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Converting inventions into innovations to address cancer grand challenges: The role of scientific and digital search intensity

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Abstract

The present study seeks to shed further light on what favors the conversion of inventions into innovations in for-profit firms and to advance our understanding of how to tackle cancer grand challenges (CGCs). Specifically, following the literature on knowledge search and recombination, we analyze whether and how cancer-related inventions developed through an intense adoption of scientific knowledge (scientific search intensity) result in (i) a higher number of approved drugs and (ii) a shorter approval time for new drugs. Notably, while the role of science with regard to technological development has been widely studied, the extent to which science-based solutions relate to new product introduction, especially in terms of coping with grand challenges such as approved cancer drugs, is less known. Furthermore, considering the digitization of (health) R&D and the role of information and communication technologies (i.e., digital technologies) to address grand challenges, we examine whether and how cancer-related inventions developed through an intense adoption of digital knowledge (digital search intensity) directly affect the extent and speed of cancer drug approval, as well as whether interaction effects between scientific and digital search intensity exist. We develop hypotheses that we test on a sample of 65,861 cancer-related patents owned by 139 for-profit firms, collected from the USPTO Cancer Moonshot Patent Data. These have a priority date between 1990 and 2010, and have led to 1035 approved drugs. Results reveal that scientific search intensity is not associated with the number of different drugs developed from a single cancer-related invention but is associated with the speed at which the invention leads to a newly approved drug. Digital search intensity appears not to directly affect cancer drug approval, but it lessens the effects of scientific search intensity, thus pointing to a limit of digitization in cancer R&D and innovation processes.

KEYWORDS

cancer grand challenges, digital search intensity, invention to innovation, scientific search intensity, search and recombination

1 | INTRODUCTION

It has long been argued that the development of a new invention—front-end of innovation (Markham et al., 2010)—is based on the recombination of existing knowledge components (Ju et al., 2023; Savino et al., 2017; Schumpeter, 1934). Depending on the recombinant search processes adopted for their development, inventions will encounter either more or fewer difficulties in becoming new products (Chen, 2023; Katila & Ahuja, 2002; Li et al., 2013). Along these lines of reasoning, this paper focuses on addressing the grand challenge of cancer from the perspectives of product development and management, by introducing a novel perspective on the way cancer-related inventions—new compounds, materials found in nature such as genes, and new related properties and forms—become innovations (i.e., the way new drugs are approved). Specifically, we are interested in comprehending the recombinant search processes that support the conversion of cancer-related inventions into new approved drugs.

Broadly speaking, one reason for addressing this issue lies in the fact that grand challenges (GCs) are by nature ill-defined and complex. Consequently, guiding the direction of search and recombination of knowledge has proven crucial in shaping innovation to effectively address these challenges (Chen & Liu, 2023; George et al., 2021; Ju et al., 2023; Ritala, 2024). However, current research on GCs on this topic has been somewhat limited. Aside from general suggestions on pooling different knowledge bases (Bertello et al., 2022; Petersen et al., 2021), it has not explored in any depth what specific sort of knowledge should be adopted in recombinant search processes and to what extent such knowledge drives innovation to solve these GCs. Moreover, there has been a disproportionate emphasis on the system level (Cagnin et al., 2012; Olsen et al., 2016; Ritala, 2024), neglecting the role played by for-profit firms. These firms play a significant part in tackling GCs and must at the same time strive for economic returns (Calfee & DuPré, 2012; Christofi et al., 2024).

Therefore, it becomes essential to focus on this type of organization in relation to GCs if one wants to gain a deeper understanding of how they can reconcile the need to address global and societal interests while also considering their economic needs. We seek to overcome these general gaps. Accordingly, with a focus on the GC of cancer, we acknowledge that for-profit firms are a key source of new (cancer) drugs (e.g., Als-Nielsen et al., 2003; Calfee & DuPré, 2012; Christofi et al., 2024) for which it is especially relevant to identify ways of reducing uncertainty, costs, and timing of drug R&D processes. Consequently, such firms play a pivotal role in addressing cancer grand challenges (CGCs), as dealing with critical and complex issues in cancer research and treatment, as well as developing novel cancer therapies. Yet, outcomes from drug and cancer R&D are quite unpredictable; they present significant costs and require a long timeframe to attain outcomes, if any, as compared with other technology-intensive (economic) sectors (Adams, 2012; Getz & Kaitin, 2015; Mullard, 2022). A better comprehension of the front-end of innovation for cancer R&D in terms of recombinant search processes might help alleviate those issues and thereby provide for-profit firms with insight into how to develop cancer-related inventions that are more likely to become new drugs, and so to face CGCs while also introducing new (profitable) products to the market.

We look in detail at whether and how cancer-related inventions originating in an intense adoption of scientific

Practitioner points

- Increasingly relying on scientific knowledge during the front-end innovation process makes it possible to reduce the time required to exploit an invention through the new product development route.
- Intense digital search does not seem to directly favor the conversion of inventions into new products and does not add to the benefits of an intense scientific search, calling managers to be more aware of the role of digital search, particularly in association with scientific search.
- Digital search that supports scientific research to address CGCs may require more experimentation to be truly effective in increasing the number of drugs that can be developed as well as the time-to-approval of a cancer drug.
- Policy actions and initiatives should be devoted to helping reconcile science and digitization, as their interplay is strengthening, but the benefits from their interaction seem yet to come.

knowledge (hereafter referred to as "scientific search intensity") and/or digital knowledge (hereafter referred to as "digital search intensity") become new drugs. The former reflects a recombinant search process thoroughly based on scientific knowledge, while the latter is a recombinant search process based primarily on knowledge pertaining to the domain of information and communication technologies (ICTs), that is, digital technologies (Ardito & Capolupo, 2022; Gupta et al., 2023; Martínez-Navalón et al., 2023; OECD, 2016).

We analyze the role played by scientific search intensity because, while the interplay between science and innovation has long been demonstrated to be positive in relation to technology development (Fleming & Sorenson, 2004) and may be relevant to address GCs (Gehlert et al., 2017), "[t]he extent to which scientific advances support marketplace inventions [as opposed to technology development] is largely unknown" (Ahmadpoor & Jones, 2017, p. 583), especially in the context of health GCs (Efstathiou, 2016). Additionally, we recognize that the continuous advancements of scientific knowledge have made it possible to understand the biological processes and phenomena related to several types of disease, including cancer, that, in turn, have helped to develop new (cancer-related) inventions over time (Foulkes & Sharpless, 2021). Still, only a few papers assess whether cancer-related inventions strongly based on scientific knowledge result in a higher number of new drugs and at what speed they do so, without reaching a general understanding of the role played by an intense scientific search (Ardito & Svensson, 2023; Su & Lin, 2018; Wagner & Wakeman, 2016) in these processes.

In this vein, we contend that further investigation into the role played by scientific search intensity is needed, both in general and in the specific domain of cancer. Furthermore, we analyze the role played by digital search intensity in light of the constant improvements of digital technologies, alongside related systems and services, occurring since the early 1990s. Indeed, such improvements are leading to disruptive changes in the social and economic arenas (Del Giudice et al., 2017) which affect firms' ability to tackle GCs (Davidson et al., 2023; George et al., 2021), thus affecting their invention and innovation processes (Lanzolla et al., 2021). This is particularly noticeable in the domain of health where digitization is enhancing "the potential of addressing the increasing complexities associated with providing high-quality health care under budget constraints and dramatically increasing demand" (Sánchez-Polo et al., 2019, p. 509). In consequence, here we see emerging a megatrend offering new innovative opportunities in the pharma and cancer domains (Hariry et al., 2022). Such opportunities are not only related to the adoption of digital technologies for improving data analytics techniques (Appio et al., 2017) and decision-making support through artificial intelligence (Alami et al., 2021), but also to the way scientific principles can be employed in conjunction with digital knowledge components in developing cancer-related inventions and subsequent drugs (Dougherty & Dunne, 2011; Felin et al., 2021). This is the case, for instance, of Smart Pills (Chehri & Mouftah, 2020; Zhu et al., 2020), which contain digital sensors or be manufactured through 3D printing techniques for a controlled release of the active principle. Nonetheless, despite the evolving landscape, there remains a dearth of empirical evidence regarding the advantages of transitioning drug and cancer R&D toward a robust reliance on digital knowledge.

Following the foregoing discussion, we pose the following research questions: (i) (How) do cancer-related inventions based on scientific search intensity lead to the approval processes of new cancer drugs? (ii) (How) do cancer-related inventions based on digital search intensity lead to the approval processes of new cancer drugs? (iii) (How) does digital search intensity interact with scientific search intensity upon entering the cancer drug approval processes? In accordance with the need of for-profit firms to reduce R&D costs and save time even as they also improve their innovative outcomes, we investigate cancer drug approval processes in terms of magnitude and timing. Indeed, broadly speaking, the approval event signifies that a cancer-related invention has led to a functioning drug being permitted to be sold.[1] Magnitude and timing are two important, albeit distinct, phenomena in the drug approval process. The first looks at the number of drugs generated (and that can be sold) by a single cancer-related invention. The second places emphasis on the speed with which the drug, originating in a cancer-related invention (referred to as time-to-approval) gains approval (if indeed it does).

To answer our questions, we rely on the literature on knowledge search and recombination (Savino et al., 2017) to develop a set of hypotheses. The hypotheses are then tested on a sample of 65,861 cancer-related patents, with priority date between 1990 and 2010, that have led to 1035 drug approval applications by 139 for-profit firms. Cancer-related patents and respective approved drugs were gathered from the USPTO Cancer Moonshot Patent Data. Additional data on the identified patents were collected from the Orbit Intelligence database.

Our results show that scientific search intensity does not affect the number of approvals achieved by drugs deriving from a single cancer-related invention but does increase the speed at which the invention leads to a

[1]See https://www.fda.gov/drugs/development-approval-process-drugs.

newly approved drug. Digital search intensity affects neither the number of approved drugs nor the time-to-approval; still, it negatively interacts with scientific search intensity when referring to both considered outcomes.

All in all, from the perspectives of product development and management, answering our research questions means dealing with the fact that the number of inventions being developed is growing, as is testified, for instance, by the rising number of patents in almost all sectors (WIPO, 2019), but for-profit firms "often struggle with commercializing new technologies via the product development route" (Capozzi et al., 2010; Nasirov et al., 2021, p. 522), that is, the route from invention to innovation (Schumpeter, 1934). This means that what explains the conversion of for-profit firms' inventions into innovations, albeit a longstanding topic in the innovation management literature (e.g., Chandy et al., 2006), is still not completely understood. This is further demonstrated by the recent publication of some notable studies on the topic (e.g., Ardito et al., 2020; Ardito & Svensson, 2023; Maurseth & Svensson, 2020; Nasirov et al., 2021), stressing the need to further delve into the factors supporting the invention-to-innovation route. We do so by examining the recombinant search processes—with a focus on search intensity (Li et al., 2013)—adopted at the front-end of innovation that lead to (cancer) inventions being developed by for-profit firms to become new products.

From the perspective of addressing cancer grand challenges (CGCs), there is a huge gap between the number of cancer-related inventions and the approved drugs that emerge from them (Adams, 2012; Batta et al., 2020; Getz & Kaitin, 2015), and this leads to significant losses for for-profit firms in the sector, given that investments in drug R&D are particularly expensive and rising, while cancer drug revenues increased by 96% between 2010 and 2019 and bring in most pharma revenues.[2] This is considered a GC because converting cancer-related inventions into drugs is complex in nature and requires significant investments in R&D with unpredictable innovative outcomes (Foulkes & Sharpless, 2021; Kuhlmann & Rip, 2014; Mullard, 2022). Therefore, the answers to our research questions will be particularly helpful for comprehending and providing insight into how to reduce the above-mentioned gap, while also supporting economic returns of for-profit firms. Concurrently, we link the literature on search and recombination to the emerging stream of literature focusing on designing management practices that allow responding to GCs more effectively (e.g., George et al., 2016; Haddad & Bergek, 2023; Howard-Grenville, 2021; Sawyer & Clair, 2022), CGCs in particular (Foulkes & Sharpless, 2021), also in light of the peculiarities of cancer drug R&D and the digitization phenomenon (Popkova et al., 2022; Yokoi et al., 2021). This viewpoint recalls and extends prior studies that emphasized the need to guide the direction of search and recombination of knowledge as a way to shape innovation for the sake of effectively addressing GCs.

Finally, from the perspective of the literature on knowledge search and recombination, first, we advance this stream of the literature as it has been primarily used to assess technological performance, such as impact on subsequent technologies (e.g., Appio et al., 2017; Fleming, 2001). However, such performance does not in effect guide recombinant search processes underlying an invention toward its conversion into new products. Furthermore, very few studies have formally considered the digital world as a space to be searched for innovation purposes (Ardito & Capolupo, 2022). In particular, we focus on search intensity over search selection given that the adoption of certain knowledge components is not beneficial or detrimental per se but is so in relation to the intensity of its adoption. Finally, this is the first attempt ever to examine the role played by digital search in new product introduction.

2 | THEORETICAL BACKGROUND

2.1 | Recombinant search processes and search intensity

Inventions and innovations are not the same thing. Within the innovation process, inventions are developed first (front-end of innovation; Markham et al., 2010) and then, if they are commercialized through the product development route, they become innovations (Nasirov et al., 2021; Schumpeter, 1934). The literature on knowledge search and recombination helps explain conversion of inventions into innovations. Indeed, innovation can be conceived of as the result of the search and recombination of different knowledge components performed by a searching agent (Fleming, 2001; Fleming & Sorenson, 2004; Jia et al., 2021; Nelson & Winter, 1982; Savino et al., 2017). The agent searches for different knowledge components that can be recombined to generate a novel solution to a technological problem (Fleming, 2001), that is, the invention. The invention is characterized by the types of knowledge components selected in the recombinant search process and the intensity with which knowledge components belonging to the same domain are adopted. That is, there are two key mechanisms of search: search selection (location of

[2]See https://dailynews.ascopubs.org/do/sales-revenue-cancer-drugs-has-doubled-among-top-pharmaceutical-companies-last-10-years.

knowledge search) and search intensity (effort and persistence in the adoption of certain knowledge) (Li et al., 2013; Posen et al., 2018). Variation in the selection and intensity of search determines the opportunities and challenges that arise which then move the invention in direction of the product development route (Ardito & Svensson, 2023; Chen, 2023; Katila & Ahuja, 2002).

Concerning search selection, two major locations to search for knowledge are the space of scientific discoveries as a source of scientific knowledge, and the space of prior technological developments as a source of applied knowledge (Lim, 2004; Martin & Scott, 2000). Scientific knowledge is often unconstrained by outside controls and unfettered by market interests, as it provides simply the basis for understanding a given phenomenon (e.g., Cassiman et al., 2018). Leveraging scientific knowledge in recombinant search processes (defining the scientific search) may play an extremely important role in guiding firms toward the development of new inventions by providing the equivalent of a map (Fleming & Sorenson, 2004) that points to a valuable solution to a problem by enlarging the firms' search space (Gruber et al., 2013). On the other hand, scientific knowledge is not considered to be readily available for innovation as it requires extra effort to make it relevant for practical applications, with the result that the relationship between scientific search and marketplace invention is yet largely undetermined (Ahmadpoor & Jones, 2017). In this vein, we go beyond discourses relating to search selection, which emphasize the need to search for scientific knowledge, and direct our attention to the extent to, or the intensity with, which, scientific knowledge is adopted in recombinant search processes; a greater or lower reliance on scientific knowledge can further elucidate its influence on the conversion of inventions into innovation.

On the other hand, applied knowledge refers to information or expertise that has already found an application to solve a technological problem with market interests. An invention performing a certain task can thus be considered applied knowledge (Cowan & Zinovyeva, 2013). Digital knowledge is a part of applied knowledge in that it constitutes information or expertise about how ICTs have been adopted in working solutions. In the last few years, leveraging digital knowledge in recombinant search processes has become pervasive in distinct industrial sectors, even if they are not conventionally related to the ICT domain (Jiao et al., 2022; Lanzolla et al., 2021; Matzler et al., 2018; Mele et al., 2023), and it opens the door to the development of new inventions by combining sector-related knowledge with digital knowledge. While the potential benefits of relying on digital knowledge have been emphasized, it must be stressed that such an approach represents a discontinuity in many a firm's knowledge base and modus operandi (Lanzolla et al., 2021). The level of this discontinuity may also have to do with the intensity with which digital knowledge enters recombinant search processes (Ardito & Capolupo, 2022). Accordingly, the focus on search intensity over selection should be emphasized in this case as well.

2.2 | Converting inventions into innovations to address cancer grand challenges

In the last few years, political debate has paid increasing attention to GCs (Haddad & Bergek, 2023). Broadly speaking, GCs are defined as "ambitious but achievable goals that harness science, technology, and innovation to solve important national or global problems and that have the potential to capture the public's imagination" (Office of Science and Technology Policy, 2013). However, they are wicked in nature and require sensitive investments with unpredictable innovative outcomes (Kuhlmann & Rip, 2014). Accordingly, some governments, such as the European Union and the United States, have recently set up several initiatives and funding schemes (e.g., Horizon 2020) to seek better solutions to addressing GCs that are related to inequality, health, sustainability, bioeconomy, transport, and energy-saving issues (Directorate-General for Research and Innovation (European Commission), 2013; Office of Science and Technology Policy, 2013). Management scholars have recognized the relevance of GCs and have begun to call for research aimed at addressing them. Some managerial studies have answered this call by providing broader insight into how to face GCs in general or some of them specifically (Doh et al., 2019; George et al., 2016; Howard-Grenville, 2021; Popkova et al., 2022; Sawyer & Clair, 2022; Yokoi et al., 2021).

With our work here we seek to contribute to the academic debate that focuses on the domain of health GCs (Christofi et al., 2024; Vakili & McGahan, 2016), with a particular emphasis on CGCs (Foulkes & Sharpless, 2021; Mullard, 2020). Notably, only some, not all, health issues constitute GCs (Directorate-General for Research and Innovation (European Commission), 2013), as in the case of CGCs. Indeed, in 2019, the World Health Organization (WHO) indicated cancer as a leading cause of death for people younger than 70 (WHO, 2020). Moreover, death by cancer is expected to grow in the next few decades (Puska, 2021). Hence, launching new cancer treatments still represents a set of GCs that our society is called on to address for the sake of improving the living conditions and life expectancy of the population.

In this context, the contributions of for-profit firms are especially relevant since they are largely involved in cancer R&D and the launch of new cancer drugs (Calfee & DuPré, 2012). Promptly finding new and multiple treatments has assumed particular importance for for-profit firms that have to reconcile two objectives: tackling CGCs and maintaining economic returns. On the one hand, developing more drugs from a single cancer-related invention may increase the breadth of treatments available to oncologists and provide higher returns; on the other hand, enhancing the speed of the cancer drug approval process may in turn make it possible to increase the likelihood of steadily launching new cancer drugs on the market, while at the same time providing the healthcare system with alternative or new therapies for people lacking or requiring additional ones due to potential drug resistance (Foulkes & Sharpless, 2021; Hait, 2010). In reality, however, despite relevant efforts and investments in cancer R&D by for-profit firms, only a few cancer-related inventions result in approved drugs (Getz & Kaitin, 2015). What is known as the technological valley of death (Adams, 2012) highlights the high risk of failures that for-profit firms face when developing cancer-related inventions. For instance, overall only 45 new drugs were approved in 2015 (Mullard, 2022) despite the fact that more than 3000 patents were filed yearly in the period between 1995 and 2015, and this in the cancer domain alone.[3] According to a study by Wong et al. (2019) using 108, 248 clinical trial data points for 24,448 unique drug development programs across 40 types of cancer from 2000 to 2018, the overall estimated phase 1-to-approval chance of success for all oncology-related drug development programs is 3.3%.

With this in mind, we are interested in offering a better understanding of what moves cancer-related inventions developed by for-profit firms from the front-end of innovation (Markham et al., 2010) toward the product development route in terms of both the number of cancer drugs approved emerging from a cancer-related invention and the time required to approve the first drug. Specifically, in line with the relevance of managing knowledge to guide innovation efforts to cope with GCs (Bertello et al., 2022; Petersen et al., 2021; Ritala, 2024; Vakili & McGahan, 2016), we follow the literature on knowledge search and recombination (Savino et al., 2017) and deem it important to reveal whether scientific and digital search intensity and combinations thereof enable this kind of outcome.

Focus on scientific search intensity finds its roots in the pivotal role played by scientific knowledge in cancer R&D, which has led to several initiatives like the "Cancer Moonshot" and the "Cancer Grand Challenges." The former was born when the US Congress passed the 21st Century Cures Act in December 2016, which authorized US $1.8 billion in funding for the Cancer Moonshot, run by the United States, over 7 years[4]; the organization aims to accelerate scientific discovery, fostering collaboration, and improving the sharing of scientific knowledge on cancer-related issues. "Cancer Grand Challenges," recently launched by the Cancer Research UK and the National Cancer Institute, aims instead to stimulate new thinking and to unleash scientific creativity to cope with ambitious CGCs.[5] These initiatives acknowledge that despite cancer drug R&D being science-based (e.g., Du et al., 2019), leveraging scientific knowledge in the research process does not ensure the actual development of new drugs (Puska, 2021), leaving CGCs still unresolved. For instance, in 2016, the US Government needed to establish an ad-hoc panel, that is, the Blue Ribbon Panel[6], tasked to advise the National Cancer Advisory Board and set out a roadmap of recommendations aimed at enabling science-based cancer-related inventions to lead to the goal of producing approved drugs for cancer (Jaffee et al., 2017). We follow this effort by delving into the role played by scientific search intensity in developing cancer-related inventions that are conducive to new cancer treatments.

As far as the focus on digital search intensity is concerned, one should acknowledge that integrating digital knowledge with a given sector-specific knowledge is opening the doors to developing new inventions and innovations in many sectors (e.g., Nambisan et al., 2017). The pharma context is not an exception. Adding digital knowledge to scientific knowledge is reshaping the recombination opportunities for developing inventions that can lead to new drugs (Hird et al., 2016). Stated differently, digitization in drug R&D does not relate only to the emergence of bioinformatics or data analytics techniques that support recombinant search processes (Appio et al., 2017), but also to drugs that embed and whose effectiveness depends on digital knowledge. One example is drugs containing ingestible sensors that can travel the bloodstream to alert the user to health issues, as we see in the concepts of Internet of Pharma Things and Smart Pills/Drugs (Chehri & Mouftah, 2020). In this case, digital knowledge (i.e., sensors) is part of the drug and not a tool to get and elaborate information to create the drug. A

[3]Based on analysis of our dataset.

[4]See https://www.cancer.gov/research/key-initiatives/moonshot-cancer-initiative.

[5]See https://cancergrandchallenges.org/about.

[6]See https://www.cancer.gov/research/key-initiatives/moonshot-cancer-initiative/blue-ribbon-panel.

second example is the use of 3D printing to print pills with complex structures to make the dosage, and its release thereof, more accurate (Zhu et al., 2020). Again, digital knowledge, alongside scientific knowledge, directly comes into play. Still, it is worth noting that the digitization of cancer drug R&D is probably more disruptive than that in other sectors (manufacturing, automotive, etc.), thus making it unclear to what extent reliance on digital knowledge is beneficial. Accordingly, in this case, too, the role of digital search intensity over search selection to develop cancer-related inventions that are conducive to new cancer treatments should be considered.

Finally, although the adoption of digital knowledge in combination with pharma scientific principles is an ongoing practice characterizing the front-end of innovation (Dougherty & Dunne, 2011; Felin et al., 2021), the way digital search intensity may interact with scientific search intensity and influence both the extent and speed at which new (cancer) drugs are approved is yet to be investigated. As such, we investigate the interaction effects between scientific and digital search intensity to address CGCs.

2.3 | The role of scientific search intensity

The extent of scientific knowledge leveraged during recombinant search processes may strongly affect the characteristics and the potential innovative value of the resulting inventions (Fleming & Sorenson, 2004; Natalicchio et al., 2017), especially in relation to a science-based context such as the pharma context (Gambardella, 1995). Indeed, intense scientific search allows researchers to increase and deepen their understanding of the underlying natural phenomena characterizing the object of investigation (e.g., Ahuja & Katila, 2004; Fleming & Sorenson, 2004). As a consequence, they may use this cognition to carry on an invention process directed at addressing the root natural causes of a problem in a broader manner, rather than focusing on its specific manifestations. Therefore, intense scientific search may result in an output of an R&D process that has the characteristics of a general invention and, for this reason, could spur a higher number of applications (Gambardella, 1995; Nightingale, 1998; Papazoglou & Spanos, 2018).

This reasoning is especially relevant in the health-related context, where understanding how to address the root causes of a disease is paramount to effectively countering its harmfulness for humans (Foulkes & Sharpless, 2021). For instance, the broader scientific knowledge that allows us to comprehend the life cycle and pathogenesis of a virus may be helpful in developing an invention that will spur the production of vaccines and therapeutics against the virus itself but also for other viruses that rely on the same biological mechanisms (Du et al., 2009). Consequently, the invention resulting from intense scientific search may be used to discover multiple drugs. In contrast, limiting scientific search intensity may result in a focalized solution that, although valuable and effective, may bring about the discovery of a lower number of drugs (e.g., only those addressing a specific disease, rather than the diseases generated by the same root cause). Thus, since scientific search intensity favors a better and broader understanding of the natural phenomena underlying a health-related problem, it may promote the development of more general inventions that may lead to a higher number of drugs addressing different variations of the focal problem.

Furthermore, through intense scientific search, researchers may overcome established routines and problem-solving mechanisms, hence favoring the development of novel inventions (Nelson & Winter, 1982; Nightingale, 1998). In turn, these inventions may support researchers in facing cancer-related problems from a new perspective, hence providing the potential to come up with multiple innovations (Ahuja & Lampert, 2001). That is, overcoming established routines and problem-solving mechanisms may lead to cancer-related inventions that can subsequently open multiple new drug discovery paths, thus increasing the number of pharmaceutical products spawned by a single invention. According to this reasoning, we can pose the following hypothesis:

> **Hypothesis 1a.** Scientific search intensity is positively related to the number of approved cancer drugs based on a focal invention.

As mentioned above, intense scientific search allows cancer researchers to better understand the root characteristics of natural phenomena and broaden their perspectives in addressing CGCs (Ahuja & Katila, 2004; Fleming & Sorenson, 2004; Lopez-Vega et al., 2016; Nightingale, 1998). In turn, a broader view of the potential solutions to addressing the root causes generating a disease may increase emerging recombination opportunities that researchers can scrutinize during the R&D process (Fleming & Sorenson, 2004; Gambardella, 1995; Gruber et al., 2013; Natalicchio et al., 2017). In other words, as pointed out in the literature on knowledge search and recombination, by leveraging a larger extent of scientific knowledge, a researcher may spot and concurrently evaluate different directions of development that can lead to valuable

inventions (Fleming & Sorenson, 2004; Gambardella, 1995; Gong et al., 2023; Gruber et al., 2013; Nelson & Winter, 1982; Zhao et al., 2023). Therefore, among the different paths of invention development, it is likely that the researcher may spot a noticeably promising one that may lead them toward the development of an effective invention that can promptly and smoothly be used to develop a new drug, thereby reducing its time-to-approval.

Furthermore, the health context may be particularly complex, in the sense that different features of the problem underlying CGCs interact among themselves and make the development of a solution with high innovative potential more difficult (Fleming & Sorenson, 2001; Hebar et al., 2013). For instance, a small change in a compound may, due to the interaction between different elements, significantly alter its effects (e.g., Bode et al., 2002). Indeed, a stronger reliance on scientific knowledge in recombinant search processes may help researchers overcome complexity-related issues. That is, intense scientific search may make it possible to spot a promising path of cancer-related invention development, effectively addressing the complex issues related to the specific field of investigation and, in turn, avoid wasting time on unfruitful attempts to commercially exploit the invention (Gruber et al., 2013; Nightingale, 1998). This may result in shortening the time required to have a drug approved. Stated differently, scientific search intensity affects the invention process by driving researchers to focus on development paths leading to the most valuable inventions, especially when the search process is characterized by complexity (Fleming & Sorenson, 2004). Therefore, it is more likely that a cancer-related invention originating in intense scientific search arises as a more valuable and reliable solution that can more easily and quickly be approved when proposed as a new drug. Based on the above reasoning, we state the following hypothesis:

> **Hypothesis 1b.** Scientific search intensity is positively related to the time-to-approval of a cancer drug, that is, it leads to a shorter time-to-approval.

2.4 | The role of digital search intensity

In the last few years, digitization has increasingly permeated many industrial sectors. As a consequence, widespread diffusion of digital technologies is redefining the search space for knowledge used as an input to generate new inventions (Lanzolla et al., 2021). This trend is becoming particularly impactful in the drug discovery context, which is typically characterized by complexity (Dougherty & Dunne, 2011). In fact, due to the novelty of this approach in the health context (Dara et al., 2022; Vamathevan et al., 2019), relying on a high degree of digital knowledge during the invention process may provide pharmaceutical firms with a fresh and non-trivial perspective to deal with a problem. For instance, by leveraging digital knowledge (knowledge about Bluetooth technology, in this case), researchers were able to develop smart pills containing sensors to control the drug assimilation process, which may eventually be used to increase the effectiveness of treatments (Litvinova et al., 2022). Therefore, digital search intensity in drug discovery may increase the likelihood of overcoming extant paradigms and promote the development of a wave of multiple innovations based on the focal invention (Ahuja & Lampert, 2001; Dosi, 1982). Especially in the health context, as in the case of cancer R&D, novel results based on increased digital knowledge may support scientists in envisioning new drug possibilities, and this may pave the way to the development of a higher number of drugs (Dougherty & Dunne, 2011).

Furthermore, intense digital search may also support researchers in exploring new development patterns to cope with diseases and this may spawn novel inventions (Dougherty & Dunne, 2011). Moreover, the novelty of inventions resulting from intense digital search may open up new streams of drug discovery that favor the development of many new drugs. Based on these arguments, we can state the following hypothesis:

> **Hypothesis 2a.** Digital search intensity is positively related to the number of approved cancer drugs based on a focal invention.

The recent widespread diffusion of digital technologies in several industries has been reshaping the way R&D processes are performed. As previously mentioned, digital search intensity may support cancer researchers in assuming a fresh perspective to address complex problems. By tackling health challenges from new perspectives and by contributing to disentangling the complexity of health-related problems, digital knowledge may provide health researchers with a better understanding of diseases and their characteristics, and this may be exploited to develop novel and particularly effective inventions (Dougherty & Dunne, 2011). In such cases, the outcome of the digital search process can be leveraged to discover a drug that may provide clinical benefits and address unmet medical needs in a highly effective manner, so that the approval process may be faster (Mulder et al., 2020). Hence, digital search intensity may open an invention development trajectory that could constitute a breakthrough for research in the health context.

Consequently, due to its potential value for patients, the approval process of related drugs may be smoother, and hence faster, in comparison with the approval process of more traditional drugs.

Furthermore, digital search intensity may provide opportunities for ex ante compound design and screening, thus providing early validation (Vamathevan et al., 2019). In turn, this may limit the likelihood of incurring undesirable effects and adverse reactions during the drug approval process. Consequently, the time required to approve a new cancer drug may be shortened when researchers intensively rely on digital knowledge to develop new solutions to health-related problems. Therefore, we can present the following hypothesis:

> **Hypothesis 2b.** Digital search intensity is positively related to the time-to-approval of a cancer drug, that is, it leads to a shorter time-to-approval.

2.5 | The interaction between scientific and digital search intensity

In the last few years, diffusion of digital knowledge is increasingly affecting the recombinant search processes in the pharma sector and, thus, it may influence the way companies respond to relevant health-related challenges (Chehri & Mouftah, 2020; Hird et al., 2016; Lerer & Piper, 2003). Therefore, during the invention process, researchers are more and more likely to concurrently pursue intense scientific and digital knowledge search. The consequent interactions between scientific and digital knowledge may affect the outcome of the R&D process itself. Actually, intense scientific and digital search may push cancer researchers to eventually recombine knowledge components belonging to very different domains. Although this is an inherently risky and uncertain process, this may result in the development of particularly novel inventions (Fleming, 2001; Rosenkopf & Nerkar, 2001), meaning that the more intense the concurrent scientific and digital search, the higher the novelty of the resulting output.

However, while a highly novel invention may definitely advance the state-of-the-art, it may also generate criticalities in the commercialization path (Aarikka-Stenroos & Lehtimäki, 2014; Colombo et al., 2017). Indeed, when developing new products, such as drugs based on highly novel inventions, firms may face market, organizational, and resource uncertainty (Leifer et al., 2001). In turn, this may call on firms to deploy additional resources and greater commitment to being effectively managed, consequently pushing them to focus on a limited number of products to be commercialized. Furthermore, firms may also need knowledge, technical capabilities, and specialized assets to be effective in the commercialization phase (Tripsas, 1997). Nonetheless, due to the novelty inherent to these inventions, firms may lack enough specialized knowledge and assets to allow them to develop and bring to the market a high number of products (Nerkar & Roberts, 2004; Roberts & McEvily, 2005). Therefore, even though inventions resulting from intense scientific and digital search may generate more opportunities for pharma firms, the high demand on resources and effort they require to reach the market, may, due to their novelty, collide with the firms' resource constraints. As a matter of fact, firms may be forced to exploit a subset of the available opportunities of development. Hence, the novel inventions developed through intense scientific and digital search may result into the development of a limited number of drugs. Consequently, we do expect that the concurrent reliance on intense scientific and digital knowledge search may ultimately spur a limited number of drugs. Stated more formally:

> **Hypothesis 3a.** The interaction between scientific search and digital search intensity is negatively related to the number of approved cancer drugs based on the focal invention.

Interaction between intense scientific and digital search may also affect the time required to approve a cancer-related drug. Indeed, cancer researchers working in conventional labs may be less experienced in absorbing and using digital rather than scientific knowledge, and researchers working with digital technologies (applied knowledge) may be less versed in purely scientific knowledge (Dougherty & Dunne, 2011). Therefore, difficulties may emerge in accurately understanding, recognizing, and exploiting the full potential of inventions based on a high extent of recombination of pieces of knowledge that could belong to distinct domains (i.e., digital as opposed to scientific knowledge; Nagle & Teodoridis, 2020; Teodoridis et al., 2019). In other words, in these cases, researchers may require subsequent notable effort in terms of time to properly assimilate the invention itself and be able to actually use it to develop an effective new drug (Kranz et al., 2016; Lanzolla et al., 2021; Savino et al., 2017). Therefore, the higher the reliance on both scientific and digital knowledge in developing the focal invention, the higher the time needed by researchers to eventually complete the invention-to-innovation process.

Furthermore, the conversion into a product of inventions resulting from intense scientific and digital search

could be a process with uncertain outcomes (Fleming, 2001). Hence, the invention-to-innovation process may require more resources to reduce its inherent uncertainty and effectively and timely yield an innovation (Roberts & McEvily, 2005). Given that firms are endowed with limited resources and generally committed to several concurrent product development processes, they may choose to allocate a suboptimal stock of resources to the invention-to-innovation process (e.g., Verma & Sinha, 2002), consequently increasing the time to develop and approve a new drug from an invention.

Finally, it must be considered that the commercial exploitation of inventions based on intense digital and scientific search may slow down the authorization process. Let us consider, for instance, the fact that a person will ingest a pill containing an electronic sensor in addition to releasing its active principle (McCaffrey et al., 2008). This represents a departure for the pharma industry, regardless of the reliability of accompanying scientific principles, while it may also introduce novel safety concerns. Due to the novelty for the pharma sector, regulatory agencies are likely to carry out thorough and longer-term analyses to ensure that drugs resulting from intense scientific and digital knowledge search are actually harmless for humans and provide benefits when used in the treatment of diseases. Stated differently, the authorization entity will likely need more time to test the new type of drug and approve it. According to this reasoning, we pose the following hypothesis:

> **Hypothesis 3b.** The interaction between scientific search and digital search intensity is negatively related to the time-to-approval of a cancer drug, that is, it leads to a longer time-to-approval.

3 | DATA AND METHODS

Granted patents relevant to the cancer domain (cancer-related patents) are used to capture cancer-related inventions. These patents are available in the database named the Cancer Moonshot Patent Data (CMPD). This database was created under the "Horizon Scanning Tool" program. The program was a joint effort between the US Government and the USPTO as a part of the broader Cancer Moonshot initiative. Specifically, the program first categorized patents as cancer-related by relying on a panel of experts in the cancer domain selected by the US Government. Cancer-related patent data were then combined with two external data sources: the National Institutes of Health (NIH) Research Portfolio Online Reporting Tools (RePORTER) and the US Food and Drug Administration (FDA)'s Approved Drug Products with Therapeutic Equivalence Evaluations (the Orange Book). As a result, cancer-related patents were respectively linked to data on upstream funding, as represented by NIH grants, and downstream commercialization efforts, as represented by drug approval out of a patent. Spanning the 1976 to 2016 period, the CMPD comprises about 270,000 cancer-related patents with indication of whether they have received a NIH grant and have led to approved drugs. For this final dataset, some patent information was included (i.e., patent number, title, classification, and grant date), and high-level technology categories were identified (i.e., drugs, diagnostics, surgical devices, data analytics, and genomic-based inventions).

To collect patent-drug linkages in the cancer domain, we queried the CMPD through Google BigQuery. All patents included in the dataset, alongside related drugs, were collected. Since the phenomenon we investigated is related to drug approval based on a cancer-related patent, we retained only those patents in the technological category "drugs," as defined by the CMPD. Indeed, the other types of patents may lead to other types of products (i.e., medical devices), for which no information is provided. Furthermore, since we are interested in the digitization phenomenon, going too far back in time would lead to biased results. Accordingly, as the earliest priority year eligible for including a patent in the study, we considered the year following the origin of the World Wide Web (1990), which represented a turning point for the use of ICTs. Finally, information about drug approval goes until June 30, 2016. This means that patents applied for close to this date had fewer chances of being counted as sources of new drugs, hence representing another source of biased results. Eventually, we considered 65,861 patents spanning the 1990–2010 period. We matched identification numbers of these patents with the Orbit Intelligence database, thus gathering full bibliographic information, such as claims, references to prior patents (alongside their bibliographic information) and non-patent documents, inventors, and assignees. About 1.3% of patents led to at least one product. This is consistent with the very low share of inventions leading to drugs in the pharma domain (Adams, 2012; Getz & Kaitin, 2015). Moreover, 11% of those patents led to more than one drug.

We acknowledge that the focus on the US context may appear to limit the scope of our investigation. This notwithstanding, it is worth mentioning that the United States represents the largest pharmaceutical market (40% of the world's pharmaceutical revenues), often acting as the benchmark in the scientific drug regulatory system (Du et al., 2019; Friedman, 2010). Moreover, the

United States is often chosen as the first target market by most worldwide pharma firms, making it a good context in which to study related innovation activities (Friedman, 2010). Finally, the patent-drug linkage system is particularly effective in the United States, since, according to the 1984 Hatch-Waxman Act, firms are required to list on the Orange Book patents issued in relation to drug approval. Consequently, patent-drug linkages originating in the Orange Book have been considered a reliable source for innovation studies (e.g., Dunlap et al., 2016).

3.1 | Variables

3.1.1 | Dependent variables

This study has two dependent variables. The first one counts the number of approved drugs resulting from a patent (*Drug Count*). The second one represents the time elapsed, in years, between the priority date of a patent and the FDA approval date of the earliest drug associated with the patent (*Time-to-Approval*). Information to compute these variables is included in the CMPD.

3.1.2 | Independent variables

To measure the extent of scientific search leading to the development of a cancer-related invention, we refer to citations for non-patent literature (NPL) made by a cancer-related patent. Indeed, NPL represents prior-art knowledge, excluding prior patent documents, reflecting the scientific character of R&D (e.g., Fleming & Sorenson, 2004). Actually, NPL is an imperfect proxy since it may include technical content (e.g., manuals and technical reports) (Callaert et al., 2012). Thus, we followed the approach taken by Sung et al. (2015) to identify only those NPL that relate to papers in scientific journals, conference proceedings, and books—in other words, science-based NPL. The independent variable was then operationalized as the number of science-based NPL for each patent, where the higher the number of NPL, the more intense the reliance on scientific knowledge in recombinant search processes (*Scientific Search Intensity*). 77% of all NPL falls within the three considered publication types. This is in line with previous findings, according to which "[t]he majority of all non-patent references are journal references, which provide ample possibilities for large-scale analyses focusing on the extent to which technological developments are situated within the vicinity of scientific knowledge" (Callaert et al., 2006, p. 3); even when references are not linked to content in scientific journals, they may relate to conference proceedings and books that can still be categorized as scientific sources (Houdou, 2018). Also, science-based NPL is much more frequent in patents related to human necessities and the pharma domain, rather than in patents from other sectors (e.g., Callaert et al., 2012; Marx & Fuegi, 2020).

The second independent variable looks at cited patents that represent a proxy for the prior art deemed applied knowledge searched and combined during technological development (e.g., Jaffe & Trajtenberg, 2002). Specifically, we counted the number of cited patents that belong to any of the International Patent Classification (IPC) codes associated with ICTs, as defined by a recent OECD report (Inaba & Squicciarini, 2017). That is, the more ICT-related cited patents, the higher the reliance on digital knowledge searched and recombined during technological development (*Digital Search Intensity*). This choice is in line with the notion that ICTs are enablers of digital innovation processes (OECD, 2016), and that relying on ICT-related technical knowledge can be considered a proxy for reliance on digital knowledge (Ardito & Capolupo, 2022).

Overall, count measures have been previously adopted to capture search intensity (Brennecke et al., 2021; Jung & Lee, 2016). Moreover, the distinction between NPL and cited patents to capture the character of scientific and digital searches recalls the view that more applied knowledge is often codified in patents, while scientific knowledge results in documents such as those previously mentioned (Cowan & Zinovyeva, 2013; Rogers, 1983).

3.1.3 | Control variables

To improve the reliability of the model, several control variables were included. First, we included the total number of cited patents (*Cited*) (Fleming, 2001). Second, we included the patent scope, hence counting the number of claims to novelty (*Claims*) and the number of different IPC codes assigned to a focal patent (*Components*) (Novelli, 2015). Third, we accounted for the geographic dispersion of prior art knowledge by computing a revised version of the originality index; it considers the priority country of the cited patents instead of their IPC codes (*Country Originality*) (Lee, 2021). Fourth, we added a variable assessing the temporal distance between the focal patent and the prior art knowledge (*Maturity*), according to findings highlighting its relevance to innovation performance (Katila & Ahuja, 2002; Nan, 2023). Fifth, we controlled, through a dummy variable, for the fact that technological development was financially supported by the US NIH (*Dummy NIH*), as indicated in the Moonshot

Patent Data. A value of one means having received a grant from the NIH. Sixth, the number of inventors working on the patented invention was included (*Inventors*), since it influences recombinant search processes (Taylor & Greve, 2006). Seventh, to account for inter-organizational collaborations during technological development, we counted the number of organizations owning the intellectual property of the patent (*Assignees*) (Messeni Petruzzelli, 2011). Eight, we added a dummy variable assuming the value of one if the priority country is the United States (*Dummy US*). Ninth, a dummy variable was added to control for the fact that the patented invention mainly pertains to the pharma domain (value of one) (*Dummy Pharma*). This distinction has been made by checking if the main IPC code of the focal patent pertains to the pharma domain or the biotech domain through well-established concordance schemes (OECD, 2009). Tenth, we included a dummy variable taking the value of one if the focal patent relates to an additional high-level technology domain, as defined by the Moonshot Patent Data, along with belonging to the drug category (*Dummy Other Drugs*). Finally, we included a set of four dummy variables indicating, respectively, if the priority date of the focal patent falls within the period, 1990–1994, 1995–1999, 2000–2004, and 2005–2010 (omitted category) (*Dummy Priority*).

3.2 | Model specification

Hypotheses 1a, 2a, and 3a involve the adoption of a count, non-negative dependent variable, that is, *Drug Count*, hence calling for the adoption of the Poisson or the Negative Binomial regression approaches. According to Table 1, *Drug Count* is over-dispersed (i.e., its standard deviation is higher than the mean). Thus, the Negative Binomial regression approach should be preferred over the Poisson one (Wooldridge, 2013). Finally, an excess of zero counts characterizes this dependent variable, which may require using a model based on a zero-inflated probability distribution—that is, a distribution that allows for frequent zero-valued observations. In line with this reasoning, a Zero-inflated Negative Binomial regression was considered. A Vuong test (Vuong, 1989) comparing the zero-inflated model to its non-zero-inflated counterpart suggested the adoption of the zero-inflated model.

Hypotheses 1b, 2b, and 3b involve the adoption of the time of the event of drug approval within a defined time-frame as the dependent variable. The time-frame ranges between a patent's priority date and June 30, 2016 (i.e., the censoring date). Thus, we have right-censored data for the dependent variable. In this case, a survival model is the most appropriate (Allison, 2014). Such a model allows us to control for the fact that each patent comes into analysis at different points in time, as represented by the different priority dates, and the event of drug approval associated with the given patent is observed till the censoring date. The possibility of accounting for this issue is relevant because innovation and related knowledge-creation dynamics are time-dependent.

In detail, let *Time-to-Approval* be the "failure time" (i.e., when the event occurs, if it occurs), and X be the corresponding covariate vector. We aim to make inferences about the effect of X on the response variable *Time-to-Approval*. Non- and semi-parametric (i.e., Cox proportional-hazard) survival models are commonly used, since they allow leaving unspecified the distribution assumed by the time-to-event random variable underlying the hazard function. However, non-parametric models were excluded because they only produce comparative measures and do not provide actual estimates of time-to-event distributions. Furthermore, our main goal is to assess whether some covariates delay or accelerate the onset of an event (e.g., delay or accelerate drug approval), rather than assessing whether they reduce or increase the overall proportion of units that observe the event through time, which is instead the main outcome of the Cox proportional-hazard semi-parametric model (Patel et al., 2006). Also, even though the Cox proportional-hazard model does not require assumptions about the distribution of the hazard function, the ratio of the hazards for any two subjects must be constant over time, that is, they must be proportional.

Conceptually, this is a strong assumption considering that the timing strongly affects the prevalence of an invention over another in innovation dynamics (Chiesa & Frattini, 2011; Mahajan & Muller, 1996). This means that the ratio of the hazards of drugs approved for any two patents is unlikely to be constant over time. For these reasons, the Cox proportional-hazard model should be excluded. In this vein, we formally ran a proportional hazard assumption test based on the Schoenfeld residuals (Allison, 2014), which confirmed the unsuitability of the Cox proportional-hazard model. Parametric, or accelerated failure time (AFT), models are an alternative to non- and semi-parametric models in the analysis of survival observations and may overcome their shortcomings. Indeed, they allow assessing the influence of covariates in terms of an effect on the expected duration/termination of an event, and they do not have proportionality assumptions (Patel et al., 2006; Svensson, 2007; Wei, 1992). On the other hand, the random error must be assumed to follow one of several distributions. To identify the most appropriate distribution, we ran several AFT models, each assuming a different distribution for the

TABLE 1 Descriptive statistics and pairwise correlations.

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18
1-Drug Count	1																	
2-Time-to-Approval	−0.116*	1																
3-Scientific Search Intensity	0.003	−0.033*	1															
4-Digital Search Intensity	0.008	−0.067*	0.173*	1														
5-Cited	0.053*	−0.136*	0.416*	0.408*	1													
6-Claims	0.016*	0.064*	0.024*	0.001	0.008*	1												
7-Components	0.012*	0.270*	−0.015*	−0.012*	0.018*	0.026*	1											
8-Country Originality	0.038*	−0.099*	0.014*	0.022*	0.119*	0.001	0.087*	1										
9-Maturity	0.006	−0.122*	0.004	0.015*	0.059*	−0.007	−0.019*	0.194*	1									
10-Dummy NIH	−0.015*	0.070*	0.081*	−0.007	−0.038*	0.019*	−0.034*	−0.129*	−0.036*	1								
11-Inventors	0.006	−0.116*	−0.027*	0.030*	0.066*	0.019*	0.103*	0.130*	−0.012*	−0.082*	1							
12-Assignees	−0.004	0.005	0.019*	−0.008*	−0.000	0.015*	−0.019*	0.003	0.018*	0.018*	0.068*	1						
13-Dummy US	0.005	−0.001	0.240*	0.070*	0.140*	0.042*	−0.043*	−0.264*	−0.020*	0.162*	−0.079*	−0.010*	1					
14-Dummy Pharma	0.065*	−0.119*	−0.244*	−0.032*	0.026*	−0.005	0.006	0.221*	0.168*	−0.113*	0.146*	−0.030*	−0.117*	1				
15-Dummy Other Drugs	−0.057*	−0.068*	0.295*	0.076*	0.065*	−0.015*	−0.059*	−0.161*	−0.143*	0.082*	−0.105*	0.027*	0.116*	−0.553*	1			
16-Dummy 90_94	0.004	0.536*	−0.027*	−0.034*	−0.067*	0.018*	0.084*	−0.043*	−0.077*	0.038*	−0.051*	0.005	−0.031*	−0.065*	−0.045*	1		
17-Dummy 95_99	0.004	0.520*	−0.034*	−0.052*	−0.102*	0.052*	0.120*	−0.081*	−0.062*	0.047*	−0.093*	0.001	0.025*	−0.075*	−0.071*	−0.199*	1	
18-Dummy 00_04	0.011*	−0.070*	0.039*	0.026*	0.053*	−0.002	0.148*	0.046*	0.015*	−0.021*	0.034*	−0.003	−0.005	0.043*	0.053*	−0.217*	−0.431*	1
Mean	0.016	14.035	24.381	0.508	30.255	2.533	10.208	0.359	5.683	0.058	4.001	1.153	0.683	0.498	0.398	0.091	0.283	0.320
S.D.	0.160	5.070	27.276	2.889	59.265	3.565	10.963	0.247	4.805	0.233	2.853	0.525	0.465	0.500	0.489	0.288	0.450	0.467
Min.	0	0	0	0	1	0	0	0	0	0	1	1	0	0	0	0	0	0
Max	10	26	190	399	1509	376	183	0.897	105	1	42	27	1	1	1	1	1	1

Note: Dummy NIH is a dummy variable controlling for the fact that technological development was financially supported by the US NIH. Dummy 90_94, Dummy 95_99, and Dummy 00_04 are dummy variables indicating if the focal patent has a priority date falling within the periods 1990–1994, 1995–1999, and 2000–2004, respectively.

*$p < 0.050$.

TABLE 2 Results of the zero-inflated negative binomial regression.

	Model 1	s.e.	Model 2	s.e.	Model 3	s.e.	Model 4	s.e.
Scientific Search Intensity (SSI)			0.002	0.002			0.003	0.002
Digital Search Intensity (DSI)					−0.019	0.017	0.056	0.032
SSI × DSI							−0.002**	0.001
Country Originality	1.048***	0.175	1.040***	0.175	1.048***	0.175	1.013***	0.175
Cited	0.006***	0.001	0.006***	0.001	0.006***	0.001	0.006***	0.001
Components	−0.001	0.003	−0.000	0.003	−0.000	0.003	−0.000	0.003
Maturity	−0.024**	0.009	−0.024**	0.009	−0.024**	0.009	−0.024**	0.009
Dummy NIH	−0.705**	0.235	−0.728**	0.237	−0.708**	0.236	−0.734**	0.237
Inventors	−0.019	0.013	−0.018	0.013	−0.018	0.013	−0.018	0.013
Assignees	−0.037	0.081	−0.037	0.081	−0.037	0.081	−0.040	0.081
Claims	0.038***	0.012	0.038***	0.012	0.038***	0.012	0.037**	0.012
Dummy US	0.398***	0.087	0.382***	0.089	0.398***	0.087	0.371***	0.089
Dummy Pharma	1.090***	0.103	1.105***	0.104	1.085***	0.103	1.103***	0.104
Dummy Other Drugs	−1.078***	0.120	−1.094***	0.120	−1.071***	0.120	−1.086***	0.120
Dummy Priority	Yes		Yes		Yes		Yes	
Constant	−5.824***	0.195	−5.846***	0.197	−5.822***	0.195	−5.852***	0.197
Log-pseudolikelihood	−4664.558		−4663.945		−4663.629		−4659.573	
Wald-chi(2)	718.46***		719.69***		720.32***		728.43***	

Note: Standard errors (in parentheses) estimated from the observed information matrix (OIM) (Cirillo et al., 2018).
*$p < 0.050$; **$p < 0.010$; ***$p < 0.001$.

random error (i.e., Exponential, Lognormal, Loglogistic, and Weibull). We found that the AFT model assuming random errors following the Lognormal distribution has the highest Log-likelihood and the lowest values of Akaike Information Criterion and Bayesian Information Criterion (Ishak et al., 2013; Wei, 1992). Therefore, we eventually adopted an AFT model assuming random errors following a Lognormal distribution for hypothesis testing.

4 | RESULTS

Table 1 shows descriptive statistics and pairwise correlations. Correlation values are below the 0.70 threshold, indicating that the defined variables do not suffer from potential multicollinearity issues (Cohen et al., 2002). We also computed variance inflation factors (VIFs) for all variables in all models. The average VIF is 1.7, and the highest individual VIF is below the value of 5.5, further suggesting no severe multicollinearity issues (Wooldridge, 2013).

Table 2 shows the results of the Zero-inflated Negative Binomial regression approach. Model 1 is the baseline model, with control variables only. Model 2 includes the independent variable *Scientific Search Intensity*. Model 3 includes the independent variable *Digital Search Intensity*. Model 4 is the full model, including the interaction term (*Scientific Search Intensity* X *Digital Search Intensity*). The full model corroborates the results of prior models; therefore, we follow Model 4 for providing results. Concerning control variables, a single invention may spawn a higher number of approved drugs if it is mainly based on prior technological knowledge ($\beta = 0.006$, $p < 0.001$), is based on geographically dispersed knowledge ($\beta = 1.013$, $p < 0.001$), claims many novelties ($\beta = 0.037$, $p < 0.010$), has a US priority ($\beta = 0.371$, $p < 0.001$), and mainly pertains to the pharma domain ($\beta = 1.103$, $p < 0.001$). Conversely, relying on older knowledge components ($\beta = -0.024$, $p < 0.010$), receiving a grant from the NIH ($\beta = -0.734$, $p < 0.010$), and belonging to a high-level technology category, as defined by the CMPD, other than drugs ($\beta = -1.086$, $p < 0.001$) reduces the number of approved drugs associated with a given invention. Concerning independent variables, there is no evidence that a more intense scientific or digital search leads to more approved products, since respective coefficient estimates are not significant, hence do not support H1a and H2a. Still, the coefficient estimate of the interaction term is negative and significant ($\beta = -0.002$, $p < 0.010$), thus supporting H3a. That is, inventions heavily embodying both scientific and digital knowledge lead to a smaller number of products. Figure 1

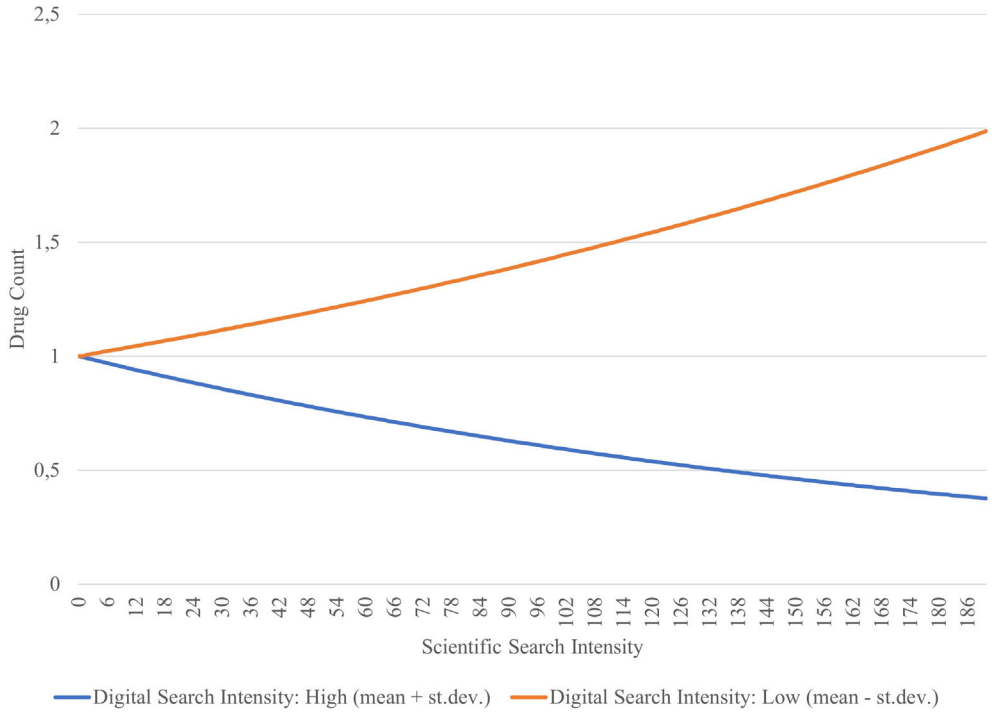

FIGURE 1 Predicted effect of scientific search intensity at different levels of digital search intensity.

depicts the relation between *Scientific Search Intensity* and *Drug Count* at a low (one standard deviation below the mean) and a high level (one standard deviation above the mean) of *Digital Search Intensity*, further supporting H3a.

Table 3 shows the results of the AFT model. Included models follow the rationale of Table 2. It is worth noting that the interpretation of the estimated parameters of the AFT model is as follows: a positive covariate coefficient means the survival time increases by a certain percentage, as indicated by the coefficient value. However, a longer survival time is equivalent to a lower conditional probability (hazard) of the failure event—that is, approval in each time period—and, accordingly, a lower probability of the patent leading to an approved drug. In other words, a negative covariate coefficient implies a positive association between a given covariate and *Time-to-Approval*.

Concerning the findings, the full model is inconsistent with other models only with regard to the effect of *Digital Search Intensity*. Thus, we follow Model 4 for providing results except for what concerns H2b. Specifically, according to Model 4, the analysis of control variables reveals that the speed at which a drug is approved increases (lower *Time-to-Approval*) if the underlying invention is heavily based on prior technological knowledge ($\beta = -0.003$, $p < 0.010$), is based on geographically dispersed knowledge ($\beta = -0.717$, $p < 0.001$), shows a higher number of claims ($\beta = -0.011$, $p < 0.010$), presents a US priority ($\beta = -0.282$, $p < 0.001$), and mainly relates to the pharma domain ($\beta = -0.894$, $p < 0.001$). Conversely, leveraging older knowledge components ($\beta = 0.015$, $p < 0.050$), obtaining a grant by the NIH ($\beta = 0.658$, $p < 0.001$), involving many inventors ($\beta = 0.020$, $p < 0.050$), and being related to a high-level technology category other than Drugs ($\beta = 0.957$, $p < 0.001$) increases the time-to-approval. Looking at the independent variables, the more intense the scientific search, the shorter the time-to-approval of a cancer drug originating from a focal invention ($\beta = -0.005$, $p < 0.010$), hence supporting H1b. Digital search intensity negatively affects the time-to-approval of a cancer drug, but Model 3 shows that this result is not robust. For the sake of prudence, we thus consider H2b as not confirmed. The coefficient estimate of the interaction term between the independent variables is positive and significant ($\beta = 0.001$, $p < 0.010$), hence supporting H3b (longer time-to-approval). The quantitative interpretation of the estimated parameters is as follows: if the number of science-based NPL increases by 1, the time to drug approval decreases by 0.4%.[7] Similarly, if interaction term increases by 1 due to more science-based NPL and/or citations to digital patents, the time to drug approval increases by 0.1%.

[7]The quantitative interpretation of the effect of the explanatory variables (also dummies) on survival time is carried out as follows. If the explanatory variable increases by 1 unit, the survival time changes by $100(e^{\beta} - 1)\%$.

TABLE 3 Results of the accelerated failure time (AFT) model.

	Model 1	s.e.	Model 2	s.e.	Model 3	s.e.	Model 4	s.e.
Scientific Search Intensity (SSI)			−0.005***	0.001			−0.005***	0.001
Digital Search Intensity (DSI)					0.019	0.014	−0.041*	0.019
SSI × DSI							0.001**	0.000
Country Originality	−0.775***	0.135	−0.735***	0.135	−0.774***	0.135	−0.717***	0.136
Cited	−0.004***	0.000	−0.003***	0.000	−0.004***	0.000	−0.003***	0.000
Components	0.002	0.003	0.002	0.003	0.002	0.003	0.002	0.003
Maturity	0.014*	0.007	0.015*	0.007	0.014*	0.007	0.015*	0.007
Dummy NIH	0.613***	0.191	0.658***	0.192	0.613***	0.191	0.658***	0.192
Inventors	0.020*	0.010	0.020*	0.010	0.020*	0.010	0.020*	0.010
Assignees	−0.026	0.054	−0.024	0.054	−0.026	0.054	−0.022	0.055
Claims	−0.011***	0.004	−0.011**	0.004	−0.011***	0.004	−0.011**	0.004
Dummy US	−0.336***	0.067	−0.290***	0.068	−0.337***	0.067	−0.282***	0.068
Dummy Pharma	−0.861***	0.082	−0.898***	0.083	−0.858***	0.082	−0.894***	0.083
Dummy Other Drugs	0.912***	0.096	0.964***	0.098	0.905***	0.096	0.957***	0.097
Dummy Priority	Yes		Yes		Yes		Yes	
Constant	13.826***	0.228	13.879***	0.230	13.825***	0.228	13.879***	0.230
Log-pseudolikelihood	−4696.7966		−4689.9139		−4695.422		−4683.8758	
Wald-chi(2)	836.58***		850.34***		839.33***		862.42***	

Note: Standard errors (in parentheses) estimated from the observed information matrix (OIM) (Cirillo et al., 2018).
*$p < 0.050$; **$p < 0.010$; ***$p < 0.001$.

For robustness, first, we ran the Negative Binomial regression model without zero inflation and alternative AFT models (Exponential, Lognormal, Weibull). These provided results consistent with the main chosen models. Second, we computed the independent variable as the share of ICT-related cited patents over the total number of cited patents (*Cited* was excluded due to multicollinearity issues). In this case, too, findings are confirmed. Third, we measured the scientific search intensity variable as a dummy variable assuming value one if the focal patent cites at least one science-based NPL document, and zero otherwise. In this case, scientific search intensity appeared not significant, thus emphasizing the importance of considering the extent to which the focal patent is based on scientific knowledge. Fourth, we considered alternative timeframes (i.e., 1990–2006, 1995–2010, and 2000–2010) for including patents in the study. Our findings still held. Finally, we substituted *Drug Count* with a dummy variable taking the value of one if an invention led to at least one product (i.e., likelihood measure). Results were consistent with the count measure.

5 | DISCUSSION

Based on a sample of 65,861 cancer-related patents, this paper delves into the question of whether the intensity of searching for certain types of knowledge during the front-end process of innovation (i.e., the development of a cancer-related invention) has any influence on the translation of inventions into marketable products. We do so by specifically examining whether cancer-related inventions based on intense scientific and/or digital search lead to multiple approved drugs and gain approval faster. Results reveal that scientific search intensity speeds up drug approval but does not increase the number of drugs originating from a single invention. Digital search intensity appears not to affect drug approval directly. However, the interplay between scientific and digital search intensity hampers both innovation performances that were considered. It is our belief that these findings provide relevant implications for theory and practice.

5.1 | Theoretical contributions and implications for research

Broadly speaking, first, we contribute to the innovation management field. We do so by providing additional insight into a longstanding, albeit unresolved, innovation management issue—that is, converting inventions into innovations (Nasirov et al., 2021). Indeed, some recent research has highlighted that much is still unknown

about the factors that facilitate the conversion of inventions into marketable products (e.g., Ardito et al., 2020; Maurseth & Svensson, 2020; Su & Lin, 2018), also when referring to cancer research (Getz & Kaitin, 2015). Among these understudied factors, we reveal that the conversion of inventions into innovations may depend on the recombinant search processes underlying the inventions (scientific and digital search intensity, in our case). This recalls and adds to the idea that heterogeneity in the conversion process is due to the fact that not all inventions contribute equally to innovation due to idiosyncratic characteristics (Ardito et al., 2020) as their knowledge base (Ardito & Svensson, 2023; Martin & Scott, 2000). Furthermore, our results highlight that while, per se, the intensity of knowledge search provides positive or neutral results when considering scientific or digital knowledge, the interaction between scientific and digital search intensity produces negative effects on the invention-to-innovation process in terms of the number of drugs that are developed and in terms of the speed of the process. Accordingly, we point out that the concurrent search and recombination of different typologies of knowledge may generate non-trivial and complex influence on the invention-to-innovation process.

Second, considering our research setting (i.e., the cancer domain), we contribute to the emerging management field by calling for identifying innovation management practices that allow coping with GCs (George et al., 2016), CGCs in particular (Foulkes & Sharpless, 2021) also in light of the digitization phenomenon (Popkova et al., 2022; Yokoi et al., 2021). Notably, till now there has been an overemphasis on technology development in response to CGS, while neglecting actual innovation in terms of resulting commercial offers (Foulkes & Sharpless, 2021; Kuhlmann & Rip, 2014). Actually, this is an aspect that should not be undervalued, due to the role for-profit firms play in driving R&D activities to cope with the complex and uncertain process of converting cancer-related inventions into drugs. Therefore, drawing on the literature on knowledge search and recombination (Savino et al., 2017), we provide evidence that differences in recombinant search processes in the cancer domain, characterizing the front-end of innovation, explain subsequent innovation performance, as reflected by new drug approvals out of developed cancer-related inventions. This improves our understanding of CGS because converting cancer-related inventions into drugs is not straightforward and often ends up with failures (Foulkes & Sharpless, 2021; Kuhlmann & Rip, 2014; Mullard, 2020). Particularly, we find that cancer-related inventions based on intense scientific search lead to new drug approvals faster. At least as far the time to commercialization in the pharma context is concerned, this result corroborates the study by Su and Lin (2018) over the one by Wagner and Wakeman (2016), which instead found a non-significant effect of scientific search.

Third, our in-depth analysis of the influence of recombinant search processes on innovation performance also adds to the literature on the (fuzzy) front-end of innovation (Markham et al., 2010), by providing evidence about where to search within the search space to innovate (Lopez-Vega et al., 2016), particularly highlighting the role of intense scientific and digital search (Ardito & Capolupo, 2022; Fleming & Sorenson, 2004). To be specific, to the best of our knowledge, this is the first attempt empirically to examine the role played by digital search intensity in actual innovation performance—even if it provides non-conclusive findings. This, of course, may be due to context specificity; on the other hand, it is coherent with prior evidence, both general and in the health domain, underlining that the pros and cons of digitization are difficult to reconcile (Champagne et al., 2015; Hariry et al., 2022), thus making its performance outcomes difficult to predict. Also, prior research had highlighted the need to investigate the impact made by interaction between reliance on basic (i.e., scientific) and applied (i.e., digital) knowledge because such interaction reflects more complex recombination processes (Tödtling & Grillitsch, 2015). We embrace this notion and reveal the existence of a negative interaction effect between heavily scientific and digital searches. Furthermore, in addition to previous studies that focused on the search and recombination of knowledge components originating in different fields (e.g., Fleming, 2001), our study focuses on the intensity of search, thus contributing to a specific stream of investigation within the search and recombination literature (Li et al., 2013; Posen et al., 2018).

Finally, we underline that we looked at actual technology commercialization via new products instead of examining the effectiveness of recombinant search processes for innovation through proxies like patent citations. Moreover, we looked at two different innovation phenomena that are rarely considered simultaneously, especially in the context of CGS: the number of new products emerging from one invention (a cancer-related invention) and the speed at which it leads to a marketable product (a drug). The second phenomenon is particularly relevant in relation to the emerging issue of accelerated innovation (Spanjol & Noble, 2021), which is gaining more and more relevance as a means to cope with unforeseen crises like the COVID-19 pandemic (Howard-Grenville, 2021).

5.2 | Implications for practice and policy

Our study may also inspire managers. First, our results indicate that relying increasingly on scientific knowledge

during the front-end innovation process makes it possible to reduce the time required to exploit an invention through the new product development route. This outcome is extremely relevant in the current economic scenario, characterized by the shortest conceivable product life cycles, thus requiring promptness in product development to establish and sustain a competitive advantage, especially in contexts as complex as the pharma context (e.g., Jaffee et al., 2017). In this vein, we point out the need to implement more effective practices to access and adopt scientific knowledge in the front-end of innovation. For instance, managers may decide to develop scientific knowledge internally through dedicated R&D units enriched with the presence of scientists and/or by favoring university–industry interactions, which the extant literature has demonstrated to be an effective way to tap into scientific knowledge (e.g., Perkmann & Walsh, 2007).

In addition, we advise managers that, at least so far, intense digital search has not directly favored the conversion of inventions into new products; actually, it hampers the influence of scientific search intensity, thus highlighting potential limits in the digitization phenomenon. This should particularly warn pharma managers, as anecdotal evidence shows that pharma firms have been increasingly relying on digital knowledge so as to enhance their innovation processes (e.g., Appio et al., 2017). Therefore, they should further analyze how the digitization of pharma R&D has evolved before further investing in the adoption of digital search, particularly in association with scientific search, maybe by placing attention on how the cross-fertilization of the pharma domain with the digital domain has been managed and whether it is possible to identify any shortcomings. Another suggestion could be to launch pilot innovation projects relying on digital knowledge with deep controls and check throughout its phases to clearly examine how well it works, its strengths and weaknesses to be further examined and, potentially, solved. Furthermore, managers should ensure the commitment of adequate resources and the development of appropriate capabilities to successfully cope with the novelty of inventions based on the interactions of scientific and digital knowledge and effectively manage the invention-to-innovation process. All in all, our results may provide advice to managers that make the front-end of innovation less fuzzy, thus helping firms attain higher and faster returns on their investments in R&D.

The results of our study may also reveal implications for policymakers. Specifically, science can explain how innovation can be driven toward CGCs and comparable contexts. Therefore, policies aiming to further increase the development of scientific knowledge in the cancer field within firms, universities, and research centers, and the ramifications of that for drug development may result in paramount contributions to improving the population's life expectancy and wellbeing. We emphasize that these policies (research grants, tax exemptions for research activities in the field, and so on) should not only relate to basic research activities aiming to boost scientific advancements but particularly to the applications of already existing scientific discoveries.

More generally, our focus on the extent and speed of drug approval may be relevant in launching ad-hoc initiatives when accelerated innovation is needed—say, for example, in pandemic crises. In this vein, policymakers may call for looking at existing scientific discoveries that may apply to such critical events, though perhaps neglecting, in such cases, to promote knowledge search strategies that are too distinct from the scientific base of the event domain (e.g., combining scientific search and digital search in the cancer domain). This does not mean that distant search and, specifically, digital search that supports scientific research to address CGCs should be fully disregarded; but it may be that this approach requires more experimentation to be truly effective in increasing the number of drugs that can be developed as well as the speediness of the process.

With this in mind, policy actions and initiatives should be devoted to helping reconcile science and digitization, as their interplay is strengthening; still, gaining advantages from this interaction appears yet to be difficult. For instance, policymakers may launch ad-hoc calls for projects aiming to rediscover and/or apply cancer-related scientific principles through digital knowledge. Moreover, policymakers may also sustain such cancer drug development projects by supporting involved firms in their need to secure more resources for their projects. This could be done, for instance, by setting up research consortia combining public and private partners, by lowering taxes for firms that address CGCs, and by lending important support when dealing with bureaucracy in the drug approval process. Additionally, designing educational trajectories aimed at developing life science researchers endowed with digital skills may be useful in better assimilating knowledge originating in different domains and improving their recombination capabilities. At the same time, placing firms in a better position to address CGCs will provide important social benefits and higher returns also for governments when R&D initiatives are funded by public money.

As a final remark, we highlight that this research is based on open data about a specific set of grand challenges (CGCs) made available by the US Government through the Cancer Moonshot initiative. It is our belief that such an initiative is a significant way to advance research on CGS; hence we suggest that governments conduct similar initiatives around other relevant grand challenges.

5.3 | Limitations and future research directions

Our study is not exempt from some limitations that, however, may inspire further research.

First, we measured the scientific search intensity as the number of science-based NPL. Even though this choice is supported by extant literature and is particularly adequate in the pharma context, it would be interesting to dig deeper into the specific features of the NPL documents cited. This analysis would be helpful for better understanding the characteristics of the scientific knowledge that may result and thus make it more useful for boosting firms' innovative zeal. For instance, future analyses may aim to discuss the impact of the scientific knowledge distance, with respect to the chosen field of research, on the resulting patent's role in enhancing a firm's innovation performance.

Second, we could not specifically analyze digital knowledge in terms of big data analytics, artificial intelligence, and so on. Indeed, patent-based classifications for those specific digital solutions are not fully reliable, and it was out of the scope of this paper to provide a new methodology to retrieve patents about those specific inventions, which could make it possible to confirm our findings in the future. Still, there is evidence of a strong overlap with the ICT codes we adopted, as they include, for instance, "Digital computing or data processing equipment or methods, specially adapted for specific applications" (IPC G06F19/00) in relation to Big Data analytics (Saheb & Saheb, 2020) or "Methods or arrangements for reading or recognizing printed or written characters or for recognizing patterns, for example, fingerprints" (IPC G06K09/00) in relation to AI (Abadi & Pecht, 2020). This is also consistent with the notion of digital innovation (Inaba & Squicciarini, 2017), where reliance on ICT is emphasized.

Third, our findings relate to CGCs. While the presented results show robustness, and the cancer domain is a high-tech and science-based context like the energy, nanotech, and semiconductor contexts (Hohberger, 2016; Pisano, 2010), the health context is characterized by a degree of complexity that may be quite different in other settings. Furthermore, researchers in the health industry are significantly familiar with scientific knowledge compared with R&D employees in other settings. Consequently, further studies may test our hypotheses in other contexts and come to understand the similarities and differences across different typologies of GCs.

Fourth, and partially related to the previous point, our analysis is performed on the time interval 1990–2011 and we rely on information on drugs that were approved before 2016. Accordingly, replication of this study in the same context, yet with more recent time intervals at hand, may contribute to increasing the reliability of our findings. For instance, while the use of digital knowledge in drug development has been rapidly rising in the last few years (e.g., Appio et al., 2017), this is not yet a pervasive trend and the leveraging of digitization in the pharma industry may still be in its infancy.

Fifth, future studies may jointly consider invention-level and higher-level factors (e.g., firm characteristics) to perform a broader multilevel analysis of the invention-to-innovation process.

Finally, our research underlines the potential of innovation management research in relation to CGCs, thus suggesting that it may be relevant in other contexts characterized by GCs (particularly developing ones).

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

ETHICS STATEMENT

The authors have read and agreed to the Committee on Publication Ethics (COPE) international standards for authors.

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Investigations on publication malpractices (according to the COPE Ethical Guidelines). Moreover, he has been newly appointed by the Ministry of Education in Italy as one of the five Commissioners for the National Scientific Qualification (ASN), for the field of Management Sciences. He is serving as Expert Evaluator for the Campania Region, the National Research Council of Norway, and the European Commission in the areas of innovation and technological management and forecasting. His main research interests deal with knowledge management, technology transfer, innovation, and technology management.

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