ELSEVIER

feature

When more isn't merrier: pharmaceutical alliance networks and breakthrough innovation

John Qi Dong, john.dong@rug.nl **and Killian J. McCarthy,** k.j.mccarthy@rug.nl

Strategic alliances, in particular strategic alliances with universities, are widely thought to be beneficial to the drug discovery process. However, the discussion of alliances and their effect has tended to focus on single alliances and has ignored the fact that firms tend to participate in multiple alliances simultaneously. Here, we show the importance of adopting a portfolio perspective of strategic alliances. We build a model of the U.S. pharmaceutical industry, and show how 2298 alliances, announced over a 15-year period, impact the alliance portfolios of 324 pharmaceutical firms, and how that, in turn, impacts the breakthrough innovations that these firms produce. In doing so, we show the stengths and benifits of strategic alliances, but we also show the dangers of adopting a more the merrier approach to strategic alliance making.

Strategic alliances and innovation

There are many different types of innovation and many ways to classify innovation [1]. One common approach is to differentiate between radical innovation (creating new and previously unimagined products) and incremental innovation (improving or upgrading existing products). In the context of the pharmaceutical industry, incremental innovation is about finding new applications for existing drugs, whereas radical, or breakthrough, innovation is about creating first-in-class drugs.

Cleary, both types of innovation are important: to survive, the firm must invest in incremental innovation and must extend product lines and life cycles [2]; however, to thrive, the firm must develop breakthrough innovation. Research supports this proposition and shows that firms that create breakthrough innovation perform better and survive longer [3,4]. However, research also shows that firms find it difficult to develop breakthrough innovation by themselves. Innovation comes from recombining new knowledge inputs [5] and, internally, firms typically lack the diversity of knowledge necessary to spark a breakthrough.

Increasingly, therefore, firms have selectively disintegrated [6], have opened up their innovation processes [7,8], and have formed strategic alliances [9,10] with industry and/or university partners [11,12] in their search for breakthrough innovation. Strategic alliances are formal arrangements, made by otherwise independent entities, to achieve a common objective; by making strategic alliances, firms hope to find the types of new knowledge necessary to spark a breakthrough. Most research supports this suggestion and shows that, whereas an individual alliance might be disappointing [13], firms that engage in alliances, in general, tend to perform better. Indeed, in the pharmaceutical context, strategic alliances are known to be essential to the drug discovery process [9,10] and to be particularly important for the development of breakthrough innovations [14].

Alliance portfolio and network

However, the existing discussion on strategic alliances is incomplete: it tends to focus on the impact of a single alliance, in isolation, and tends to ignore the reality that alliance-making firms often participate in multiple alliances simultaneously.

For example, Pfizer formed an alliance with University of California San Francisco (UCSF) in 2011, and with Merck in 2014, which, in 2011, formed an alliance with Parexel. In 2018, Parexel

https://doi.org/10.1016/j.drudis.2019.01.002

partnered with CHA Medical group, and Immutep joined the Pfizer–Merck alliance. In this way five firms and one university became linked in an alliance network. Therefore, the performance of one alliance depended not only on the parties in that alliance, but also on the other alliances of the firms involved. In other words, the performance of the Pfizer–UCSF alliance will be affected by the existence of the Pfizer–Merck alliance, which will be further affected by the existence of the Merck–Parexel alliance. Therefore, a study of the innovation effects of the Pfizer–UCSF, in isolation, will be incomplete and might be misleading.

We claim that, to really understand the impact of alliances on breakthrough innovation, we need to move from a bilateral to a network perspective of the strategic alliances; we need to move from the study of one individual alliance to the study of the alliance portfolio of a firm. Doing so, we suggest, will not only allow us to more accurately represent the realities of the pharmaceutical industry but, as we will show, also allows us to draw on the knowledge network theory [15,16], to explain how the alliance portfolio of a pharmaceutical firm can be better managed to increase the number of breakthrough innovations that it produces.

Alliance network position and composition

Knowledge network theory considers how the ways in which organizations are connected affects knowledge transfer. It has been applied to a variety of research settings. Applied to our context, knowledge network theory highlights two important factors: the position of the firm in the alliance network and the composition of its alliance portfolio.

The importance of alliance network position

First, knowledge network theory suggests that the position of a firm in an alliance network is important because the benefits of a network are not evenly shared; the more central the firm is in the network, the more benefits that it can reap from the network. Centrality, in its simplest form, refers to the number of connections that the firm has, relative to the maximum number of possible connections. Centrality matters because central firms are exposed to more of the information and knowledge that are created in the network. Therefore, firms that are central can combine more of the diverse knowledge that is available in the network, which increases the chance of developing breakthrough innovation [17].

However, more isn't always merrier. Firms have a limited absorptive capacity, that is, a limited ability to acquire external information, to assimilate it,and to apply it to the commercial ends, meaning that there is a maximum level of new knowledge that the firm can process [18]. The speed at which this saturation point is achieved is influenced not only by the quantity of information, but also by the degree of difference between the new information and the existing knowledge of the firm. Once the maximum level is achieved, more information can lead to a random drift of the knowledge base of the firm [18], which then in fact reduces the chance of developing breakthrough innovation.

Therefore, in the context of the above example, centrality implies that Pfizer is wise to build alliances with Merck and UCSF, and that Pfizer is wise to connect to more organizations. As a central firm in the network, Pfizer will be able to access more of the information generated in the network and, therefore, will be more likely to develop breakthrough innovation than Parexel. However, at the same time, Pfizer should be cautious of adding too many alliances to its portfolio. As it approaches the limits of its absorptive capacity, the marginal benefit from each new alliance decreases and, once it crosses the limit, it runs the risk of becoming overwhelmed, which will be detrimental to its efforts to develop new breakthrough innovations. Pfizer's first alliance brings new knowledge, but with each new alliance, the amount of effort required to digest that new knowledge that it brings increases, and beyond a certain point, the effort to digest the knowledge is greater than the benefits of digesting it. Firms, in other words, should be central enough to be able to get access to the knowledge in the alliance network, but should not be too central as to become overwhelmed by it.

The importance of alliance portfolio composition

Second, knowledge network theory suggests that the composition of the alliance portfolio of a firm matters because different types of partner can bring different types of knowledge to the focal firm, which has implications for the speed with which the firm will reach the limits of its absorptive capacity. For example, the Pfizer–Merck alliance is an industry–industry partnership, and industry partners are market-based knowledge creators [19]; they tend to have similar, applied knowledge, with clear commercial applications, and tend to form alliances to supply market needs. By contrast, the Pfizer–UCSF alliance is a university–industry partnership, and university partners are science-based knowledge creators [19]; they tend to have dissimilar, basic knowledge, with few direct commercial applications, and tend to form alliances to add to the academic knowledge. It follows that the Pfizer–Merck and the Pfizer–UCSF alliances provide Pfizer with different types of partner, and the composition of the Pfizer alliance portfolio will affect the chance that it develops breakthrough innovation.

In more general terms, an alliance portfolio with more industry partners is likely to offer more similar knowledge to that of the firm. Similar knowledge is more digestible, which will slow the speed at which the firm reaches the limits of its absorptive capacity. However, breakthrough innovation requires a diversity of knowledge, meaning that an alliance portfolio dominated by industry partners is less likely to produce breakthrough innovation. By contrast, an alliance portfolio with more university partners is likely to have abundant dissimilar knowledge to spark a breakthrough innovation. However, the level of difference between the knowledge base of the firm and a university will accelerate the speed with which the firm reaches the limits of its absorptive capacity, meaning that an alliance portfolio dominated by university partners is also less likely to produce breakthrough innovation. Simply put, the composition of the alliance portfolio of a firm matters and, to be successful, the firm should have enough but not too many university and industry partners.

Data from the pharmaceutical industry

To demonstrate this, we built a model of the U.S. pharmaceutical industry. We constructed the model using data collected from the Thomson Reuters' SDC Platinum database, which has data on 2298 pharmaceutical alliances, announced by 324 unique pharmaceutical firms. We constructed the industry alliance network for each year, in the period 1985–2001[*]; Fig. 1 illustrates the result for the year 2001. For each firm, we then measured its centrality as the number of alliances that the firm had, compared with the size of the alliance network, and we categorized its portfolio as being industry dominant or university dominant, based on the ratio of industry to university partners. We then considered how changes in these variables, over the period of our analysis, affected the number of breakthrough innovations generated.

[*] The period was determined based on practical issues concerning access to data.

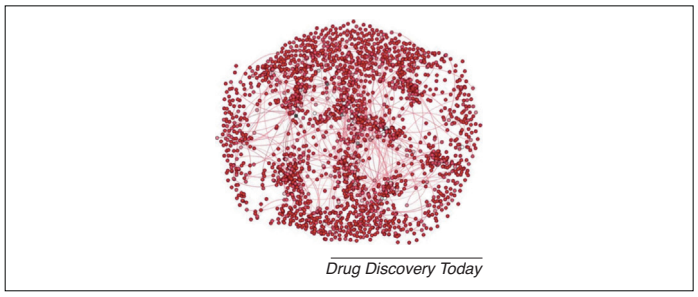

FIGURE 1

Alliance network of the U.S. pharmaceutical industry in 2001. We modeled the way in which 324 unique U.S. pharmaceutical firms connected to each other, through the 2298 alliances that had been announced over a 15-year period.

We used patents to quantify the effects of strategic alliances on pharmaceutical innovation, and made use of forward citations (an innovation measure commonly used in both academic and policy discussions) to distinguish between patents that led to either incremental or breakthrough innovations. However, what is a forward patent citation?

A patent citation is a reference to a previous patent that is important to the development of the focal patent. In Fig. 2, for example, four patents in period *t* (Patents A1, A2, A3, and A4) build upon and, therefore, cite Patent A, which was filed in period *t* – 1. By contrast, only one patent in period *t* (Patent B1) cites Patent B. Put another way, Patent A has four forward citations and B has one patent, meaning that Patent A has led to more innovation in period *t* than has Patent B. In this way, we can use the number of forward citations to identify those foundational, breakthrough innovations that spark a series of new patents.

Concretely, we define breakthrough innovations as the most heavily cited (top 3%) patents, in each three-digit U.S. patent classification (USPC) category.[†] Given that more recently granted patents have less time to gain forward citations, and to avoid comparing apples with oranges, we counted the number of forward citations received by each patent over the 5 years after the initial application. We retrieved the patent and citation data to do this from the U.S. Patent and Trademark Office (USPTO), which has records on 3 million patents and 24 million patent citations in the period of analysis. We calculated the percentage of breakthrough patents, per firm per year, as the number of breakthrough patents produced by each firm, per year, divided by total number of patents produced by the firm, per year.

Position, composition, and breakthrough innovation

Figure 3 documents the relationships between the alliance network of the firm and the percentage of breakthrough patents that it generates. The level of the centrality of the firm is represented on the horizontal axis (it varies from 0, meaning the firm has no connections with other organizations in the network, to 1, meaning the firm has all possible connections) and the percentage of breakthrough patents is on the vertical axis. The clear inverted U-shaped curve supports the suggestion that, although it is good to be central and connected, because central firms develop more breakthrough innovations, firms that are too central end up with fewer breakthrough patents. Figure 3 shows, in fact, that a firm with no alliances is more likely to make a breakthrough innovation than is a firm that is overwhelmed with too many.

Figure 4 then looks at the role of network composition. Again, the level of centrality is represented on the horizontal axis and the percentage of breakthrough patents on the vertical axis. The stripped line represents the case of firms with an alliance portfolio dominated by universities, and the solid line represents the case of firms with a portfolio dominated by industry partners. Figure 4 shows that firms with a portfolio dominated by universities are more likely to develop breakthrough innovation than are those with a portfolio dominated by industry partners, when centrality is low. As such, Fig. 4 supports the view that university partnerships are crucial to the innovation process. However, Fig. 4 also shows that the marginal benefit of adding additional universities to the portfolio is nonexistent, because more universities will reduce the likelihood of developing a breakthrough innovation. By contrast, we see clear benefits to working with more industry partners, and advantages to becoming more central in a network that is dominated by industry partners. Importantly, however, Fig. 4 shows that the maximum benefit of working with more industry partners (i.e., becoming more central) is never as high as that of working with a university.

Limitations of the study

Of course, a study of 324 firms and 2298 alliances, announced over a 15-year period, comes with its assumptions and limitations. In our case, several

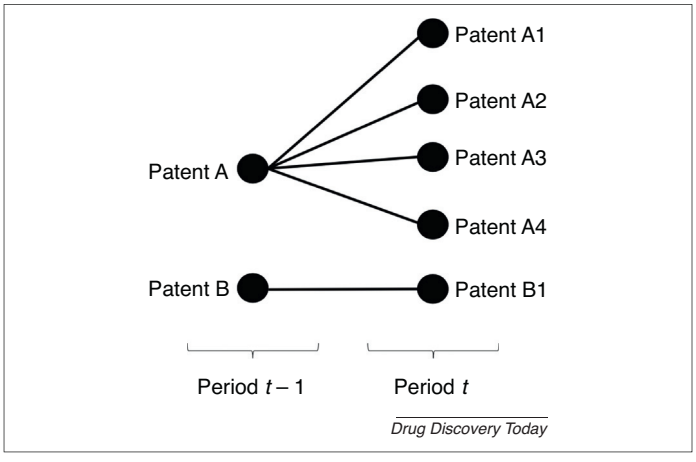

FIGURE 2

Forward patent citations. All patents are innovation, but by looking at forward citations, we were able to distinguish between radical, breakthrough patents, such as Patent A, which lead to new streams of development, and incremental patents, such as Patent B, which have a more modest effect.

[†] However, for robustness-checking purposes, we also used more conservative (top 1% and 2%) and less conservative (top 5% and 10%) measures of breakthrough innovation, and found consistent results.

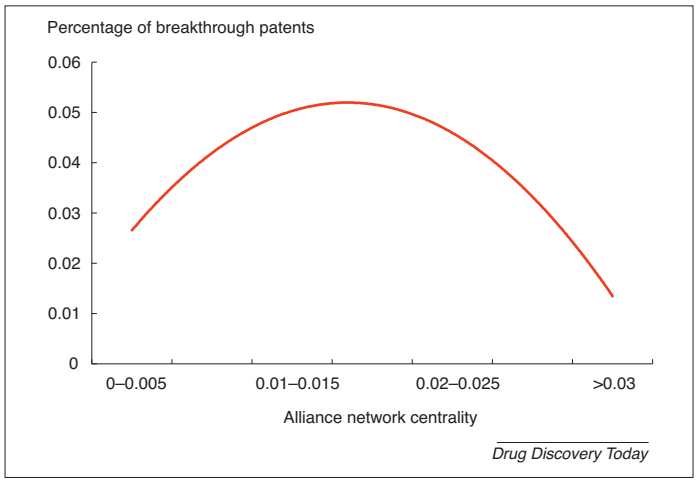

FIGURE 3

Alliance network centrality and breakthrough patents. How does the number of alliances or, put another way, the level of centrality of a firm in the industry alliance network, impact the number of breakthrough innovations that it produces? Surprisingly, it is not a case of the more the merrier: firms with no alliances are more innovative than are firms with too many alliances.

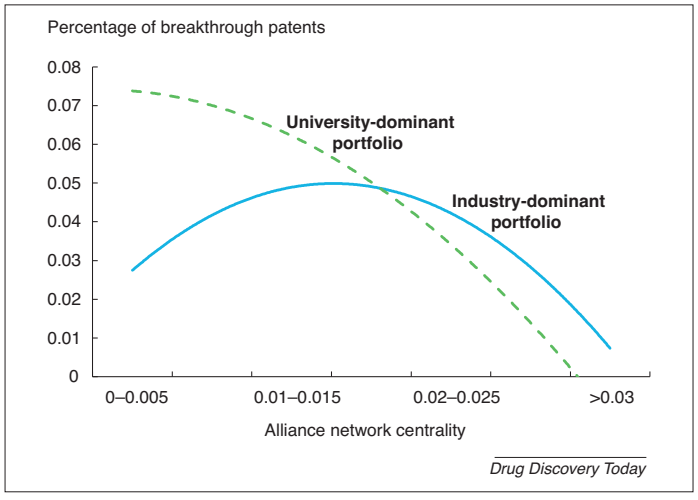

FIGURE 4

Alliance partner type and breakthrough patents. Who you ally with matters: the maximum benefit of working with more industry partners is never as high as that of working with a university, but adding additional universities to the alliance portfolio of a firm only decreases the percentage of breakthrough patents.

are noteworthy. First, we assumed that all pharmaceutical alliances are aimed at developing breakthrough innovation. This might not be the case, and firms might partner with universities, for example, simply to improve their innovative appearance or to open doors for future clinical trials. Unfortunately, we were unable to tease out these details in this project. Second, we only discuss one type of innovation, namely patentable knowledge. In doing so, we ignore issues, for example, such as the medical need of the technology, or its commercial value. Again, however, because of the level of the analysis, we were unable to match patents to products, or to medical needs, and, therefore, were unable to provide a richer picture regarding of the consequences of these breakthrough patents. Finally, our sample was constrained to the period of our analysis because of data limitations. However, anecdotal evidence suggests that alliance-making activity in the pharmaceutical industry has only increased in recent years, which means that the effects we documented are likely on the conservative side.

Concluding remarks

Our study makes several contributions. First, and by studying the innovation and alliance-making behavior of U.S. pharmaceutical firms over a 15-year period, we have provided large-scale empirical support for the widely accepted fact that strategic alliances can and do positively contribute to their development of breakthrough innovation.

Second, and by describing alliances as building blocks in a network, we have not only provided a more accurate depiction of alliances in the pharmaceutical industry, but have also offered important insights into the ways in which alliance portfolios can be managed to increase the percentage of breakthrough patents generated. We offer three insights in particular, as detailed below.

The network perspective is crucial

We showed that: (i) the position of a firm in its alliance network matters, because it affects the amount of knowledge that the firm is exposed to; and (ii) the composition of the alliance portfolio of a firm matters, because the different organizations bring different types of knowledge. We would call on managers to recognize this fact, and to adopt a network perspective, in which each new alliance is not only considered by its individual merits, but also by how it affects the portfolio of alliances of the firm. In this way, the firm can manage the probability of developing a breakthrough.

Alliances do not follow the more the merrier principle

Alliances bring access to new information and knowledge and the reduction of risks and costs when developing breakthrough innovation. So why not make more alliances? Our findings warn managers that each firm has a maximum level of information that it can efficiently utilize and, once the maximum capacity is passed, the effect can be detrimental on the number of breakthrough innovations created. In fact, we showed that firms with no alliances create more breakthrough innovations compared with firms with too many. Again, we would call on managers to recognize this fact, and to exercise caution when adding alliances to the portfolio of a firm.

The portfolio should include a university

We found that there are significant advantages that come from working with a university; a portfolio with one university is more likely to result in a breakthrough innovation than is a portfolio with the maximum number of industry partners. In other words, all firms looking to develop breakthrough innovations should form alliances with university partners. Again, however, we must warn managers that partnerships with universities come with significant costs, which might quickly outweigh the benefits. Universities have different objectives and

different types of knowledge and, although this helps spark breakthroughs, the effect of working with universities can quickly become detrimental. Therefore, we call on the manager to make alliances with universities, but to exercise extreme caution when adding additional universities to the alliance portfolio of the firm.

References

1 Garcia, R. and Calantone, R. (2002) A critical look at technological innovation typology and innovativeness terminology: a literature review. *J. Prod. Innov. Manage.* 19, 110–132

2 Bader, M.A. *et al.* (2012) Getting the most out of your IP: patent management along its life cycle. *Drug Discov. Today* 17, 281–284

3 Hill, C.W.L. and Rothaermel, F.T. (2003) The performance of incumbent firms in the face of radical technological innovation. *Acad. Manage. Rev.* 28, 257–274

4 Cha, M. and Yu, F. (2014) *Pharma's First-to-Market Advantage.* McKinsey & Co.

5 Schoenmakers, W. and Duysters, G. (2010) The technological origins of radical inventions. *Res. Policy* 39, 1051–1059

6 Ekins, S. *et al.* (2013) Four disruptive strategies for removing drug discovery bottlenecks. *Drug Discov. Today* 18, 265–271

7 Cavalla, D. (2003) The extended pharmaceutical enterprise. *Drug Discov. Today* 8, 267–274

8 Schuhmacher, A. *et al.* (2013) Models for open innovation in the pharmaceutical industry. *Drug Discov. Today* 18, 1133–1137

9 Havenaar, M. and Hiscocks, P. (2012) Strategic alliances and market risk. *Drug Discov. Today* 17, 824–827

10 Williams, R.J. *et al.* (2012) Collaborative approaches to anticancer drug discovery and development: a Cancer Research UK perspective. *Drug Discov. Today* 17, 185–187

11 Breimer, D.D. (1996) University–industry collaboration in the pharmaceutical sciences. *Drug Discov. Today* 1, 403

12 Wellenreuther, R. *et al.* (2012) Promoting drug discovery by collaborative innovation: a novel risk-and reward-sharing partnership between the German Cancer Research Center and Bayer HealthCare. *Drug Discov. Today* 17, 1242–1248

13 Grindley, J.N. (1998) Success rates for strategic alliances: are they good enough? *Drug Discov. Today* 3, 145–146

14 Dong, J.Q. *et al.* (2017) How central is too central? organizing interorganizational collaboration networks for breakthrough innovation. *J. Prod. Innov. Manage.* 34, 526–542

15 Ghosh, A. and Rosenkopf, L. (2015) Shrouded in structure: challenges and opportunities for a friction-based view of network research. *Organ. Sci.* 26, 622–631

16 Phelps, C. *et al.* (2012) Knowledge, networks, and knowledge networks: a review and research agenda. *J. Manage.* 38, 1115–1166

17 Kilduff, M. and Brass, D.J. (2010) Organizational social network research: Core ideas and key debates. *Acad. Manage. Annu.* 4, 317–357

18 Cohen, W.M. and Levinthal, D.A. (1990) Absorptive capacity: a new perspective on learning and innovation. *Adm. Sci. Q.* 35, 128–152

19 Du, J. *et al.* (2014) Managing open innovation projects with science-based and market-based partners. *Res. Policy* 43, 828–840

John Qi Dong
Killian J. McCarthy*

Faculty of Economics and Business, University of Groningen, 9747 AE Groningen, The Netherlands

**Corresponding author.*