has received substantially less attention than product innovation in past research (Crossan and Apaydin 2010). As a result, much uncertainty remains about the true impact of process innovation on firm's performance (Benner and Tushman 2003). This work seeks to address this gap by exploring in depth and quantifying the association between process innovation and economic performance. In particular, we aim to address the following overarching research question: How does a firm's process-innovation portfolio relate to this firm's economic performance?

We choose the pharmaceutical industry as the context for this work for several reasons. First, as a major employer and driver of economic growth and given its critical importance for public health, the pharmaceutical industry is important "in its own right" (Pisano 1997: p.20). Second, R&D spending in the pharmaceutical industry (as a percentage of sales) is higher than in any other high-tech industry (Cardinal 2001). As a result, studies of innovation across literature streams, including operations management (e.g., Schlapp et al. 2015, Taneri and De Meyer 2017), have focused on this setting. Third, the importance of process innovation is rapidly growing in the pharmaceutical industry, making it a privileged setting for our study. For example, so-called Advanced Manufacturing Technologies (AMTs) (cf., Gerwin 1993), that have long proved their value in assembled-goods industries, are now starting to receive increased attention in the pharmaceutical industry, where a push for a transition from batch to continuous manufacturing is underway (Harrington et al. 2017). This relatively recent emphasis on process innovation, in an industry long dominated by product innovation, is likely the result of a few key developments. First, pharmaceutical firms' ability to pursue "blockbuster medicines" has been declining recently because "even when promising products reach the market, few become blockbusters and generate a sufficient level of profitability relative to investment" (Carroll 2009). Concurrently, new legislation has facilitated the growth of the generics' market by significantly lowering barriers to entry (Morton 1999). Thus, investing in process innovation, rather than product innovation, may represent an important opportunity for pharmaceutical firms to ensure future growth.

In order to investigate the effect of process innovation, we focus on drugs that have lost product-patent protection (in the remainder of the paper, we use the term "drug" to refer to the set of all

bio-equivalent pharmaceutical products, i.e., all products that are based on the same key molecule, which includes the original brand product and any potential generic(s) for that product). Once a drug's product patent expires, the originating pharmaceutical firm faces competition from bio-equivalent versions, i.e., "generics". Thus, competitive advantage for these drugs depends mainly on process improvements (Morton 1999). In other terms, by looking at drugs open to competition from generics, we can compare the performance of different firms which are utilizing manufacturing processes of varying levels of innovativeness to deliver otherwise equivalent products.

Among pharmaceutical products, we choose to focus specifically on the antineoplastics drug category (i.e., drugs which are used in the treatment of cancer) for two main reasons. First, their sales tend to occur directly to hospitals through tenders (OECD 2016). This allows us to control for the effect of pharmaceutical firms' advertising efforts and overall brand awareness, which are very limited for drugs that are dispensed through hospitals compared to drugs dispensed through retail pharmacies (Caves et al. 1991). Consequently, any benefits that would derive from process innovation would be more readily observable in this context. Second, this market is significant from both an economic and a political point of view. Antineoplastics "rank first in terms of global spending by therapeutic class" and "figure prominently in discussions over health reform, alternately symbolizing wasteful spending and biomedical progress" (Howard et al. 2015, p. 140).

We rely on process patents as our indicator of process innovation as they represent concrete outputs of the firms' process-related R&D activities (Griliches 1990) and have been found to be the prevalent tool to protect intellectual property in the pharmaceutical industry (Mansfield 1986). This measurement allows for a granular investigation of the value of process innovation by capturing innovations that are both product-specific and available to a single organization. As such, our study aims to contribute to the operations management literature, which has typically considered broader instances of process innovations. These include, among others, novel software- and hardware-intensive production technologies (Ettlie and Reza 1992 and Ettlie 1998), new machinery and computer-integrated manufacturing systems (Zahra and Das 1993), and AMTs targeted at design, manufacturing, or administrative processes (Gerwin 1993).

For each drug in our sample, we longitudinally observe firms' corresponding process-patent portfolio, i.e., the collection of process patent(s) that apply to the production of that drug. In order to capture variation in the characteristics, and hence in the potential value, of these portfolios (Trajtenberg 1990), we collect independent ratings from three experts for each individual portfolio across three key dimensions: i) degree of novelty (thereafter referred to as "novelty"), ii) scope of protection against competition (thereafter referred to as "scope"), and iii) locus of application

in the production process (thereafter referred to as "locus"). To best capture a firm's degree of competitiveness relative to other firms in the market, we use its country-level market share for a drug as our measure of economic performance. Our final sample covers 50 drugs, whose sales are observed across four countries over a ten-year period. The resulting dataset includes quarterly observations for 206 firms which own a total of 282 distinct process patents, grouped into 216 unique portfolios of one or more patents.

Our study contributes to the literature on operations and innovation management in three substantial ways. First, we more accurately capture a firm's product-level process innovation by evaluating relevant patent portfolios. This is a unique proposition of our work since existing studies that use patents tend to conduct their analysis at the firm level and only rely on individual-patent characteristics. Second, we construct a unique longitudinal panel dataset that includes the simultaneous evaluation of every firm's product-level process-patent portfolio across novelty and scope dimensions. This allows us not only to identify the presence, but also to measure the extent of process innovation across multiple dimensions and over time. Third, our novel measure of locus allows us to observe the specific steps of the production process to which a process innovation applies. We are thus able to investigate potentially varying relationships between process innovation and performance, depending on the operational characteristics of the focal production phase. To the best of our knowledge, such in-depth examination of the association between the multiple characteristics of process innovation and performance is unique in the literature.

Econometric analyses on this large-scale longitudinal dataset suggest that ownership of a portfolio of patented process innovations for the production of a given drug is associated with a market share (for that drug) that is on average 5.4% higher relative to non-process-innovative competitors. We further find significant relationships between the qualitative characteristics of a firm's process-innovation portfolio and its economic performance. In particular, among process-innovative pharmaceutical firms, ownership of a high-novelty portfolio of patented process innovations is associated with a 2.4% higher market share, on average, relative to ownership of a low-novelty portfolio. Moreover, the association between novelty of portfolio and firm performance is more pronounced when the portfolio is characterized by a broader scope of protection. Finally, these relationships appear dependent on the production process' phase to which the portfolio applies. In particular, it may not be economically beneficial to invest in high-novelty process innovations in early production stages, which are characterized by numerous opportunities to innovate with potentially higher but less predictable economic payoffs. On the other hand, at later stages of the production process, where the opportunities to innovate are less numerous with potentially lower but more predictable

economic payoffs, portfolios that are jointly characterized by high novelty and high scope could be more valuable. Overall, our results not only contribute to the literature on process innovation but also provide important practical insights that can inform process-related R&D investments across industries.

2. The technological landscape of pharmaceutical manufacturing

We conceptualize the pharmaceutical manufacturing process as consisting of seven stages (detailed in Online Appendix A and depicted in Figure 1 that can be grouped into two broader phases: I) Production of API (stages 1 to 4), and II) Manufacturing of Final Dosage Form (FDF) (stages 5 to 7). This characterization is consistent with the Good Manufacturing Practice guidelines (Bennett and Cole 2003).

Drug production commences at a primary manufacturing site, which is responsible for housing the entire API phase, and continues at a (typically separate) secondary manufacturing site, which is responsible for housing the entire FDF phase. At the API phase, the firm's principal operational objectives relate to cost and quality since the focus is on the development of a manufacturing process that is cost-efficient, safe and can reliably scale-up while respecting a strictly-defined regulatory environment (Burns 2012). The key challenge in this phase is the selection of appropriate starting materials and their combination through chemical synthesis or fermentation, i.e., a series of chemical or biological reactions, to produce the API (cf., Hickey 2001). To achieve this, a firm should be capable of successfully integrating a complex technological skill set that relies on engineering, chemistry and microbiology (Bennett and Cole 2003). This suggests that API-phase operations are mainly technology-driven (Nusim 2016).

The main operational objectives at the FDF phase relate to flexibility and delivery since the goal is to develop a manufacturing process that uses the bulk API to efficiently produce the final pharmaceutical in various dosage forms, while ensuring preservation of the originating drug's therapeutic efficacy. Thus at the FDF phase, the primary process-related challenge is to manage the operational complexity that arises from the need to frequently produce a given drug in multiple

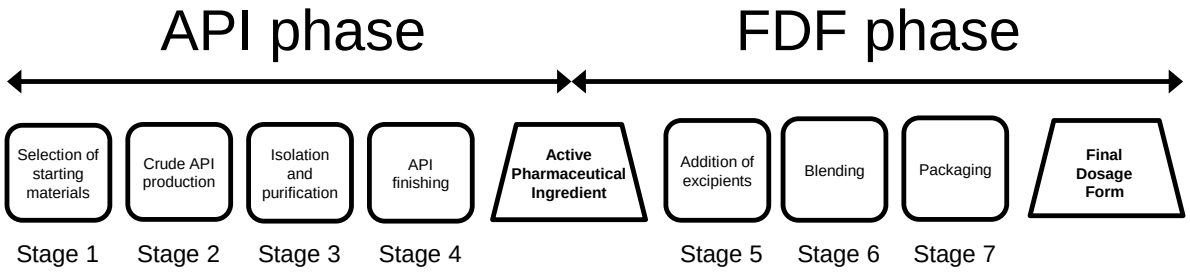

Figure 1 The seven stages of the pharmaceutical manufacturing process

strengths and supply it to different countries, each requiring a unique packaging. Such requirements lead to an explosion in the number of stock-keeping units (SKUs). Thus, differently from the API phase, where the main challenge is to master the underlying technology, efficient on-site operations are a key priority at the FDF phase (Burns 2012). As we will highlight throughout the development of our hypotheses, the different operational priorities between API and FDF phases suggest different opportunities for process innovation, as well as different economic implications of such innovation.

We use the concept of "technological landscape" as the main underlying thread for our arguments. This concept has been used extensively in the operations management and strategy literatures (e.g., Mihm et al. 2015, Fleming and Sorenson 2004) as the organizing framework for examining a firm's innovation activities. Researchers have argued that "the world of potential technological innovations can be conceived of as a landscape, with each potential position on the landscape corresponding to a particular configuration of components" (Aharonson and Schilling 2016: p.82). These components relate to either attributes of the final product or practices employed to manufacture that product (Fleming and Sorenson 2004).

In the context of drugs open to competition from generics, the final product is essentially identical across competing firms. Thus, each set of bio-equivalent pharmaceutical products, i.e., each drug, can be thought of as having its own technological landscape. A firm's position on the landscape is determined by its current configuration of technological choices across the API and FDF phases (Kauffman et al. 2000). Following this conceptualization, process innovation, as reflected in a firm's portfolio of process patent(s), becomes a means to occupy a unique, and potentially more valuable, position on the technological landscape.

3. Literature review and hypothesis development

3.1. Process innovation and firm performance

We begin our investigation by examining whether a firm's ownership of a portfolio of patented process innovations is associated with improved economic performance.

3.1.1. Presence of process innovation A broad stream of operations management research has examined the managerial implications of process innovation in manufacturing. This literature has considered, among others, the challenges associated with successfully adopting process innovations (e.g., Ettlie and Reza 1992), the association between the intensity of process R&D and economic performance (e.g., Ettlie 1998), the patterns of investment in process innovations (e.g., Boyer 1999), the association between organizational complexity and process innovation (e.g., Damanpour 2008), and the association between HR practices and manufacturing process innovation (e.g., MacDuffie 1995). In these studies, the presence of process innovation is mostly measured

through surveys that aim to obtain information about the extent to which manufacturing organizations have adopted or developed novel production technologies. Thus, the unit of measurement is typically the organization itself or an organization's plant(s).

A common argument in this literature is that organizations that successfully adopt or develop process innovations should enjoy superior performance in the marketplace. However, despite some supporting evidence (e.g., Ettlie 1998, Zahra and Das 1993), the association between adoption of process innovations and economic performance has not received the necessary degree of attention. This is echoed by Benner and Tushman (2003) who argue that the available literature on the effects of process management (broadly defined to include process mapping, process improvement and process adherence techniques) has not reached a definitive conclusion.

Relative to existing studies, our work is, to the best of our knowledge, unique in that we measure the presence of process innovation using objective patent data that we link to individual products (i.e., drugs in our setting). Our usage of patent data implies that the process innovations that we consider are outputs of scientifically-driven process-development efforts that have gone through a rigorous evaluation process to establish their patentability and are uniquely available to the patent-holding firm. Ownership of a strong portfolio of patented process innovations can offer the owning firm exclusive access to superior production processes and protect its technological choices by impairing competitors' ability to venture close to its position on the technological landscape.

While such an approach may narrow our "universe" of considered process innovations (e.g., we do not explicitly consider the adoption of novel production equipment or the implementation of novel managerial procedures), it allows us to conduct our investigation at the individual product level, as opposed to the firm level, and directly test and measure the link between product-specific process innovation and product-specific firm performance (as measured by market share for that product in a given country). Conducting the analysis at the product level is beneficial because multi-product firms that may operate innovative production processes for some of their products may not necessarily do so, or face the same level of competition, across their entire product line.

In addition to lowering production costs, and consequently enabling lower prices, such manufacturing process innovations in the pharmaceutical industry have the potential to impact hospital purchasing decisions in various important ways. For instance, practical considerations such as storage requirements, drug shelf life, packaging, and route of administration can all be impacted by process innovations (Staniforth 2007). To illustrate this point consider the case of Vinorelbine, a drug in our sample that is used to treat lung and breast cancers (drug-specific examples throughout the paper have been identified with the assistance of expert patent attorneys; additional background information can be provided upon request). Its prior-art formulation had to be stored in a

refrigerator, whereas the process innovation patented by Pierre Fabre allows the production of a formulation that can be stored at room temperature. Thus, the new formulation has the potential to significantly decrease transportation, holding, and handling costs for hospitals. Process innovations can therefore have a large impact on cost not just at the beginning, but along the entire drug's lifecycle (Pisano 1997), which is increasingly taken into consideration when hospitals choose among otherwise bio-equivalent pharmaceuticals.

The above arguments lead us to hypothesize that:

H1a: Process innovation is positively associated with firm performance.

3.1.2. Locus of process innovation Process innovation can apply to different steps of the pharmaceutical production process, which may lead to different effects on a firm's performance. We use the term "locus" to refer to the specific phase(s) of manufacturing production to which a portfolio of patents applies. To the best of our knowledge, a detailed examination of the relation between the locus of process innovation and economic performance has not been undertaken in previous research, despite its potential to allow more targeted R&D efforts.

As introduced in Section 2, the pharmaceutical manufacturing process can be divided into two broad phases, a technology-driven API phase that targets cost effectiveness and high quality, and an efficiency-driven FDF phase that targets high flexibility and fast delivery. To illustrate process innovation at the API phase, consider the case of Idarubicin, an anti-leukemia drug included in our sample. Due to a manufacturing process that originally consisted of 12 distinct chemical steps, yield in API manufacturing was only 5%, resulting in an average price of $2,000 per gram. When Synbias Pharma developed an innovative manufacturing method that used only four chemical steps the yield increased to 30%, a process innovation that catapulted Synbias Pharma to become the world market leader for this drug. Our earlier example, in Section 3.1.1, of Pierre Fabre developing a dosage form for Vinorelbine that can be stored at room temperature, illustrates process innovation at the FDF phase.

Mirroring their markedly different operational objectives, the API and FDF phases represent very different proportions of the total cost of pharmaceutical production. Indeed, while the cost of API manufacturing as a percentage of total costs can vary significantly from drug to drug, it is widely considered as the largest component of direct manufacturing costs (Pinheiro et al. 2006). For generics, one can assume that API manufacturing represents at least 50% of total drug cost on average and this can reach as much as 90% for specialized molecules, such as those contained in the anti-cancer drugs that compose our sample (Sampath 2010).

The relatively large proportion of costs borne by the API compared to the FDF phase would suggest that innovations at the API phase might have the potential to lead to higher cost reductions

than at the FDF phase. For example, shortening a chemical-synthesis route from seven to five steps may cut costs by approximately 50% (Adler et al. 2006). Because cost is a key driver of performance in the studied setting, this leads us to the following hypothesis:

H1b: Process innovation at the API phase has a stronger association with firm performance than process innovation at the FDF phase.

3.2. Dimensions of process innovation and firm performance

Using a binary measure of process innovation to categorize firms as innovative versus non-innovative precludes from qualitatively differentiating process innovations and may hide important insights. Thus, we next focus on two key dimensions of process innovation, i.e., novelty and scope, in order to achieve a more nuanced understanding of its association with economic performance.

Past research that has measured innovation's novelty or scope using patent data, has typically done so at the patent level (Verhoeven et al. 2016, Novelli 2015). Having expert patent attorneys evaluate patent portfolios allows us to more accurately capture the characteristics of process innovation for a given product, by accounting for the potential overlap and complementarities between patents that belong to the same portfolio (the experts' evaluation process is further detailed in Section 4.2.2 and in Online Appendix B).

3.2.1. Novelty of process innovation Patented process innovations, by their virtue of having received patent protection, necessarily introduce something novel relative to the state of the art ("prior art") at their time of filing. They can nonetheless vary considerably in terms of their degree of novelty, which is defined as the technological distance between the patented innovation and the prior art (Reitzig 2003). Going back to our concept of technological landscape, a more novel process patent portfolio would enable the owning firm to identify and occupy a more distant (and likely superior) position on the technological landscape, relative to the competition.

Nevertheless, the adoption of novel process innovations at an industrial scale may introduce a certain degree of uncertainty in a firm's manufacturing operations (Ettlie and Reza 1992, Verhoeven et al. 2016). This is because, as explained in Pisano (1997), "plants are complex environments, and the nuances in equipment, procedures, and people that make up its capabilities cannot be fully characterized ahead of time" (p.133). Consequently, as the degree of novelty of process changes increases, so does the associated implementation difficulty. More novel process changes are more likely to require non-trivial changes in plant design and equipment usage (Dennis and Meredith 2003) or necessitate additional employee training (Pisano 1997). These arguments suggest that the expected economic or other benefits of novel process innovations may not necessarily be fully realized.

However, existing research, which relies on various patent-based measures of innovation novelty (e.g., Verhoeven et al. 2016), typically posits a positive link between innovation novelty and firm value. In line with Hall (2000)'s concluding remark that the "market value of the modern manufacturing corporation is strongly related to its knowledge assets" (p.198), we state the following hypothesis:

H2a: Novelty of process-patent portfolio is positively associated with firm performance.

3.2.2. Scope of process innovation Apart from their degree of novelty, patented process innovations can also vary substantially in terms of scope, defined as the degree of difficulty for competitors to operate a similar technological configuration without infringing on the process-patent portfolio. Our construct of scope is closely related to the concepts of patent "breadth" (e.g., Lerner 1994) and "width" (e.g., Klemperer 1990) that have received attention in previous literature as meaningful qualitative differentiators of innovation. Using the technological landscape terminology, a patent portfolio with a broader scope would suggest that the firm may not only uniquely occupy a technological position, but also maintain exclusive access to a broad set of related technological configurations. Thus, the broader the portfolio's scope, the higher the expected ability for the owning firm to implement its innovation while denying competitors a similar position on the technological landscape (Mihm et al. 2015).

Broader inventions may however, during their transfer from lab to plant, require higher refinement efforts and increased experimentation for identifying the optimal configuration among this broader set of alternative implementation choices (Leonard-Barton 1988). This observation suggests a mechanism through which innovations of broader scope may induce some loss of efficiency as they are being translated into specific operating routines, thereby potentially mitigating the potential benefits associated with broader innovation scope.

Nevertheless, existing studies assume that ownership of patents of broader scope is positively associated with various measures of firm value (e.g., Gilbert and Shapiro 1990, Novelli 2015). Because we expect process patents of broader scope to allow the owning firm to benefit from improved production processes in a relatively secluded technological position, and thus to secure a substantial market share, we hypothesize that:

H2b: Scope of process-patent portfolio is positively associated with firm performance.

3.2.3. Complementarity between novelty and scope As we argued in Sections 3.2.1 and 3.2.2 above, we expect a portfolio of process innovations that is, ceteris paribus, more novel and/or of broader scope to be associated with better firm performance. However, when considered simultaneously, higher novelty doesn't necessarily imply a broader scope and vice versa. To illustrate the

case of high novelty-low scope process innovation consider Mesna, a drug in our sample that is used in the treatment of chemotherapy-related cystitis. While UCB Pharma developed and patented a highly novel process for the preparation of this drug, the resulting patent was of narrow scope, according to our patent experts, because it could be circumvented relatively easily. For instance, Altan Pharma Ltd, Fresenius AG, and Sagent Pharmaceuticals Inc all found a way around this particular patent. This example points to one of the principal risks associated with high-novelty but narrow-scope process patents. Because, due to the narrow scope, protection is relatively weak, competitors may free-ride on a firm's innovation, which becomes public knowledge as soon as the patent application is published.

For an example of a low novelty-high scope process innovation consider Oxaliplatin, a drug in our sample that is used in the treatment of colorectal cancer. Fresenius AG developed and patented a modified method for stabilizing the final dosage form through different stabilization agents, which permitted longer shelf life. According to our patent experts, the innovation was low in novelty because similar methods were already known, yet broad in scope because an entire family of related stabilization agents was identified and included in the patent. A potential risk from developing well-protected low-novelty process innovations is that they may create a false sense of security for the innovating firm. Indeed, this may force the competition to target its efforts in different regions of the technological landscape which might result, in the long run, in these other firms succeeding to identify high-novelty (and likely more profitable) process innovations (Verhoeven et al. 2016). This is exactly what we observed with Fresenius AG who briefly achieved market dominance for Oxaliplatin but was soon outperformed by Pfizer, who, over time, succeeded in developing its own high-novelty high-scope portfolio of process innovations.

Although, to our knowledge, no existing study considers both the novelty and the scope of process innovation, the above arguments imply that important competitive advantages might stem from the complementarity between these dimensions. Thus, we hypothesize:

H2c: The association between process-patent portfolio's scope and firm performance is stronger when the portfolio's novelty is higher.

3.3. Dimensions of process innovation and locus of application

We now build on our discussion in Sections 3.1.2 and 3.2 to explore how the association between the dimensions of novelty and scope and firm performance may differ depending on the manufacturing phase to which the innovation applies.

3.3.1. Locus of process innovation's novelty Recall from our discussion in Section 3.1.2 that the principal objective for the design of a pharmaceutical's API manufacturing phase is to develop a technology-driven manufacturing process that reflects the chosen sequence of chemical or biological reactions and will consistently and cost-effectively deliver an output, i.e. the API in bulk form, with the desired physicochemical attributes (Nusim 2016). Because of the large number of possible chemical-synthesis routes from which a given firm may choose, with many of these routes including over twenty distinct intermediate reactions (Bennett and Cole 2003), many radically new technological configurations are potentially available to the firm in this manufacturing phase.

During the FDF phase, firms focus on managing the operational complexity associated with frequently and quickly producing multiple dosage forms of multiple drugs using common, and typically existing, infrastructural designs and equipment (Gad 2008). This is very different from the API phase, where the selected technological configuration will often determine the design of the API manufacturing plant itself (Nusim 2016). Therefore, according to our patent experts, process innovations for the FDF phase are aimed at improving the properties of a pharmaceutical product's formulation so as to optimize its shelf life, storage, disposal, and handling without drastically changing the nature of the underlying manufacturing process. Consequently, the set of technological configurations available to a firm is narrower in the FDF phase relative to the API phase.

These arguments suggest that patents of higher novelty could be much harder to achieve in the FDF phase and could thus constitute a greater source of competitive advantage. Thus, we state the following hypothesis:

H3a: The association between process-patent portfolio's novelty and firm performance is stronger when the portfolio applies to the FDF compared to the API manufacturing phase.

3.3.2. Locus of process innovation's scope Similarly, because numerous technological configurations are available to each firm in the API phase, having a portfolio of patents that is broader in this phase might not be very effective at limiting competitors' opportunities to achieve a different, yet economically comparable technological position. This is supported by our patent experts who noted that patented API process innovations can block a particular synthesis route but cannot prevent competitors' market entry completely. A practical example is found in the case of Letrozole, a drug in our sample used to treat breast cancer. After product patent expiration, Mylan Laboratories patented an improved, and broadly protected, API production process, which likely allowed them to capture the majority of the U.S. market for that drug during 2011 and part of 2012. However, it also revealed a previously hidden part of the technological landscape for Letrozole that allowed Sun Pharmaceuticals to patent an additional relatively small but key improvement

(i.e., the removal of one step), thereby bypassing Mylan's scope of protection. The cost and quality benefits stemming from this patented improvement are likely to have aided Sun in replacing Mylan Laboratories as the market leader for Letrozole in the U.S.

On the other hand, because of the much fewer technological configurations available to a firm in the FDF phase, a process-patent portfolio that broadly covers a drug's set of possible FDF-related technological configurations may not only protect a firm's intellectual property but could also prevent competing firms from occupying any economically-viable position on the technological landscape (Ceccagnoli 2009). This is illustrated by Celgene's Lenalidomide (a multi-billion blockbuster drug in our sample, which is used in the treatment of myeloma), where a broad process-patent portfolio consisting of 48 patents that apply to the FDF phase is predicted to allow Celgene to maintain market dominance long after the expiration of its product patent in 2019. Similarly, Pierre Fabre has maintained worldwide sales monopoly for the Vinorelbine drug for the last 15 years without product-patent protection because of its broad portfolio of three process patents that apply to the FDF phase (*Sources:* IMS Health, Newport).

These arguments suggest the following hypothesis:

H3b: The association between process-patent portfolio's scope and firm performance is stronger when the portfolio applies to the FDF compared to the API manufacturing phase.

3.3.3. Locus and complementarity between novelty and scope Our final hypothesis tests whether the complementarity between process innovation's novelty and scope dimensions could depend on the specific manufacturing step to which the process-patent portfolio applies. Recall from our discussion in Section 3.2.3 that we expect portfolio's novelty to be more valuable when the portfolio is also broad in scope, i.e., we expect a complementary effect between process innovation's novelty and scope. Recall also from our discussion in Sections 3.3.1 and 3.3.2 that we expect a portfolio of process innovations that is more novel or of broader scope to be more valuable when it applies to the FDF rather than the API manufacturing phase. Combining these discussions, we hypothesize that:

H3c: The complementarity between process-patent portfolio's novelty and scope, with regard to firm performance, is stronger when the portfolio applies to the FDF compared to the API manufacturing phase.

4. Dataset and variables

4.1. Dataset

We conduct our investigation using a unique dataset which combines primary and secondary data sources. We focus on drugs that have lost product-patent protection and as a consequence face

competition from generics, i.e. bio-equivalent pharmaceuticals. Thus, competitive advantage for these drugs depends mainly on process improvements (Morton 1999). We further focus on drugs included in the L1 subgroup of the drug classification system that has been developed (and is being maintained) by the European Pharmaceutical Marketing Research Association. This subgroup includes all antineoplastic (i.e., anti-cancer) drugs. We choose this broad, self-contained category of drugs because of its economic and political significance, and the fact that sales of antineoplastics tend to occur directly to hospitals through tenders. This suggests that price and other practical considerations, rather than marketing efforts, are the principal drivers in hospitals' purchasing decisions (and hence the key determinants of market share).

We collect data from four countries: the U.S. (33.7% of the global generics market), France (9.8% of the European generics market), Spain (6.5% of the European generics market), and Italy (2.5% of the European generics market) (*Source:* IMS Health). We choose these specific markets because the U.S. is the largest pharmaceutical market worldwide, and France, Italy, and Spain are all within the top five European pharmaceutical markets. Moreover, all four countries' overall markets for generics (with the exception of market size) are characterized by qualitatively similar competition characteristics. In Online Appendix C, we present a detailed characterization of these markets using Porter's "Five Forces" framework (Porter 2008).

The entire L1 subclass of antineoplastics covers 208 drugs, 148 of which have lost product-patent protection prior or during the time frame of our study, and which therefore qualify for our sample. We further exclude 46 drugs that did not receive market authorization in any of the four studied countries. Next, we exclude 22 drugs which have global sales of less than $10M. This amount is considered as the industry threshold for a pharmaceutical firm to consider investing in the development of a generic version of a drug (Morton 1999). When global sales are expected to be below the $10M threshold it becomes increasingly unlikely that firms will be able to recover their fixed investment costs. This suggests that market share observations for generics that relate to drugs with lower global sales volumes are likely to be determined through mechanisms different from those that typically govern competition in this setting (Tenn and Wendling 2013). Such a separate treatment of "small" drug markets is consistent with the literature (e.g., Reiffen and Ward 2005, Tenn and Wendling 2013). Finally, we exclude 30 drugs because of the lack of any related process innovation (i.e., any active process patent for that drug) across all firm-country-quarter combinations. This results in a final sample of 50 drugs.

For each of the 50 drugs included in our final sample, we collect all firm quarterly sales observed in each of the four countries considered, as well as all related process patents, over a period of 40

Country	Number of drugs	Number of unique pharmaceuticals	Number of firms	Number of individual patents	Number of patent portfolios	Number of patent portfolios with at least two patents
USA	50	366	105	234	132	105
France	46	232	55	194	96	79
Spain	45	240	67	210	104	84
Italy	45	243	85	196	96	79

Table 1 Overview of data by country

quarters, from January 2005 (when our data provider implemented its current database structure) to December 2014 (the latest data available when we initiated this study). The resulting final dataset includes 43,280 drug-firm-country-quarter observations that relate to 675 unique pharmaceuticals (original and generic versions) produced by 206 global corporate groups (referred to as "firms" in the remainder of the paper). These firms own a total of 282 individual process patents, which can be further grouped into 216 unique portfolios–with 61% of these portfolios consisting of two or more patents. Table 1 details the number of drugs, firms, patents, and portfolios by country in our final dataset.

4.2. Variable definitions and sources

4.2.1. Firm performance $SHARE_{ikjq}$ represents the share of the market for drug i that is captured by firm k in country j during quarter q, and is used as our measure of economic performance. We rely on Intercontinental Medical Statistics (IMS) Health's MIDAS pharmaceutical sales proprietary database to compute this measure. This database tracks the sales of nearly every pharmaceutical product sold worldwide by firm, product, and quarter and is considered to be the most reliable source of sales information in the pharmaceutical industry (Kanavos 2014). MIDAS brings together data obtained from IMS Health's detailed audits of actual invoiced retail pharmacy and hospital sales. The accuracy of the data ranges between 93% and 95%.

For each drug included in our sample, we collect quarterly sales data from the MIDAS database for the original pharmaceutical and all related generics sold between January 2005 and December 2014. We measure the size of the market for a particular drug as the total sales (in kgs of pure API) for the drug in a given quarter and country, thereby not distinguishing between different dosage forms or strengths. Such a volume-based calculation of market share is commonly used in the pharmaceutical policy literature (e.g., Caves et al. 1991, Kanavos 2014). Thus, in quarter q, firm k's market share in country j for drug i is computed as the ratio of quarterly sales of firm k's version of drug i divided by country j's total quarterly sales for drug i, i.e. total sales across all versions of that drug in that country. That is:

$$SHARE_{ikjq} = Sales_{ikjq} / \sum_{k} Sales_{ikjq} \tag{1}$$

$SHARE$ in our dataset ranges from 0.00% to 100% with a mean of 13.71%. Consistent with our dependent variable, we measure each independent variable for drug i, firm k, country j, and quarter q. However, for conciseness, we do not repeat these subscripts when describing these variables.

4.2.2. Process innovation For each drug in our dataset, we collect complete sets (i.e., portfolios) of the process patents owned by each firm for the original pharmaceutical and all related generics for each quarter of the ten-year timeframe considered. We use the Thomson Reuters Newport database to obtain all relevant information for each patent (e.g., related drug, owning firm, filing and expiration dates and detailed description). The Newport database is considered as the reference database in the pharmaceutical industry for the collection of patent data and other intellectual-property information (Grimaldi et al. 2015).

To assess overall process innovation, we use a binary variable, $ACTIVE$, set to 1 in a given quarter if the focal firm shows positive sales and has at least one current process patent in the focal country for its version of the focal drug, and set to 0 otherwise. In our final dataset, 4,217 observations (i.e., 9.74% of the sample) relate to an active portfolio.

To measure the novelty, scope, and locus of each active process-patent portfolio, we developed, in collaboration with three expert patent attorneys, survey questions based on the formal definition provided for each construct in Section 3. We then asked the three patent experts, who are highly experienced in patent litigation and have extensive chemical and biotechnological backgrounds, to rate each portfolio of process patents along each of these items.

We provide a detailed description of the evaluation process for each active portfolio of patents in Online Appendix B, along with inter-rater reliability statistics. In summary, the evaluation of the portfolios consists of two steps. First, experts evaluate individually each current patent within a portfolio along novelty and scope dimensions and identify which manufacturing step(s) is(are) covered by the patent's claims. This step of the evaluation process is particularly time-consuming given that patents are dense technical documents whose length ranges, for our sample, from 9 to 165 pages. In total, our patent experts evaluated 282 individual patents. Second, portfolio-level measures are determined. While the locus of each portfolio simply corresponds to the step(s) covered by its individual patents, experts rely on both their patent-level measures and a comprehensive assessment of each portfolio in its entirety to determine measures of novelty and scope at the portfolio level. Indeed, the presence of human experts is crucial in this second step to identify and take into account the possible overlap and complementarities between the individual patents that are current within a given portfolio at a given point in time. Every time there is a change in a portfolio through the filing of a new patent or the expiration of an existing patent, the entire

portfolio needs to be re-evaluated across all three dimensions. In total, our patent experts rated 216 portfolios. To the best of our knowledge this multi-dimensional evaluation of process innovation at the portfolio level is a unique proposition of our study.

We denote by $NOVELTY$ the level of novelty of the process-patent portfolio for each drug-firm-country-quarter observation. $NOVELTY$ is coded as "none" if the firm has no active portfolio covering its version of the focal drug in the given country and quarter, and as "low", "medium", or "high" otherwise. Levels of novelty are based on patent experts' responses to the question "How would you evaluate the overall novelty of the portfolio of process patents with respect to the state of the art at the time of the latest patent filing/expiration?". Among active portfolios in our final sample, 15.46% (n=652) of the observations are low novelty, 55.16% (n=2,326) are medium novelty, and 29.38% (n=1,239) are high novelty.

$SCOPE$ measures the scope of the process-patent portfolio for a firm's version of a drug in a given country and quarter. Similar to our construct of novelty, $SCOPE$ is an ordinal variable coded as "none" in the absence of active portfolio and as "low", "medium", or "high" otherwise. In the presence of an active portfolio, it is measured using patent experts' answers to the question "How broad are the claims of the portfolio of process patents with respect to the state of the art at the time of the latest patent filing/expiration?". Among observations related to active portfolios in our final sample, 6.45% (n=272) are low scope, 45.60% (n=1,923) are medium scope, and 47.95% (n=2,022) are high scope.

We denote by $LOCUS$ the locus of application of the patent portfolio for a firm's version of a drug in a given country and quarter. This categorical variable is coded as "none" if there is no active portfolio, as "API-only" if the active patent portfolio covers production steps within the API manufacturing phase only, as "FDF-only" if it covers production steps within the FDF manufacturing phase only, and as "both" if it covers production steps within both the API and FDF phases. In our final sample, 28.55% (n=1,204) of the observations for active portfolios apply to the API phase only, 36.50% (n=1,539) apply to the FDF phase only, and 34.95% (n=1,474) apply to both the API and FDF phases.

Finally, we include AGE in our regressions to control for the average age of the process-patent portfolio for a firm's version of a drug in a given country and quarter. We measure the age of an individual patent as the number of quarters since the patent was filed and the age of a portfolio as the average age of its respective patent(s). We expect that as a portfolio ages, the protected innovation will gradually become less economically valuable as the competition identifies alternative manufacturing approaches that may erode the portfolio holder's competitive advantage without

Variable	Definition	Measurement	Source
SHARE	Firm's share of drug sales in a country	Percentage of firm's sales (in kgs of pure API) to total country sales	IMS Health
ACTIVE	Presence of a currently active process-patent portfolio	Binary variable (0=no active portfolio; 1=active portfolio)	Newport
NOVELTY	Distance between the portfolio's patented invention(s) and the prior art	Ordinal variable (levels = none, low, medium, high)	Expert evaluations
SCOPE	Breadth of the patent portfolio's claims	Ordinal variable (levels = none, low, medium, high)	Expert evaluations
LOCUS	Manufacturing phase(s) to which the patent portfolio applies	Categorical variable (0=no portfolio; 1=API-only; 2=FDF-only; 3=both)	Expert evaluations
AGE	Average age of a portfolio's patent(s)	Average number of quarters since patent(s)' activation	Newport

All variables are measured at the drug-firm-country-quarter level.

Table 2 Variables' definitions, measurement and sources

	SHARE	*NOVELTY*	*SCOPE*	*AGE*
SHARE	1			
NOVELTY	0.138	1		
SCOPE	0.273	0.135	1	
AGE	-0.223	0.063	0.053	1

Table 3 Pairwise correlations for active portfolios (N=4,217)

infringing on its patent(s) (Gilbert and Shapiro 1990). In our final sample, *AGE* for active portfolios ranges from 1 to 86 quarters with a mean of 35 quarters (i.e., 8.75 years).

Table 2 provides a summary of variables' definitions, measurement, and sources. Pairwise correlations for the *SHARE*, *NOVELTY*, *SCOPE* and *AGE* measures among active portfolios are reported in Table 3.

5. Analyses and Results

5.1. Model specification

We use the system generalized method-of-moments (system GMM) estimation approach (Arellano and Bover 1995, Blundell and Bond 1998, Kuhnen and Niessen 2012, Senot et al. 2016, Pennetier et al. 2018) to model market share using the xtabond2 command in STATA15. This approach allows us to include multiple important considerations into the model specification.

First, the persistence of a firm's market share has been discussed extensively in past research. Researchers argue that higher market shares may, in part, be indicative of superior firm capabilities that tend to change slowly over time. We thus include lagged market share as a control in our model to capture the effect of such persistent and unobservable firm characteristics (Fresard 2010). Estimating such dynamic model with either an OLS or a fixed effects approach would lead to a "dynamic panel bias" (Nickell 1981, Bond 2002). Second, a firm's past market share would not only affect its current market share but might also influence the level of resources available for current innovation efforts (Pennetier et al. 2018). This raises endogeneity concerns for our key independent

variables, which characterize these innovations. The System GMM estimation approach, which uses lags of variables as instruments, addresses both these issues (Blundell and Bond 1998).

In addition to time dummies, our model also needs to account for unobserved heterogeneity across different drugs, firms, and countries that would potentially affect realized market share. Country-specific market characteristics include, for example, the overall market size, the country's regulatory environment, and the overall degree of generics' penetration. Firm-level characteristics include aspects such as size, intensity of R&D investment, financial leverage, and labor quality. Finally, drug-level characteristics include the cost and complexity associated with developing an appropriate manufacturing process and the competition from potential substitute treatments for the same disease. Because these sets of characteristics are all intertwined (e.g., the competition for a drug will ultimately depend on the overall market size, regulatory environment, labor quality, etc.), we include a fixed effect at the drug-firm-country level in our model.

In order to test our hypotheses, the market share for drug i produced by firm k in country j during quarter q is generally defined as follows:

$$SHARE_{ikjq} = \beta_1 \cdot SHARE_{ikjq-1} + \beta_2 \cdot AGE_{ikjq} + \beta_3 \cdot QUARTER_q + \beta_Z \cdot Z_{ikjq} + \mu_{ikj} + \epsilon_{ikjq} \quad (2)$$

where Z_{ikjq} represents the characteristics of interest of the process-patent portfolio and β_Z a vector of associated estimated coefficients; μ_{ikj} denotes the drug-firm-country fixed effect and ϵ_{ikjq} is the observation-specific error. In line with our earlier remarks, the lagged dependent variable, $SHARE_{ikjq-1}$, is specified as pre-determined; all process-patent portfolio's characteristics, i.e., AGE_{ikjq} and Z_{ikjq}, are specified as potentially endogenous; and the time variable, $QUARTER_q$, is considered strictly exogenous (Roodman 2009a).

To further ensure the validity of our approach and reliability of our estimates we conduct various tests whose results are shown in Tables 4 and 5, along with the coefficients' estimates. First, for each analysis, we report both the number of instruments and the number of drug-firm-country groups included. In every instance, the number of groups is significantly larger than the number of instruments, which suggests that instrument proliferation is unlikely to be an issue (Roodman 2009a). Second, we report the p-value for the Arellano-Bond test for AR(2) auto-correlation. This value, which is consistently far greater than 0.10, suggests that our choice to instrument the potentially endogenous explanatory variables starting from lag 2 is appropriate. Third, we report the p-value for both the Hansen test of over-identifying restrictions and the Difference-in-Hansen test of the system GMM instruments. For each analysis, both tests failed to reject the null hypothesis that the instruments are uncorrelated with the error term, which supports the validity of the instrument set. Fourth, we note that for all models the lagged $SHARE$ coefficient has an absolute

value below unity, which ensures the convergence of the estimation process (Blundell and Bond 1998). Moreover, for each model, we verify that this coefficient is between its lower bound estimated through fixed-effects regression and its upper bound estimated through OLS regression (cf., Bond 2002). Overall, all tests satisfy the standard criteria for the use of system GMM and support the reliability of our estimates.(Roodman 2009a, Roodman 2009b).

5.2. Process innovation and firm performance

In line with equation (2), we estimate the following specific model to test Hypothesis $H1a$, which states that process innovation is positively associated with firm performance:

$$\begin{aligned} SHARE_{ikjq} = \beta_1 \cdot SHARE_{ikjq-1} + \beta_2 \cdot AGE_{ikjq} + \beta_3 \cdot QUARTER_q \\ + \beta_4 \cdot ACTIVE_{ikjq} + \mu_{ikj} + \epsilon_{ikjq} \end{aligned} \tag{3}$$

where $ACTIVE_{ikjq} = 1$ when firm k has a process-patent portfolio that is active in country j during quarter q covering some parts of the manufacturing process for drug i. Otherwise, we set $ACTIVE_{ikjq} = 0$. $H1a$ would then imply that $\beta_4 > 0$. The results from the estimation of Model (3) are presented in Table 4. Coefficient β_4 is positive and significant (0.054, $p < 0.01$), which supports $H1a$. This suggests that firms that own active portfolios of patented process innovations that apply to the production process of a given drug enjoy a market share that is on average 5.4% higher (95% CI=[1.4%, 9.4%]) relative to the market share of non-process-innovative firms for the same drug.

Hypothesis $H1b$ states that the positive association between process innovation and performance will be stronger if the portfolio applies to the API than if it applies to the FDF manufacturing phase. We thus estimate the following model to test this hypothesis:

$$\begin{aligned} SHARE_{ikjt} = \beta_1 \cdot SHARE_{ikjt-1} + \beta_2 \cdot AGE_{ikjt} + \beta_3 \cdot QUARTER_q \\ + \beta_{4A} \cdot API_{ikjt} + \beta_{4F} \cdot FDF_{ikjt} + \mu_{ikj} + \epsilon_{ikjt} \end{aligned} \tag{4}$$

where $API = 1$ if the portfolio applies to the API phase (i.e., $LOCUS = \{1, 3\}$) and zero otherwise, and $FDF = 1$ if the portfolio applies to the FDF phase (i.e., $LOCUS = \{2, 3\}$) and zero otherwise. Full support for $H1b$ would imply that $\beta_{4A} > \beta_{4F} \geq 0$. The results from the estimation, which are presented in the column (Model 4) in Table 4, show that $\beta_{4A} = 0.043$ ($p < 0.05$) and $\beta_{4F} = 0.035$ ($p < 0.05$). Nevertheless, a Wald test cannot reject the null hypothesis that $\beta_{4A} = \beta_{4F}$ ($p > 0.10$), thus $H1b$ is not formally supported. Our results from the estimation of Model (4) suggest that when considering the mere presence of process innovation, there is no statistically distinguishable benefit from it applying to the API versus the FDF manufacturing phase.

Taken together, results for $H1a$ and $H1b$ suggest that, overall, process-innovative firms might enjoy economic benefits in terms of higher market share, and this irrespective of the manufacturing phase targeted by the innovation(s).

	SHARE				
	(Model 3)	(Model 4)	(Model 5)	(Model 6)	(Model 7)
$SHARE$ (Lagged 1 quarter)	0.940***	0.946***	0.930***	0.930***	0.952***
	(0.032)	(0.029)	(0.036)	(0.035)	(0.023)
AGE	-0.001***	-0.001***	-0.001***	-0.001***	-0.001***
	(0.000)	(0.000)	(0.000)	(0.000)	(0.000)
$ACTIVE$	0.054***				
	(0.020)				
API		0.043**			
		(0.019)			
FDF		0.035**			
		(0.018)			
$NOVELTY_{LOW}$			0.042**$_{H}$		
			(0.018)		
$NOVELTY_{MEDIUM}$			0.053**		
			(0.021)		
$NOVELTY_{HIGH}$			0.066***$_{L}$		
			(0.020)		
$SCOPE_{LOW}$				0.029*	
				(0.016)	
$SCOPE_{MEDIUM}$				0.052***	
				(0.015)	
$SCOPE_{HIGH}$				0.068**	
				(0.026)	
$NOVELTY_{LOW} \times SCOPE_{LOW}$					0.018
					(0.018)
$NOVELTY_{LOW} \times SCOPE_{MEDIUM}$					0.047**
					(0.019)
$NOVELTY_{LOW} \times SCOPE_{HIGH}$					0.048**
					(0.020)
$NOVELTY_{MEDIUM} \times SCOPE_{LOW}$					0.052**
					(0.024)
$NOVELTY_{MEDIUM} \times SCOPE_{MEDIUM}$					0.048***
					(0.017)
$NOVELTY_{MEDIUM} \times SCOPE_{HIGH}$					0.052**$_{HH}$
					(0.022)
$NOVELTY_{HIGH} \times SCOPE_{LOW}$					0.015$_{HM,HH}$
					(0.017)
$NOVELTY_{HIGH} \times SCOPE_{MEDIUM}$					0.059***$_{HL}$
					(0.020)
$NOVELTY_{HIGH} \times SCOPE_{HIGH}$					0.077***$_{HL,MH}$
					(0.028)
Observations	42,198	42,198	42,198	42,198	42,198
Number of groups (drug-firm-country)	1,082	1,082	1,082	1,082	1,082
Number of instruments	375	332	379	379	603
Arellano-Bond test for AR2 (p-value)	0.916	0.926	0.911	0.910	0.912
Hansen Test of overid. restr. (p-value)	0.473	0.738	0.397	0.420	0.909
Hansen Difference (null H = exogenous) (p-value)	0.638	0.808	0.183	0.612	0.167

Notes: *p<.10; **p<.05; ***p<.01. Drug-firm-country and time (quarter) fixed effects are included in all regressions. Robust standard errors are provided in parentheses. Subscripts indicate significant differences from coefficients within the same model with L, M, and H, referring respectively to low, medium, and high level of novelty and/or scope. For instance, in Model 5, 0.042_{H} for $NOVELTY_{LOW}$ is significantly different from 0.066 for $NOVELTY_{HIGH}$. Similarly, in Model 7, 0.059_{HL} for $NOVELTY_{HIGH} \times SCOPE_{MEDIUM}$ is significantly different from 0.015 for $NOVELTY_{HIGH} \times SCOPE_{LOW}$.

Table 4 System GMM estimation results for testing of H1a&b and H2a,b,&c

5.3. Dimensions of process innovation and firm performance

Hypothesis $H2a$ posits a positive association between novelty of process-patent portfolio and firm performance. As described in Section 4.2.2, we measure the level of novelty for active portfolios as "low", "medium", or "high" – with "none", i.e., the absence of process innovation, being our base

category. We thus test $H2a$ using the following model:

$$SHARE_{ikjq} = \beta_1 \cdot SHARE_{ikjq-1} + \beta_2 \cdot AGE_{ikjq} + \beta_3 \cdot QUARTER_q + \sum_{n=1}^{3}(\beta_{4n} \cdot NOVELTY_{ikjq}) + \mu_{ikq} + \epsilon_{ikjq} \quad (5)$$

where β_{4n} is the estimated coefficient for level of novelty n – with $n = 1$, 2, and 3 corresponding to low, medium, and high novelty, respectively. Full support for $H2a$ would translate into $\beta_{43} > \beta_{42} > \beta_{41} \geq 0$. The results from the estimation of Model (5) are provided in Table 4. Separate Wald tests do not reject the null hypotheses that i) $\beta_{41} = \beta_{42}$ ($p > 0.10$) and ii) $\beta_{42} = \beta_{43}$ ($p > 0.10$). However, a Wald test rejects the null hypothesis that $\beta_{41} = \beta_{43}$ ($p < 0.10$) which indicates that $\beta_{43} > \beta_{41}$ and provides partial support for $H2a$. In particular, this result suggests that firms with a high-novelty portfolio of patented process innovations have a market share that is, on average, $\beta_{43} - \beta_{41} = 2.4\%$ (90% CI=[0.2%, 4.5%]), higher than firms with a low-novelty portfolio, ceteris paribus.

Hypothesis $H2b$ posits a positive association between scope of process-patent portfolio and firm performance. Similar to novelty, we measure the level of scope as "low", "medium", or "high" for active portfolios, with "none" as our base category. We estimate the following model to test $H2b$:

$$SHARE_{ikjq} = \beta_1 \cdot SHARE_{ikjq-1} + \beta_2 \cdot AGE_{ikjq} + \beta_3 \cdot QUARTER_q + \sum_{s=1}^{3}(\beta_{4s} \cdot SCOPE_{ikjq}) + \mu_{ikj} + \epsilon_{ikjq} \quad (6)$$

where β_{4s} is the estimated coefficient for level of scope s – with $s = 1$, 2, and 3 corresponding to low, medium, and high scope, respectively. Full support for $H2b$ would translate into $\beta_{43} > \beta_{42} > \beta_{41} \geq 0$. The results from the estimation of Model (6) are provided in Table 4. Separate Wald tests do not reject the null hypotheses that i) $\beta_{41} = \beta_{42}$ ($p > 0.10$), ii) $\beta_{42} = \beta_{43}$ ($p > 0.10$) and iii) $\beta_{41} = \beta_{43}$ ($p > 0.10$) such that there is no statistically distinguishable economic benefit among levels of scope.

Testing for Hypothesis $H2c$ – complementarity between novelty and scope – requires us to extend our estimation model to account for a potential interaction between level of novelty and level of scope of the process-patent portfolio. We thus estimate the following model :

$$SHARE_{ikjq} = \beta_1 \cdot SHARE_{ikjq-1} + \beta_2 \cdot AGE_{ikjq} + \beta_3 \cdot QUARTER_q + \sum_{n=1}^{3}\sum_{s=1}^{3}(\beta_{4ns} \cdot NOVELTY_{ikjq} \times SCOPE_{ikjq}) + \mu_{ikj} + \epsilon_{ikjq} \quad (7)$$

where β_{4ns} is the estimated coefficient for a portfolio with novelty level n and scope level s – with n=0 and s=0, i.e., the absence of process innovation, as our base category. Note that since our interacting variables of novelty and scope are both categorical, overall results would remain the same but would be harder to directly interpret if we were to include each variable independently in

addition to their interaction in Model (7). Since $H2c$ formally states that the association between scope and performance is stronger when the portfolio's novelty is higher, we expect to find stronger evidence that $\beta_{4n3} > \beta_{4n2} > \beta_{4n1} \geq 0$ as the level of novelty n increases.

The results from the estimation of Model (7) are provided in Table 4. Looking at coefficients' estimates at low and medium levels of novelty, i.e., β_{41s} and β_{42s}, we do not observe any significant difference between coefficients. However, when novelty is high, Wald tests reject both null hypotheses that i) $\beta_{431} = \beta_{432}$ ($p < 0.10$) and that ii) $\beta_{431} = \beta_{433}$ ($p < 0.05$), thus indicating that $\beta_{432} > \beta_{431}$ and that $\beta_{433} > \beta_{431}$. These results can be interpreted as follows: ceteris paribus, a highly novel portfolio is associated with a market share that is on average 6.2%–95% CI=[1.1%, 11.4%] (4.4%–90% CI=[0.6%, 8.2%]) larger if its scope is high (medium) as opposed to low. These results provide support for $H2c$ as they indicate that level of scope is only associated with performance for high-novelty patent portfolios.

Overall, results for $H2$ suggest that a process-patent portfolio of high novelty could be more valuable ($H2a$), and that high novelty appears complemented by high scope ($H2c$). However, for $H2a$ we only find a statistical difference between low- and high-novelty portfolios, and we do not find any support for an individual effect of scope ($H2b$). This could potentially be explained by the lack of differentiation, so far, between the two major phases of pharmaceutical production, i.e. the portfolio's locus of application.

5.4. Dimensions of process innovation and locus of application

The next set of hypotheses requires us to match levels of novelty and scope with the specific phase of manufacturing to which they apply. Therefore we drop from our dataset the 23 drug-firm pairs for which $LOCUS = 3$ for at least one quarter during our ten-year timeframe, i.e., that have a process-patent portfolio that simultaneously applies to the API phase and the FDF phase at any time during our observation window.

Hypothesis $H3a$ states that the association between portfolio's novelty and firm performance is stronger when the portfolio applies to the FDF than when it applies to the API manufacturing phase. To test H3a we estimate the following model:

$$\begin{aligned} SHARE_{ikjq} = {} & \beta_1 \cdot SHARE_{ikjq-1} + \beta_2 \cdot AGE_{ikjq} + \beta_3 \cdot QUARTER_q \\ & + \sum_{n=1}^{3} (\beta_{4nA} \cdot NOVELTY_{ikjq} \times API_{ikjq}) + \sum_{n=1}^{3} (\beta_{4nF} \cdot NOVELTY_{ikjq} \times FDF_{ikjq}) \\ & + \mu_{ikj} + \epsilon_{ikjq} \end{aligned} \quad (8)$$

where β_{4nA} and β_{4nF} are the estimated coefficients for a portfolio with novelty level n that applies to the API phase and to the FDF phase, respectively. Support for $H3a$ would imply that, we

find stronger evidence that $\beta_{43F} > \beta_{42F} > \beta_{41F} \geq 0$ than that $\beta_{43A} > \beta_{42A} > \beta_{41A} \geq 0$. The results from the estimation of Model (8) are provided in Table 5. We do not find any evidence that $\beta_{43A} > \beta_{42A} > \beta_{41A}$, i.e., the level of novelty does not appear to matter in the API phase. However, at the FDF phase, separate Wald tests reject the null hypotheses that i) $\beta_{41F} = \beta_{43F}$ ($p < 0.05$) and ii) $\beta_{42F} = \beta_{43F}$ ($p < 0.05$) providing support for $\beta_{43F} > \beta_{41F}$ and $\beta_{43F} > \beta_{42F}$. This indicates that high portfolio novelty appears more valuable than medium or low portfolio novelty at the FDF phase providing support for $H3a$.

We further compare the coefficient estimates for a given level of novelty across the API and FDF phases. Wald tests reject both null hypotheses that i) $\beta_{41A} = \beta_{41F}$ ($p < 0.10$) and that ii) $\beta_{43A} = \beta_{43F}$ ($p < 0.05$), which indicates that $\beta_{41A} > \beta_{41F}$ and that $\beta_{43A} < \beta_{43F}$. While high novelty appears more valuable at the FDF phase (in accordance with our previous findings), these results suggest that a portfolio of low novelty could actually be more beneficial in the API than in the FDF phase. Overall, these findings provide strong evidence that the value derived from higher novelty for a portfolio depends on the manufacturing phase that is covered by the patented process innovation(s).

Hypothesis $H3b$ mirrors Hypothesis $H3a$ but relates to the scope, rather than the novelty, of the process-patent portfolio. We thus estimate the following model:

$$\begin{aligned} SHARE_{ikjq} = {} & \beta_1 \cdot SHARE_{ikjq-1} + \beta_2 \cdot AGE_{ikjq} + \beta_3 \cdot QUARTER_q \\ & + \sum_{s=1}^{3} (\beta_{4sA} \cdot SCOPE_{ikjq} \times API_{ikjq}) + \sum_{s=1}^{3} (\beta_{4sF} \cdot SCOPE_{ikjq} \times FDF_{ikjq}) \\ & + \mu_{ikj} + \epsilon_{ikjq} \end{aligned} \tag{9}$$

where β_{4sA} and β_{4sF} are the estimated coefficients for a portfolio with scope level s that applies to the API phase and to the FDF phase, respectively. Support for $H3b$ would translate into finding stronger evidence that $\beta_{43F} > \beta_{42F} > \beta_{41F} \geq 0$ than that $\beta_{43A} > \beta_{42A} > \beta_{41A} \geq 0$. The results from the estimation of Model (9) are provided in Table 5. They provide no evidence to support $H3b$ and suggest that the association (or lack thereof) between scope and performance is not dependent on the targeted manufacturing phase.

Our final hypothesis, H3c, posits that the complementarity between novelty and scope of process-patent portfolio will be stronger at the FDF than at the API phase. This is tested using the

	SHARE		
	(Model 8)	(Model 9)	(Model 10)
SHARE (Lagged 1 quarter)	0.923***	0.922***	0.955***
	(0.034)	(0.036)	(0.021)
AGE	-0.001***	-0.001**	-0.001***
	(0.000)	(0.000)	(0.000)
$API \times NOVELTY_{LOW}$	$0.100^{***}{}_{[F]L}$		
	(0.036)		
$API \times NOVELTY_{MEDIUM}$	0.068**		
	(0.028)		
$API \times NOVELTY_{HIGH}$	$0.057^{**}{}_{[F]H}$		
	(0.024)		
$FDF \times NOVELTY_{LOW}$	$0.038^{**}{}_{[F]H,[A]L}$		
	(0.017)		
$FDF \times NOVELTY_{MEDIUM}$	$0.048^{**}{}_{[F]H}$		
	(0.024)		
$FDF \times NOVELTY_{HIGH}$	$0.105^{***}{}_{[F]L,M,[A]H}$		
	(0.040)		
$API \times SCOPE_{LOW}$		0.054	
		(0.039)	
$API \times SCOPE_{MEDIUM}$		0.052**	
		(0.021)	
$API \times SCOPE_{HIGH}$		0.058*	
		(0.032)	
$FDF \times SCOPE_{LOW}$		0.027	
		(0.028)	
$FDF \times SCOPE_{MEDIUM}$		0.038**	
		(0.017)	
$FDF \times SCOPE_{HIGH}$		0.076*	
		(0.042)	
$API \times NOVELTY_{LOW} \times SCOPE_{LOW}$			N/A
			(.)
$API \times NOVELTY_{LOW} \times SCOPE_{MEDIUM}$			$0.064^{***}{}_{[A]HM}$
			(0.021)
$API \times NOVELTY_{LOW} \times SCOPE_{HIGH}$			0.029
			(0.022)
$API \times NOVELTY_{MEDIUM} \times SCOPE_{LOW}$			0.047*
			(0.025)
$API \times NOVELTY_{MEDIUM} \times SCOPE_{MEDIUM}$			0.039*
			(0.022)
$API \times NOVELTY_{MEDIUM} \times SCOPE_{HIGH}$			0.041**
			(0.020)
$API \times NOVELTY_{HIGH} \times SCOPE_{LOW}$			0.029
			(0.062)
$API \times NOVELTY_{HIGH} \times SCOPE_{MEDIUM}$			$0.029^{*}{}_{[A]LM}$
			(0.018)
$API \times NOVELTY_{HIGH} \times SCOPE_{HIGH}$			$0.038^{*}{}_{[F]HH}$
			(0.021)
$FDF \times NOVELTY_{LOW} \times SCOPE_{LOW}$			$-0.007\ {}_{[F]LM,LH,HM,HH}$
			(0.008)
$FDF \times NOVELTY_{LOW} \times SCOPE_{MEDIUM}$			$0.029^{*}{}_{[F]LL}$
			(0.015)
$FDF \times NOVELTY_{LOW} \times SCOPE_{HIGH}$			$0.040^{**}{}_{[F]LL,HH}$
			(0.019)
$FDF \times NOVELTY_{MEDIUM} \times SCOPE_{LOW}$			0.058
			(0.040)
$FDF \times NOVELTY_{MEDIUM} \times SCOPE_{MEDIUM}$			0.026
			(0.020)
$FDF \times NOVELTY_{MEDIUM} \times SCOPE_{HIGH}$			$0.030\ {}_{[F]HH}$
			(0.019)
$FDF \times NOVELTY_{HIGH} \times SCOPE_{LOW}$			N/A
			(.)
$FDF \times NOVELTY_{HIGH} \times SCOPE_{MEDIUM}$			$0.049^{***}{}_{[F]LL}$
			(0.016)
$FDF \times NOVELTY_{HIGH} \times SCOPE_{HIGH}$			$0.127^{**}\ {}_{[F]LL,MH,LH,[A]HH}$
			(0.058)
Observations	40,114	40,114	40,114
Number of groups	1,042	1,042	1,042
Number of instruments	367	367	854
Arellano-Bond test for AR2 (p-value)	0.779	0.795	0.773
Hansen Test of overid. restr. (p-value)	0.233	0.397	0.910
Hansen Difference (null H = exogenous) (p-value)	0.114	0.161	0.320

Notes: *p<.10; **p<.05; ***p<.01. Drug-firm-country and time (quarter) fixed effects are included in all regressions. Robust standard errors are provided in parentheses. Subscripts indicate significant differences from coefficients within the same model with L, M, and H, referring respectively to low, medium, and high level of novelty and/or scope. [A] refers to API stage and [F] refers to FDF stage. For instance, in Model 8, $0.100_{[F]L}$ for $API \times NOVELTY_{LOW}$ is significantly different from 0.038 for $FDF \times NOVELTY_{LOW}$. Similarly, in Model 10, $0.064_{[A]HM}$ for $API \times NOVELTY_{LOW} \times SCOPE_{MEDIUM}$ is significantly different from 0.029 for $API \times NOVELTY_{HIGH} \times SCOPE_{MEDIUM}$.

Table 5 System GMM estimation results for testing of H3a,b,&c

following model:

$$\begin{aligned} SHARE_{ikjq} = {} & \beta_1 \cdot SHARE_{ikjq-1} + \beta_2 \cdot AGE_{ikjq} + \beta_3 \cdot QUARTER_q \\ & + \sum_{n=1}^{3}\sum_{s=1}^{3}(\beta_{4nsA} \cdot NOVELTY_{ikjq} \times SCOPE_{ikjq} \times API_{ikjq}) \\ & + \sum_{n=1}^{3}\sum_{s=1}^{3}(\beta_{4nsF} \cdot NOVELTY_{ikjq} \times SCOPE_{ikjq} \times FDF_{ikjq}) \\ & + \mu_{ikj} + \epsilon_{ikjq} \end{aligned} \tag{10}$$

where β_{4nsA} and β_{4nsF} are the estimated coefficients for a portfolio with novelty level n and scope level s that applies to the API phase and to the FDF phase, respectively. In line with the finding for $H2c$ that high portfolio novelty is complemented by high portfolio scope, support for $H3c$ would translate into finding stronger evidence of an association between novelty and performance as the level of scope s increases at the FDF, i.e., for $\beta_{43sF} > \beta_{42sF} > \beta_{41sF} \geq 0$, than at the API phase, i.e., for $\beta_{43sA} > \beta_{42sA} > \beta_{41sA} \geq 0$. The results from the estimation of Model (10) are provided in Table 5 (we note that there are no observations to allow estimates for β_{411A} and β_{431F}).

When looking at each level of scope at the API phase, Wald tests do not show any significant differences among coefficients for different levels of novelty, which provides no evidence for a complementarity between novelty and scope at the API phase. In fact, Wald tests only reject the null hypothesis that $\beta_{432A} = \beta_{412A}$ ($p < 0.10$), which indicates that $\beta_{432A} < \beta_{412A}$, rather than the reverse. This would suggest that low novelty may actually be *more* valuable than high novelty for a process-patent portfolio characterized by medium scope. When looking at each level of scope at the FDF phase and comparing coefficients for different levels of novelty, Wald tests only reject the following null hypotheses: i) $\beta_{413F} = \beta_{433F}$ ($p < 0.10$), and ii) $\beta_{423F} = \beta_{433F}$ ($p < 0.05$). This indicates that $\beta_{433F} > \beta_{413F}$ and $\beta_{433F} > \beta_{423F}$, and suggests that, at the FDF phase, having high novelty is beneficial but only when combined with high scope.

In addition, when comparing coefficients for a given level of scope and novelty between the API and FDF phases, a Wald test rejects the null hypothesis that $\beta_{433A} = \beta_{433F}$ ($p < 0.05$), which implies that $\beta_{433A} < \beta_{433F}$. This result further suggests that a high-novelty, high-scope portfolio of process patents is more valuable at the FDF rather than the API phase. Together, these results suggest that the complementarity between high novelty and high scope found in section 5.3 might in fact only exist at the FDF phase, which supports $H3c$.

Overall, results for $H3$ suggest that having a process-patent portfolio of high novelty is only valuable at the FDF phase and could potentially be detrimental at the API phase ($H3a$). In addition, we find further evidence that the value of a portfolio's broader scope is not standalone ($H3b$) but instead appears related to its ability to protect high novelty at the FDF phase of the manufacturing process ($H3c$).

5.5. Robustness checks

5.5.1. Alternative estimation approaches As described in section 5.1, the inclusion of a lagged dependent variable as a predictor in our model leads to a dynamic endogeneity issue, commonly referred to as the "Nickell bias" (Nickell 1981). The System GMM approach is thus most adapted to estimating our model (Blundell and Bond 1998, Kuhnen and Niessen 2012). However, the magnitude of this bias reduces significantly as T increases and would be relatively small if T is greater than 30 periods, as is the case for our dataset (Arellano 2003, Cornelius and Gokpinar 2019). Therefore, estimation of our models using simpler approaches such as fixed-effects or OLS regressions can be used to check the robustness of our results. A Hausman test comparing fixed- and random-effects regressions indicates that the fixed-effects specification is better adapted here. Thus we re-estimate every model using fixed-effects regressions and find that, despite minor variations in coefficients, all main results remain consistent.

The System GMM estimation approach clusters errors at the panel level, i.e., for each drug-firm-country combination. Given that the same drug is sold by many firms and across multiple countries, there could be some cross-sectional dependence. Thus, we re-estimate all models using fixed-effects regressions, clustering errors by drugs. Results are consistent with those of our main analyses except for H2c, where we fail to find significant differences across groups. However, the magnitude of each coefficient is still ranked as expected. We also note that results are fully consistent when adding $LOCUS$ to the interaction (i.e., H3c).

Our dependent variable, $SHARE$, is bounded by 0 and 1. To explicitly accommodate this feature, we re-run all analyses using a fractional logit model (Papke and Wooldridge 1996). We would like to note that this estimation approach does not control for the Nickell bias, which would explain some variation in the results. Overall, results remain consistent with the only notable difference being that, for H3a the results show $\beta_{42F} < \beta_{41F}$ ($p<0.01$) (though we continue to find evidence that $\beta_{41F} < \beta_{43F}$ and $\beta_{42F} < \beta_{43F}$). Thus, estimation using the fractional logit model still supports our main conclusion for this hypothesis, i.e., high novelty benefits market share at the FDF phase. This further supports the overall robustness of our results.

5.5.2. Potential endogeneity of price If manufacturers set their prices partly based on production costs, then price could potentially be endogenous to our model to the extent that process innovation affects production costs. Thus, we conduct additional analyses to determine whether price should be included as a mediating variable in our model. We combine the sales data of each product in our sample obtained from IMS Health with our original data on sales volume (measured in kgs) to compute average quarterly prices as the ratio of dollar sales to volume. To

assess price positioning relative to competition, we normalized each price within their respective drug-country-quarter combination to obtain the $PRICE$ variable. We then followed the procedure outlined by Baron and Kenny (1986) for mediation analyses to test H1a, i.e., overall effect of process innovation on market share. We find that process innovation is indeed, on average, negatively related to price ($p < 0.10$). However, although a lower price appears on average related to a higher market share, when controlling for process innovation, this effect becomes insignificant, while the coefficient for process innovation remains positive and significant ($p < 0.01$). Overall, these results minimize endogeneity concerns related to price in our model.

5.5.3. Comparison among countries Although our analyses include country-level fixed effects, they assume constant relationships between our predictors and market share across U.S. and E.U. countries. As discussed in Section 4.1 and shown in Online Appendix C, this is supported by the similarity of key characteristics among these markets. Nevertheless, we further verify this assumption by estimating each model separately for the U.S. and the E.U. countries in our dataset. Due to the resulting reduced sample sizes, only H1a can be tested using System GMM estimation. We thus use fixed effects regressions for all other hypotheses. Overall results across both sub-samples are all consistent with our main results.

5.5.4. Consideration of portfolio's concentration Some portfolios are more concentrated than others across the technological landscape, which could translate into greater value for the owning firm, due to deeper knowledge of the focal product. We test for such phenomenon using two distinct Herfindahl-Hirschman Indexes (HHI) to capture a portfolio's concentration. In line with previous literature (Aharonson and Schilling 2016), our first concentration measure uses patents' 3-digit class as determined by the U.S. Patent Classification (USPC) system. Each USPC-classified patent in our sample has between 1 and 5 corresponding USPC codes with a median of 2 codes. The concentration for each portfolio reflects the combined spread of its respective patent(s) across USPC-classes with higher values corresponding to more concentrated portfolios. The second concentration measure is computed similar to the first one but using the stages of the manufacturing process to which the patents within a portfolio apply–as illustrated in Figure 1–rather than their USPC-classes. Each patent in our sample applies to between 1 and 7 manufacturing stages with a median of 3 stages. Here again, a higher value for this index imply a more concentrated portfolio. While the first concentration measure can only be computed for U.S. portfolios, this alternative measure can be computed for our entire sample. We added each concentration measure as a control in our analyses involving scope and novelty (i.e., to test hypotheses-sets H2 and H3). While results for our key predictors remain consistent, we do not find a significant relationship between

the USPC-based concentration measure and market share across models, while the stages-based concentration measure appears weakly related to market share both in significance and magnitude (β_2<0.001 across all hypotheses). Thus, it appears that portfolio's concentration is not a key predictor in our model.

6. Discussion and concluding remarks

Our study offers specific guidance in addressing one of the principal questions found in the process innovation literature: How should a manufacturing firm manage its R&D spending so as to maximize its expected return on investment (Pisano 1997, Pennetier et al. 2018)? Because in the pharmaceutical context, "successful process development [...] requires an organization to couple the worlds of leading-edge science with the realities of plant operations" (Pisano 1997, p.21), our findings are also likely to carry implications for other high-technology industries. In addition, by framing innovations within the context of a technological landscape, which is a concept that broadly applies to several industries, our findings can provide important preliminary insights across a wide range of settings.

Our results suggest that high novelty may be beneficial, even as a standalone feature, while broad scope mainly appears to complement high novelty. This underlines the importance for researchers to systematically consider process innovation as a multi-dimensional construct. Practically, this suggests that firms might want to restrict investments in broad protection unless seeking to develop (or acquire) high-novelty process-patent portfolios. Our consideration of locus further suggests that choosing which part of a manufacturing process to target depends not only on the process's cost structure but also on its technological landscape. Indeed, despite the API phase being responsible for the largest proportion of overall manufacturing costs, we do not find any evidence of a positive association between novelty and performance in this phase, and this irrespective of the portfolio's scope. Since a large number of technological configurations can be used in the API phase to obtain similar outcomes, firms might want to favor low novelty portfolios, which would provide some cost benefits while not being as appealing to the competition, and thus not attracting the same circumvention efforts. At the FDF phase, because the available set of viable technological positions is much smaller (Burns 2012), a portfolio's level of protection is expected to more effectively mitigate competition, thus ensuring a more predictable competitive advantage for highly-innovative firms.

These observations are important because the development of process innovations that are more novel or more general (such that they can subsequently permit broader patent protection) is a costly, risky and time-consuming undertaking (Verhoeven et al. 2016) and their implementation is

likely to be more disruptive to a firm's operations (Tushman and Nadler 1986). Therefore, what our results imply is that in the case of manufacturing processes characterized by wide underlying technological landscapes, the additional R&D resources that would have to be invested to obtain qualitatively superior process innovations may not provide the same level of return as R&D investments in processes characterized by narrower technological landscapes. Essentially, our analysis indicates a complex interaction between manufacturing processes' characteristics such as their cost structure and underlying technological landscape, and competition and invite additional research on how, depending on a process's technological landscape, R&D efforts that are more explorative in their nature (and therefore more likely to lead to more novel or more general innovations) should be balanced with more exploitative R&D efforts.

As with all studies of this type, our work has some limitations. First, some authors have raised concerns on the use of patents as a measure of innovative output because not all patentable innovations are patented (Griliches 1990). Nevertheless, in the pharmaceutical industry firms generally prefer choosing patent protection to other forms of intellectual-property protection (e.g., trade secrecy). As a result, the percentage of patentable innovations that are patented is estimated to be higher than 80%; the highest among all industries according to Mansfield (1986). There are several reasons for this when it comes to process innovations. First, infringement of a process patent for pharmaceuticals may be detected through the "chemical fingerprint" that a manufacturing process leaves on the final product (Deconinck et al. 2008) or through on-site inspections of suspected infringing competitors (Blakeney 2005). Second, when a pharmaceutical firm applies to public health authorities for the license to sell a product, it must typically disclose the full details of its manufacturing process (Cartwright 2016), which could potentially be accessed by competitors through future court orders. Third, protection via trade secrecy is inherently risky because competition may successfully reverse-engineer a firm's invention, independently discover it or even hire away from the inventing firm key personnel with the necessary technical knowledge.

Second, in the pharmaceutical industry, process and product innovation may not be as straightforward to completely disentangle and measure separately because process development frequently results in changes in features of the final product and vice versa (Pisano 1996). As explained in Pisano (1997) (p. 11), in pharmaceuticals, product and process technologies "not only evolve rapidly, but also must be well synchronized". In fact, in manufacturing of some pharmaceuticals, process characteristics can play such a critical role for product characteristics that, from the perspective of regulators, "the process actually constitutes the product" and drug efficacy "can only be known through the specification of its process" (Lim et al. 2006, p.13). However, we mitigate this

concern through the following. First, we focus on generics which are, by definition, bio-equivalent substitutes for the original drug. In addition, we rely on our expert patent attorneys to identify and include only patents that primarily focus on the methods, i.e, the processes, through which active pharmaceutical ingredients and final dosage forms are being produced.

Third, our study relies on market share as a measure of economic performance. Exploring the association between process innovation and other indicators (e.g. firm value, profitability, sales growth, etc.) could further our understanding of the mechanisms through which process innovation might impact a firm's performance.

Finally, our study focuses on the pharmaceutical industry, and more specifically on drugs open to competition from generics. Although such narrow setting allows us to derive greater insights into the value of process innovation, it also limits their generalizability. We believe that future studies aimed at testing our findings in other contexts would hold great value.

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