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Dynamic impact of uncertainty on R & D cooperation formation and research performance: Evidence from the bio-pharmaceutical industry

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ABSTRACT

Our study concentrates on the dynamic research and development (R & D) process in the pharmaceutical industry, which is characterized by high uncertainty and a low probability of success in passing research phases. We evaluate whether R & D cooperations are appropriate instruments to help firms counter various types of uncertainty in different R & D markets and across the drug development process. Our study uses a novel and comprehensive database on the pharmaceutical industry that tracks firms' drug pipelines, R & D success rates, new drugs launched on the market and the formation of R & D cooperations throughout different research phases and research (therapeutic) markets from 1990 to 2011. We provide interesting and insightful results regarding technological, demand and profit uncertainty and their impacts on R & D cooperation formation across the drug development process. For example, we find that technological, demand and profit uncertainty vary drastically across R & D markets, and most types of uncertainty are significantly higher in the early research phase than in the late research phase. R & D cooperations are formed at the early stage of the R & D process to counter high technological, demand and profit uncertainty and to increase the likelihood of successfully passing drug development phases. In contrast, R & D cooperations formed at the late stage of the R & D process are less motivated by these types of uncertainty and more motivated by R & D funding scarcity. Our calculation shows that an early-stage R & D cooperation would increase life expectancy for the U.S. population by 2.6 million years and a late-stage R & D cooperation would decrease life expectancy by 56,000 years.

1. Introduction

In many industries, technologies are increasingly complex and firms experience a high pace of innovation.[1] Research projects associated with high risk and uncertainty result in development failures and often leave firms with unsuccessful projects and no products to commercialize.[2] This is concerning for firms and policy makers since they invest large amounts of money in research and development (R & D). Governments frequently intervene with the intention of promoting the development of new technologies and new products. A series of support programs has been put in place by federal and state governments in the form of providing financial support and promoting R & D cooperations. Firms frequently engage in R & D cooperations to overcome innovation impediments, share R & D costs, pool resources, exchange technologies, benefit from synergy effects and overcome financial constraints.[3] Policy makers and managers consider the formation of R & D cooperations an important instrument to achieve beneficial impacts on innovation, and many countries have established research programs that support the formation of R & D cooperations. Examples are the National Cooperative Research Act enacted by the U.S. and the Ministry of International Trade and Industry in Japan, as well as several framework programs offered by the European Union.[4] Even though firms frequently operate in highly uncertain research environments, to date, no empirical study investigates the dynamic impact of uncertainty on R & D cooperations and research performance throughout the drug development process. This is a relevant topic for firms, managers and

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[1] Examples are the electronics, semiconductor, aircraft, pharmaceutical, software and telecommunications markets, among many others.

[2] In a general sense, uncertainty refers to a situation characterized by a lack of information (see Knight, 1921; Galbraith, 1973).

[3] See Kogut (1988) for a summary on research cooperation incentives. Many excellent studies focus on evaluating the impact of R & D cooperations on firms' investment and innovation incentives (see also Das et al., 1998; Eisenhardt and Schoonhoven, 1996; Hagedoorn, 1993; Hagedoorn et al., 2000; Lorenzoni and Lipparini, 1999; Mowery et al., 1998, among others). Further prominent empirical studies are Sakakibara, 2002; Cassiman and Veugelers, 2002; Irwin and Klenow, 1996; Kaiser, 2002; Duso et al., 2014; Roeller et al., 2007; Nicholson et al., 2005; Higgins and Rodriguez, 2006; Arora et al., 2009; Grabowski and Kyle, 2012, among others.

[4] For an overview of research joint ventures registered with the U.S. Department of Justice from 1985 to 1995, see Vonortas (1997).

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policy makers since it provides insights into promoting research incentives and overcoming research obstacles. The aim of the current study is to evaluate whether R & D cooperations are appropriate instruments to help firms counter various types of uncertainty in different R & D markets across drug development phases. We also investigate the impact of R & D cooperations formed at different research stages on research performance.

Our study focuses on the pharmaceutical industry, a natural setting in which to analyze these research questions for several reasons. First, the pharmaceutical industry is one of the most research-intensive industries (Danzon et al., 2005). The drug development process in this industry faces major challenges, since it is time consuming, very expensive and highly uncertain.[5] Drug development projects have low success rates of only 4% and cost, on average, $873 million dollars.[6] Even though numerous R & D cooperations exist in the industry, few empirical studies focus on R & D cooperations in the pharmaceutical industry, and most work concentrates on cooperations in clinical trials. Prominent studies in this area are Arora et al. (2009), DiMasi and Grabowski (2007), Danzon et al. (2005), Nicholson et al. (2005), Pisano (1997) and Powell et al. (1999). Second, the drug development process in the pharmaceutical industry is inherently dynamic since newly developed drugs have to successfully pass several R & D stages before the Food and Drug Administration (FDA) will approve them for market launch. The R & D stages are characterized by specific aims, objectives and requirements and have different aims, objectives and success probabilities.[7] The nature of the dynamic R & D process enables us to track drug development projects across research phases and to measure the extent to which uncertainty differs across research stages. Moreover, R & D cooperations are formed at different R & D stages, which supports the fact that they serve different purposes and achieve different impacts across research stages. This allows us to determine whether changes in uncertainty across research stages provide differential incentives for firms to form R & D cooperations. It also enables us to evaluate the impact of R & D cooperations on research performance throughout different research stages.

Third, the industry is characterized by various forms of uncertainty that can have implications on firms' entry, exit and investment decisions and frequently result in the abandonment of research projects.[8] Ghosal and Ye (2015) recognize that the development of new products is characterized by various types of uncertainty. They distinguish between technological, demand and profit uncertainty, among others. Technological uncertainty is often associated with the failure rates between clinical testing phases. Sherbloom (1991), DiMasi et al. (1991) and DiMasi (2000, 2001) show that research projects at the early stage (preclinical testing phases) are highly complex. Of about 250 compounds entering the preclinical testing phase, only one new compound is eventually approved by the FDA. Powell and Brantley (1992) emphasize that a single biotechnology firm rarely has all the necessary technical skills to succeed in the early research stage and firms are, therefore, dependent on working in teams of interdisciplinary scientists and forming R & D cooperations. Even if research projects successfully complete all stages, other types of uncertainty remain. Hence, we also consider demand uncertainty, which relates to unknown market factors determining the sale of products. Demand uncertainty can be caused by further competition from generic drugs entering the market (Branstetter et al., 2014, 2016) or caused by an unknown drug acceptance across the population in the market. Until a drug reaches the population, the drug's true effectiveness and all the side effects are unknown. Hartman (1976) and Holthausen (1976) have shown that firms respond to demand uncertainty by investing less in capital. Profit uncertainty is another type of uncertainty that results from the fact that investments in research projects are often considered a sunk cost that vary across firms, treatment classes and development stages. Ghosal (1995, 1996, 2009) provides empirical evidence that greater profit uncertainty significantly reduces firms' investments.

Our study uses a novel and comprehensive database on the pharmaceutical industry that tracks firms' drug pipelines, R & D success rates, new drugs launched on the market and the formation of R & D cooperations throughout different research phases and R & D (therapeutic) markets from 1993 to 2011. In accordance with previous studies, we categorize the drug development process into an early research stage (that concentrates on inventing and exploring the chemical stability of promising molecules) and a late research stage (that includes clinical testing).[9] Our study provides interesting and insightful results regarding technological, demand and profit uncertainty and the dynamic impact of R & D cooperations across the drug development phases. Interestingly, we find that all three types of uncertainty vary drastically across R & D markets and across research stages; they are significantly higher in the early stage than in the late stage.

We find that firms use early-stage R & D cooperations as an instrument to counter technological, demand and profit uncertainty. Our results show that early-stage R & D cooperations are formed to alleviate uncertainty and exploit synergy effects. Early-stage R & D cooperations increase the number of R & D projects firms are working on and improve the likelihood of successfully completing drug development phases (i.e., the rate of drugs proceeding from the early to the late research stage). Late-stage R & D cooperations, however, are less motivated to counter technological, demand and profit uncertainty, but more motivated by R & D funding scarcity. Late-stage R & D cooperations are formed in R & D markets characterized by lower technological, demand and profit uncertainty. Moreover, they significantly reduce the number of R & D projects during the late research stage and also reduce the success rate of drugs passing from the late research stage to the approval stage. This finding suggests that re-optimization and selection of R & D projects take place after firms engage in late-stage R & D cooperations, presumably to discontinue research projects of low quality and avoid wasteful duplication of research projects.

The remainder of the paper is organized as follows: The next section provides an industry description. Section 3 presents a description of the data sources and the variable definitions. Section 4 discusses the empirical model and the estimation results. We conclude in Section 5.

2. Industry description

The pharmaceutical industry is vital for the treatment of disease and improving our quality of life. It is a research-intensive industry, and pharmaceutical companies are under constant pressure to discover new drugs. The drug development process is time consuming and expensive (see, e.g., DiMasi et al., 2003). The high uncertainty and low success rate of drug development are concerning industry features for firms and policy makers.[10] To improve drug development productivity, much research is funded by the public sector, which involves institutions, foundations, universities and specialized government agencies, e.g., the National Science Foundation and the National Institutes of Health (see also Cohen et al., 2002 and Arora et al., 2004 for more details).[11] Approximately one-third of drug development costs are paid by the

[5] See also DiMasi et al., 2003.

[6] See also Paul et al. (2010), DiMasi et al. (2016) for more information on drug development costs.

[7] Details about the different research phases are introduced later in the industry description. See also DiMasi et al. (1991) for further information on success rates across drug development phases.

[8] Several studies consider R & D investments as a sunk cost and analyze the impact on firms' investments (see, e.g., Pindyck, 1993 and Pindyck and Dixit, 1993).

[9] More detailed information is provided in the next section.

[10] Berndt et al. (2015) find that diminished returns in R & D success is a serious concern for earning rents and an impediment for biomedical innovation. Grabowski and Vernon (1990, 1994) find that only drugs in the top few deciles earn premium returns.

[11] The National Institutes of Health is the largest public funder of biomedical research in the world, investing more than $30 billion a year.