DISS. ETH NO. 26429

PRACTICING REPURPOSING IN THE PHARMACEUTICAL INDUSTRY: UNCOVERING NEW USES FOR POTENTIAL RESOURCES

A thesis submitted to attain the degree of

DOCTOR OF SCIENCES of ETH ZURICH

(Dr. sc. ETH Zurich)

presented by

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2019

I dedicate this dissertation to my parents, who have provided me endless support in my intellectual journey and taught me how to love.

Let the beauty of what you love be what you do.

Rumi

ACKNOWLEDGEMENTS

Above all, I want to thank my two supervisors, Prof. Dr. Georg von Krogh and Dr. Shiko Ben-Menahem, who accompanied me during my journey from being a young PhD candidate to a junior scholar. I would like to express my deepest gratitude to Georg, who always supported me in following my intellectual curiosity and welcomed my ideas and feelings with his open-minded and open-hearted attitude. Whenever my PhD process seemed to go off-track, he centered me with his kindness and compassion. I feel very lucky that I have gotten a chance to work with not only an excellent scholar but also a true intellectual. The safe atmosphere he provided in our group is one that every PhD student would want to have.

I am particularly grateful to Shiko, who has become my main mentor during this journey. He has put his mind and heart into my growth, sometimes even giving from himself to make me grow. As I often like to joke (but it is true), he has become my PhD program and provided me with fundamental knowledge about the management field, whether about theory, methods, academic writing, or academic culture. As parents teach their kids how to walk, Shiko has taught me how to walk on an academic path.

I feel fortunate that my roads crossed with Prof. Dr. Samer Faraj, first during the process of the Special Issue in ISR, then during the KIN Summer School and at many conferences. Our past conversations gave me many inspirations and expanded my horizons about academia in management.

One particular person among my friends deserves special thanks: Christian! Sharing office space with him for five years has led to the flourishing of a lifetime friendship and a sense of kinship. When far from our homes and families, nothing is more valuable than seeing someone every day in the office who has become a family member.

The years I spent at MTEC have also brought many wonderful friendships to my life. I thank my lovely friends Simge, Nina, Johanna, Zeynep, Ecaterina, and Ece for being here for me whenever I needed them. I'm blessed to be surrounded by such beautiful people.

I am also very grateful to my dear current and past team members, particularly my Nepali guru Yash; my IT friend (you know what it means!) Thomas; smiling-faced Patrick; my sweet, supporting runner friend Vivianna; and of course, my flower-child big sister Hilde!

During my PhD program, I also had the chance to meet and work with many inspiring people. I thank all of my former students, particularly Tino and Valerie, and my collaborators Prof. Dr. Joerg Goldhahn and Dr. Juerg Gasser, who have played an essential role in developing papers in my dissertation. I also thank Dr. Katharina Dittrich for providing feedback on my research. I also express my endless gratitude to Aris Persidis, Bruce Bloom, Steve Naylor, and Tim Hoctor; their passion for saving the lives of patients suffering from diseases without cures gave me the courage and energy to continue running.

A huge thanks goes to my dear friends—my soul family—around the globe! As the saying goes, distances don't separate; silence does. They have always continued to be part of my life with the fun, love, and nurturing they shared over written words and their voice! I am very grateful to my dear friend Berna, who had already put a lot of effort into my PhD journey before I moved here and who has grounded me whenever I felt confused! Words cannot describe my gratitude to my two beautiful friends Aydan and Merve, with whom I talk almost every day. Without you both, I wouldn't be the same person, and this dissertation wouldn't be here! I am very grateful to my sister from another mother, Damla, for offering her beautiful heart and endless support. I also thank Gizem, who has witnessed my growth as a person and always supported me. I also thank my lovely friends Aydin, Aytunc, Barbara, Elif, Ezgi, Gorkem, and Simon. Love you all so much!

And my family! My academic journey actually dates back to the time when I was a lucky little child sitting on the ground in front of our bookshelves and reading the Encyclopedia Britannica. Since this time, my parents have supported my intellectual journey tirelessly and worked day and night to provide me a safe and supportive environment. One phrase best describes my parents' attitude toward me: unconditional love! I am so grateful to have been born into such a beautiful family. I also express my gratitude to my brother Burak, my sister-in-law Katya, and the jewel of my life, my sweet niece Melisa!

I cannot end my words without mentioning a particular group of people: academics in Turkey and around the world, who strive for academic excellence but suffer from a lack of academic freedom. During my PhD studies, many of them experienced a lot of unfortunate events. Because I know from the inside how important academic freedom is, they deserve a few lines in my dissertation. I express my endless respect to them for their courage. Thank you.

Burcu Kucukkeles

Zurich, 2019

Abstract

By focusing on a set of practices and challenges in the pharmaceutical innovation process, this dissertation offers implications on the management theory and practice in three ways. Study I focuses on the question of how existing objects (i.e., tangible and intangible assets that actors act on) gain new use values by investigating a novel practice of drug repurposing—i.e., seeking new therapeutic applications for existing drugs. Study II examines the societal challenge of rare diseases, which have been largely neglected by commercial pharmaceutical companies. To this end, study II analyzes the practices of two non-profit organizations that were effective in circumventing market and government failures underlying rare diseases by repurposing off-patent (generic) drugs. Study III focuses on a highly relevant empirical problem of delays in termination decisions of research projects during the drug development process.

Study I takes on a practice theory perspective on resources (i.e., resourcing perspective), and contributes to the literature on the resourcing perspective by developing a framework of intentional and systematic resourcing processes. Study II provides new insights into the mutual constitution of organizational arrangements for societal challenges, particularly social entrepreneurship, and the practices they host. Study III identifies factors catalyzing delays in termination decisions during the drug development process and provides recommendations for practitioners and researchers working on drug discovery and development.

The studies in the dissertation suggest several future research avenues, centering on future research questions that studies have indicated from a practice theory perspective, and on extending implications of studies to different empirical settings.

Zusammenfassung

Durch die Fokussierung auf eine Reihe von Praktiken und Herausforderungen im pharmazeutischen Innovationsprozess hat diese Dissertation drei Implikationen für die Management-Theorie und Praxis. Studie I widmet sich der Frage wie bereits existierende Objekte (materielle und immaterielle Güter, auf Grundlage derer Akteure handeln können) neuen Wert erlangen, indem die neuartige Praktik der Umnutzung von existierenden Arzneimitteln erforscht wird. Studie II untersucht die gesellschaftliche Herausforderung von seltenen Krankheiten, die von großen kommerziellen Pharmafirmen weitgehend vernachlässigt wurden. Zu diesem Zweck analysiert Studie II die Praktiken zweier gemeinnütziger Organisationen, die erfolgreich Markt- und Gesetzesversagen, die typisch für die Erforschung seltener Krankheiten sind, umgangen haben, indem sie nicht patentgeschützte (generische) Arzneimittel umgenutzt haben. Studie III konzentriert sich auf ein hochrelevantes empirisches Problem der Verzögerung von Abbruchentscheidungen von Forschungsprojekten im Entwicklungsprozess von neuen Arzneimitteln.

Studie I nimmt eine praxeologische Perspektive auf Ressourcen ein (d.h. Ressourcenperspektive). Die Studie trägt zur Literatur der Ressourcenperspektive bei, indem sie ein Rahmenwerk für zielgerichtete, absichtliche und systematische Resourcing-Prozesse entwickelt. Studie II generiert neue Erkenntnisse über die gemeinsame Konstitution von organisatorischen Arrangements für das Bewältigen von gesellschaftlichen Herausforderungen – im Speziellen im Bereich des sozialen Unternehmertums und den damit verbundenen Praktiken. Studie III identifiziert Faktoren, die Verzögerungen bei Abbruchentscheidungen während des Medikamentenentwicklungsprozesses katalysieren, und gibt Empfehlungen für Praktiker und Forscher, die an der Entdeckung und Entwicklung von Medikamenten forschen. Die Studien in dieser Dissertation zeigen mehrere Wege für zukünftige Forschung auf. Insbesondere zeigt diese Dissertation zukünftige

Forschungsmöglichkeiten auf, die eine praxeologische Perspektive nutzen und die die in dieser Dissertation gewonnen Erkenntnisse in anderen empirischen Kontexten testen.

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1. INTRODUCTION

"The social is a field of embodied, materially interwoven practices centrally organized around shared practical understandings." T. R. Schatzki (2002, p. 3)

How do objects that are treated as garbage or leftovers become useful resources? How do we take an available object and make a new use out of it? This dissertation centers on the processes and practices of uncovering new uses for existing objects (i.e., tangible and intangible assets that actors act on). The main studies in this dissertation originated from empirical observations of serendipitous discoveries of additional uses for existing drugs (e.g., Viagra). Merton and Barber (2004) defined serendipity as "finding something while searching for something else" (p. 194). Central to this dissertation is the question of whether such discoveries are indeed based only on fortuitous findings. Casting doubt on this question has led me to investigate the practices underlying such discoveries.

Practice theory scholars consider social life as a continuous production of people's recurring actions (Feldman & Orlikowski, 2011). Practices refer to "open and spatially, temporally dispersed sets of doings and sayings organized by common understandings, teleology (ends and tasks) and rules" (Nicolini, 2017, p. 21; Schatzki, 2002). By centering on practices, practice theory scholars reconceptualize how we perceive various organizational phenomena and shift the focus to agency rather than agents (e.g., to organizing rather than organization; Nicolini, 2013). Although there is no unified theory of practice (Schatzki, 2001), past work on practice theory shares some common principles (Feldman & Orlikowski, 2011).

Practice theory scholars argue that the social life is produced and reproduced through people's everyday actions and reject the separateness implied by dichotomies (e.g., body/mind, structure/agency) (Feldman & Worline, 2016; Nicolini, 2013). Practice theory scholars further suggest that a phenomenon can only be understood in relation to another

phenomenon (Feldman & Orlikowski, 2011). The same principles of practice theory also guided Study I and II in this dissertation. In this dissertation, I focus on the practice perspective on resources (resourcing) (Feldman, 2004; Feldman & Worline, 2011) as well as on a MacInyrean perspective on social practices (MacIntyre, 1981).

Feldman (2004) develops a practice theory perspective on resources by challenging earlier assumptions in the strategy literature (Barney, 1991, 2001; Pfeffer, 1982; Salancik & Pfeffer, 1978) about resources being valuable because of their inherent characteristics, and develops a theory of resourcing. In the resourcing perspective, objects only become valuable when they are put into use (Feldman, 2004; Feldman & Worline, 2011). Past work on the resourcing perspective provided important insights into the role of resourcing practices during organizational change processes and in triggering the change by often depicting emergent, often improvisational, resourcing processes (Sonenshein, 2014). However, little is known about more directed, intentional resourcing processes. In Study I, by analyzing practices of identifying additional uses for existing drugs—drug repurposing—my coauthors and I develop a framework on resourcing processes whereby existing objects gain new use values. Study I contributes to the resourcing perspective (Feldman, 2004; Feldman & Worline, 2011; Sonenshein, 2014) and provides implications on several phenomena, including innovation processes.

Starting from an empirical hunch based on the fieldwork I conducted for Study I, Study II investigates practices in circumventing market and government failures regarding a grand societal challenge: rare diseases. Prior research provides insights into the emergence of certain types of organizational arrangements (e.g., social entrepreneurship) in cases of simultaneous market and government failures (e.g., Luo & Kaul, 2019; Mair & Martí, 2006; Miller, Grimes, McMullen & Vogus, 2012; Santos, 2012). However, studies on social entrepreneurship and similar organizational arrangements fall short in explaining what the

actors in these organizational arrangements do to circumvent market and government failures. By taking a practice theory perspective, we investigate two non-profit organizations—Cures Within Reach and Findacure—that effectively circumvented market and government failures by reinforcing practices of repurposing off-patent (generic) drugs for developing treatments for rare diseases. Study II contributes to practice theory and to the literature on organizational arrangements under simultaneous market and government failures, such as social entrepreneurship (Luo & Kaul, 2019; Santos, 2012).

While the first two studies focus on applying a practice theory lens to examine resourcing and organizational arrangements, Study III focuses on a core concern in the pharmaceutical drug development process: delays in termination decisions of drug development projects often due to various cognitive biases stemming from factors, such as incentive systems (Paul et al., 2010; Peck et al., 2015). Based on analysis of 11 drug projects in postmenopausal osteoporosis therapeutic area, Study III identifies factors catalyzing the progression-seeking behavior when terminating projects in drug development processes. Study III complements the first two studies by further investigating the pharmaceutical development process and provides important insights to practitioners in the pharmaceutical industry as well as translational research in the drug discovery and development.

In Chapter II, I provide a background on practice theory, and Chapter III and IV extend the theoretical background used in this dissertation to study resources from a practice theory perspective as well as organizational arrangements, respectively. Chapter V summarizes the empirical contexts investigated in the studies, and Chapter VI provides a brief overview of three studies of this dissertation. In Chapter VII, I discuss the studies' limitations and introduce future research questions derived from the studies.

2. THEORETICAL FOUNDATIONS

This chapter introduces the fundamental principles and key concepts of practice theory, which is the primary lens I used in Studies I and II.

Practice theory constitutes a set of ideas that emphasize practices, which are "organized constellations of material activities performed by multiple people" (Nicolini, 2017, p. 20; Schatzki, 2002). Central to practice theory is that things (e.g., material assets, ideas, organizations) take on meanings through practices (Feldman & Worline, 2016). Although there is no unified approach to practice theory (Schatzki, 2001; Nicolini, 2013), practice theory studies share a common assumption that "social life is an ongoing production and thus emerges through people's recurrent actions" (Feldman & Orlikowski, 2011, p. 1240). Practice theory suggests that fundamental aspects of human life, such as knowledge, power, organizations, and discourses, should be studied by analyzing practices. Hence, practice theory studies prevalently focus on practices as the unit of analysis (Nicolini, 2013; 2017).

Practice theory has three fundamental principles. First, practice theory scholars argue that "everyday actions are consequential in producing the structural contours of social life" (Feldman & Orlikowski, 2011, p. 1241). Practices recursively generate and regenerate social life (i.e., social structures, Giddens, 1984; or habitus, Bourdieu, 1990). Thus, practices constitute the core of organization and are consequential in creating organizational life (Orlikowski, 2010). Rather than seeing organizing as a top-down approach in which rules and norms of organizations impose a certain set of practices on organizational actors, practice theory scholars suggest that practices also shape organizing processes.

Second, practice theory rejects the dualism(s) between concepts (e.g., body/mind, structure/agency) and instead focuses on the inherent relationship between them (Feldman & Orlikowski, 2011; Reckwitz, 2002). For practice theory scholars, such dichotomies are

inherently inseparable. For example, the fundamental premise of structuration theory is to reject the dualism of structure and agency (Giddens, 1984). Third, relational thinking is fundamental in practice theory. No concept can be understood without looking at another concept, and concepts are mutually constitutive (Feldman & Orlikowski, 2011, Osterlund & Carlile, 2005). Relational thinking in practice theory implies that one cannot understand practices only by observing human action; rather, practices should be studied in relation to the structure wherein practices unfold.

Feldman and Worline (2016) explain three fundamental principles of practice theory by drawing on an example of the microfinance approach to banking – the practice of providing banking services, such as loans, to people who formerly did not have access to such services. The traditional form of banking relies on the assumption that banks cannot provide loans to poor people because they do not have material assets that banks can use as collateral. However, microfinance practices (e.g., creating support groups where individuals can be accountable for each other's loans) transformed the banking such that everybody can get loans, and banks can use both material and nonmaterial (social) assets as collateral.

Thus, the microfinance example illustrates that using nonmaterial assets as collateral was consequential in shaping the idea of lending and structural contours of poverty (consequentiality of everyday action). Microfinance practices made actors question common dualities such as poor-rich and material-nonmaterial by treating them relational rather than dichotomously (rejection of dualisms). Banking practices structure lending practices, and the availability of microfinance practices shapes and reshapes banking practices (relationality of mutual constitution) (Feldman & Worline, 2016, p. 313).

Taking a practice theory lens offers opportunities for management scholars to understand various social, technological, and organizational phenomena. Especially in the advent of increasingly complex organizational forms and dynamics, a practice theory lens can

help management scholars to explain the dynamics of emergent and novel forms of organizational phenomena (Feldman & Orlikowski, 2011). When studying an organizational phenomenon from a practice theory perspective, researchers observe practices rather than simply observing the subjects of those practices (i.e., practitioners). However, analysis of a phenomenon from a practice theory perspective goes beyond observing the daily actions of organizational actors, and practice theory scholars avoid naïve empiricism—the idea that observing the world in detail makes one closer to reality (Nicolini, 2013). To go beyond naïve empiricism, practice theory perspective requires a method-toolbox and the use of certain types of approaches (Nicolini, 2013).

Feldman and Orlikowski (2011) differentiate three ways of engaging in the practice theory in research. First, in the empirical approach, studies answer the question of "what" of a practice theory perspective. In this approach, the everyday actions of organizational actors are the main focus of the studies rather than the structural properties of organizations. Such studies challenge those studies that primarily focus on organizations' structural properties to explain an organizational phenomenon. In this line of research, scholars focusing on practices do not necessarily contribute to the practice-based perspective. Rather, they use practices as constituents of everyday organizing in organizations without explicitly drawing on the principles of practice theory.

Second, in the theoretical approach, studies focus on the question of "how" by putting the fundamental assumptions of practice theory to the center of studies (e.g., Bourdieu, 1977, 1990; Giddens, 1976, 1979, 1984). Here, practice theory provides a theoretical lens, through which an organizational phenomenon of interest is theorized about from a practice theory perspective. Such scholars take a theoretical approach to the practices to explain "the dynamics of everyday activity, how these [practices] are generated, and how they operate within different contexts and over time" (Feldman & Orlikowski, 2011, p. 1241).

Third, the philosophical approach to practice theory focuses on the fundamental epistemological stance of practice theory scholars. In this line of research, scholars propose that "practices are fundamental to the production of social reality" (Feldman & Orlikowski, 2011, p. 1241). This approach answers the question of "why" of a practice theory perspective by drawing the ontological perspective on practices as constituents of social reality (e.g., Gherardi, 2006; Lave, 1988).

In Studies I and II of this dissertation, two particular principles about practice theory are central. First, in contrast to the positivist perspective, in practice theory, the meanings of things (such as ideas, organizations, and resources) are socially constructed through practices, rather than having innate characteristics (Feldman & Worline, 2016). Second, central to practice theory is "the relationship between specific instances of situated action and the social world in which the action takes place" (Feldman & Orlikowski, 2011, p. 1241). Thus, in Studies I and II, I study practices in relation to the contexts in which they are situated.

To date, practice theory scholars have investigated various organizational phenomena, including knowledge (e.g., Carlile, 2002, 2004; Nicolini, 2011), sociomateriality (e.g., Orlikowski, 2000, 2007), and strategy (e.g., Whittington, 2006, 2007; Jarzabkowski, 2005, 2008). In this dissertation, I focus on two perspectives within practice theory: a practice theory perspective on resources (Feldman, 2004) and the role of social practices in co-constituting practices and organizations (MacIntyre, 1981). In the next chapter, I give a more detailed background on the theoretical perspectives I use in Studies I and II of this dissertation.

3. PRACTICES AND RESOURCES

In this chapter, by taking stock of existing perspectives on resources in the organizational theory and strategy literature, I introduce the notion of resourcing process and explain the prior studies that have taken a resourcing perspective. First, I provide a short overview on the traditional perspectives on resources. Then, I introduce the resourcing perspective, which refers to a practice-based perspective on resources (Feldman, 2004; Feldman & Worline, 2011, 2016), and I address the question of "how to tap into a variety of resources and put them to use in new ways that enable creative, resourceful approaches to management" (Feldman & Worline, 2016, p. 305).

3.1. Traditional Perspectives on Resources

How organizations create value from resources has been a central question to strategy literature (Barney, 1991, 2001; Salancik & Pfeffer, 1978). Three perspectives on resources are predominant in the strategy literature. First, the traditional set of theories, such as the resource dependency theory (Pfeffer, 1982; Salancik & Pfeffer, 1978) and the power-dependence model (Thompson, 1967), suggests that an organization's ability to create value from resources depends on its ability to control externally available resources. Thus, in the first set of theories, controlling the flow of resources from the external environment is a crucial determinant of an organization's success. Second, in relation to the resource-dependency theory, an institutional perspective on resources adds the insight that the value of resources is defined at the field level, and it depends on the configurations of field actors at any given moment (Leblebici, Salancik, Copay & King, 1991).

In the third set of theories, the attention regarding the value-creation process of resources moves to an organization's internal dynamics and internal ability to create value from resources. The resource-based view of the firm and the dynamic-capabilities perspective, based on the resource-based view of the firm, analyze the relationship between

an organization's competitive advantage and valuable, rare, non-imitable, and non-substitutable resources (Barney, 1991, 2001; Eisenhardt & Martin, 2000; Helfat & Peteraf, 2003). Thus, a central question in the resource-based view of the firm and the dynamic capabilities perspectives has become how firms use capabilities for "creation, extension and modification of resources" (Stadler, Helfat & Verona, 2013, p. 1782). Within these theories, studies have suggested that rather than being entirely dependent on externally available resources, an organization can create its own resources, which might lead to competitive advantage in return. Thus, this line of strategy literature has focused on the dynamics of creating value from resources, which can be completely internal or can be achieved through collaboration with other organizations (Barney, 2001; Das & Teng, 2000; Eisenhardt & Schoonhoven, 1996).

While existing perspectives on resources have provided explanations for various organizational phenomena, some scholars (e.g., Priem & Butler, 2001a, b; Priem, Butler & Li, 2013) have argued that the studies primarily focused on the value-capture processes while falling short in explaining the value-creation processes, whereby value is created from the resources. In particular, attention has been lacking on value creation for an organization's customers and eventually users, while most of the attention has been given to the value captured by an organization (Priem et al., 2013). Priem and Butler (2001a) also argued that although there have been many studies on value creation and value capture processes, what determines value of resources remains unclear (Bowman & Ambrosini, 2000). In an attempt to "fill the blanks for value" (Priem & Butler, 2001a, p. 36), Bowman and Ambrosini (2000, 2010) developed a conceptualization of value, which I also use in Study I.

Bowman and Ambrosini (2000, 2010) define two types of value—use value and exchange value—based on the differentiation made by classical economists. Use value refers to "the specific qualities of the product perceived by customers in relation to their needs"

(Bowman & Ambrosini, 2000, p. 2). Consequently, use value refers to the individual utility that a customer gains from using a product (i.e., a resource) and is hence subjective. Exchange value, on the other hand, refers to the monetary gain that an organization (i.e., a firm) can get by selling a product (i.e., a resource) and is determined by the perceived use value and total monetary value, or the amount of money that a customer is willing to pay for a product (Bowman & Ambrosini, 2000, 2010).

Despite attempts to provide more value-creation explanations in the traditional strategy research, questions still remain about the processes whereby value is created from the resources. As Priem et al. (2013, p. 472) clearly indicate, the focus on the strategy research is primarily on "strategic decisions rather than day-to-day operating decisions." I subscribe to Feldman's (2004) argument that a closer examination of not only strategic decisions but also day-to-day activities might be necessary to understand value-creation processes. Hence, a practice-based perspective on resources (i.e., the resourcing perspective) can fill this gap. In the next section, I introduce the resourcing perspective and studies conducted on the resourcing perspective to date.

3.2. Resourcing Perspective

Resourcing perspective takes a practice-based perspective to develop a dynamic, structurational account of the processes whereby potential resources (objects) obtain value (e.g., Feldman, 2004; Feldman & Quick, 2009; Feldman & Worline, 2011). Thus, the resourcing perspective brings attention to processes rather than entities (Feldman & Worline, 2011). Drawing upon the relational ontology assumption of the practice theory, resourcing studies argue that resources cannot be defined independently of their use (Orlikowski, 2000). Studies on the resourcing perspective suggest that the existing theoretical perspectives' definition of resources limits our understanding of how resources become valuable in value-creation processes (Feldman, 2004; Feldman & Worline, 2011). For example, Eisenhardt and

Martin (2000, p. 1107) define resources as "specific physical (e.g., specialized equipment, geographic location), human (e.g., expertise in chemistry), and organizational (e.g., superior sales force) assets that can be used to implement value creating strategies." Similarly, Helfat and Peteraf (2003, p. 999) define resources as "asset[s] or input[s] to production (tangible or intangible) that an organization owns, controls, or has access to on a semi-permanent basis." Consequently, the traditional perspective on resources provides a fixed account on resources.

In studies on the resourcing perspective, on the contrary, resources are dynamic entities that not only affect internal value-creation processes within an organization but also are affected by the processes (Feldman, 2004). Thus, the resourcing perspective expands the definition of resources to "anything that allows an actor to enact a schema" (Feldman & Worline, 2011, p. 631; Sewell, 1992). In other words, the resourcing perspective emphasizes "how organizational members take up and use assets as they pursue activities in line with what they wish to make happen in the world" (Feldman & Worline, 2011, p. 631). Resources are thus enacted (Feldman & Worline, 2011), rather than being static tangible and intangible assets. However, the resourcing perspective does not imply that resources do not have innate qualities, rather, studies on the resourcing perspective argue that potential resources only become resources in use "when actors act upon these qualities by deploying them for a particular purpose" (Deken, Berends, Gemser & Lauche, 2018).

Looking from the practice-based perspective, Feldman (2004) suggests that resources are only potential resources (i.e., objects) until they are used, and makes a clear distinction between potential resources and resources-in-use (Deken et al., 2018; Feldman, 2004; Feldman & Worline, 2011). Resources become different resources depending on the particular instance in which they are used: "it is the ways that things are used that makes them into particular resources" (Feldman & Orlikowski, 2011, p. 1246). Thus, Feldman (2004) defines the processes whereby a potential resource becomes a resource-in-use as

resourcing. The resourcing perspective addresses the lack of process explanations in the resource literature by shifting the focus from entities to processes within organizations (Feldman & Orlikowski, 2011).

3.3. Studies on the Resourcing Perspective

To date, a great deal of attention in the resourcing studies has been given to analyzing emergent and dynamic change processes in organizations (Feldman, 2004; Howard-Grenville, 2007; Nigam & Dokko, 2019; Sonenshein, 2014; Quinn & Worline, 2008; Wiedner, Barrett & Oborn, 2017). The change processes studied in the resourcing studies are typically bottom-up processes triggered by individual practices and the interactions among them (Nigam & Dokko, 2019). Thus, in resourcing studies, practices are central to resourcing processes, and practices can become resources in a change process (Feldman & Worline, 2011).

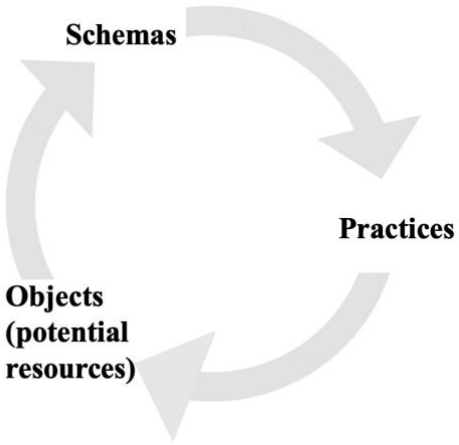

Figure 2: Resourcing Cycle*: Adapted from Feldman (2004, p. 296)*

For example, by using a single case study over four years, Feldman (2004) shows how changes in organizational routines have led to new resources being created. She shows the cyclical process of resourcing (Figure 1), in that the new resources being created as a result of changing practices enacted schemas. Since potential resources become valuable in the process of enactment through practices, the resourcing perspective provides a useful lens to

study emergent change processes. Feldman (2004) proposes that understanding the relationship between practices and resource creation can help to better explain change processes and resistance to change. These studies highlight the emergent role of new practices, resources and schemas such that the dynamic process of resourcing can lead to unexpected outcomes (Feldman, 2004), and conclude that "how people use potential resources, not their distribution per se, … influence[s] whether and how change will occur" (Wiedner et al., 2017, p. 7).

In a related line of resourcing studies, scholars have focused on understanding how practices among organizational actors can trigger change. Some commonly studied mechanisms include mutual adjusting (Feldman & Worline, 2011), juxtaposing the familiar with unfamiliar (Howard-Grenville, Golden-Biddle, Irwin & Mao, 2011), narrating (Quinn & Worline, 2008), and framing (Kannan-Narasimhan & Lawrence, 2018). For example, Feldman and Worline (2011) suggest that adopting a resourcing perspective can help scholars to understand how organizations can create ampliative cycles with which to reinforce positive spirals in organizing. By energizing positive frameworks through the resourcing process, organizations can trigger ampliative cycles of compassion in organizing (Dutton et al., 2006) and thriving at work (Spreitzer et al., 2005).

While scholars have used the resourcing perspective as a lens through which to study change processes (i.e., the relationship between change processes and how actors use resources; see Wiedner et al., 2017), few studies have investigated the actual resourcing processes (Deken et al., 2018; Sonenshein, 2014). Using a resourcing perspective, Deken et al. (2018) define the prospective resourcing as the process of "how managers create resource complementarity to articulate an innovative strategic initiative and initiate collaboration" (p. 1939). Thus, prospective resourcing explains the interplay between strategizing and interorganizational collaboration by challenging the assumption that strategy precedes

collaboration. Since the value of resources depends on their future use, the resourcing is prospective. The prospective resourcing process includes three subpractices: resource exploration, envisioning the resource use, and configuring resources. In a dynamic interaction of three subpractices, actors in an interorganizational collaboration process create resource complementarities through prospective resourcing (Deken et al., 2018).

In another study, by analyzing a family-owned company in two different resource-endowment episodes, Sonenshein (2014) explains how organizational actors created new resources from existing ones in changing resource environments. He describes the process of creative resourcing as "the manipulation and recombination of objects in novel and useful ways to solve problems" (Sonenshein, 2014, p. 814). Sonenshein (2014) distinguished between two types of resourcing processes—autonomous and directed resourcing—depending on managers' resource endowments in each resourcing process. In this way, Sonenshein (2014) contributes to the resourcing and creativity literature by explaining which kind of actions managers must take to facilitate creativity given different resource endowments.

While few studies have investigated the resourcing processes in relation to different organizational phenomena (Deken et al., 2018; Sonenshein, 2014), the studies primarily focused on resourcing activities during the improvisation process (Wiedner et al., 2017). However, "agents are primarily drawn to those things [potential resources] they value highly, either because they are personally dependent on, or familiar with them . . . or because they are deemed valuable in the wider field" (Wiedner et al., 2017, p. 40). Thus, actors' strategic interests and preferences might *direct* resourcing processes (Wiedner et al., 2017). I argue that in addition to analyzing resourcing processes that emerge during organizational activities such as coordination and creative problem-solving, a closer examination is needed of processes in which actors identify new uses for objects that they deem to be potentially

valuable. In Study I of this dissertation, departing from the perspective that resourcing processes constitute problem-solving activities (Sonenshein, 2014), I elaborate upon the resourcing theory by asking *how existing objects gain new use values*. In investigating this question, I draw on Bowman and Ambrosini's (2000, 2010) definition of use and exchange values that I introduced in the previous chapter.

3.4. Materiality Perspective

In this section, I expand upon the discussion on materiality and objects from the practice-based perspective (e.g., Carlile, Nicolini, Langley, & Tsoukas, 2013), which I have found increasingly relevant to studying resourcing. Although the materiality perspective is not central to any of my studies, I briefly discuss some of the key ideas of the materiality literature as I mention them in the future research agenda chapter. While I define objects as both material and nonmaterial assets as described in the resourcing perspective (e.g., Feldman, 2004; Sonenshein, 2014), in the materiality literature, objects refer to "the collection of artifacts that individuals work with—the numbers, blueprints, faxes, parts, tools, and machines that individuals create, measure, or manipulate" (Carlile, 2002, p. 446).

While the idea that theoretical perspectives in management should include materiality and objects dates back to earlier studies on "socio-technical systems" (STSs; e.g., Pickering, 1995; Trist & Bamford, 1951), the language turn in social sciences has directed attention to interpretations or discourses while reducing the attention on materials and objects. Responding to the critiques provided by studies in social sciences, including Barad (2003) and Knorr-Cetina (1997), practice-based scholars have brought the materiality back in studying organizational phenomena—technology, in particular (e.g., Carlile, 2002, 2004; Carlile et al., 2013; Orlikowski, 2007; Orlikowski & Scott, 2008). A practice-based perspective on materiality and objects introduces the idea that "the social and the material are

considered to be inextricably related—there is no social that is not also material, and no material that is not also social" (Orlikowski, 2007, p. 1437).

The materiality literature proposes three insights that I find particularly relevant to my studies. First, in line with the view that objects, from a resourcing perspective, are valuable when they are enacted through schemas (Feldman, 2004), an object matters "as a consequence of its web of relationships and the relational movements that it enables" (Endrissat & Noppeney, 2013, p. 60). Thus, the value of objects depends on the situational relationships among a network of actors as well as the relationship between actors and objects (Law, 2002). An object that is valuable in one situation might not be valuable in another (Carlile, 2002), and its use can also change over time (Nicolini, Mengis & Swan, 2012). In other words, in addition to the assertion from the resourcing perspective that an object only becomes valuable when it is enacted through practices (Feldman, 2004; Feldman & Worline, 2011), its value also depends on the fit between situational requirements (e.g., boundaries) and the material constitution of an object (Endrissat & Noppeney, 2013). Thus, objects interact with spaces they are embedded in and that "are political . . . because they set limits to the conditions of object possibility" (Law, 2002, p. 102).

Second, objects can be epistemic beings, and knowledge can be inscribed in objects because knowledge practices are often concentrated around objects (Knorr-Cetina, 1997; Nicolini, 2013). Similar to Knorr-Cetina's (1997) argument, "objects become epistemic when they embody what one does not yet know" (Nicolini et al., 2012, p. 614). Finally, there is a finite number of possibilities for an object to get new uses through human action; "no amount of creativity can permit a toaster to be used as a cell phone" (Jarzabkowski & Pinch, 2013, p. 582; Pentland & Feldman, 2008). Thus, as the materiality literature acknowledges, the materiality of an object matters (Carlile et al., 2013). In the next chapter, I introduce theories I used in Study II.

4. PRACTICES AND ORGANIZATIONAL ARRANGEMENTS

I investigated the relationship between practices and resources in Study I of this dissertation, and in this chapter, I explore the mutual constitution between practices and organizations in Study II. When I was conducting my field research to investigate drug repurposing for Study I, I increasingly began to realize that some types of practices are hosted in certain types of organizations. To research this empirical hunch further, I started to look into the literature on organizational arrangements for types of arrangements that are present under certain contexts, such as simultaneous market and government failures in the case of Study II, and then provide a practice theory lens to study these organizational arrangements. In this chapter, I introduce organizational arrangements that are present under simultaneous market and government failures and then briefly discuss the motivation behind introducing a practice lens to study organizational arrangements.

4.1. Market and Government Failures and Organizational Arrangements

Market failures refer to a situation where the allocation and distribution of goods and services are not Pareto efficient—that there is a way to reallocate and redistribute goods and services by benefiting some actors without harming others (Bator, 1958; Krugman & Wells, 2006). Market failures often stem from information asymmetries and inefficient and incomplete markets (Bator, 1958). Thus, market failures result in situations where a group of actors (e.g., consumers) cannot benefit from goods and services due to inefficiencies in the distribution of goods and services.

Studying market failures raise a critical question in understanding major societal challenges, such as clean energy, food security, and access to healthcare, as the existence of market failures might imply that markets are not efficient in addressing the needs of a group of consumers. Indeed, economics and management scholars have long sought answers to understand which types of organizational arrangements can be effective in correcting market

failures (e.g., Appold, 2004; Krugman & Wells, 2006; Santos, 2012; Stiglitz, 1989). A typical mechanism for correcting market failures is public-sector involvement (Stiglitz, 1989). One commonly studied arrangement for resolving market failures through public-sector involvement is public–private partnerships (e.g., Appold, 2004; Hagedoorn, Link & Vonortas, 2000; Zervos & Siegel, 2008).

Proponents of the public–private perspective argue for three cases where partnerships between public institutions (e.g., governments, public universities) and private (e.g., companies) can be effective. First, early-stage technology development is typically resource intensive, and private actors might not have sufficient resources at the early stages of the technology development processes (e.g., space exploration). Second, despite a high public need, for instance, in certain areas of healthcare, incentives might not be in place for private actors to enter a market. Third, there might be high expected social benefits in investing new technologies (e.g., clean energy technologies). Under these three cases, public–private partnerships can be an effective mechanism for resolving market failures (Appold, 2004; Hagedoorn et al., 2000; Siegel & Zervos, 2002; Zervos & Siegel, 2008).

Governments, however, might not always have sufficient influence for resolving market failures. Because actors in public institutions do not necessarily have more information than private actors, information asymmetries underlying market failures, therefore, can persist (Stiglitz, 1998). Moreover, governments might not foresee all possible market failures and also might not have sufficient resources or the ability to resolve market failures; therefore, the governments' lack of capacity to solve market failures can result in government failures (Williams & Coase, 1964; Stiglitz, 1998; 2008). The literature on social entrepreneurship (e.g., Luo & Kaul, 2019; Mair & Martí, 2006; Miller et al., 2012; Santos, 2012; Seelos & Mair, 2005) indicates that social entrepreneurship can be an effective mechanism under simultaneous market and government failures to "provide a distributed

mechanism for society to identify neglected problems with positive externalities, develop innovative solutions to address them and, often, change institutional arrangements so that the externality becomes visible and is internalized" (Santos, 2012, p. 348).

Social entrepreneurship, or "entrepreneurial activity with an embedded social purpose" (Austin, Stevenson & Wei-Skillern, 2006, p. 370), and related nonprofit arrangements primarily focus on creating social gain rather than capturing private gains (Santos, 2012). To date, social entrepreneurship and nonprofit literature has provided important insights into the underlying causes of major societal challenges and potential forms of organizational arrangement under simultaneous market and government failures (e.g., Johnson & Prakash, 2007; Luo & Kaul, 2019; Santos, 2012; Weisbrod, 1991; 1997). However, we know little about what actors in such organizational arrangements do to achieve social gains and to solve market and government failures. To address this question, my coauthors and I introduced a practice theory perspective to understand how actors prioritizing social gains over private gains resolved market and government failures in the societal challenge of rare diseases in Study II of this dissertation.

According to MacIntyre's view on social practices, practices are essential for an organization's existence (Geilinger, 2016; MacIntyre, 1981). A MacIntyrean perspective on practices highlights that

> any coherent and complex form of socially established cooperative human activity through which goods internal to that form of activity are realized in the course of trying to achieve those standards of excellence which are appropriate to, and partly definitive of, that form of activity, with the result that human powers to achieve excellence, and human conceptions of the ends and goods involved, are systematically extended. (MacIntyre, 1981, p. 187)

In Study II, by highlighting the notion of standards of excellence in the MacIntyrean perspective on practices, my coauthors and I investigate the question of what organizational actors do to circumvent the market and government failures underlying societal challenges.

5. EMPIRICAL CONTEXT

All three studies in this dissertation investigate empirical contexts in the pharmaceutical industry. In the first study, I analyze an increasingly common practice in the pharmaceutical industry—drug repurposing, which refers to identifying additional disease indications of existing drugs. In the second study, I analyze a context in which field participants repurpose off-patent (generic) drugs to develop treatments for rare diseases. For this concept, I collected data from two nonprofit companies, Cures Within Reach and Findacure, to investigate how their practices enhance generic repurposing practices for rare diseases. In the last study, I focus on an empirical question about project termination by analyzing 11 drug projects in the postmenopausal osteoporosis therapeutic area to identify factors influencing delays in termination decisions during the drug discovery processes. In the following sections, I provide a summary of the empirical contexts I analyzed in the studies of this dissertation.

5.1. Pharmaceutical Industry

Drug discovery and development in the pharmaceutical industry is known to be a knowledge-intensive process that involves the knowledge integration of multiple researchers from different disciplinary backgrounds (Ben-Menahem, von Krogh, Erden & Schneider, 2016). Despite rapid scientific and technological developments in the last century, the drug discovery and development process remains a lengthy and costly process. DiMasi, Grabowski, and Hansen (2016) estimate that developing a single drug costs, on average, $1395 million and can take about 12 years to do so (Smith, 2003).

Recently, there is an increasing concern about surging R&D costs due to high attrition rates in the pharmaceutical industry. Around 95% of drug candidates fail in clinical trials despite increasing levels of investment (Arrowsmith & Harrison, 2012). Some of the reasons often attributed to the productivity crisis in the pharmaceutical industry include increasing

complexity of the drug discovery and development process as easier-to-discover drugs ("low-hanging fruits") are already on the market and increasing standards of clinical trials (Arrowsmith & Harrison, 2012). The industry is seeking remedies to cope with decreasing R&D efficiency and industry profits.

All the studies in this dissertation relate to issues that have emerged as a response to the productivity crisis and the lack of treatments for certain groups of patients in the pharmaceutical industry. While Study I and Study III propose complementary practices to increase the number of treatments in the market, Study II relates to a societal grand challenge of rare diseases, where patients facing difficulties having treatments for their diseases.

5.2. Drug Repurposing

Historically, field participants in the pharmaceutical industry have discovered new drugs by studying traditional cures, such as plant-derived extracts, or through fortuitous findings. Modern drug discovery, however, started with developments in chemistry at the end of 19th century. Focusing on beneficial therapeutic outcomes, field actors in the pharmaceutical industry generally lacked a deep understanding of the biological mechanism of action (i.e., the process linking drugs and their targets in the human body) that underlies the desired therapeutic effect. Limited understanding about why a certain drug works in the human body has resulted in a drug discovery and development process that is often serendipitous. Indeed, penicillin, one of the most important drugs in the history of the pharmaceutical industry, was discovered serendipitously by Alexander Fleming in 1929. Later, other serendipitous discoveries such as thalidomide and Viagra entered the pharmaceutical industry market.

Following scientific advances in computational chemistry and molecular biology in the late 20th century, however, scientists began to develop a deeper understanding of disease-causing genes and proteins. In particular, the human genome project—an international

research effort to sequence and map all of the genes in the human body—revolutionized the development of new therapeutic methods. The pharmaceutical industry has shifted more and more toward a "rational" drug discovery and development process, whereby field participants first identify candidate drug compounds based on the biochemical properties of diseases then test the compounds in clinical trials (Drews, 2000). In the process of drug repurposing, however, instead of starting from a disease and discovering a novel drug for that disease, researchers attempt to identify existing drugs that can have a positive therapeutic effect on different disease indications.

Given the complex nature of scientific problems being addressed in the drug discovery and development process, a high percentage of new drug candidates fail to reach the pharmaceutical industry market. Although candidate compounds might fail to demonstrate efficacy in treating a disease of interest, they might still be safe for patient use and might be efficacious in treating other diseases. Indeed, some experts estimate that over 90% of drugs on the market are approved for indications other than those for which they were initially developed and used (Frail & Barratt, 2012; Gelijns, Rosenberg & Moskowitz, 1998).

In the last few decades, field actors in the pharmaceutical industry have started to recognize the potential value of drug repurposing and to consider it as a potential remedy for decreasing R&D efficiency and profitability in the pharmaceutical industry. Because field participants can start the drug discovery and development process from an existing drug, drug repurposing can make the discovery of drugs "cheaper, quicker and less-riskier." Thus, drug repurposing has become an increasingly used practice in the pharmaceutical industry. In Studies I and II, I focus on the practice of drug repurposing. More specifically, in Study I, I delve into the practices of drug repurposing, and in Study II, I show how field actors perform repurposing off-patent (generic) drugs to increase the number of treatments for rare diseases.

5.3. Rare Diseases

A rare disease refers to a disease that only affects a limited number of people in a population (Schieppati et al., 2008). The definition of rare diseases varies from one country to another; for instance, they are defined in the United States as diseases that affect less than 200,000 people and, in the European Union, less than 5 in 10,000, although the majority of rare diseases affect much fewer people (Aronson, 2006). It is estimated that nearly 7,000 rare diseases affect 25 to 30 million people in the United States (Griggs et al., 2009) and 30 million people in Europe (Wästfelt, Fadeel & Henter, 2006).

Rare diseases are often genetic and chronic conditions that cause physical and mental disabilities that significantly impact life expectancy and life quality of patients. Around 50% of rare diseases affect children (Wright, FitzPatrick & Firth, 2018). Because most rare diseases are hereditary conditions, a rare disease might be a common condition in a family but be uncommon in society. This imposes a significant burden on families with rare diseases by limiting their economic and social opportunities (Schieppati et al., 2008). Despite the challenges imposed on the patients, families, and society by rare diseases, historically, most of the rare diseases were left unattended by the pharmaceutical industry due to their small market size.

In the last 30 years, following an increase in public awareness about rare diseases, governments started introducing regulatory incentives to enhance the development of drugs for rare diseases. The U.S. government introduced the Orphan Drug Act in 1983, and other countries also introduced similar acts, including Japan in 1985, Australia in 1987, and the European Community in 2000 (Aronson, 2006; Lavandeira, 2002). The governments commonly introduced regulatory incentives about rare diseases around three categories: publicly funded research and tax benefits, access to fast-track regulatory approval processes, and extended market exclusivity for drugs with an effect on rare diseases (Arronson, 2006).

Although the regulatory incentives have had a positive effect on the increase of drugs approved for rare diseases, the field actors agreed that the regulatory incentives have not been sufficient in providing necessary momentum for the drugs' development (Haffner, Torrent-Farnell & Maher, 2008).

Field actors in the pharmaceutical industry often highlighted the potential benefit of using repurposing practices to increase the number of treatment options for rare diseases (Melnikova, 2012). In particular, field actors considered the discovery of potential rare disease indications of generic drugs as a beneficial approach because the drugs are already on the market and patients can access them at a cheap cost (Muthyala, 2011). During my fieldwork on drug repurposing (Study I), I realized that some nonprofit organizations enhance repurposing practices for rare diseases by collaborating with other actors in the pharmaceutical industry. Departing from this empirical hunch, I analyzed how the practices of two nonprofit organizations, Cures Within Reach and Findacure, have been successful in enhancing treatment options for rare diseases.

5.4. Delays in the Termination Decisions of Drug Projects

Drug discovery and development literature has suggested that factors such as incentive mechanisms and the lack of a stopping culture in pharmaceutical companies often lead to delays in termination decisions about drug development projects (Kola & Landis, 2004; Paul et al., 2010; Peck et al., 2015). Given that the drug development process is a costly process, delays in termination decisions result in loss of financial and human resources and contribute further to decreasing profits in the pharmaceutical industry. Study III investigates the factors underlying the delays in termination decisions by analyzing 11 drug projects in the postmenopausal disease area.

6. OVERVIEW OF THE STUDIES

This dissertation consists of three coauthored studies to analyze a highly complex knowledge creation process in the pharmaceutical industry and, specifically, to investigate a novel practice of repurposing, the mutual constitution between practices and organizations in a societal grand challenge setting, and challenges in termination decisions in the process of developing resources-in-use from objects. While Studies I and II focus on the practice theory perspective, Study III takes on a more general perspective in identifying challenges in the resource creation process by targeting a practitioner audience. Figure II illustrates each study by focusing on the journey of drugs from being objects to resources-in-use.

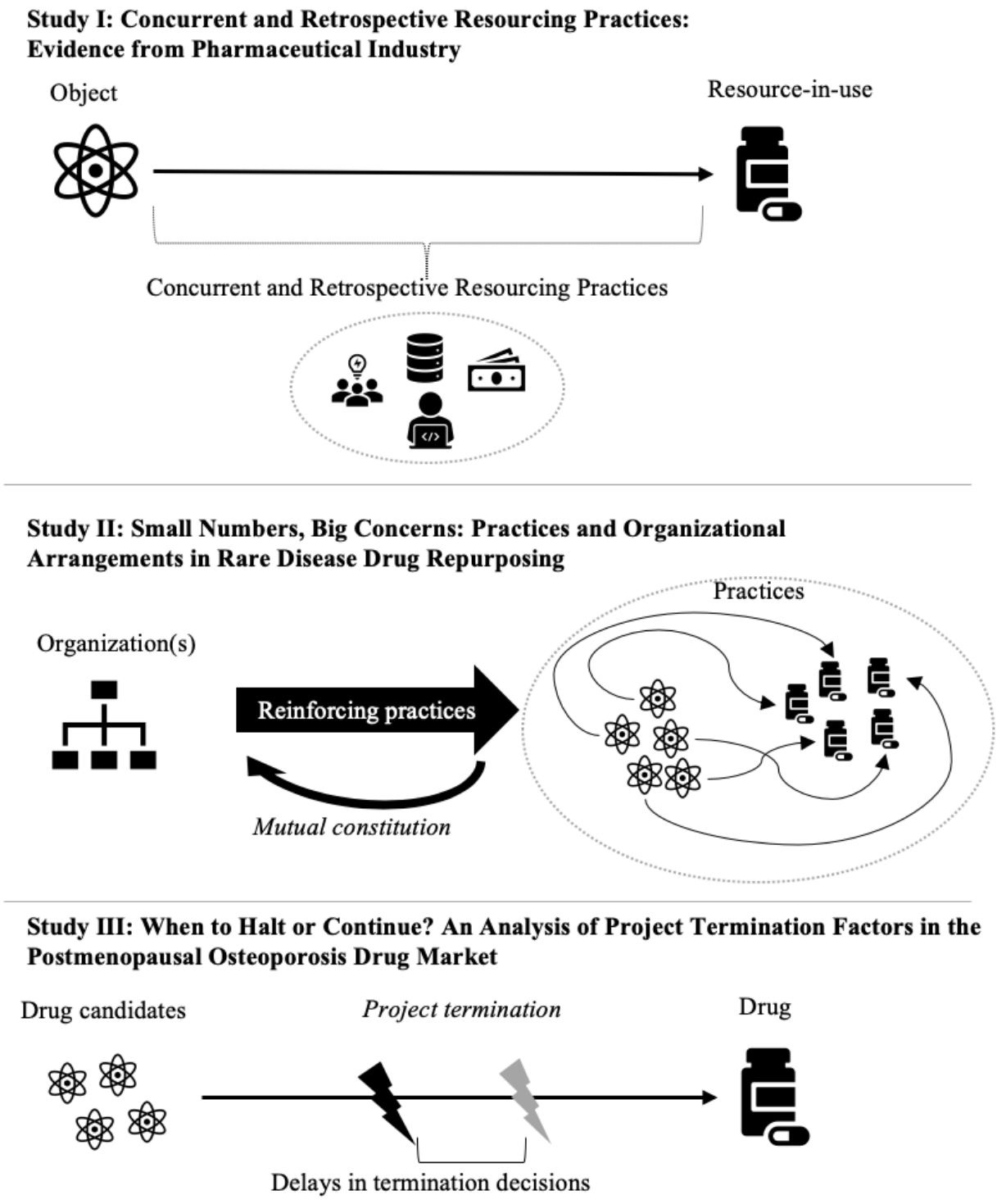

Figure 2: Overview of Studies

6.1. Summary of Essay I: Concurrent and Retrospective Resourcing Practices: Evidence from Pharmaceutical Industry

Coauthors: Shiko Ben-Menahem, Georg von Krogh

6.1.1. Motivation and Research Question

The purpose of this study is to investigate how existing objects (i.e., tangible and intangible assets that field actors act on) become resources-in-use from a practice theory perspective on resources (Feldman, 2004; Feldman & Worline; 2011; Sonenshein, 2014). To address the lack of process explanations about value creation processes in past works on resources (Priem & Butler, 2001a, 2001b) and to challenge the assumption that resources are valuable because of their innate characteristics (Barney, 1991, 2001; Pfeffer, 1982; Salancik & Pfeffer, 1978), Feldman (2004) develops a practice theory perspective on resources, resourcing perspective, by defining a resourcing cycle.

Feldman (2004) argues that resources only become valuable when they are put into use. Thus, practices through which field actors uncover the values of resources are central to the resourcing perspective (Feldman & Worline, 2011). To date, most of the studies on the resourcing perspective have focused on the role of emergent, often improvisational, resourcing practices in the change process and in triggering the change (Feldman, 2004; Howard-Grenville, 2007; Nigam & Dokko, 2019; Quinn & Worline, 2008; Sonenshein, 2014; Wiedner et al., 2017). However, some scholars argue that the actors' perception about the perceived use of resources can direct resourcing processes (Wiedner et al., 2017). To explore this insight further, this study investigates a novel practice in the pharmaceutical process, drug repurposing, to produce insights into the processes whereby existing resources gain new use values as a result of systematic processes. In analyzing this question, I (together with my coauthors) draw on a differentiation made by Bowman and Ambrosini (2000, 2010) on the definition of value of resources as use and exchange value.

6.1.2. Methodological Approach

In this study, we adopted an inductive and qualitative single-case study approach (Yin, 2003) based on the analysis of the field of drug repurposing (i.e., discovering additional disease indications in existing drugs). The main data source of this study comprises 52 formal and 15 informal interviews[1] with field actors spanning various organizations, including big pharma companies, small companies focusing on drug repurposing, and academia. We complemented the dataset with presentations from field-configuring events, field notes from the events, as well as secondary data such as scientific publications and books on drug repurposing.

6.1.3. Findings and Contributions

Based on an analysis of the practices found in the drug repurposing field, we develop a framework on the repurposing process, which is a form of resourcing processes, and identify two temporal modes of repurposing practices: concurrent and retrospective repurposing. We show that the following three mechanisms, which are schemas in resourcing cycles, differentiate between the two temporal modes: decay of knowledge about objects, ownership of objects, and potential exchange values of objects.

The study makes several contributions to the resourcing perspective by developing a framework on intentional repurposing processes and demonstrating the relationships between the field actors' schemas derived from a context wherein they perform practices and uncover new use values for existing resources. The study also has implications on practices involving technology and innovation practices on repurposing.

6.1.4. Contribution of the Author

I (and occasionally accompanied by one of my coauthors) collected all the data and performed the data analysis. I developed the theoretical lens and framework together with my

[1] 15 informal interviews are also part of the dataset of Study II.

two coauthors. I also developed initial drafts of the study, and was involved in every stage of the writing process.

6.1.4. Publication Status

The study is planned to be submitted to *Administrative Science Quarterly*.

6.2. Summary of Essay II: Small Numbers, Big Concerns: Practices and Organizational Arrangements in Rare Disease Drug Repurposing

Coauthors: Shiko Ben-Menahem, Georg von Krogh

6.2.1. Motivation and Research Question

Although repurposing off-patent (generic) drugs could potentially be a promising practice in developing treatments for rare diseases, which are largely neglected by commercial R&D due to small market sizes, neither the market nor government activities are sufficient enough to capture the positive externalities of generic drugs. Thus, market and government failures persist in rare disease markets (Santos, 2012). Departing from our empirical hunch in Study I that some nonprofit organizations are successful in circumventing market and government failures, we adopt a practice theory perspective to understand their approaches to circumvent failures.

6.2.2. Methodological Approach

Similar to Study I, I (together with my coauthors) adopted an inductive, qualitative single-case study approach in this study. First, we conducted 23 interviews with field actors in the rare disease drug repurposing field, and then we extended our interviews with five more actors from the nonprofit organizations we analyzed, Cures Within Reach and Findacure.

6.2.3. Findings and Contributions

From our findings, we developed a theoretical framework (reinforcement) based on MacIntyre's (1981) social practice theory. The study provides insights on the mutual constitution between practices and organizations in a societal challenge context. The study further demonstrates that a practice theory perspective could potentially be a useful lens in studying societal grand challenges and provides implications for the social entrepreneurship theory (Luo & Kaul, 2019; Santos, 2012).

6.2.4. Contribution of the Author

I was involved in the data-collection process (which was partially collected by a master's student whom I supervised and I was largely involved in the development of the thesis) and analyzed data. I also developed the initial version of the paper submitted to the journal (where we published the study), and was also involved in every stage of the writing process. For theoretical background and development, I shared the tasks with my coauthors.

6.2.4. Publication Status

The study is published in *Academy of Management Discoveries*.

https://doi.org/10.5465/amd.2018.0183

6.3. Summary of Essay III: When to Halt or Continue? An Analysis of Project Termination Factors in the Postmenopausal Osteoporosis Drug Market

Coauthors: Tino Anthamatten, Shiko Ben-Menahem, Juerg Gasser, Georg von Krogh, Joerg Goldhahn

6.3.1. Motivation and Research Question

This study is driven by our motivation to understand stopping decisions in the R&D process. Although the study primarily targets the practitioner audience in the pharmaceutical industry and aims to contribute to the translational science literature in drug discovery and development, the study lays the groundwork for future studies on the topic of interest as well as enhances our knowledge on the pharmaceutical innovation processes.

In the pharmaceutical industry, it is widely known that there are delays due to scientific, organizational, and cultural factors in giving termination decisions about drug projects (Paul et al., 2010; Peck et al., 2015). Scholars in the drug development field often associate such delays with the progression-seeking behaviors of actors in drug projects (Peck et al., 2015). To investigate this issue further, this study aims to identify factors catalyzing progression-seeking behavior in the drug development processes.

6.3.2. Methodological Approach

Similar to Studies I and II, this study takes an inductive, qualitative research approach to analyzing data. The primary data source of this study includes 21 semi-structured interviews with researchers and managers who have worked in drug projects in the postmenopausal osteoporosis therapeutic area, which we focused on because of two reasons. First, all drug projects are closed in the postmenopausal disease area; thus, there is not much activity left in this therapeutic area. Second, two of my coauthors (Juerg Gasser and Joerg Goldhahn) are known experts in the therapeutic area, and this helped us to have a comprehensive understanding of the therapeutic area as well as activities and actors in it.

6.3.3. Findings and Contributions

We identify four factors catalyzing progression-seeking behavior in drug development projects. The study demonstrates that a biased interpretation of competitive factors and market sizes, abundance of resources, empty pipelines of companies, and individual attachment to drug projects are factors that further result in progression-seeking behavior. The study contributes to the drug development literature and has a number of implications for practice.

6.3.4. Contribution of the Author

I am largely involved in the data analysis process. I also handled research design, developed the framework, and wrote up the study.

6.3.4. Publication Status

The study is planned to be submitted to *Nature Reviews Drug Discovery.*

7. CONCLUSION, LIMITATIONS, AND FUTURE RESEARCH

The studies in this dissertation have several implications for future research that are discussed in depth in full-length versions in the Appendices. In this chapter, I focus on the limitations of conducting research in the empirical contexts I studied, as well as the broader future research agenda that the studies in this dissertation imply. I also discuss potential future research avenues based on Study III by asking how this study could be framed from the management theory perspective.

The first set of limitations of the studies in this dissertation relates to specific features of the pharmaceutical industry. The pharmaceutical industry is a highly regulated industry, where value capture from resources is strongly connected to intellectual property rights. The regulated nature of the industry has implications not only for the value capture from resources but also the behavior of field actors. For example, in all of the studies, we observed that knowledge-sharing behavior is highly restricted and secretive, especially in the case of big pharma companies. This limits the potential value creation and capture from existing resources by external parties to an organization, as in the case of drug repurposing, since accessing the existing resources of organizations might imply sharing trade secrets and highly protected ideas. Even in the case of academic research, researchers often face limitations in publishing their results in the academic community because publications might imply a nonpatentability issue in the future. Thus, a natural departure point for the studies in this dissertation, Study I and Study II in particular, is to extend our implications to and test our results in other empirical contexts.

Future studies can extend our implications in two ways, empirically and theoretically. First, by taking a similar theoretical practice theory lens, future scholars can test the boundary conditions of our implication in Study I and II. Second, by taking a slightly different theoretical approach, future studies can investigate how different theoretical lenses are

effective in explaining similar phenomena that we investigated in the studies, Study I in particular. Some of the relevant theoretical lenses to Study I include, but are not limited to, the knowledge reuse perspective (e.g., Majchrzak, Cooper & Neece, 2004; Haefliger, von Krogh & Spaeth, 2008), exaptation literature (e.g., Dew, 2009; Garud, Gehman & Giuliani, 2018), and bricolage (e.g., Baker & Nelson, 2005). Future studies are needed to fully explore these relationships. However, this approach of looking at a question from different theoretical lenses implies having to go through the assumptions underlying each theoretical lens thoroughly. For example, to a large extent, the practice lens is not present in studies of bricolage or knowledge reuse or the exaptation literature. In my view, adopting a different lens might imply a fundamental shift in the basic principles of practice theory, the structuration principle in particular. However, I argue that other theoretical lenses could still have important insights that can benefit practice scholars.

A second future research avenue that I have increasingly found intriguing and potentially useful is conducting studies with a stronger emphasis on the theoretical perspectives on materiality and material objects. Here, the pharmaceutical industry has several advantages to studying materiality and objects. Drugs might constitute objects that make it effective to study materiality. In pharmaceutical innovation processes, drugs are one obvious material object to study, although there can be many others (e.g., machinery, technologies). Because drugs are carriers of knowledge and practices are organized around drugs, the pharmaceutical industry can be a relevant research setting for future materiality research.

Similar implications in relation to the pharmaceutical industry being a regulated industry impose limitations on the results of Study II, as we discussed in the original manuscript of the paper (see Appendix). In addition to future research avenues we discussed in the original manuscript, I suggest that there are additional benefits of using a practice

theory perspective in studying societal challenges, social entrepreneurship in particular. While conducting Study II, we realized that the practice theory lens is largely absent in the nonprofit and social entrepreneurship literature. Some studies use practice theory lens from an empirical perspective (i.e., analyzing practices) (e.g., Shaw & Carter, 2007); however, I argue that scholars in social entrepreneurship literature should more closely link their studies to the theoretical principles of the practice theory. For example, using the relationality assumption of practice theory in Study II enabled us to identify the mutual constitution between organizational arrangements and practices. Hence, scholars in future studies should not only study practices but also study them in relation to other concepts such as schemas and resources. In particular, given that social entrepreneurship literature deals with ethical issues, a MacIntyrean social practice perspective could offer important insights to future studies on social entrepreneurship.

Although Study III is not primarily intended for scholars in management research, it still promises several implications to management research and opens new research avenues, as the core concern in Study III is a highly relevant organizational problem. Although there are studies in management literature investigating similar issues about project termination decisions from a cognitive biases perspective and employing concepts such as information filters, which blur the perception of actors in interpreting information, (e.g., Van Oorschot, Akkermans, Sengupta & van Wassenhove, 2013), project-termination decisions can be studied from a practice theory perspective and in materiality research in particular. For example, Knorr-Cetina (1997) proposes several insights about actors in knowledge creation processes, often in scientific settings, and their relationships with objects of interest. Indeed, in a study on objects and emotion, Endrissat and Noppeney (2013) report from their field notes, “Personal attachment, intimacy, and projection characterize the relationship between the concept and the creative director” (p. 72). Actors closely identify themselves with objects

because their activities are organized around objects and their expertise is also inscribed in these objects. This also implies that actors are unwilling to give up objects as they build connections with them. Indeed, one of the factors we identified in Study III that catalyzes progression-seeking behavior is the attachment of actors to drugs; the actors often say that making termination decisions about drug projects feels "as if giving up their baby." Hence, I suggest that future studies can look closer to the relationship between objects and actors working on the objects, and delays in project-termination decisions.

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9. APPENDICES: STUDIES AND CV

Concurrent and Retrospective Resourcing Practices:

Evidence from Pharmaceutical Industry

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Abstract

Understanding how resources obtain value is a central question in strategy and organization theory. The literature on the resourcing perspective proposes that objects become valuable resources in practice—that is, through practices field participants undertake to make objects useful. Prior work acknowledges that field participants' schemas about the perceived value of objects drive them to engage in specific practices and objects for repurposing, yet few studies explain how field participants can uncover new use values of objects. Building on an inductive study of drug repurposing—an emerging problem-solving approach in the field of drug discovery aimed at finding novel uses for existing drugs—we explain how objects can obtain new use values. By describing two temporal modes of repurposing, concurrent and retrospective, we develop a model of repurposing processes whereby field participants explore and effectuate new uses of existing objects by using tools and technologies and turn them into valuable resources in practice.

Keywords: resourcing, repurposing, problem-solving, field, drug discovery.

How organizations create value from resources is a core question in management practice and research. Strategy and organization theory scholars have long sought to understand how the availability, ownership, and redistribution of resources enables organizations to create value (Barney, 1991; Barney, 2001; Pfeffer, 1982; Salancik & Pfeffer, 1978). Extending this line of research, scholars have recently increased their focus on the processes whereby actors enact resources to create value (Deken, Berends, Gemser, & Lauche, 2018; Feldman & Orlikowski, 2011; Feldman & Worline, 2011; Wiedner, Barrett & Oborn, 2017). Taking a practice-based perspective, studies on the resourcing perspective explain how individuals turn potential resources (i.e., objects, tangible and intangible assets that field participant act on) into "resources-in-use" (e.g., Feldman, 2004; Feldman & Worline, 2011; Howard-Grenville, 2007; Sonenshein, 2014; Wiedner et al., 2017). In this line of research, resourcing is conceptualized as an emergent process wherein the relationships between schemas, potential resources, and practices shape the value of enacted resources (Feldman, 2004).

While prior research on the resourcing perspective illuminated insights into various organizational phenomena, including change processes (Feldman, 2004; Howard-Grenville, 2007; Kannan-Narasimhan & Lawrence, 2018; Nigam & Dokko, 2019; Quinn & Worline, 2008; Sonenshein, 2014; Wiedner et al., 2017), the processes whereby objects become resources-in-use by gaining new use values remain poorly understood. In this study, by drawing on a practice perspective on resources, the resourcing perspective (e.g., Feldman, 2004; Feldman & Worline, 2011, 2016), we develop a model of repurposing, the processes whereby field participants identify new uses of an object (e.g., taking a ladder and repurposing it as a bookshelf). Here, we draw on the distinction made by Bowman and Ambrosini (2000, 2010) in defining the value as *use value* and *exchange value*. Whereas use value refers to the "properties of products and services that provide utility," exchange value

refers to the "monetary amount exchanged between a firm and its customers and suppliers when UVs [use values] are traded" (Bowman & Ambrosini, 2010, p. 480). Thus, we study the question of how existing objects gain new use values.

Using a field study of a practice in drug discovery and development in the pharmaceutical industry known as drug repurposing, we explore how field participants uncover additional disease indications of existing drugs. Drug discovery is known to involve a costly and lengthy process of interdependent problem-solving efforts by specialists from a wide range of scientific disciplines including chemistry, biology, and pharmacology (Ben-Menahem, von Krogh, Erden & Schneider, 2015). Given the complex nature of the scientific problems addressed in drug discovery, a high share of candidates for a new drug fails to reach the market due to either a lack of efficacy or safety concerns. About 1 in 6 compounds nominated as a candidate compound makes it into clinical trials, out if which 1 in 12 successfully finds its way through clinical development to the market (Waring et al., 2015). Failed drug candidates are shelved in so-called "compound libraries," and information about them is stored in company databases and disseminated to the industry through publications, patents, and clinical trial reports.

Drawing on the understanding that a single drug compound can be effective in treating multiple disease indications, field participants have recently increased systematic efforts to identify additional uses of existing drugs—a practice known as drug repurposing. Drug repurposing has become an increasingly important practice in the pharmaceutical industry as the decreasing R&D returns in the pharmaceutical industry have led field participants to seek out alternative practices to develop drugs for unmet medical needs. Field participants engage in drug repurposing to develop drugs more cheaply, more quickly, and with lower risk. Using a multiyear field study of drug repurposing, we investigated practices whereby field participants uncovered new uses of existing drugs. Drug repurposing is not

associated with one particular company or research organization, but instead emerged as a novel approach to drug discovery at the field level. Accordingly, we approached our analysis of the processes of drug repurposing by focusing on the broader field level.

From our findings, we developed an integrative theoretical framework of repurposing practices. Our analysis of drug repurposing revealed that an increasing understanding of scientific mechanism behind drug repurposing has led field participants to develop intentional (systematic) practices of repurposing existing drugs. We identified two temporal modes of repurposing practices based on a differentiation on the timing of repurposing. Whereas *retrospective repurposing* refers to repurposing an existing object that was developed in the past and is either in use for another purpose or not in use (i.e., the scrap or junk of an initial process), *concurrent repurposing* refers to the process of constantly checking for additional use values of an object that is in the development process. Our theoretical framework shows that timing affects the temporal mode of repurposing practices as retrospective or concurrent through three mechanisms that relate to knowledge decay, object ownership, and potential exchange values of resources-in-use.

Our study has important implications for management theory and practice. In the age of big data and digital technologies (see for example George, Osinga, Lavie & Scott, 2006; Henfridsson, Nandhakumar, Scarbrough & Panourgias, 2018), we have both an increasing amount of digital resources (data points, programs, etc.) and an increasing possibility of digitalizing knowledge about organizational resources. Our findings show that the availability of practices using technology co-created repurposing practices by leading to the creation of a space in which it is possible to store and use knowledge about existing objects as well as algorithms uncovering the relationships between existing objects and their potential new uses. We also show that intentional practices can be used to uncover unexpected (i.e., novel) uses of existing objects. While field participants historically uncovered unexpected uses of

resources through serendipitous events, we argue that performing problem-solving practices by using algorithms in an unbiased manner (non-hypothesis driven) may lead to unexpected associations between an existing resource and its potential new use.

From our findings, we extend the resourcing perspective by developing a model of intentional resourcing processes, as well as showing how field participants' value perceptions derived from the context in which they are embedded drive resourcing practices (Wiedner et al., 2017). We also show the potential benefit of using a resourcing lens to study various innovation phenomena and technology-in-use.

THEORETICAL BACKGROUND

Resourcing: A Practice Theory Perspective on Resources

The resourcing perspective suggests that instead of viewing resources as fixed entities with innate qualities, resources should be seen as dynamic objects whose value depends on their use in their own contexts (Feldman, 2004; Feldman & Orlikowski, 2011; Feldman & Worline, 2011; Sonenshein, 2014). Although some scholars criticized earlier perspectives on resources for falling short in explaining value creation processes whereby value is generated from a resource (Priem & Butler, 2001a, 2001b), the resourcing perspective takes a practice-based approach to develop a dynamic account of the processes whereby a potential resource (object)—such as assets, skills, knowledge, money, time, trust, or qualities of relationships—becomes a resource-in-use, which is referred as a resourcing process (Feldman, 2004).

The resourcing perspective expands the definition of potential resources (hereafter, objects) to the tangible and intangible assets that field participants must act on (Feldman, 2004; Feldman & Worline, 2011, 2016; Sonenshein, 2014), and proposes a separation between objects and resources-in-use. This view acknowledges that objects do not become resources or resources-in-use until field participants act on them (Feldman, 2004; Feldman & Worline, 2011). While the traditional perspectives on resources often considered resources as

influencing rather than being influenced by practices of field participants (Barney, 1991, 2001; Pfeffer, 1982; Salancik & Pfeffer, 1978), the resourcing perspective acknowledges that the relationship between resources and practices are mutually constitutive (Feldman, 2004; Feldman & Worline, 2016). In this way, the resourcing perspective differs from the earlier perspectives on resources such as resource-based and resource dependency theories (Barney, 1991, 2001; Pfeffer, 1982; Salancik & Pfeffer, 1978), which consider resources as static entities (Feldman, 2004).

Feldman (2004) defines a resourcing cycle as a process where objects allow field participants to enact their schemas and perform practices to create resources from the objects. Departing from the relationality assumption in practice theory (Feldman & Worline, 2016), the resourcing practice highlights the interrelationship between objects, schemas, and practices (Feldman, 2004; Feldman & Worline, 2011, 2016). In resourcing cycles, schemas "map our experience of the world, identifying both its relevant aspects and how we are to understand them" (Bartunek, 1984, p. 355). To date, several studies have applied the resourcing perspective to study various organizational processes (Feldman, 2004; Feldman & Worline, 2011; Howard-Grenville, 2007; Howard-Grenville, Golden-Biddle, Irwin & Mao, 2011; Quinn & Worline, 2008; Sonenshein, 2014; Wiedner et al., 2017).

Feldman and Worline (2016, p. 312) point out that the resourcing perspective provides a powerful lens particularly "when [a] new schema is resourced or when schema that could not be pursued by established practices are made available through new practices." Indeed, a substantial literature has emerged on how a resourcing lens illuminate insights into change processes (Feldman, 2004; Howard-Grenville, 2007; Kannan-Narasimhan & Lawrence, 2018; Nigam & Dokko, 2019; Quinn & Worline, 2008; Sonenshein, 2014; Wiedner et al., 2017). Scholars particularly look into emergent and dynamic change processes in which the change was unexpected (e.g., Wiedner et al., 2017).

For example, by analyzing a strategic change process within the English National Health Service, Wiedner et al. (2017) explained the emergence process of strategic change in unexpected places of the organization triggered by strategic change initiatives. They argued that contrary to what is expected, the change did not happen in the parts of the organization where the resources were abundant. Instead, the lack of resources and attention in other parts of the organization resulted in free space for resourcing where field participants could enact their personal schemas and use resources freely. Furthermore, Wiedner et al. (2017, p. 40) suggest that "the value agents [field participants] associate with potential resources plays an important role in terms of shaping their willingness to associate themselves with them, appropriate them, challenge others, and participate in certain practices." Thus, they argue that resourcing processes can be directed by field participants' perceptions about potential values of objects.

Although past works have provided critical insights into understanding the change processes from a resourcing perspective, scholars have given little attention to the actual processes of how objects gain values. In recent years, two studies have outlined some practices relating to the processes of how objects gain values from a resourcing perspective (Deken et al., 2018; Sonenshein, 2014). In a study, Sonenshein (2014) explores the relationship between resource endowments and creativity by analyzing creative resourcing processes in a multiyear field study in a retail company. The study defines creative resourcing as a problem-solving practice where field participants manipulate and recombine objects "in novel and useful ways to solve problems" (Sonenshein, 2014, p. 2014). The study focuses on the relationship between the provision of different levels of resource endowments and creativity rather than unpacking problem-solving practices in creative resourcing.

In another study, Deken et al. (2018) investigate the process of establishing resource complementarities during interorganizational collaboration processes. Deken et al. (2018)

provides insights into the processes of how objects gain uses by identifying practices of prospective resourcing (resource exploration, envisioning resource use, and configuring resource) that mediate the interplay of strategizing and initiating collaboration. Since the motivation of field participants to initiate a collaboration is to seek for complementary resources that they do not have internally, field participants are often "in no position to assess what would be needed and to envision what could be accomplished with certain resources" (Deken et al., 2018, p. 43). Thus prospective resourcing practices entail experimentation activities rather than systematic practices of seeking particular resources.

While we know the general importance of processes of how objects gain new values in resourcing cycles (Deken et al., 2018; Sonenshein, 2014), a greater understanding may be gained by looking deeper into the practices underlying such processes. The purpose of this study is to investigate the practices of how existing objects become resource-in-use. Particularly, departing from the insight that resourcing processes can be directed (Wiedner et al., 2017), our study draws on a qualitative fieldwork on drug repurposing to illuminate how field participants uncover new uses of objects intentionally and systematically.

In investigating this question, we acknowledge three assumptions. First, while the resourcing perspective shifts the focus on processes of creating resources rather than innate qualities of resources, studies on the resourcing perspective acknowledge that objects have innate qualities that might limit the extent to which an object has potential as resources for particular uses (Feldman & Worline, 2016). Indeed, Pentland and Feldman (2008) suggest that "no amount of creativity can permit a toaster to be used as a cell phone" (Jarzabkowski & Pinch, 2013, p. 582). Second, past materiality research has highlighted that the social and material are entangled (Orlikowski, 2007), and the value of objects depends on the relationship between objects (i.e., materials) and the broader field-level dynamics (Bourdieu, 1990; Law, 2002; Nicolini, 2013).

Third, for explaining resourcing practices in drug repurposing, we draw on a differentiation that prior research has made in defining the value of resources (Bowman & Ambrosini, 2000, 2010). While the use value refers to the utilities that field participants can get by using a resource, the exchange value refers to the monetary gains that an organization can obtain by exchanging a resource in trade markets (Bowman & Ambrosini, 2000, 2010). Although uncovering new use values is central to the resourcing perspective, past works on the resourcing perspective did not explicitly specify the notion of value. Based on Bowman and Ambrosini's (2000, 2010) differentiation in the definition of value, we focus our analysis on uncovering new use values for existing objects.

METHODS

Case Selection and Overview

We adopted an inductive, single-case study approach that allows for an in-depth understanding of our research question (Yin, 2003). Ideal research settings are those in which the phenomenon of interest occurs in abundance (Eisenhardt, 1989; Yin, 2003). In the early stages of our investigation, we were guided by the question of how resources obtain new meanings through serendipitous discoveries. The history of the pharmaceutical industry is rich in examples of serendipitous discoveries. We decided to review historical case studies such as Viagra and conducted pilot interviews with drug discovery experts. As our data collection and analysis unfolded, we found that the discoveries of such drugs were far less serendipitous than we had expected. There were many intentional efforts and much scientific knowledge present during their discovery, and narratives of examples of serendipitous discoveries have led to a practice called drug repurposing[2]—the identification of additional disease indications of existing drugs in a systematic manner. We reasoned that such a

[2] Drug repurposing can also be called "drug repositioning." For the sake of simplicity, we stick to "drug repurposing" in our study.

revelatory case (Siggelkow, 2007) of drug repurposing might help us to elaborate theory on resourcing and decided to focus on drug repurposing.

Drug repurposing is an increasingly common phenomenon in the pharmaceutical industry. The actors in drug repurposing span various forms of organizations, including big pharmaceutical companies, small biotech companies focusing on drug repurposing, technology platform companies, and academia. There is also a growing community of practice organized around repurposing that publishes books (Frail & Barratt, 2012), forms professional LinkedIn groups, and organizes conferences. We also realized that there is a surge in the number of articles published on drug repurposing. For example, when we searched "drug repurposing" or "drug repositioning,[1]" on Web of Science, while there were only 20 articles published on drug repurposing in 2010, this number jumped to 454 in 2018. This increase is often attributed to the increasing availability of tools and technologies, and the promise of drug repurposing in potentially decreasing risk, duration, and cost of the drug development process (Pushpakom et al., 2019).

Drug repurposing provides a suitable case for studying repurposing for two reasons. First, there is a focal object (a drug) for which we were able to trace its origins, new uses, and practices of identifying new uses as an existing drug. Second, our early access to participants in the drug repurposing field, which is a subfield of drug discovery and development, enabled us to identify relevant actors, institutions, and events in the field of drug repurposing. An ability to understand the field enabled us to gain in-depth knowledge about the field itself, practices, and resources. Thus, we focused our data collection efforts on the practice and field of drug repurposing. For the rest of our study, we refer to drugs or compounds as objects, drug repurposing as a practice, the set of actors and institutions involved in drug repurposing as a field, and actors in the field of drug repurposing as field participants.

Data Collection and Sample

We started our data collection on the drug repurposing field with exploratory interviews with field participants. Our primary data source was 52 formal and 15 informal interviews with 57 key field participants between June 2015 and July 2019. We also collected archival data from scientific publications, books, company websites and publications, and news articles to establish the historical context of our empirical setting and develop our interview questions (Vaara & Lamberg, 2016). Table 1a shows an overview of the data sources and Table 1b shows an overview of informants. Table 2 illustrates the types of organizations involved in drug repurposing.

We used a purposeful sampling strategy in our data collection process (Patton, 2002). We started our data collection effort by establishing relationships with the main actors in the drug repurposing field during conferences, and by identifying critical informants from archival resources, publications, and networking websites. Because drug discovery is rooted in the scientific research domains of biology, chemistry, and pharmacology, the most significant discoveries are well-documented in scientific publications, patent filings, and records of regulatory authorities such as the U.S. Food and Drug Administration (FDA).

To increase our sample size, we applied two approaches. First, we identified an initial set of informants from archival resources, publications, and networking websites, and we asked each informant to recommend additional names. In particular, we largely relied on Naylor, Kauppi, and Schonfeld's (2015) analysis of key actors in drug repurposing. Second, we attended the main conference on drug repurposing at an early stage of our data collection. Conferences and networking events, are often considered as field-configuring events. Attending such events is a commonly applied approach to collect data and identify main discussions in field studies. Indeed, scholars have argued that such events are the places where field participants discuss the meaning of the field (Garud, 2008; Grodal, 2007; Meyer,

Gaba & Colwell, 2005) and manifest the "cognitive, social and political dynamics" of a field (Anand & Watson, 2004; Zilber, 2014, p. 103).

For each of the organization that we identified, we approached at least one key informant. We also obtained access to the contact details of all past participants of the main drug repurposing conference, and approached those involved in drug repurposing activities or who held critical positions as opinion leaders in the pharmaceutical industry. We also regularly checked networking websites such as LinkedIn groups to make sure that we involved all relevant parties. We continued to sample informants until our informants kept referring back to the same names, at which point we concluded we had reached saturation in our sampling of key informants. Not only did the informants start recommending the same people, but our theoretical insights also became saturated, and we ended our data collection efforts from interviews. In this way, we reached out to 57 informants. Interviews lasted between 45 and 120 minutes and were recorded and transcribed unless recording was not possible. For the interviews that we could not record, we used detailed interview notes for analysis.

We asked our informants to define drug repurposing in their own words, to explain how they started working on drug repurposing, to describe their daily drug repurposing activities, and to describe critical events and developments that influenced the emergence of drug repurposing practice. To keep the interviews close to the informants' practice, we asked for detailed accounts of their recent experiences (Miles & Huberman, 1994; Miller, Cardinal & Glick, 1997).

To validate our findings, we triangulated our insights from interviews with the archival materials, publications, discussions in networking websites, and our notes from informal meetings with drug discovery experts and conference presentations. We attended the main field conferences in 2015 and 2016. We had an opportunity to access the archive of

presentations of the conference between 2012 and 2016, totaling 68 presentations. We also attended an academic drug repurposing conference in May 2017 where a group of European academics discussed opportunities and methods of drug repurposing. Furthermore, to discuss our ideas and to validate our inferences from the data, we organized a roundtable discussion with 10 experts from a research unit of a major pharma company.

Data Analysis

We organized and coded our interview data using NVivo 9.0, a software for qualitative data analysis. During our data analysis, we took an iterative approach between data and theory (Locke, Golden-Biddle & Feldman, 2008). To analyze our interviews, we initially engaged in open coding of the interviews (Strauss & Corbin, 1998) and identified activities performed by field participants. We kept our initial codes close to the day-to-day reality of field participants. We took the practices underlying drug repurposing as our unit of analysis. Although drug repurposing might involve various types of activities, tools, and artifacts, our informants used "drug repurposing" as an overarching term to refer to practices used to search for additional disease indications for existing drugs.

Second, we used axial coding to identify similarities between the activities we identified from the open coding and then clustered them into higher-level practices (Gioia, Corley & Hamilton, 2013). For example, we grouped codes from the open coding stage, such as "combining data from various resources," and "manually curating data" as "generating the knowledge base for repurposing." We employed regularly archived material to contextualize our data. Being aware of the technical language in our empirical context, we made sure that we understood concepts correctly by engaging with field resources such as scientific publications and books. We also repeatedly consulted key informants, including owners of drug repurposing companies, executives at big pharma companies, and academic scientists, to aid in our interpretation of technical data.

After clustering the practices underlying repurposing, we identified two temporal modes of repurposing practices, concurrent and retrospective, depending on when field participants perform repurposing practices in comparison to the time at which the original object is created. When field participants mentioned one temporal mode or another, they often explained why they chose to perform one of each. Departing from the insights they provided about the mechanisms differentiating two temporal modes, we identified three mechanisms by following a similar set of steps of open and axial coding.

While analyzing our interview data, we started developing preliminary models and developed higher-order constructs by iterating between data and theory (Locke et al., 2008). Finally, we triangulated our findings by using archival resources, publications, our field notes, discussions in networking websites, and conference presentations. In particular, we coded conference presentations and used them largely to triangulate emerging dimensions from our interviews. The next section shows our findings from the analysis.

REPURPOSING PRACTICES

In this section, we introduce practices that field participants perform to repurpose drugs systematically. Hereafter, by drug repurposing, we refer specifically to the *systematic and intentional* efforts of finding additional disease indications of drugs that are known to be safe. Milton, a chief data scientist in the healthcare branch of a global information technology company, explained,

> Rather than developing an entirely new drug, which takes years of development to be sure that is safe for human use and does not have any serious adverse side effects, we can take some of the drugs that already exist and use them for the treatment of other diseases. It is a lot cheaper than going in and developing a brand-new drug.

Lucas, a vice president of life sciences at a data analytics company, highlighted, “The advantage is that basically most of your clinical studies have to be solely on efficacy because all of the safety studies for the most part are done.”

Our analysis of repurposing practices was based on two assumptions. First, we define repurposing as the process of taking an object and identifying its new uses. Second, before field participants start with a repurposing practice, an object that was initially developed for a different purpose is available. In the pharmaceutical industry, as Milton explained, drugs that are known to be safe, drug candidates that already passed through Phase I (safety) clinical trials, are objects for repurposing. Three sets of drugs could be objects for repurposing: drugs that are shelved in compound libraries of big pharma companies, drugs that are still in the development process, and drugs that are on the market for other disease indications.

In the next sections, we first explain practices involved in repurposing. Then, we introduce two temporal modes of repurposing: retrospective and concurrent repurposing.

Generating the knowledge base for repurposing. Field participants draw on knowledge bases for performing repurposing practices. Generating the knowledge base for repurposing refers to practices of creating, collecting, integrating, curating, and harmonizing data sources about objects and potential uses. Here, by knowledge bases, we specifically mean knowledge repositories, including databases. These practices often constitute continuous processes, and field participants constantly revisit, extend, and curate their databases for repurposing projects. In drug repurposing, field participants collect data about drugs and diseases and generate databases about them. Lucas, a vice president of life sciences at a data analytics company, explained,

> We combine data from multiple platforms. We have a platform which is the essential source for every potential drug. This platform has all targets indicated, all the secondary indications for every drug that has ever been released into the market. We have another

> platform which gives us the complete biologic or systems pathway to identify mechanisms that implicate the targets for diseases for any active component.

By creating and combining multiple knowledge resources through tools and technologies, field participants create their technological platforms (i.e., technological platforms that consist of databases about drugs and diseases, as well as algorithms for repurposing). In addition to their internally developed databases, field participants draw on public databases to combine publicly available knowledge with their internal knowledge bases. Harold, a business development and strategic partnerships manager at a drug repurposing company, explained,

> The databases that are available in the public domain have a lot of information. However, most of the information is unstructured; it is there but all over the place. We manually curate the information to build the database. We remove whatever is not relevant for the repurposing practice. We keep only the drug, target, and disease relationships in this picture. We then integrate public databases to our internal databases that have 7 million compounds, 86000 biomarkers and clinical trial outcomes from a given clinical trial in the public domain. We constantly record and maintain them.

Thus, repurposing practices involve constant curation of databases to keep the platforms ready for repurposing. When repurposing is performed, databases might come from any possible source that is reliable. For example, Ned, a scientist and department head at a research institute, highlighted the following:

> There are lots of chemistry companies out there which make compounds. They know that an interesting compound is published as a lead in a leading academic journal such as Nature Medicine. Within three months that compound becomes available in their catalogues.

However, field participants often argue that although the amount of knowledge resources that could potentially be used for repurposing is abundant, there are challenges in

integrating them. Informing the challenges of using external databases, some field participants choose to focus on the internal databases that they develop by conducting experiments and curating data continuously. Eliot, a vice president of business development at a drug repurposing company, underlined,

> [Our] data is all interrelated to every experiment that we do because we are using the same protocol, and we are using very strict controls and we are normalizing a lot of our data across time to account for things like batch effects [sources of variation due to the sampling] and environmental effects. With every experiment we do, we are adding new results to this cumulative, aggregate amount of information that is really relatable. But that's only doable because we have amassed a data set that's relatively relatable to itself.

Thus, although there are ways to integrate various knowledge resources through data curation and harmonization activities, field participants highlight that the internal data creation processes contribute to more reliable results because it enables field participants to control variations due to experimental designs and make the data harmonization more straightforward.

Identifying the scope of repurposing. Identifying the scope of repurposing refers to practices of determining and constraining choice sets of objects and potential uses for repurposing. As Mike, a manager at a big pharma company, mentioned, "the science is not necessarily everything when it comes to progressing with a compound . . . the decision might be based primarily on scientific reasons or resource issues." The selection criteria for objects and potential uses often depend on idiosyncratic preferences of field participants regarding organizational and scientific needs. Although field participants often choose to constrain the scope of repurposing to a limited set of objects and potential uses, they can also choose to stay agnostic about them. Adam, a computational biologist and a senior fellow at a big pharma company, mentioned the following:

> We do not actually think about marketed drugs a lot as we are a big pharma and we have a very large IP-protected pipeline. We are typically looking around our own IP-protected assets [drugs] and seeing how we can find new indications for them. The more advanced the drug is [in the company's pipeline], the more repurposing value it has. We are not trying to find ways of taking other people's drugs that are off-patent or patented by others, and finding a way around for repurposing. (Adam)

Denis, a professor of computational chemistry, explained the selection criteria for drugs from an academic's perspective:

> For us, the idea is that you start with a drug that has already been approved and given to people so that you understand its basic properties, including toxicology profile, pharmacokinetics, and side effects. You can have at least an idea of how the drug behaves. I am aware that in big pharma, for example, they would consider drug repurposing as an activity where they look at compounds that have made it through Phase II or even Phase III clinical trials. In theory, an academic could do that too; it's just trickier to get somebody else's IP and then say, "Hey guys, I just found a new potential therapeutic indication for you!" So, for academics, it is easier to focus on off-patent drugs for which the patents have expired. This is also what we do.

Adam noted that they decide not only on the drugs in which they are interested but also on the diseases:

> The indications we are looking at might be 100 diseases that might be of interest for [my company]. So, we do not even start with things that we know we will not be interested in.

Traditionally, big pharmaceutical companies typically focus on a couple of disease areas, where they build expertise in terms of both scientific knowledge and organizational factors, such as building a sales force. Thus, as Adam also highlighted, field participants from big pharma companies tend to focus on these disease areas in their repurposing practices. Harold, a business development manager from a drug repurposing company, explained that in

his organization, they often work with external companies (often big pharma) and repurpose their partners' drugs:

> There might be seven to ten indications [additional indications for a drug]. Before that, we sit down with the client to define inclusion-exclusion criteria. They might say that they don't want cancer or CNS [central nervous system diseases]. So that happened, and out of those ten, we have only five therapeutic indications that they [the client] are interested in. We do not identify and deep dive into the science before defining the inclusion-exclusion criteria.

Not only field participants from big pharma companies and drug repurposing companies providing service to big pharma companies but also field participants from drug repurposing companies with internal pipelines could restrict drugs and diseases that they focus on. Andrea, a CEO of a drug repurposing company, explained,

> Ten years ago, we had an idea for developing drugs in a therapeutic area, neuro rehabilitation, that surprisingly was not being addressed by the pharmaceutical industry, the biotech industry or even academic research. There are reasons why the industry has not focused on that. Part of it is because there are not good animal models, part of it is because of the industry tendencies; at least the companies that have a neuroscience franchise tend to be focused on a few very specific neurological indications like Alzheimer's and Parkinson's disease, and schizophrenia. But it was very clear for us almost ten years ago that the area of neuro rehabilitation defines a very large area of unmet medical need.

As highlighted by Andrea, a fundamental criterion for selecting diseases for repurposing is to find the ones with high unmet medical need, which constitutes the main value driver (both social and financial) in the pharmaceutical industry. Thus, field participants often focus on unmet medical needs, diseases, in their repurposing practices, although their technologies also allow for identifying drugs for diseases for which there are

already drugs available. Field participants argue that identifying a drug for such a disease would only makes sense if the new drug would be significantly better than the available one. Although we found instances of such cases, such cases often arise by chance rather than as a result of intentional practices.

After deciding on which diseases and drugs to involve in the repurposing practice, field participants gradually start questioning what other criteria they might need to consider. Mike, a manager at a big pharma company, explained,

> It is important for us to focus on a drug that patients are able to tolerate at different doses, has good distribution in the body, has no critical issues in terms of safety, and is bioavailable, etc. Having very good human safety data about the drug is also one of the primary parameters when we are looking at a compound initially. It is also important to understand whether or not we have sufficient quantities of the drug. We sometimes lack sufficient quantities; in such cases, if there is not a clear repurposing idea yet, we do not want to go ahead and spend the money to make large quantities of the drug.

Problem-solving for repurposing by using algorithms. Problem-solving for repurposing refers to practices of identifying the relationship between an object and its potential use by means of tools and technologies. Problem-solving practices constitute the core activities of a repurposing practice. After field participants identify the scope of repurposing, hence defining their starting points, they perform a set of practices by using multiple tools and technologies to expand their knowledge about focal objects and potential needs that they are interested in meeting. Leroy, a data scientist from a drug repurposing platform company, explained, “When you start with a disease, you first try to understand what the disease is: its biology, physiology, pathways regulating the disease, interacting pathways, which other proteins and genes are involved.”

Diane, a scientist at a drug repurposing company, said, “We need to read what other people are doing, and we need some other out-of-the box thinking and multiple brainstorming sessions.” Morgan, a head of clinical operations at a drug repurposing company, explained,

> For every single program, we search all the information available on the internet. . . . Thanks to all the information, we build a competitor pipeline in terms of development phases: how many products are on the market, how many Phase II or III projects are currently underway. Then we try to differentiate ours from the rest. We also predict when our product is going to reach the market and when the competitors are going to reach the market. In this way, we build a business case.

In this way, Morgan and his colleagues try to find out whether a specific drug repurposing project makes sense to proceed with. Milton, a chief data scientist in the healthcare branch of a global information technology company, highlighted,

> The issue in the health care is that there is way more information available now than any human mind can comprehend in any given disease area. There are so many publications, and so much raw data that is being produced on a daily basis. It is impossible to be up to date nowadays. So, it is no longer reasonable to try to read this information by yourself, as a doctor or as a scientist, or as a drug discovery practitioner. You need to have a system like [a computational platform developed by his company]; it can read it all for you and partner with you to help you understand what you don’t know that could be relevant to your disease. It is a necessity to augment computers to our thinking now to make us better.

Mason, a vice president of healthcare at a data analytics company, explained,

> Before the age of big data, drug repurposing was something that kind of strictly happened in the lab. A researcher would run experiments, do a lot of reading and research, go to conferences, and at some point, connect the dots with a different indication. However,

> now, big data narrows down the world from countless possibilities into something you can really wrap your head around.

In drug discovery and development, scientists commonly develop hypotheses about the causal linkages between a drug molecule's chemical structure and its biological activity on a disease target (i.e., "structure-activity-relationship"). Hypothesis strength refers to the extent to which prior beliefs about the relationship between an object and its potential new uses drive repurposing practices. In drug repurposing practices, field participants perform two types of problem-solving depending on the hypothesis strength: hypothesis-driven problem-solving and non-hypothesis-driven problem-solving. Whereas in hypothesis-driven problem-solving, field participants first develop a hypothesis about a drug or disease and its potential mechanism of action in the human body based on prior knowledge, in non-hypothesis-driven problem-solving, field participants pretend that they do not know anything about this relationship. Thus, they initiate an unbiased process. As a result of problem-solving practices, hypothesis-driven or non-hypothesis-driven, field participants establish a link between a drug and its potential new use.

Ryan, a CEO of a drug repurposing company, described hypothesis-based problem-solving as follows:

> The best way to think about hypothesis-based problem-solving is in terms of whether the discovery process is focused on mechanisms and specific therapeutic targets. Does the process begin with an assumption around a therapeutic area target? Is the process really built on a foundation that certain biological pathways or proteins are critical in the description of the disease of interest? If that is incorporated into the architecture of the discovery process, then the process is hypothesis-based.

Olivia, a senior director of clinical development at a big pharma company, gave an example of repurposing based on hypothesis-based problem-solving:

> Esketamine [originally developed as an anesthetic] has been approved as a rapid antidepressant in patients that have treatment-resistant depression as well as patients that are acutely suicidal and depressed and who are in need of a rapid treatment. . . . The understanding of neuro-mechanisms of depression led investigators to take esketamine from the shelf and to test this hypothesis because of its specific properties that make it suitable for psychiatric diseases.

Diane, a scientist at a drug repurposing company, explained how they do it:

> When we start with a drug, we look into the drug space completely, such as the structural and chemical properties of the drug, what target it is binding to, what off-target effects it has, the side-effect information . . . many more like its chemical role and mechanism of action in the disease. Then, we identify diseases that our drug's target and genes are related to by using our computational platforms. So, we collect information on the drug, the target, and the disease, and we try to connect the dots among these three.

Olivia described a case of starting with a disease, whereas Diane described a case of starting with a drug. Regardless of their starting point, whereas repurposing practices based on hypothesis-driven problem-solving start with an assumption about the link between diseases or drugs and related targets, in repurposing practices with a non-hypothesis-driven approach, such assumptions are relaxed. Ryan, a CEO of a drug repurposing company, explained, "In non-hypothesis-driven [problem-solving], we take a compound and, without any particular hypothesis in mind, evaluate across a broad range of models or a broad therapeutic space."

Adam, a computational biologist and a senior fellow at a big pharma company, explained,

> Most of our methods, including the connectivity mapping approach, are hypothesis-free [non-hypothesis-driven]. It is just saying, "Let's look at all drugs and what they do, and let's look at all diseases and what they do in terms gene expressions, and see which one

> [drug] matches with what [disease].” We don’t have any biases or hypothesis in performing connectivity mapping.

Jeremy, a cofounder of a computational drug repurposing company, explained,

> The matching is multivariate. We’re creating a profile of a drug-disease relationship in a similar way to how dating algorithms work by asking, “What’s your religion? What do you like to read? What do you do on the weekends? What are your hobbies?” We just change the variable names: “What molecules are you attracted to? What are the states of this pathology?” Based on the similarity between diseases, [our platform] tells me which existing drugs are talking to these molecules. Which of these drugs have common friends with these pathologies? So that’s how we arrive at probabilistic models of what diseases may be cured by molecules that have not been tried yet.

Field participants can either start from a drug or a disease, or they can run two-sided matching algorithms using computational platforms. One way to perform repurposing based on a non-hypothesis-driven approach is to use pure in-silico (computational) platforms, and another is to use experimental methods. Eliot, a vice president of business development at a drug repurposing company, explained an experimental method, phenotypic screening, and how they use it for repurposing:

> Phenotypic screening starts with defining two states: what a healthy cell looks like physically and what a very specific disease looks like physically, which we need to understand in very robust, reproducible, and statistically significant ways. We define both of those two states using hundreds of different features of a cell. Then we take compounds, and we apply them to those disease cells, and we look for compounds that reverse those physical features back to what we believe to be a healthy cell.

As Eliot explained, field participants use experimental methods to identify potential diseases for drugs based on a rapid trial-and-error process. Field participants often see the

advantage of non-hypothesis-driven problem-solving as allowing for more surprises and unexpected links. Eliot continued,

> The beauty of non-hypothesis-driven approaches such as phenotypic screening is that it's unbiased. So, we are able to identify compounds or drug classes that rescue a disease model in an otherwise unexpected way. We're looking at a thousand-dimensional space using machine vision. We turn the problem-solving logic on its head. Hence, we are looking outside the searchlight of otherwise known biology and just letting the science speak for itself. Then we are just deconvoluting it on the backend.

Hence, field participants use various tools and technologies to identify the relationship between an object and its potential new use, and propose new uses for a potential resource.

Human interpretation of algorithmic problem-solving. Human interpretation of algorithmic problem solving refers to the activities in which field participants analyze, discuss, and use their expertise to perform problem-solving by using technologies and tools, and to interpret the results of algorithmic problem-solving. As field participants identify potential relationships between an object and its potential new use, there is a recurrent process of human interpretation of technology- and tool-based results. Carter, a professor of computer science and bioengineering, discussed the necessity for human interpretation complementing technology:

> We do not intend to replace humans (e.g., physicians), but we are just helping them to find possible drugs faster. . . . Computers are good at going through all search space, much bigger space than humans can go through, and identify a lot of links that humans cannot reach. Then, we evaluate these results with a team of experts, who have experience in a particular domain.

Indeed, Milton, a chief data scientist in the healthcare branch of a global information technology company, highlighted that "humans help to understand what is a real discovery

and what is junk, and without that loop of human interpretation, we would just be generating noise." James, a drug discovery manager at a drug repurposing company, explained,

> What we find ourselves quite often that we have to discard the results that we analyze through our computational platform because the relationship that we find between a disease and a drug has already been published. From the computational point of view, results are okay and promising, but for us, it is not possible to use them because there is no point of proceeding with an already patented or published idea.

As James highlighted, not all the critical criteria might be embedded in algorithms, and field participants need to go through the results to make sure that the results are relevant to their idiosyncratic preferences. Leroy, a data scientist at a drug repurposing platform company, explained how they integrate human interpretation at several stages of the repurposing process:

> At the beginning of a repurposing process, we call for a meeting and allocate projects to team members. The decision is often based on an interest or prior experience (e.g., somebody might have worked on a drug or a disease during his PhD). We organize interim meetings to share information among each other. . . . After we collect data and do the computational analysis, we rely heavily on the human interpretation. Any algorithm would not give you, "Oh, this is a very novel idea, look at here, listen!" Although machines display everything, we can only understand pathology, disease biology and condition through a thought process. Technology can you give dots and some relationships, but it depends on the human mind to connect these dots in a proper way to draw a very nice picture to show to the world.

Walter, a professor of computational chemistry, explained,

> Human interpretation is critical at the points where there are some spontaneous and creative ideas, and intuitive associative and interdisciplinary thinking. The machine provides a scientist with opportunities: try this molecule for this indication, try that one,

> there might be something here, some opportunity there. Then the chemist, the biologist, the human mind looks at these five to ten suggestions - not the millions of data points - and decides, in discussion with his team members, what to do next. So it's a two-step approach: to use machines to sift through the big data, and then to have the human mind to transfer thinking.

Thus, in a recursive process between human interpretation and using tools and technologies, field participants arrive at the identification of a potential new use of an object. In the next section, we explain two temporal modes of repurposing: retrospective and concurrent repurposing.

TEMPORAL MODES OF REPURPOSING

We identified two temporal modes of repurposing practices, depending on the moment at which an original object is created: concurrent and retrospective repurposing. In concurrent repurposing, field participants identify additional uses of an object during the process of its original creation, whereas in retrospective repurposing, field participants uncover additional uses of an object that already exists through retrospective analysis. Although in both of the temporal modes, field participants perform a set of practices similar to those that we introduced in the previous sections, the timing of practices changes depending on the temporal mode of repurposing.

Systematic drug repurposing originated from the idea of identifying additional indications of existing drugs that are shelved or already on the market, which we call retrospective repurposing. Indeed, Jackson, a manager at a big pharmaceutical company, described drug repurposing as "finding some old compound on the shelf [drugs that failed due to the lack of efficacy and are stored in the compound libraries] ten or twenty years ago and repurposing it into a new indication." However, recognizing the potential value of repurposing drugs for their additional indications at earlier stages, pharma companies integrate the practices of checking additional indications of drugs during the process of the

development of a drug for its original indication (i.e., concurrent repurposing). Matt, a scientific expert of biochemistry at a big pharma company, explained,

> These days when we think about indications, we have a different strategy, and we systematically look at all potential indications that we think a particular drug could maybe reach right from the start. . . . We have the awareness that you can use drugs in various indications and how it will make best use of them.

Adam, a computational biologist and a senior fellow at a big pharma company, added,

> Nowadays, drug repurposing does not only happen in retrospective fashion. It happens everywhere in the organization. During the entire process, they [researchers and clinical scientists at the company] are always thinking about what other indication the drug might work for. They are thinking about mechanisms, they look at the literature, they see what other diseases might be connected as well.

Figure 1 shows the critical points in a drug's lifetime. Based on the lifetime of a drug, we identified three mechanisms that motivate field participants to perform either retrospective or concurrent practices (Figure 1).

Decay of knowledge about objects. When field participants repurpose existing objects, at each stage of a repurposing practice, they need to access and use the existing knowledge of an object. Our informants repeatedly underscored the difficulties of using existing knowledge of drugs as time passes. Linda, a scientific manager at a big pharma company, explained,

> It [repurposing] is a little bit retrospective thinking as well as prospective. In a pharmaceutical company, once the project is closed, the project teams are dispersed. People move to other projects and have other things on their plate. There is also a lot of movement within the pharmaceutical industry. So, two or three years down the road, many of the people that were on the original project team may not even be employees

> anymore. So, it is extremely difficult to go backward and to fill in those gaps [to complete missing information]. The system is really not built for reverse engineering the projects.

As Linda underscored, lots of knowledge is lost due to the movement of researchers within and outside of companies. Rebecca explained,

> There is an operational complexity of restarting something. . . . When people leave the organization and you start to lose institutional knowledge and memory . . . I think the sooner the repurposing happens after the initial stop decision, the more likely it is to be successful because you've got that institutional memory there and you still have enthusiasm about the program.

Similarly, Lucas explained that it is challenging to obtain comprehensive data when they need to revisit information about drugs that field participants developed a long time ago:

> In companies, they [researchers] probably don't always maintain the libraries. The person that created those compounds is probably gone. They have to go back and read. . . . You have to go find Dr. X's notebook from 15 years ago and hope that it is comprehensive and detailed enough. So, then you will have to have somebody else come in and guess.

Ned, a scientist and head of an international research institute, argued,

> We have datasets, which are sort of incomplete or have errors in them, which make it difficult to generate new hypotheses. I think in order to create the data you need, to support those models, you better design upfront what the experiments might be, what data you might need, and then generate all of that data on consistent conditions.

Adam, a computational biologist and a senior fellow at a big pharma company, compared retrospective and concurrent repurposing as follows:

> Since the value for concurrent drug repurposing is already so high [and it is performed in the traditional drug development process], retrospective drug repurposing can help uncover value where they [researchers] might have missed it, or when the connection is less obvious to uncover the connections that the biologist would miss.

Because field participants experience problems in accessing past knowledge and using it, the knowledge of objects constitutes temporal knowledge that can age and decay. This mechanism hence affects the field participants' choice of temporal mode of repurposing practices.

Ownership of objects. Accessing the past knowledge of an object as well as the object itself constitutes a mechanism that interacts with the temporal mode of repurposing practices. Until a drug becomes off-patent, an organization that developed the initial drug has control over the drug. Even after the drug becomes off-patent, the organization has most of the knowledge about producing the drug, and field participants who want to repurpose the drug might need to obtain access rights from the company to be able to perform practices (e.g., run experiments) to repurpose the drug.

Field participants stressed that one of the common challenges they face is the fear of losing control. Travis, a founder of a drug repurposing company, explained how legal liability is a critical issue in gaining access to compounds,

> When a big pharma company out-licenses a drug to me, they are giving me all their data. I do my own trials, and then if something bad happens in these trials—such as a serious side effect or death—some lawyers may argue that [the adverse events] could have been prevented by having more thorough data from previous preclinical trials performed by the big pharma company. And guess what, they will not sue me [a small repurposing company], because I have no money. They will sue the big pharma company for negligence. And even if it doesn't end up costing them millions of dollars, it is bad PR.

As Travis elucidated, when a drug owner grants access to the drug, they continue to be the liable legal entity in case of any unexpected side effects. Matt further explained,

> There is a risk that a negative reputation follows back in the primary indication, where you [a company that initially developed the drug] are the market authorization holder. That has to be assessed when you agree or not to help out with repurposing.

As Matt underscored, relinquishing control over compounds might bring not only potential legal threats but also the threat of a bad reputation. Roy, an innovation manager from a big pharma company, explained,

> [The compounds that are still active in development] we hope are going to bring us financial returns in the future, but those are also the ones which are most attractive for the academic community because these are newer compounds [with] newer mechanisms, so there is a lot of excitement. It has been a progressive struggle within the company to convince people to be a little bit more willing to make those compounds available to the external community and to relinquish complete hands-on control [when] a novel clinical study is going to be done with those compounds. We have successfully accomplished that with a few compounds within [the company]. Most companies have struggled with that because they don't want to lose any control.

Control issues potentially obstructed repurposing practices even if field actors were aware of the potential opportunities of finding novel uses. Indeed, Nick likened pharma companies' compound libraries to "family jewels." Lisa, a manager of a drug repurposing unit in a big pharma company, underscored the reluctance of her colleagues to provide access to compounds, "I think this is what a lot of project leaders are worried about. You make the compounds, and then somebody goes off and does something with it and then they generate data that is threatening to the lead indication."

Thus, control and ownership issues limit the possibilities to access objects and knowledge around them. Leonard, a chief executive officer and cofounder of a drug repurposing company, stated,

> Large companies that we've talked to oftentimes have drug repurposing teams who are looking to repurpose drugs based on signals from clinical trial data. Obviously, we don't have kind of the level of access to that data to even incorporate it into our algorithm. If we had the data, we could. . . . If you're one of the top ten big pharmas, you have massive

> datasets of blood tests and everything from all the patients, on lots of clinical trials, and you can look for signals that might be informative.

As Leonard indicated, in many circumstances, ownership of drugs determines who can access the knowledge and thus repurpose the drugs.

Potential exchange values of objects. In the pharmaceutical industry, intellectual property rights are key determinants of whether an organization or a field participant can generate financial returns on innovation outcomes (i.e., exchange value of objects). Thus, the intellectual property constitutes a core concern for field participants in repurposing practices. Ryan, a chief executive officer of a drug repurposing company, explained,

> On one side, you have to have the freedom to operate and be able to use the drug. On the other side, you need [the drug] to be patentable so that you can exclude others from using it . . . [A drug] could be the next best candidate for Alzheimer's disease. But if there's only two years of patent [protection] left, there may be no motivation for a company to spend 20 to 50 million dollars to conduct a clinical trial, if they can't be assured that they're going to get exclusivity when they get this to market. So, it has nothing to do with the validity of the idea.

Similarly, Jackson highlighted patents as one of the primary considerations in making decisions about repurposing drugs,

> The fundamental principle is that you have a drug with sufficient patent life that makes it worthwhile to spend all the money and take all the risks to develop it. . . . Once you file the patents, you've got 20 years of protected time, some of which is lost during the development period, to recoup your whole investment and make your whole profit. Once the key patents expire, then any company can come in and make something equivalent, and it will be cheap and widely available for the rest of eternity. So, there's a huge risk from when patents are filed to when you get a drug on the market and make hay while the

> sun is shining. The key thing about repurposing is you've already lost some of that time, and the question becomes: Is there still enough patent life to make it worthwhile?

Indeed, in drug repurposing field meetings, patents are one of the core topics of presentations. Such presentations often focus on generating patent protection for repurposed drugs creatively. If the initial patent over a drug has expired, field participants can still get additional IP protection over the new use of an existing drug (i.e., method-of-use patents) and access to market exclusivity rights if they successfully repurpose a drug. However, field participants considered use patents much weaker than the patent over a new drug molecule. Field participants referred to patents as "a hotbed of pharmaceutical creativity" or used terms such as "bulletproofing patent estate" to underline the importance of patent protection for repurposed drugs. Therefore, IP issues constitute the key drivers behind why big pharma companies often choose to focus on concurrent repurposing or retrospective repurposing of their recently failed drug candidates.

Field participants indicated that they repurpose drugs whose patents have expired or with weak patentability possibilities only if they have a strong interest in the use values of the drugs. Indeed, this kind of case is prevalent in the cases of orphan diseases. Matt a, scientific expert of biochemistry in a big pharma company, explained,

> Patient organizations, especially for orphan diseases, which have been desperate because no research has been done in the past, have a high interest in repurposing drugs. If there is anything available, they will grab it and try to help funding of studies, which would support theses indications. Then it's more the medical need, the pressure from the patient point of view that lead to repurposing.

As Matt described, in the instances that the potential value of using drugs can benefit a group of field participants, there might be an interest in repurposing drugs without any patent protection. Hence, field participants interested in such disease areas often repurpose

off-patent drugs retrospectively, even though there are often no financial returns on their investments. In the next section, we discuss the emerging framework of our study's findings.

EMERGING FRAMEWORK

Based on our findings, we propose a model of temporal modes of repurposing practices. Our model depicts two repurposing practices: concurrent and retrospective repurposing. Three mechanisms differentiate two temporal modes of repurposing practices: decay of knowledge about objects, ownership of objects, and potential exchange values of objects.

Repurposing Practices

To unfold repurposing practices, we identified four practices that recursively constitute the process of repurposing. Generating the knowledge base for repurposing is the foundational practice of repurposing practices, which we define as systematic and intentional practices. Unless field participants generate a knowledge base about objects and potential uses, they can only uncover additional uses of objects serendipitously (e.g., Dew, 2009; Garud, Gehman & Giuliani, 2018). Indeed, the traditional form of identifying additional disease indications of drugs in the pharmaceutical industry has been the serendipitous identification of new uses based on clinical signals (e.g., Viagra case; see Tiefer, 2006). The difference that we highlight in repurposing practices lies in the field participants' intentionality in performing repurposing practices.

In repurposing practices, data quality and integration present a key challenge since field participants are dependent on the knowledge that they can abstract from the data during repurposing practices. Indeed, existing literature on information systems has emphasized the importance of data quality in the success of knowledge management systems (e.g., Lee, Strong, Kahn & Wang, 2002; Wixom & Watson, 2001). Both data quality and the interrelatedness of data contribute to the key challenge of repurposing practices. As our

informants repeatedly suggested, when they were unable to harmonize data about objects and potential uses, they struggled to perform repurposing practices even with the availability of vast amount of knowledge about objects and potential uses. In this sense, field participants faced a big-data problem, where the data is available but not useful (Günther, Mehrizi, Huysman & Feldberg, 2017). Our findings, therefore, demonstrate the importance of preparing for repurposing (i.e., an informant defined it as prospective thinking)—that is, to record data about objects and potential uses by keeping in mind that field participants can use this data in the future for repurposing.

The idiosyncratic preferences of field participants or organizations that the field participants are embedded in, shape the scope of repurposing. When field participants identified the scope of repurposing, they introduced boundary conditions about which objects and potential uses they were interested in repurposing. Our findings indicate that field participants imposed boundaries on not only the set of objects and potential resources that they had an interest in repurposing but also on the novelty of a mechanism that connects an object with its potential new use. In other words, the innovativeness of repurposing practice lies in the novelty of the mechanism that connects an object with its new use. Our findings demonstrate that field participants were able to define novelty at a local or field level. The mechanism between an object and its potential new use could be novel to a group of field participants at the local level, but if the mechanism is not novel at a field level, field participants repurposing an object would not gain an exchange value from an object-in-use in an industry as the pharmaceutical industry, where IP rights are crucial determinants of exchange values of resources. These findings further enhance the implications of field-level dynamics on repurposing practices.

Problem-solving practices lie at the core of repurposing practices, which involve matching activities between objects (i.e., solutions) and potential uses (i.e., needs; cf. von

Hippel & von Krogh, 2016). In particular, problem-solving practices via algorithms allow field participants to process a large amount of information and utilize the power of technology to identify new repurposing opportunities. As our informants repeatedly emphasized, repurposing drugs by processing massive amounts of data would not be feasible without using algorithms that help field participants to come up with a hypothesis. In particular, artificial intelligence, machine learning, and big data algorithms constitute core artifacts of repurposing practices.

Our findings also imply that field participants could identify unexpected new uses of objects by using algorithms when they relaxed their hypotheses about the mechanism connecting objects with their potential new uses during problem-solving practices. Field participants used tools and technologies to effectively perform non-hypothesis-driven problem-solving activities, but without them, field participants could achieve such unexpected discoveries only when they stumbled across an observation by chance. Using tools and technologies enables field participants to identify unexpected uses in a systematic and intentional way without "waiting for serendipity to come," as one of our informants put it. In this way, repurposing practices highlight the performativity of material artifacts (i.e., tools and technologies) in uncovering the novel uses of objects (Carlile et al., 2013).

Human interpretation is a crucial part of problem-solving activities in repurposing practices. As our informants repeatedly emphasized, human interpretation helps identify whether the new use of an object is a meaningful finding. Even in cases where field participants used sophisticated artificial intelligence and machine learning algorithms, field participants saw the role of these technologies as complementary to human interpretation. Our informants particularly highlighted the importance of recruiting domain experts in the human interpretation process of problem-solving outcomes, in particular experts on

interpreting mechanisms between objects and new uses (e.g., biologists in the case of drug repurposing; e.g., Ben-Menahem et al., 2016; Grant, 1996; Knorr-Cetina, 1997).

Temporal Modes of Repurposing Practices

Repurposing processes represent a type of resourcing process in which an object gains new use values (Feldman, 2004; Feldman & Worline, 2011). The specificity of repurposing practices is under the assumption that an object can gain new use values without significantly changing its material properties. For example, in drug repurposing practices, although field participants can make slight modifications to the formulation of a drug, keeping an original drug as is, is desirable because its material properties can change if combined with other objects. Although the extent to which the modification of an object can affect its material properties can change across different settings, we make a clear distinction between repurposing processes and processes whereby recombinant knowledge creation processes unfold (e.g., new product development processes).

In a resourcing cycle, objects enable field participants to develop schemas, which lead field participants to perform practices. We identified three mechanisms that distinguish two temporal modes of repurposing and constitute schemas in the resourcing cycle (Feldman, 2004; Feldman & Worline, 2011). Because field participants enact different schemas in concurrent and retrospective repurposing practices, the specific activities underlying these practices and their timing vary in each temporal mode of repurposing. Schemas are constituents of structure in resourcing cycles (Feldman, 2004); hence, a particular set of schemas (i.e., structure) and activities (i.e., agency) co-create each other.

Repurposing constitutes a multisided practice where field participants integrate various knowledge domains that often originate from different organizations, to repurpose objects. At a high level, three sets of knowledge domains represent the critical dimensions of a repurposing practice: knowledge about potential uses, knowledge about objects, and

knowledge about the mechanism connecting objects with their potential uses. Because knowledge creation processes in each knowledge domain is a temporal activity of recombining knowledge (e.g., Katila, 2002; Nerkar, 2003) that decays over time (e.g., Kok, Faems & de Faria, 2019), field participants' timing to create knowledge for each knowledge domain influences the temporal modes of repurposing practices. Although the knowledge originally created around an object decays over time, and hence could make retrospective repurposing unappealing for field participants, new knowledge about objects and potential uses can also become available. Thus, as highlighted in our findings, field participants performed retrospective repurposing practices to exploit the unidentified uses of an object in the past. In contrast, they tried to exploit all potential uses they could identify during the creation process of an object in concurrent repurposing. In this sense, concurrent and retrospective repurposing practices constitute complementary processes in uncovering the new uses of objects.

In repurposing practices, the timing at which a specific knowledge is created, as well as whether field participants can access an object, has a temporal dimension. Field participants can move objects to different organizational units or even different organizations (Nicolini, 2013). Indeed, in the pharmaceutical industry, drugs, which are the objects of repurposing, is typically developed in a certain organization but then move to another organization through licensing agreements. Given that we defined repurposing as a resourcing practice whereby an object becomes a resource-in-use (e.g., Feldman, 2004), the field participants' ability to access an object becomes an integral part of repurposing practices, as field participants can only attain an object's value when they put them in use (Deken et al., 2018). Otherwise, even if field participants are able to develop ideas about an object and its potential new use, the objects do not become resources-in-use unless the field participants gain ownership over the objects to manipulate them. As organizational

boundaries become more distinct in a field and ownership rights become stronger, field participants face more boundaries in their repurposing practices. Thus, the critical points at which an object moves across different organizational boundaries influence the temporal mode of repurposing practices.

We defined repurposing practices as uncovering the use values of objects, which may result in a financial gain (i.e., exchange value; Bowman & Ambrosini, 2010); however, field participants' idiosyncratic preferences about the potential exchange value of a resource-in-use could affect the temporal mode of repurposing. In the pharmaceutical industry, as well as other industries in which intellectual property rights significantly influence the exchange values of resources, the amount of time left for an object until it becomes off-patent determines the amount of financial returns that an organization can gain over an object. Thus, field participants become unwilling to repurpose objects that would be hard to claim intellectual property rights for as this can affect the financial returns they would get back. Therefore, field participants with a high preference for gaining exchange value tend to focus on concurrent repurposing practices.

DISCUSSION

Through our unique analysis of drug repurposing, we not only elaborated upon the resourcing perspective (Feldman, 2004; Feldman & Worline, 2011) but also contributed to the agenda on this perspective. By drawing on the differentiation of use and exchange values (Bowman & Ambrosini, 2000, 2010), we unearthed a specific type of resourcing process—repurposing process, whereby existing objects gain new use values. From our findings on repurposing practices, we also uncovered a number of implications on theory that reach far beyond the resourcing perspective.

Our framework on repurposing practices offers several contributions to the resourcing perspective (Feldman, 2004; Feldman & Worline, 2011; Sonenshein, 2014). Studies on the

resourcing perspective to date have focused on processes that are emergent and often improvisational and unintended as a result of an interaction between schemas of field participants and potential objects (e.g., Quinn & Worline, 2008; Sonenshein, 2014). By showing a systematic and intentional resourcing process, repurposing process, our study extends resourcing perspective in a way that not only takes into account instantaneous interaction between schemas of field participants and potential objects but also schemas of field participants about the perceived use value of potential objects, resulting in a process whereby field participants perform practices to identify the new use values of objects. In this sense, field participants' schemas about the potential use values of objects direct their resourcing processes and make them focus on a set of potential objects and uses to perform resourcing practices. Although prior studies on resourcing (e.g., Wiedner et al., 2017) have hinted at such directed resourcing processes, our study is the first to depict how this process unfolds.

Studies on the resourcing perspective have highlighted the importance of context in constituting the meaning structure that organizational actors draw upon to define the potential values of resources (Howard-Grenville, 2007). Organizational actors cannot define resources' values independent of the context wherein actions take place (Feldman, 2004). The values of potential resources can vary from one context to another and can be dependent on multiple factors, such as organizational context (Howard-Grenville, 2007; Kannan-Narasimhan & Lawrence, 2018) or environment (Mealey & Sonenshein, 2017). This study explains how the relationship between context and practices unfolds in resourcing processes. Although prior studies (e.g., Howard-Grenville, 2007; Kannan-Narasimhan & Lawrence, 2018) have demonstrated the importance of organizational context, our study shows how not only the organizational context but also the field-level context that field participants are embedded in can shape resourcing practices. By drawing on the differentiation between exchange value

and use value (Bowman & Ambrosini, 2000, 2010), our study suggests two mechanism regarding the importance of context in resourcing processes.

When field participants are primarily interested in gaining new use values from an object, as long as they have access to the object to manipulate it, the field-level context wherein practices take place might have a lesser influence on their resourcing processes, unless the field-level context strictly prevents them from using objects (e.g., strict IP laws on the use of objects). However, when field participants are interested in gaining financial returns (i.e., exchange value) on the new use values of objects that they uncovered, the field-level context might strongly interact with their resourcing practices. In such cases, the field participants tend to focus on a set of objects and their potential uses whose exchange values they perceive are high. Although field participants can uncover unexpected potential new uses when engaging in resourcing, their schemas often constrain them to a set of possibilities that they perceive will put the objects to use. Thus, our study demonstrates how the perception of value deriving from the relationality between field participants' schemas and objects shape their resourcing practices (Bourdieu, 1990; Wiedner et al., 2017).

Studies on the resourcing perspective have proposed the potential of using resourcing perspective for exploring innovation processes (Feldman & Worline, 2011). Even though the primary objective of this study was not to necessarily contribute to the innovation literature, the findings that we derived from the drug repurposing context, which is part of an innovation process, have implications for the use of resourcing perspective in informing innovation processes. By taking a practice-based perspective, we demonstrate how existing objects can gain new uses (i.e., repurposing), which can result in innovative outcomes.

Our framework shows how repurposing practices can develop in innovation processes and how they can bring complementarities to new product development processes (e.g., Olson, Walker & Ruekert, 2001; Veryzer, 1998). Repurposing processes are inherently

connected to new product development processes because objects for repurposing are either direct outcomes of new product development processes (e.g., marketed drugs) or by-products of such processes (e.g., failed drugs; Andriani, Ali & Mastrogiorgio, 2017). Although some studies on innovation have argued that uncovering the new uses of existing objects are the result of serendipitous discoveries (e.g., Andriani et al., 2017; Garud et al., 2018), we depict a repurposing process as well as its underlying practices that are systematic and intentional. Unless field participants do not have the intention to repurpose objects that they deem as potentially valuable and have access to relevant practices, uncovering existing objects' new uses is likely to be a serendipitous process. We show that the resourcing perspective can be a powerful lens in exploring innovation processes by bringing attention to objects and practices (Feldman & Worline, 2011).

Finally, our study has important implications for technology-in-practice literature (e.g., Orlikowski, 2000, 2007; Feldman & Orlikowski, 2011) and promises the potential value of synthesizing the resourcing perspective with technology-in-practice studies. By showing how field participants use algorithmic tools and technologies in their repurposing practices, our study contributes to the broader agenda of applying big data to management (George et al., 2006; Günther et al., 2017; Henfriddson et al., 2018; Yoo, Boland, Lyytinen & Majchrzak, 2012). Furthermore, by bringing a problem-solving perspective to analyzing practices involving technology, we were able to identify the ways algorithmic problem-solving processes can enhance repurposing outcomes. We show that resourcing processes involve a need-solution problem-solving process (von Hippel & von Krogh, 2016), where field participants match objects (i.e., solutions) with their potential uses (i.e., needs). We show that by relaxing assumptions about the relationship between an object and its new use, field participants could identify unexpected and novel uses of existing objects by using tools

and technologies. In this way, we contribute to the management literature by explaining how field participants can use technologies to uncover novelty (George et al., 2006).

Boundary Conditions, Limitations, and Directions for Future Research

Our findings yield important insights not only on the resourcing perspective but also on an unexplored and novel research setting. Nevertheless, several limitations of our study merit attention. Our research setting represents a highly regulated industry where access to objects and knowledge around them are protected by intellectual property rights. Because the commercialization process in the pharmaceutical industry is strongly related to the patents and exclusivity rights, repurposing existing compounds is a big concern from a commercial perspective. In other industries where patent and exclusivity rights do not prevent companies from commercialization and profit-making, novelty-related concerns can be less important. We invite future research to look into other industry contexts where this assumption is more relaxed.

The objects we studied, drugs, have limited mutability; therefore, modifications made on objects can change their material properties and, hence, their potential use values significantly. While it is fairly common in similar industries, such as the chemical industry, future research should look at how such repurposing processes unfold under different levels of object mutability. We studied a context where material matters significantly, and we suggest that studying different contexts where materiality of objects matter much less can illuminate important insights into repurposing processes.

Based on our study, we call further attention to the potential benefits of integrating the practice level with the field level. Future studies can look into specific mechanisms that can enhance or limit resourcing opportunities. In particular, future studies can look into how field participants influence resourcing practices by altering field-level schemas. We also suggest future studies investigate the potential performance implications of resourcing processes.

Given that our research setting represents a newly emerging field, and it can take up to 15 to 20 years for a drug to go from development to commercialization in the pharmaceutical industry, we were not able to include performance criteria in our model.

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Table 1a: Overview of Data Sources

Use in the Analysis	Data source
Interviews	
Main data source	52 formal interviews and 15 informal interviews between 2015-2019, including drug repurposing company CEO's, president and founders, scientists, big pharma representatives of drug repurposing, academics, scientists and managers working for NGOs, government representatives.
Conference Presentations	
Triangulation	Drug Repositioning, Repurposing and Rescue Conference, data between 2012-2016 (from the beginning of the conference), in total 68 conference presentations.
Scholarly Publications and Other Scientific Resources	
Triangulation	Articles published in main field journals such as Nature, Drug Discovery Today, PNAS, and Lancet. Access to such articles was provided by both keyword search and recommendations by key actors in drug discovery field.
Triangulation	Books on drug repurposing.
Other Archival Resources	
Triangulation	Organizational websites and reports.
Triangulation	Groups in networking websites.
Field notes from Networking Events	
Triangulation	Roundtable discussion with 10 experts from a research unit of a big pharma company. The meeting lasted 4 hours. Participants had backgrounds in chemistry, biology, computational methods, and represented different hierarchical positions, from executive functions to operational scientists.
Triangulation	Three field conferences on drug repurposing in June 2015, June 2016 and February 2017. 40 hours of non-participatory observation.

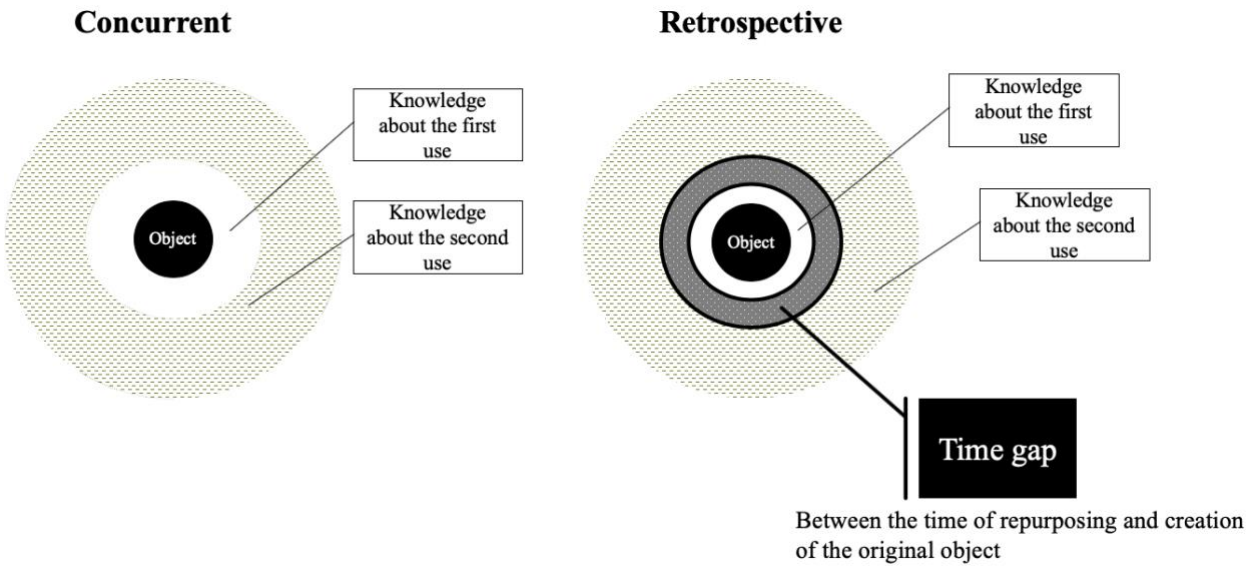
Table 1b: The Overview of Data Sources

#	Name	Organization	Position	# of interviews
1	Walter	Academic	Professor	2
2	Alicia	Academic	Senior Researcher	1
3	Carter	Academic	Professor	1
4	Gregory	Academic	Professor	1
5	Beckett	Academic	Professor	1
6	Sam	Academic	Professor	1
7	Pharrell	Academic	Professor	1
8	Walter	Academic	Professor	1
9	Harris	Big pharma	Senior Vice President, Research and Discovery	1
10	Hugh	Big pharma	VP Head of Discovery and Product Development	1
11	Logan	Big pharma	Chairman	1
12	Roy	Big pharma	Executive director	1
13	Carol	Big pharma	Manager	1
14	Kent	Big pharma	Director	1
15	Lisa	Big pharma	Senior Director	1
16	Linda	Big pharma	Associate Director	1
17	Richard	Big pharma	Senior Director	1
18	Adam	Big pharma	Senior Scientist	1
19	Mike	Big pharma	Science Policy Director	1
20	Matt	Big pharma	Global Scientific Expert	1
21	Barbara	Big pharma	Head of Diagnostics	1
22	Rebecca	Big pharma	President & co-founder	1
23	Jackson	Big pharma	Manager	1
24	Mariana	Big pharma	Manager	1
25	Daniel	Drug repurposing company	President/ Co-founder	3
26	Bob	Drug repurposing company	Chief Scientific Officer	1
27	Calvin	Drug repurposing company	Owner/ Chief Executive	2
28	Leonard	Drug repurposing company	Chief Executive Officer/ Co-founder	1
29	Travis	Drug repurposing company	Founder	2
30	Tobias	Drug repurposing company	Chief Scientific Officer	1
31	Clayton	Drug repurposing company	Founder, Chairman, President	3
32	Gabriel	Drug repurposing company	Chief Scientific Officer/ Founder	2
33	Jeremy	Drug repurposing company	Co-founder	1
34	Ryan	Drug repurposing company	CEO & President	1
35	Anthony	Drug repurposing company	Founder	1
36	Sofia	Drug repurposing company	Senior Manager	1
37	Diane	Drug repurposing company	Scientist	1
38	Leroy	Drug repurposing company	Scientist	1
39	Morgan	Drug repurposing company	Business Development	1

40	James	Drug repurposing company	Senior Scientist	1
41	John	Drug repurposing company	Advisor and Strategic Expert	1
42	Ruben	Drug repurposing company	Co-founder	1
43	Harold	Drug repurposing company	Business development	1
44	Andrea	Drug repurposing company	CEO	1
45	Eliott	Drug repurposing company	Business development	1
46	Gus	Drug repurposing company	CEO & Funder	1
47	Denis	Drug repurposing company	CEO	1
48	Gil	Drug repurposing company/ Academic	Director	1
49	Marion	Government	Program Coordinator	1
50	Ned	Government	Scientist	1
51	Adler	Non profit	Scientist	1
52	Daniel	Rare disease	President, Chief Scientific Officer	1
53	Nick	Rare disease	Scientific Advisor, Co-founder	1
54	Rene	Rare disease	Chief Scientific Officer	1
55	Mason	Service company	VP Healthcare	1
56	Lucas	Service company	Vice President	2
57	Milton	Service company	Chief Data Scientist	1

Table 2: Types of Organizations Involved in Drug Repurposing

Type of organization	Description	Profit model	Activities	Tools and artifacts
Academia	Academics and doctors working on particular diseases or diseases mechanisms. Main objective is knowledge creation.	Non-profit	• Investigation of underlying mechanisms of diseases. • Direct observation and testing with patients.	• In vivo and in vitro screening models. • Computational platforms. • Medical records.
Big pharma companies	Pharmaceutical or biotechnology companies with revenues over billions of dollars. Their main objective is typically commercialization of drugs	For profit	• Entire chain of events involved in drug discovery and development to discover new drugs to treat unmet medical needs with high profit potential. • Repurposing can be part of drug discovery and development activity or can be done separately by looking at compound libraries.	• In vivo and in vitro screening models. • Computational platforms. • Proprietary compound databases. • Medical records.
Drug repurposing companies	Repurposing companies using technological platforms for repurposing. May focus on one or more diseases.	For profit	• Identification drug repurposing opportunities that can be done by using computational platforms or experimental models such as in vivo and in vitro screening.	• In vivo and in vitro screening models. • Computational platforms. • Public compound libraries • Proprietary compound libraries (if purchased) • Medical records.
Service companies	Drug companies that provide services such as manufacturing drugs, data analytics to other organizations.	For profit	• Identification of drug repurposing opportunities based on their client needs.	• Computational platforms. • Public compound libraries • Proprietary compound libraries of their clients • Medical records.
Government	Regulatory agencies, patent offices and health related divisions of governments.	Non- profit	• Management of drug approval and patenting process. • Organizing open innovation platforms to match drug owners with academics, companies and doctors with repurposing ideas.	• Open innovation platforms • Public funds to finance repurposing projects • Patent and approval databases • Clinical trial reports
Non-profit organizations	Communities of patients and relatives searching treatments for a disease with high unmet medical need.	Non-profit	• Identification of potential drugs for particular diseases. In most of the cases, these diseases are rare and orphan diseases. • Reaching out to patients and organizing clinical trials as well as approval process.	• Open innovation platforms • Social networks and patient databases • Medical records.



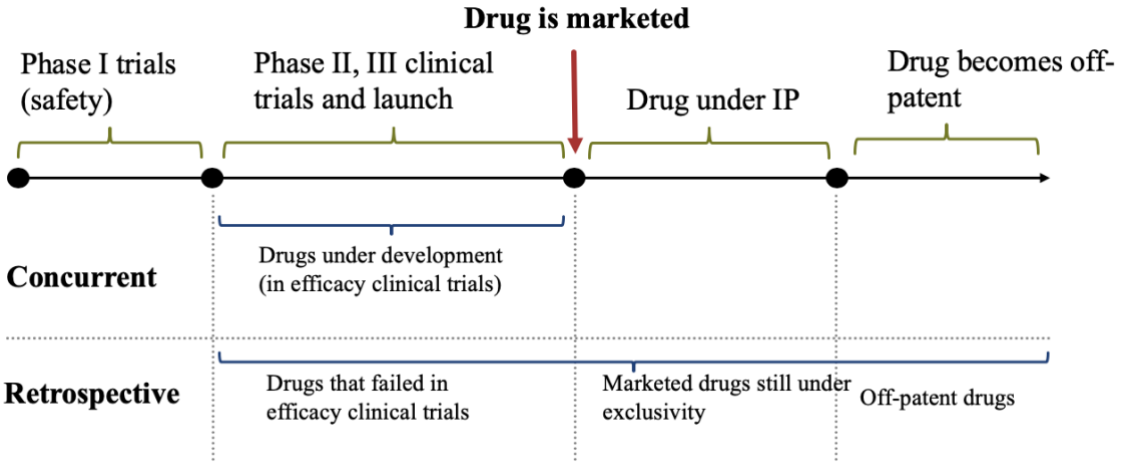


Figure 3: Temporal Modes of Repurposing

Small Numbers, Big Concerns: Practices and Organizational Arrangements in Rare Disease Drug Repurposing

Kucukkeles, B., Ben-Menahem, S., & von Krogh, G. (2019). Small Numbers, Big Concerns: Practices and Organizational Arrangements in Rare Disease Drug Repurposing. *Academy of Management Discoveries*.

https://doi.org/10.5465/amd.2018.0183

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2019, Vol. 5, No. 4, 1–23.
Online only
https://doi.org/10.5465/amd.2018.0183

SMALL NUMBERS, BIG CONCERNS: PRACTICES AND ORGANIZATIONAL ARRANGEMENTS IN RARE DISEASE DRUG REPURPOSING

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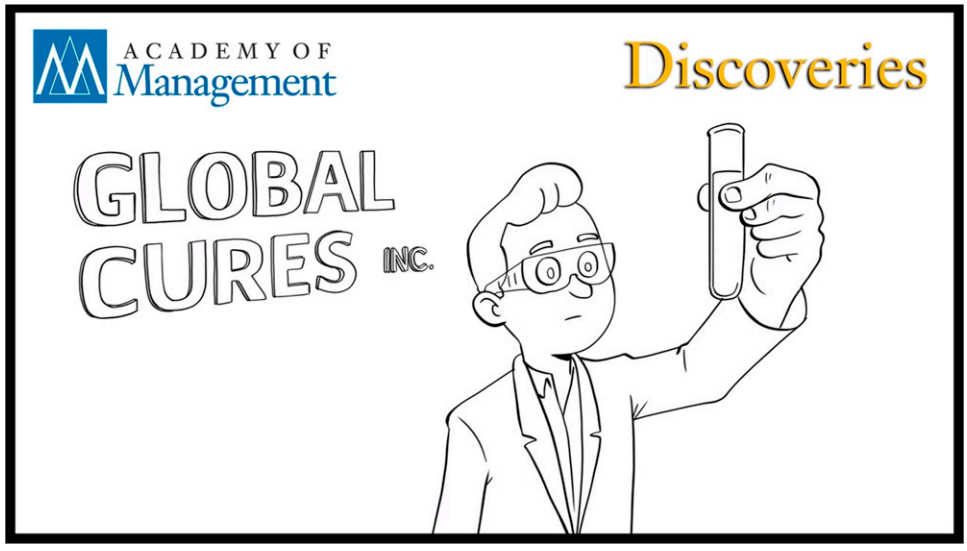

Because of their small market size, many rare diseases lack treatments. Although government incentives exist for the development of drugs for rare diseases, these interventions have yielded insufficient progress. Drawing on an in-depth case study of rare diseases therapies, we explore how the practices of two nonprofit organizations allowed them to circumvent the endemic market and government failures involving positive externalities by using generic drug repurposing—i.e., seeking new therapeutic applications for existing generic drugs. Beyond elucidating the potential of generic drug repurposing for those suffering from rare diseases, our discoveries provide important insights into the mutual constitution of organizational arrangements for societal challenges and the practices they host. By showing how organizational arrangements can both reinforce and extend practices such that they enable practitioners to achieve a standard of excellence, our study advances practice theory and research on the comparative efficacy of alternative organizational arrangements for tackling societal challenges.

INTRODUCTION

Access to safe, effective, and affordable therapeutic drugs constitutes a fundamental human development need. The challenge of developing such drugs is effectively met largely through the for-profit innovation activities (i.e., knowledge creation and commercialization) of private pharmaceutical firms. However, a growing and

We thank Stefan Thau and two anonymous reviewers for their insightful comments and suggestions throughout the review process. We are particularly grateful to Valérie Chardonnens, and members of Cures Within Reach and Findacure. We gratefully acknowledge Barbara Kohl and Natalie Reid for their editorial assistance. We are also grateful to the participants of the seminars in McGill Desautels Faculty of Management and LUISS Business School.

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substantial number of rare diseases[2] have been neglected by industry-based R&D (Austin & Dawkins, 2017). Given the relatively modest market size associated with rare diseases, investments in discovering and developing drugs and other therapies are commercially unattractive,[3] leading to an innovation market failure causing both personal suffering and severe economic and societal strain.

To tackle this social welfare issue, government policy interventions (e.g., the 1983 U.S. Orphan Drug Act [ODA]) have emerged globally in recent decades. Although partially successful at increasing the number of approved drugs for rare diseases, such interventions have also received criticism for failing to motivate extensive for-profit drug development in this space (Aronson, 2006; Côté & Keating, 2012). Some industry experts (e.g., Simoens, Cassiman, Dooms, & Picavet, 2012) have thus concluded that developing drugs for rare diseases is subject not only to persistent market failure in the for-profit private sector (Akerlof, 1970; Pitelis, 1994) but also to the failure of public administration and government policy-making (Coase, 1964; Luo & Kaul, 2019; Maskin & Tirole, 2008; Pitelis, 1994; Schmidt, 1996).

Understanding how to effectively organize solutions for such neglected societal problems is receiving increasing attention in management and organization research (George, Howard-Grenville, Joshi, & Tihanyi, 2016). Research on this issue from an organizational economics perspective (Coase, 1960; Williamson, 1989, 2000) has focused on how simultaneous market and government failures give rise to alternative organizational arrangements,[4] including nonprofits and social entrepreneurship (e.g., Luo & Kaul, 2019; Mair & Marti, 2006; Miller, Grimes, McMullen, & Vogus, 2012; Santos, 2012). An important distinguishing feature of such arrangements is their emphasis on creating value for society over capturing value for private gains. Likewise, in the case of rare diseases, organizations[5] have emerged with the primary objective of developing therapies for rare diseases.

Author's voice:
What is the social relevance of this research project?

The mechanisms leading to the emergence of organizational arrangements that prioritize social value have received significant attention in the organization literature. However, discovering therapies for rare disease represents a particularly challenging context for social value because it demands complex and costly knowledge creation with highly uncertain outcomes. Under such conditions, which practices evolve to overcome market and government failures remains poorly understood. The focus on organizational "doing" in nonprofits warrants a practice perspective emphasizing knowledge in use (Feldman & Orlikowski, 2011; Gherardi, 2001; Nag, Corley, & Gioia, 2007). Drawing on this perspective, we report discoveries that flow from our interest in understanding how field actors in the pharmaceutical industry use knowledge about existing drugs for identifying new therapeutic indications—a common practice known as drug repurposing (Barratt & Frail, 2012). While exploring this setting, we encountered two organizations that successfully applied drug repurposing to pursue their strategic intent[6] of finding new treatments for rare diseases and, in so doing, appeared to circumvent market and government failures in innovation.

From our interest in better understanding their practices, we conducted an in-depth analysis using interviews, secondary data, and observations. Our analysis shows how the two organizations placed the repurposing practice outside its traditional commercial context and reinforced it through a set of novel practices focused on (1) mobilizing collaboration among clinicians, researchers, and philanthropists; (2) leveraging the knowledge-creation potential of patients and relatives; and (3) catalyzing funding opportunities. The organizations thus helped realize positive externalities from basic and

[2] Rare diseases are defined by the European Union as those diseases/disorders affecting less than one in 2,000 inhabitants. The U.S. Food and Drug Administration (FDA) uses the criterion of fewer than 200,000 people in the United States (Aronson, 2006).

[3] Less than 10 percent of the roughly 7,000 known rare diseases have treatments. It is estimated that rare diseases collectively impact 6–7 percent of the developed world, among the millions of people suffering from them, with most of them remaining untreated (Melnikova, 2012).

[4] Organizational arrangements refer to how field actors "structure their activities and operate transactions within rules defined at the broad institutional level" (Ménard, 2014: 568); organizational arrangements thus constitute ways "to coordinate scarce resources" (Brousseau & Quelin, 1996: 1,206).

[5] Many forms of nonprofit organizations exist in the rare disease domain, including charities, single-disease societies, and patient advocacy groups. We use the term "nonprofit" to refer to those arrangements whose primary objective is to find treatments for rare disease patients.

[6] Strategic intent refers to an organization's "long-term goals and aims" (Prahalad & Doz, 1987: 52) and "directs the accumulation of necessary competencies" (Mantere & Sillince, 2007: 407).

commercial research for greater societal benefit. In this setting, the positive externality derived from the availability of generic drugs that can potentially be used to treat rare diseases.

Our discoveries provide important insights for organization scholars, policy-makers, and practitioners. We show that a practice perspective (Feldman & Orlikowski, 2011; MacIntyre, 1981; von Krogh, Haefliger, Spaeth, & Wallin, 2012) can help advance knowledge of the organizational arrangements for dealing with neglected societal issues (e.g., Luo & Kaul, 2019; Santos, 2012), even when they require complex and costly knowledge creation under high uncertainty. In particular, our findings emphasize that private nonprofit actors can deliver sustainable solutions to societal problems involving simultaneous market and governance failures with positive externalities when they create a context for prioritizing excellence in their practice. By focusing on the orchestration of practices in nonprofit organizations, our study extends the notion of stakeholder empowerment as a driving force in solving societal problems (Santos, 2012) beyond the confines of specific organizational arrangements.

Finally, our discoveries contribute to practice theory by elaborating insights on the mutually constitutive relation of practices to the organizations in which they exist (Feldman & Orlikowski, 2011; Giddens, 1984; MacIntyre, 1981). Prior work has demonstrated the tensions and struggles that frequently emerge between practices and the specific organizational context wherein they are enacted. These tensions result from the constraints that organizational attributes—such as governance arrangements and strategic objectives—can pose for agents' standards of excellence and have the potential to drive practices into more congenial organizations (von Krogh et al., 2012). However, little is known about what practices are needed to sustain a novel organizational context that helps uphold agents' standards of excellence. We contribute novel insights to this "practice-first" perspective by developing a theoretical framework (reinforcement) explaining how the drug repurposing practice may thrive under, but also breaks away from, the established organizational arrangements in for-profit drug development. The conduit in this process is the establishment of novel organizational arrangements that bolster the standards of excellence in practices.

THEORETICAL CONTEXT

Market and Government Failures

Market failures refer to inefficiencies in the distribution and allocation of services and goods in a market, leading to an unrealized outcome that can benefit certain field actors without harming others (Bator, 1958; Krugman & Wells, 2006). Information asymmetries and inefficient and incomplete markets are key drivers of market failures (Arrow, 1962). In innovation markets, failures lead not only to a distorted market structure that prevents firms from innovating adequately (Loury, 1979) but also to socially suboptimal outcomes as a consequence of failure to appropriate externalities such as knowledge spillovers (Stiglitz, 1989).

Scholars have proposed at least two organizational arrangements for resolving market failures: arrangements highlighting the importance of government intervention, such as public–private partnership (e.g., Appold, 2004; Hagedoorn, Link, & Vonortas, 2000; Zervos & Siegel, 2008), and arrangements highlighting private–actor involvement, such as social entrepreneurs (e.g., Luo & Kaul, 2019; Mair & Marti, 2006; Miller et al., 2012; Santos, 2012; Seelos & Mair, 2005) and nonprofit actors (Johnson & Prakash, 2007; Weisbrod, 1991, 1997). Proponents of the public–private partnerships perspective suggest that partnerships among commercial and public (e.g., governmental) organizations are particularly effective when there are (a) difficulties in amassing the funds for early-stage technology development, (b) weak incentives for investing in a particular type of research despite a public need, and (c) high expected social benefits from investing in new technologies (Appold, 2004; Hagedoorn et al., 2000; Siegel & Zervos, 2002; Zervos & Siegel, 2008).

Government policy can be an effective tool for dampening the harmful effects of externalities (e.g., environmental pollution). Yet, some externalities typically remain when governments allocate insufficient resources to correcting market failures (Martin & Scott, 2000; Santos, 2012)—resulting in what scholars have referred to as "government failures" (Coase, 1964; Stiglitz, 1998, 2009). Indeed, when market failures result from imperfect and costly information in innovation markets, governments can face information and incentive problems similar to those occurring in private markets (Stiglitz, 1989). The literature on social entrepreneurship (e.g., Luo & Kaul, 2019; Mair & Marti, 2006; Miller et al., 2012; Santos, 2012; Seelos & Mair, 2005) proposes that under conditions of simultaneous market and government failures, social actors can "provide a distributed mechanism for society to identify neglected problems with positive externalities, develop innovative solutions to address them, and, often, change institutional arrangements so that the externality becomes visible and is internalized by other societal actors" (Santos, 2012: 348). Specifically, social entrepreneurship centers on "entrepreneurial activity with

an embedded social purpose" (Austin, Stevenson, & Wei-Skillern, 2006: 370) aimed at creating social value rather than capturing private value (Santos, 2012). Thus, social entrepreneurship and related nonprofit arrangements (Johnson & Prakash, 2007; Weisbrod, 1991, 1997) that prioritize social gains over commercial gains can potentially offer solutions for neglected social problems under conditions of simultaneous market and government failures (Luo & Kaul, 2019; Santos, 2012).

A Practice Lens on Grand Societal Challenges

As Furton and Martin (2019: 197) propose, when classical incentive, institutional, and political mechanisms prove ineffective, "it is time to . . . focus on problems of institutional mismatch, when the rules governing institutions are ill-suited to the problems that agents confront." In line with this notion, the management and organizational economics literature have provided important insights into the root causes of societal challenges and the potential of alternative governance mechanisms such as nonprofits, social entrepreneurship, and related arrangements in solving them in the context of market and government failures (e.g., Doh, Tashman & Benischke, 2019; Lumpkin & Bacq, 2019; Luo & Kaul, 2019; Santos, 2012; Sarasvathy & Ramesh, 2018). However, a limited understanding of what actors in such alternative organizational arrangements do remains—i.e., how they inaugurate, institute, and cultivate practices to mitigate such endemic failures. Underlying the organizational arrangements discussed in the literature, a wealth of knowledge creation, problem-solving, and innovation activities are likely unfolding in emerging practices that may ultimately impinge on the effectiveness of structural solutions (e.g., Ben-Menahem, von Krogh, Erden, & Schneider, 2016). Studying such practices may allow scholars to discover entirely novel solutions to well-known market and government failures—solutions that in turn may hold wide-ranging consequences for how society and the economy may better cope with societal challenges.

Practice scholars argue that social life comes about through "ongoing production and thus emerges through people's recurrent actions" (Feldman & Orlikowski, 2011: 1,240). The practice lens encompasses three approaches. First, using practice as an empirical approach (e.g., Dutton & Dukerich, 1991), scholars foreground the centrality of practices as an expression of the human agency underlying organizational operations. Second, the theoretical approach to practice theory (e.g., Bourdieu, 1977; Giddens, 1984) asks "how practices are produced, reinforced, and changed, and with what intended and unintended consequences" (Feldman & Orlikowski, 2011: 1,241). Third, the philosophical approach (Gherardi, 2006) to practice takes an ontological stance in which practices are the constitutive elements of social reality (Feldman & Orlikowski, 2011; Schatzki, 2001; Whittington, 2011). In using a practice lens on the societal issue of rare disease drug discovery, we initially focused on understanding the activities of field actors (i.e., actors involved in seeking for solutions to tackle a societal challenge) seeking sustainable solutions to developing new treatments. As we discuss in greater detail in our Findings section and Discussion, our exploratory study also led to discoveries with implications for practice theory.

METHODS

Empirical Motivation and Research Setting

Rare diseases. A rare disease is one that affects a relatively small number of people in a population (Schieppati, Henter, Daina, & Aperia, 2008).[7] It is estimated that nearly 7,000 rare diseases affect 25–30 million people in the United States (Griggs et al., 2009) and 30 million people in Europe (Wästfelt, Fadeel, & Henter, 2006). Along with scientific advances in the pathophysiology of diseases, about 250 new rare diseases are described every year, and more specific (and thus smaller) disease categories emerge (Wästfelt et al., 2006). Rare diseases are often genetic and chronic conditions causing physical and mental disabilities that significantly impact patients' life expectancy and quality of life. At least 50 percent of rare diseases affect children (Wright, FitzPatrick, & Firth, 2018). Rare diseases thus place a significant burden on families by limiting the socioeconomic opportunities of relatives and caretakers (Schieppati et al., 2008). Moreover, because most rare diseases are hereditary, they can be widespread in a given family, although being uncommon in society.

Rare diseases constitute a societal problem that cuts across at least 6 of the 17 sustainable development goals (SDGs) defined by the UN General Assembly (Howard-Grenville et al., 2017: 106).[8] Enhancing treatment alternatives for rare diseases particularly aligns with SDG 3, ensuring healthy lives and promoting well-being for all people at all

[7] The definition of rare diseases varies between countries (e.g., less than 200,000 people in the United States, and less than 5 in 10,000 in the European Union). Most rare diseases affect a considerably smaller number of people (Aronson, 2006).

[8] See also NGO Committee for Rare Diseases, (Common Goals, n.d.), https://www.ngocommitteerarediseases.org/common-goals/.

Author's voice:
What motivated you personally to undertake this research?

ages. Furthermore, improving the life conditions of individuals with rare diseases holds great promise for reducing poverty (SDG 1), inequality among countries, and gender inequality (SDG 10) by reducing the marginalization of particular subgroups of patients—especially by improving the quality of life of mothers caring for children with rare diseases (SDG 5), improving opportunities for receiving high-quality education (SDG 4), and strengthening multistakeholder collaboration (SDG 17).

In recent decades, following increased public awareness of rare diseases, governments introduced regulatory incentives to enhance the development of drugs to treat rare diseases. For example, in 1983, the US government introduced the ODA, followed by similar acts in Japan (1985), Australia (1987), and the European Union (2000) (Aronson, 2006; Lavandeira, 2002). Governments have commonly introduced regulatory incentives in three categories: publicly funded research and tax benefits, access to fast-track regulatory approval processes, and extended market exclusivity for drugs with an effect on rare diseases (Aronson, 2006). Although regulatory incentives have contributed to increased numbers of drugs approved for rare diseases, field actors generally agree that the impact of government incentives has been inadequate (Haffner, Torrent-Farnell, & Maher, 2008; Simoens et al., 2012). Indeed, rare disease drug development has not only progressed slowly (Joppi, Bertele, & Garatinni, 2006) but also continues to lead to the high cost of treatment—with some drugs ranging up to 400,000 USD per patient per year (Haffner et al., 2018). Some experts have argued that large commercial pharmaceutical firms abuse orphan drug regulations to expedite approval for drugs for common diseases with secondary rare disease indications and increase prices (Haffner et al., 2018; Wellman-Labadie & Zhou, 2010).

As we studied the field of drug discovery and development, our empirical exploration uncovered two organizations whose practices enabled them to reinforce the practice of generic drug repurposing and, in so doing, develop sustainable solutions for rare diseases. We next discuss our sampling and data collection, and analytical approach.

Sampling and Data Collection

Our sampling strategy followed an embedded case-study approach (Yin, 1994), in which we progressed from analysis of rare disease drug discovery and development to selecting two nonprofit organizations—representing unique and revelatory cases within the rare disease setting—and their practices. In the initial stage of our study, we created an in-depth account of rare disease drug discovery and development, a setting of simultaneous market and government failures, collecting data primarily through interviews with members of a Swiss rare disease network. Next, we expanded the data collection to include experts from Germany, India, Israel, Switzerland, the United Kingdom, and the United States.

We followed a purposeful sampling strategy for selecting informants, resulting in 23 interviews with leading experts on rare diseases (Glaser, 1978; Patton, 1990; Yin, 1994). Our informants covered a wide range of roles in rare disease drug development (George et al., 2016), including academic and commercial researchers, clinicians, entrepreneurs, executives of big pharma companies, policy-makers, patent experts, and rare disease patients. To complement our interview data, we also collected articles on rare diseases from discipline-related journals and books, and regulatory agency websites. One of the authors attended three academic rare disease conferences to interact with field actors and cover the latest developments in the rare disease arena.

Drawing on our initial round of data collection and analysis, we focused our attention on two organizations, Cures Within Reach (CWR) and Findacure, both of which were unique and revelatory cases (Yin, 1994) in their approaches to creating sustainable solutions for discovering rare disease drug treatments. Four criteria guided our theoretical sampling. First, at the initial data collection stage, informants repeatedly referred to these two organizations and highlighted their successful approach to circumventing imminent market and government failures. Second, CWR and Findacure are central players in drug repurposing for rare diseases, organizing well-known conferences in their area of expertise, and were known as global pioneers in establishing an agenda and advocating for rare disease drug repurposing. Third, these organizations are transparent, allowing us broad access to their members and stakeholders. Fourth, the two organizations are unique in their strategic intent to create sustainable solutions for all untreated rare diseases, rather than limiting their focus on specific diseases or therapies.

The next stage of our data collection focused on gaining an in-depth understanding of CWR and Findacure's practices. We expanded our initial two interviews (the executives of each organization) with three additional interviews at CWR and two at Findacure. Our questions pertained to what actors

do as they pursue solutions to drug development and discovery for rare diseases.

We conducted 28 interviews, all of which were recorded, transcribed, and coded with NVivo. About half of the interviews were conducted face to face; the other half *via* video call or by phone. Interviews lasted between 45 minutes and 2 hours. Table 1 gives an overview of our informants.

To triangulate our data, we collected secondary data on the two organizations, including materials from their websites, annual reports, news articles, blog entries, and conference presentations, as well as videos of conferences, workshops, and published interviews with key stakeholders (Silverman, 2015). Table 2 shows an overview of the data sources. We next provide an overview of the two organizations.

Findacure. Findacure is a UK-based charity that aims to facilitate treatments for rare diseases. Findacure emphasizes patient needs and aims at contributing to rare disease developments both for patients and in collaboration with patients. It was founded in 2012 in Cambridge, UK, by Nick Sireau and Tony Hall. Nick has two sons who were diagnosed with an ultrarare disease that had no treatment at the time of diagnosis. Following his experience establishing a patient group[9] for the disease affecting his sons, Nick recognized the need for an organization that would facilitate knowledge sharing and learning among different patient groups. Tony is an expert on rare disease drug development with many years of experience with the challenges pharmaceutical industry drug development for rare diseases. Given these experiences, Tony recognized the need for developing a nonprofit alternative for finding rare disease treatments. Findacure has four employees, five board-of-trustee members, seven scientific advisors, and five patient-empowerment advisory committee members (Findacure, 2018a).

CWR. CWR is a public charity founded in 2005 by Goldman Philanthropic Partners in the United States with the primary mission of accelerating drug discovery for diseases with a high unmet medical need. Under the leadership of Bruce Bloom, CWR focuses on repurposing drugs for application in life-threatening diseases and on developing alternative approaches for research and funding. It currently has six employees, nine board-of director members, 11 scientific advisory board members, seven business development and commercialization committee members, and 24 young professional board members (Cures Within Reach, 2018b).

[9] Patient groups are support groups that patients, their families, and other advocates organize (typically) around a single or a group of related diseases, to share their experiences and bring awareness about diseases.

Data Analysis

We followed a qualitative research design for its strength in uncovering unknown phenomena (Arino, LeBaron, & Milliken, 2016; Bamberger, 2018; Robinson, 2019). Our research design consists of two stages. During each stage, we relied on interpretive thematic coding, drawing on some elements of grounded theory (Gioia, Corley, & Hamilton, 2013; Strauss & Corbin, 1998).

Stage one. We initially kept our research question very broad, focusing on how field actors in rare disease drug development construed a reason for the lack of treatments for rare diseases. At this stage, we kept a "willing suspension of belief" (Gioia et al., 2013: 21) about potential explanations. First, we followed an open coding strategy to map informants' interpretations of the lack of treatments for rare diseases, and their potential solutions. In the open coding stage, we stayed as close as possible to our data and developed first-order codes. For example, when one of our informants, Colin, a molecular biologist and chief scientific officer at a biotech company, mentioned that "normally, rare diseases are only addressed after a success in another disease, a strategy known as lifecycle extension. . .," which we coded as "developing drugs for rare diseases only after developing drugs for common diseases."

Next, we iterated between our data and the literature. Rather than trying to retrofit our data, this stage involved searching for potential theoretical explanations for our emerging findings and the potential theoretical contributions of our emergent insights (Gioia et al., 2013). We identified various theoretical perspectives on market and government failures in the management and economics literature (e.g., Santos, 2012; Stiglitz, 2009). While continuously iterating between theory and data, and ensuring that our emerging themes related to relevant theoretical constructs, we developed our second-order themes (Gioia et al., 2013). For example, we grouped codes relating to first-order codes, such as "developing drugs for rare diseases only after developing drugs for common diseases" and "increasing the price of drugs by first launching them for rare indications" as "construing market and government failures." In addition, we had informants validate our themes on various occasions.

We triangulated multiple data sources including interviews and secondary sources (e.g., publications, conference notes, and presentations) (Strauss & Corbin, 1998). For example, the theme "repurposing generic drugs with positive externalities as a way to find treatments for rare diseases" emerged from both our interview data and our field notes from rare disease conferences, where drug repurposing was a recurrent theme. While triangulating our data, we also paid attention to possible biases and conflicting

TABLE 1
Overview of Interviews

	Name	Role	Number of Interviews
1	Ocean	Academia/PhD researcher	1
2	Camron	Academia/head of research group	1
3	Alfonso	Patent expert	1
4	Lise	Researcher with industry experience	1
5	Tanja	Patient/researcher	1
6	Pearce	Marketing expert	1
7	Colin	Industry expert	1
8	Stanko	Senior pediatrician	1
9	Robin	Drug repurposing company	1
10	Monte	Drug repurposing company	2
11	Reid	Drug repurposing company/academia	1
12	James	Non-profit	1
13	Gregory	Academic	1
14	Beckett	Clinician/academia	1
15	Sam	Clinician/researcher	1
16	Marion	Government	1
17	Alex	Drug repurposing company	1
18	Patrick	Drug repurposing company	1
19	Travis	Drug repurposing company	1
20	Calvin	Drug repurposing company	1
		Interviews with Findacure	
21	Manuel	Cofounder	1
22	Rene	Executive	2
		Interviews with CWR	
23	Daniel	Executive/cofounder	2
24	Nina	Manager	1
25	Summer	Manager	1

views in the data. In cases of conflicting accounts, we cross-compared our insights from interviews with secondary data sources and contacted experts in the drug discovery field.

Stage two. Over the course of stage one, we became particularly intrigued by the finding that some organizations appeared to circumvent innovation market and government failures through repurposing. To better understand this finding, we focused our exploration on the interplay of market and government failures, specific organizational features, and practices within two unique and revelatory organizations. Our preliminary exploration focused on uncovering what practices allowed these organizations to successfully circumvent the market and government failures. Our unit of analysis in this stage thus centered on practices. In exploring the two organizations, we iterated between data collection and analysis until we reached an empirical saturation point where neither new informants from the organizations nor secondary data would deliver new first-order codes about their practices.

Our data analysis of the two organizations involved two steps. First, during the open coding process, we coded their activities in actors' day-to-day reality. During the axial coding, we clustered these activities into three practices. For example, we grouped the first-order codes for "organizing conferences to facilitate interaction between field actors from different domains," "creating a community by using online platforms," and "playing a bridging role between different actors in their networks" as "mobilizing cross-field collaborative knowledge creation through community building." As in the first stage, we triangulated our findings with secondary data sources, including the organizations' websites and published documents. Informal interactions with organizational members also allowed us to check our emerging insights during our research process. Table 3 shows the key themes and sample quotes from our data analysis.

FINDINGS

We present our findings in three parts. First, we report how field actors construe market and government failures that limit the development of treatments for rare diseases. Second, we describe how our informants perceived a drug development practice known as generic drug repurposing to hold

TABLE 2
Overview of Data Sources

Use in the Analysis	Data Source	Description
Data collection in stage 1: market and government failures in rare diseases		
Primary data source	Interviews	23 interviews with experts in rare diseases, clinicians, nonprofit organizations, government employees, and researchers. Interviews lasted between 45 and 120 minutes.
Secondary data source	Scholarly publications and other scientific resources	Articles published in main field journals, including Nature, Drug Discovery Today, PNAS, and PLOS One.
Secondary data source	Other archival resources	Organizational websites and reports, and news articles.
Secondary data source	Field notes from networking events	Three field conferences in June 2015, June 2016, and February 2017. 40 hours of nonparticipatory observation.
Data collection in stage 2: case organizations		
Findacure		
Primary data source	Interviews	2 additional interviews with two members. Interviews lasted between 45 and 60 minutes.
Secondary data source	Organization website	https://www.findacure.org.uk/
Secondary data source	Patient focus group reports	4 patient focus group reports: a total of 39 pages.
Secondary data source	Impact reports	4 impact reports between 2014 and 2017: a total of 58 pages.
Secondary data source	News articles, annual account, and trustee reports	3 news articles, and 4 annual accounts and trustee reports: 139 pages.
CWR		
Primary data source	Interviews	3 additional interviews with three members. Interviews lasted between 45 and 60 minutes.
Secondary data source	Organization website	https://www.cureswithinreach.org/
Secondary data source	Annual reports	8 annual reports for the years between 2009 and 2017: 124 pages.
Secondary data source	Conference presentations	4 conference presentations prepared about CWR's practices: 120 slides.
Secondary data source	Audited financial statements	Financial statements of the years 2010–2017: 100 pages.

TABLE 3
Themes and Example Quotes

Theme	Illustrative Interview Quotes
First Stage	
Construing market and government failures	*"Definitely, [pharmaceutical drug development] is a failed market. First and foremost, the industry has to be profitable, otherwise it would never exist. The incentive is for a company to make a profit even if that means [developing] an expensive drug that takes longer and is less likely to reach the market, [instead of] a cheap drug that can be quickly introduced, involves less innovation risk, and can result in a cheaper product at the end of the day."* (Alex) *"In the United States, companies can determine their drug prices. If you are able to buy it or not, that is your problem. There is a company which has a model to focus on rare diseases but in a way that it buys small companies and then rises the price for a drug when they are approved on the market. This makes it impossible to afford for patients [who] have to pay out of pocket. . .."* (Tanja).
Repurposing generic drugs with positive externalities as a way to find treatments for rare diseases	*"I wish there was even more repurposing for drugs that are not of immediate interest to [commercial] companies. If I take a generic drug that is off-patent and want to use it repurposed, usually you have to do clinical trials and all that costs money. If it's some old compound your rationale to earn money from a public source has to be very good to get it approved for your new indication. The other option is just trying to convince insurance companies to cover it. So, I think overall, there could be much more repurposing for different areas and for different reasons."* (Beckett) *"It's actually super rare that you will see new chemical entities [newly developed drugs] in rare disease. This is by default the case because of the risk. In a rare disease community, the first thing is to minimize the risk, and the risk is minimized if you can repurpose a drug, which is proven to be safe."* (Colin)
Second Stage	
Mobilizing cross-field collaborative knowledge creation through community building	*"Going to scientific conferences is key in my experience. When I went to a scientific conference a long time ago, I met a researcher who wanted to develop a model of AKU [the disease that Manuel works on] after hearing my talk, and then started developing it. These meetings do lead to a lot of connections and that's why it is worth organizing conferences dedicated to rare diseases."* (Manuel) *"CureAccelerator Live is one great example where we have had the opportunity to showcase pitches on repurposing where we select up to five finalists. The researchers come and present an eight-minute pitch for their particular repurposing clinical trial, and the attendees in these events then vote on the projects. The winner receives up to fifty-thousand dollars in funding. There have been really great events where we have not only been able to fund projects but also create exposure for the other researchers and their research."* (Nina)
Leveraging the knowledge creation potential of end users	*"This year I'm mentoring a group called PANS and PANDAS UK, pediatric autoimmune neurologic disorders. [children develop extreme psychiatric disorders due to an infection]. I'm mentoring them, and they have a big struggle. Not only is this a rare disease but also, no one really knows how the people are affected. I think peer mentoring works really well. Findacure sets the overall structure and provides the logistic help, a kick-off meeting, and peer mentoring meetings. I have Skype chats with PANS and PANDAS every two weeks to assess their progress, discuss their objectives, [help with] fundraising, all these things."* (Manuel) *"It's a lack of knowledge that leads to problems. There's a lack of knowledge about where the patients are, what the patients' issues are, what the natural progression and the mechanisms of the condition are. It's the intrinsic lack of understanding which causes problems. A lot of our work concerns directly working with those patients and patient organizations to provide them with training and support."* (Rene)
Catalyzing funding for repurposing opportunities	*"We [CWR] see ourselves as catalyzers, giving money early on to support clinical trials for repurposing [projects] that we hope will. . .get published in a bigger trial, which we already had successes with."* (Summer) *"Drug repurposing is really interesting because it bypasses so many of the problems you get in the early stages of traditional drug development, particularly safety issues. [But] the key problem in drug repositioning is the intellectual property. . .the fact that most of these repositioning drugs are generic. They may cost just a few pennies to produce and there is no return for commercial companies developing them. That is why you have to go for grants or for things like Social Impact Bonds which is a concept that [Daniel] from CWR and [Rene] from Findacure have developed for rare diseases."* (Manuel)

important opportunities for rare disease treatment, yet also considered this practice to be underused in traditional organizational arrangements such as commercial pharmaceutical companies. Third, we report how Findacure and CWR could effectively host and extend generic drug repurposing practices. Using these practices, the two organizations successfully capture positive externalities from generic drugs for rare diseases and, in so doing, circumvent market and government failure.

Construing Market and Government Failures

With very few established treatments for rare diseases, Calvin, a patent expert and owner of a biotech company, explains why the traditional "blockbuster model" of drug development—in which pharmaceutical companies formulate a strategic intent of targeting diseases with large patient populations—leaves most rare diseases unattended to:

> *It is difficult for a company to finance drug development for a small market. It takes too long to recoup development costs. And drug discovery is a risky process as it is. The risk of competition often turns out to be higher than expected, or other problems arise with [the safety and efficacy of] the drug. You need to forecast [such risks] five to seven years in advance. . . Without additional incentives, nobody would develop anything for rare diseases.*

Since the early 1980s, healthcare authorities have become increasingly aware of the need to incentivize discovery and development for rare diseases through regulation. One of the earliest government interventions was the U.S. ODA of 1983. The ODA outlines a set of incentives for the development of drugs for rare diseases by pharmaceutical companies, including additional years of market exclusivity, reduction in application fees, fast-track approvals, and tax incentives. Other countries followed suit, passing laws providing similar incentive programs. Amelia, a marketing expert in the pharmaceutical industry, reflects on these developments:

> *The ODA and similar acts in Europe in 2000 changed the industry's incentives and motivations. It lowered barriers such that companies could now enter easily and have the guarantee that they were protected from competition for at least 10 years.*

Author's voice:
Was there anything that surprised you about the findings?

Regulatory incentives for rare disease drug research indeed resulted in a significant increase in the number of rare disease drug approvals. Between 1983 and 2017, the U.S. Food and Drug Administration (FDA) granted more than 600 orphan drug designations (Lanthier, 2017). Yet many field actors argued that current incentives fail to enhance dedicated basic R&D for rare diseases. Colin, a molecular biologist and chief scientific officer at a biotech company, explains one important cause:

> *Normally, rare diseases are only addressed after success in another disease, a strategy known as lifecycle extension. [A company can extend an existing drug's patent protection] either by changing its formulation[10] or by adding a rare disease indication. In this way, you can maintain a higher price compared to its generic [off-patent] price.*

Our findings show that approximately 70 of the roughly 450 drugs approved under the ODA incentive program were initially approved for common diseases. In 2017, 47 percent of approved drugs received an orphan status (Tribble & Lupkin, 2017). Thus, the regulatory incentives proved effective in stimulating clinical trials aimed at exploring the potential use of drugs initially developed for other diseases—an important and positive outcome for rare disease patients. However, the incentives proved less effective for stimulating new projects dedicated to the many unaddressed rare diseases requiring costly basic research. Camron, a physician and clinical researcher in rare diseases, notes:

> *If you go to the websites of big pharma companies, it looks like they develop many drugs for rare diseases. The reason is that the registration of the drug is much easier if you develop a drug for a rare disease. Once the company registers the drug, they can easily reassign it for a more common disease. It's a bit of a trick enabled by the Orphan Drug Act.*

Colin further explained:

> *Companies used to go into small indications to get quick approval, and subsequently, extend the drug for general indications. . . For example, there is a drug for a disease with only 10 patients globally. [A company] submitted a new drug application based on a clinical trial with 10 patients on this super rare disease. . . . Then the company extended the application to arthritis because it works on the same mechanism of action in the human body, but has a much larger market.*

[10] Reformulation patents involve mixing a formerly used active ingredient into a new patentable mixture.

In line with Colin's comment, many of our informants observed that government incentives have primarily stimulated R&D efforts for rare diseases where implications exist for a common disease, although these incentives have been less effective in stimulating basic R&D efforts for unaddressed rare diseases where such links are absent or remain unidentified.

Informants frequently viewed increasing prices for drugs receiving orphan status as an indication of government failure. Indeed, the high prices of rare disease treatments result in a financial burden for healthcare systems and reimbursement challenges for uninsured patients. With the number of orphan disease drug applications increasing as scientists continuously identify new rare diseases and develop new treatments, experts predict that healthcare systems being able to cover the associated increases in costs is unlikely (Stephens & Blazynski, 2014). Rene, a Findacure executive, explains:

> *Concerning the reimbursement challenges, you could probably say that it is more a government failure than a market failure. Firms are responding to market signals, and are developing and marketing products at a price that it can still generate profit for them. However, such high prices are leading to reimbursement issues for rare disease patients.*

Generic Drug Repurposing and Positive Externalities

As our interviews progressed, field experts noted that—given the limited effectiveness of government policies in solving the apparent market failure in rare diseases—alternative approaches to delivering fast and affordable solutions for rare disease patients were needed. One practice that frequently emerged as a promising opportunity was generic[11] drug repurposing. By focusing on drugs with known safety profiles, drug repurposing has the potential to reduce development costs, time, and risk of failure (Barratt & Frail, 2012).

Historically, scientists and physicians discovered additional uses of marketed drugs for rare diseases serendipitously. Given the lack of sufficient treatments for rare diseases, physicians often prescribe drugs known as effective for suppressing symptoms of rare diseases or drugs serendipitously observed as effective treatments. James, a member of a patient advocacy group, explains why the potential benefits of drug repurposing are particularly appealing as a systematic solution for rare disease drug development:

> *Drug repurposing is clearly an area that can be attractive for all those diseases that are currently neglected by the pharmaceutical industry—wherever there are no powerful incentives for the development of new medicine. For rare disease patient organizations like mine, this is very attractive because we would like to deliver value for patients, and financial returns are not really the key objectives.*

Although potentially valuable, scientific evidence on how the safety and efficacy of drugs developed for common diseases could extend to rare disease indications has been lacking because of the requirements for costly additional clinical studies. Thus, the existence of unused yet potentially valuable off-patent compounds constitutes what economists call a welfare loss involving a positive externality (Bator, 1958). Rene, an executive at Findacure, further explains:

> *Reusing an existing generic [off-patent] drug can result in lower prices. However, there aren't really incentives in [commercial] pharma to do that because they can't easily protect their patents. Physicians could just prescribe another generic version of the treatment, so it is unlikely they will regain their investments. So you don't really see [big pharmaceutical companies] working that generic space so much. It lacks commercial viability.*

There are two pathways to using generic drugs known to be effective for rare disease indications. First, physicians can prescribe an existing drug for off-label use. Although many countries prohibit the advertising of off-label use without additional clinical trials proving safety and efficacy in its target patient population, off-label use accounts for up to 90 percent of rare disease drug prescriptions in the United States (Liang & Mackey, 2010; von Hippel, DeMonaco, & de Jong, 2014). Second, field actors can conduct additional clinical trials to specify a drug's safety and efficacy for the rare disease indication, and subsequently apply for regulatory approval.

However, regulatory authority requirements for costly additional clinical trials pose an important limitation for those pursuing repurposing opportunities aimed at rare disease applications. Dialog Box 1 illustrates this problem when a physician-clinical researcher and his team were developing a drug based on a natural extract for a rare indication and struggled to finance clinical trials and further stages of commercialization.

[11] A generic drug is a drug with an expired patent. When a drug becomes generic, information about it becomes publicly available, with any manufacturer allowed the right to produce it, resulting in increased market competition and lower prices.

Dialog Box 1: An interview with Camron about the discovery of serine as a potential treatment for hereditary peripheral neuropathy (HSN1).

Q: Can you explain your discovery?

A: The background is actually in a disease called hereditary sensory neuropathy type 1 or HSN1. Patients lose their sensation for pain and temperature. It's a slowly progressing disease. Typically, the symptoms start at an early age.... What we observed is that we can basically suppress the formation of disease. . .based on the natural product serine.

Q: How did you proceed with your discovery?

A: Serine is a normal amino acid—a natural substance like sugar—and is thus quite hard to protect, which raises the problem of intellectual property. . .. We can say that the use of serine for the treatment in HSN1 is protected, but this will not give any tight protection that would be of interest to any company because you can easily use it off label. Just don't label it at all and then you can use serine free of any restrictions.

Q: What was the problem in launching serine as a drug for HSN1?

A: We would need a clinical study [to prove its safety and efficacy]. Clinical studies in the field of peripheral neuropathies are quite expensive because they take a long time. If the patient already has nerve defects causing insensitivity in the feet and hands, it takes a long time to observe an effect, even if the treatment is effective. So we have a bit of a stupid situation. We have a therapy that is cheap but cannot be protected. Then, we have to prove efficiency, [but] studies are very expensive and time-consuming, and won't be financed by the industry because there is no payoff. The problem arises because of regulations. As soon as you have an indication for a chemical, it is considered a medication. So you have to perform studies, apply for permissions, and do administrative work. It's again a bit of a scurrilous situation. You tell people quietly to eat it, it's good for you, but we cannot really tell them that it's good for them.

Sam, a professor of pediatrics and cofounder of a leading repurposing platform, concludes:

> *The big challenge that we haven't figured out quite yet is the financial model of how a repurposing opportunity could get sufficient resources. . . I think that's a fundamental problem. I'm a little bit worried. . .. The investment community and venture capitalists aren't going to be interested in funding because it's generic. Governments could do it, but governments often move slowly and might not have enough resources for it. . ..*

Thus, our findings from the first step showed that generic drug repurposing—although widely considered as having potential as a tool for developing new treatments for rare diseases—lacked commercial viability within existing arrangements. Indeed, large pharmaceutical companies typically prioritize the search for novel drugs with strong opportunities for intellectual property, which enables them to recoup R&D costs (Dutfield, 2017) that often leaves generic drug repurposing out of the focus of strategic intents of large pharmaceutical companies.

In the remainder of this section, we report our findings on how Findacure and CWR, by placing generic drug repurposing outside the purview of the commercial context, were able to host a set of reinforcing practices that supported generic drug repurposing. Doing so enabled these two organizations to successfully circumvent some of the critical market and government failures.

Generic Drug Repurposing for Rare Disease Treatments: Reinforcing Practices

CWR formulates its strategic intent as "improve [ing] patient quality and length of life by leveraging the speed, safety, and cost-effectiveness of medical repurposing research, to drive more treatments to more patients more quickly" (CWR website, "Mission" (Cures Within Reach, 2018a)). Daniel, a CWR executive, explains the focus on generic drug repurposing as follows:

> *We've funded conferences, worked in integrative medicine, funded de novo research, and accidentally funded some repurposing research and a number of other things. We tried to help disease-specific non-profits. We tried all sorts of things to find where we could be the most successful, and after ten years of doing all of these different things, we realized we were having the most success in drug repurposing.*

Similarly, placing generic drug repurposing at the center of their activities, Findacure aims at creating "a world in which all rare diseases have treatments—made together with patients, for patients" (Findacure website, "About us" (Findacure, 2018a)). As Rene explained:

> *We think that the generics market is relatively untapped for repurposing. When you combine the issue of small patient population in rare diseases with the issue of repurposing in generics in terms of the lack of IP. . .it tends to be a quite unappealing industry. There are, however, potential uses for the generics in the prevention and treatment of rare diseases.*

Findacure emphasizes the role of patients and patient communities. Manuel, the cofounder of Findacure, explains:

> *We were successful with AKU [Alkaptonuria, the disease affecting Manuel's children] because. . .we had the team in place, we had done all the scientific research, we had the animal model, the clinicians, and access to the patients [globally]. We even asked an accountant from a global accounting firm to calculate how much an average AKU patient costs the NHS. After*

establishing all the necessary pillars, it was much easier to convince other stakeholders, such as the company that owns the candidate drug compound, the NHS, and the European Commission [to fund us]. After we had demonstrated success with AKU, I was frequently contacted by parents who wanted to set up patient groups for other rare diseases. So I thought it would be more helpful to set up some kind of a structured environment within which to do this because there was obviously a big gap.

Aspiring to excel in their standard of fundamentally serving rare disease patients' and caregivers' interests, CWR and Findacure reinforced the practice of generic drug repurposing beyond its use in large pharmaceutical companies. We next present findings on three practices that Findacure and CWR applied as they pursue their strategic intent of repurposing generic drugs for rare diseases to overcome the market and government failures previously described.

Mobilizing cross-field collaborative knowledge creation through community building. A primary function of repurposing for rare diseases is both the advancement of knowledge about under-researched generic drugs and finding applications for treating complex rare diseases within dispersed and small patient populations. Developing treatments for rare diseases thus involves a complex knowledge-creation process in which multiple knowledge domains need integration. These domains include clinical research findings, studies on the mechanism of action, the properties of the generic drugs (e.g., pharmacologic), knowledge of financial models, and physicians' experiences in diagnosing and treating the symptoms of rare disease patients.

For the case organizations we analyzed, community building was at the core of mobilizing cross-field collaborative knowledge creation. Mobilizing collaborative knowledge creation involves bringing together field actors within different knowledge domains (e.g., patients and patient relatives, doctors, researchers, funders, social entrepreneurs, stakeholders from pharmaceutical companies, and governmental organizations), and instilling in them a sense of community. CWR and Findacure achieve community building through online (e.g., platforms) and offline (e.g., events) channels. As the following statement from CWR executive Daniel shows, the need for community building emerges from the high dispersion and lack of central organization and integration among the knowledge creation activities of different actors in the rare disease field:

We got a call from a rare disease organization [which asked for advice about the rare disease they work on]. It's an ultra-rare disease affecting fewer than 1,000 people in the United States. They knew maybe 30 researchers around the world working on this disease. When I did a PubMed search, I found 1,400 publications on this disease, and around 420 authors working on something relevant.

Bruce, the CEO of CWR, emphasizes:

We desperately needed a place where smart and like-minded people could share their ideas and uncover new medical solutions for unsolved diseases. Funders need to know where to find the most promising projects, and researchers need exposure [to patients] to develop ideas that might transform patient lives. (Bloom & Thibodeaux, 2016)

By facilitating interaction among multiple field actors, Findacure and CWR seek to enhance the integration of these actors' knowledge, and create opportunities for knowledge creation around generic drug repurposing:

[Findacure brings] all of these groups together to promote collaboration and, ultimately, build a cohesive rare disease community. In so doing, we are providing opportunities for rare disease patient groups to make the connections they need to accomplish their own mission, as well as giving researchers the motivation to engage patients in their work. (Findacure website, "Building the Community." (Findacure, 2018b)

In 2015, CWR founded CureAccelerator, an online platform dedicated to repurposing research and proof-of-concept studies for drugs approved for human use. The stated objective of CureAccelerator is to "quickly and affordably answer the question 'will this help patients?'" (CureAccelerator website, "What is CureAccelerator?" (CureAccelerator, 2019). Specifically, the platform allows researchers to post their repurposing ideas and interact with peers and potential funders, and offers funders a way of identifying repurposing projects that they would like to support. Moreover, the platform enables clinicians to share their experiences with prescribing off-label drugs.

CureAccelerator has a growing community of approximately 2,000 users—primarily researchers, funders, and clinicians, as well as company representatives and members of patient advocacy groups. In this way, the platform not only enables knowledge exchange but also serves as a matching mechanism for opportunities (potential treatments) and resources (funding). Daniel, CWR executive, notes:

There are people who know things about rare diseases, and they don't even know that the rare

disease exists. We find out that some rare disease has a certain gene trigger or pathway involved with it, and it's the same pathway that is involved in a more common disease. The people out there working in the common disease don't even know that the rare disease exists. If we could figure out how to tie them together, then we might be able to say "Oh, this researcher over here could work with this clinician on this rare disease and bring in some new knowledge." We use a different web application [in addition to CureAccelerator]. . .to find those people by searching all the publications to see who has published on this pathway or this particular target once we find that it exists in a rare disease.

In addition to uniting people involved in rare diseases on online platforms, Findacure and CWR stimulate networking opportunities in the form of conferences and showcase events. In these conferences, field actors come together to learn about the latest developments in drug repurposing, present and discuss their research and ideas on rare diseases, meet patients and learn about their experiences living with the disease, and meet with potential collaborators. Nina, a manager at CWR, recalls:

One academic researcher, who was working on Huntington's disease, reached out to me. I told him "You know, I was talking to another researcher from your institution who also works on Huntington's disease and has served as a reviewer for one of our recent grants." I connected them, and they are now collaborating on projects. We can connect people because we're building this ecosystem, because we're building these connections, I can say, "I know somebody from your own institution who can be great for you."

Leveraging the knowledge creation potential of end users. The second practice we identified is efforts to leverage the knowledge creation potential of end users, by empowering their participation in the search for treatments. Leveraging the knowledge creation potential of end users means engaging patients and their relatives in the process of knowledge creation, and integrating their needs and experiences to enhance the knowledge creation process. Rene, a Findacure executive, explains the importance of involving patients as follows:

We have a limited understanding of the needs and experiences of patients. Furthermore, it's very difficult to understand what the drug does, what it means for a patient's daily life, what the real value of the drug is. . . . It is [also] much easier to get them reimbursed [with the help of] patient organizations that are involved in interpreting information, developing new measures, and explaining the impact of treatments.

Manuel, the cofounder of Findacure, explains:

When I set up Findacure, one of the main priorities was to really build a new patient group sector for patient mentoring, workshops, networking, and drug repurposing. . . . Although each rare disease is very different, the issues [patients] face are very similar: marginalization, difficulties in accessing funding, identifying and recruiting patients for clinical trials, and working with pharma and academia. Somewhere, someone has solved these problems, and it's just about finding them and packaging it, and teaching people how to do it.

For a number of rare diseases, patient groups have emerged to represent patient interests. Rene further notes why enabling patients to form communities is critical:

Patient communities [groups]. . .help create experts in their disease area and grow the knowledge base. They often end up collecting their own data on patients and disease progression, and fund research through community fundraising. They can also help develop treatment pathways in collaboration with clinicians and come up with ideas for treatments and new clinical trial protocols specific to rare conditions. . . . In this way, [patient communities] bridge the knowledge gap between [those suffering from the] condition and researchers. They streamline . . .and [facilitate the process] of finding a treatment.

Mary, an event manager of Findacure, explains that although patient groups are vital for rare diseases,

[*m]any of these patient groups have little organizational experience. . . Many rare diseases don't have any patient groups at all. Therefore, Findacure tries to unite these fragmented patient groups into taking control of their own conditions and getting involved in research and medical developments.* (Findacure, 2016)

Engaging patients thus enhances the process of repurposing by saving time and money. We found that CWR and Findacure supported the formation of patient groups by organizing workshops, webinars, peer mentoring, and e-learning opportunities, and by publishing information resources.

Supporting patient groups empowers end users to become active partners in R&D for rare diseases. Although patient groups are vital for repurposing drugs for rare diseases, only half of all rare diseases are

represented in a disease-specific patient group. Most patient groups are kitchen-table organizations run by volunteers with limited experience or knowledge on how to organize themselves to achieve their objectives. For example, Findacure enables patient groups to develop active communities by organizing training workshops, webinars, and peer-mentoring. In one instance, Findacure helped create the LHON Society, a patient organization for a rare hereditary disease causing vision loss. Russell—whose son lost his vision at the age of 24 years and was diagnosed with LHON—attended Findacure's workshops. After learning about the experiences of other patient groups, he decided to establish the LHON Society and became an active member of ERN-EYE, a European virtual specialist network on complex and rare diseases requiring highly specialized treatment.

Findacure also offers an e-learning portal for patients and advocacy groups to develop their knowledge of rare diseases and issues related to healthcare technologies, health economics, and patient registries, and to build a rare disease patient organization. Mary described the e-learning portal and Findacure's activities as follows:

> *We provide…a central hub of information for patient groups and rare disease advocates. The online portal empowers and encourages the creation of new patient groups and allows for [developing] existing patient groups, and ultimately builds the rare disease community by facilitating communication between its users. The online portal hosts a variety of topics at various levels…including an introduction to rare diseases, how to set up a patient group, working with pharmaceutical companies, and information on drug repurposing and fundraising. Ultimately, this larger community leads to a greater force that can create wide-scale changes within research and patient priority settings.* (Findacure, 2016)

Pippa, a patient of the rare Ehlers-Danlos syndrome that causes the body's connective tissue to become elastic and fragile, notes:

> *Most of the patient groups are run by passionate parents and patients who have found themselves in this position by chance. They're not necessarily equipped with the necessary resources. We have the same need for support groups, tools to manage our conditions, and to understand the research and get grant funding. By bringing us altogether, and facilitating and teaching us all those things, Findacure is massively improving the patient power of these support groups.* (Findacure, 2014)

Finally, Findacure and CWR publish resources—including blog posts, books, scientific articles, and disease focus reports—showing their commitment to upholding their practice standards in creating knowledge in ways that meet the standards of medical research. A notable example includes Findacure's essay competition, for which field actors write about their experiences as patients, researchers, and industry experts. Findacure also sponsors the publication of the winning essay in the Orphanet Journal of Rare Diseases.

Catalyzing funding for repurposing opportunities. Catalyzing funding for opportunities is the practice of attracting and allocating monetary resources to repurposing solutions. Findacure and CWR approached this practice both through direct funding and by developing and supporting new financial models. Daniel, a CWR executive, explains:

> *The first part of our mission is to facilitate proof-of-concept clinical trials in drug repurposing. Our primary objective is to link researchers with funders, get the project started and completed, and publish the results… We have about 45 research institution partners. Whenever we have a new funding opportunity, we make sure that they know about these opportunities both by sending emails and contacting people by phone, and by posting calls on the CureAccelerator platform. These give details about how much money is offered, the duration, and any other project restrictions.*

Nina from CWR further comments:

> *We build relationships with academic institutions and the researchers who do the work. They become more of a partner for CWR rather than somebody who is sending us research proposals for potential funding. For example, even if an academic institution does not have a proposal, we can still engage it in grant reviews. We also go back to people who applied for funding opportunities in the past and say "We have this new funding opportunity, we think that you're a great fit, let us know if you want to update your project and to be considered…" It's about relationship building.*

Nina further explains the close collaboration of CWR with research applicants:

> *We try and work closely with researchers who are applying so that they get lots of feedback along the way…. It's important that we're finding the best repurposing research opportunities out there…. Once we get reviews back from the reviewers, we feed those back to the researchers…and provide an opportunity to*

address these comments before we make the final decision. It's a very interactive and iterative process. It ends up with a stronger grant.

In one project, e.g., CWR collaborated with pediatrician David Teachey to repurpose the FDA-approved drug sirolimus for treating a rare pediatric autoimmune disease known as autoimmune lymphoproliferative syndrome (ALPS). ALPS patients typically spend 5 to 10 days a month in the hospital and rarely survive beyond their teenage years. David recalls:

Since it was a preliminary idea without a ton of data to support it at that time, a lot of the bigger agencies were not ready to spend a lot of money on it. I found CWR, who were willing to give me a chance and try it. After writing a grant application the whole process took about a year. Within two years, the medicine was in kids and started to work. (Istplifescience, 2013)

Drawing on his results in animal models, David tested sirolimus with six patients and published his results (Teachey et al., 2006; Teachey, Seif, & Grupp, 2010), which give physicians evidence for prescribing the drug for the treatment of ALPS (Cures Within Reach, 2018b). Daniel notes:

CWR has completed funding for 70 projects, out of which 15 have been successfully completed, and 22 projects are ongoing [at year-end 2018]. Two-thirds of the funding comes from disease-specific philanthropic funders—such as patient advocacy groups or wealthy individuals who are interested in finding a treatment for a particular disease. Another source of funding is corporations, but most of that money is given to us in an unrestricted form. Then the last bit of money comes from our own fundraising activities.

In addition to finding funding sources for repurposing research, Findacure and CWR develop and support alternative funding models. As the CWR case illustrates, charity funding from philanthropists and other sources can only support a limited number of all known rare diseases. Findacure and CWR thus seek to develop approaches that complement philanthropic and public funding for rare diseases. One example is a social financing model for funding clinical trials in generic drug repurposing, a model known as social impact bonds (SIBs) (see Text Box 1).

Rene explains the motivation for the SIB model as follows:

Our primary aim was to set up a new funding mechanism. . .. [A] number of clinicians. . .have ideas for the use of generic drugs for treating rare diseases. But they can't really access funding or industrial support to drive these ideas forward.

Text Box 1: Social Financing: What Is a Social Impact Bond (SIB)?

A SIB is an innovative financing mechanism in which governments or commissioners enter into agreements with social service providers, such as social enterprises or nonprofit organizations, and investors to pay for the delivery of predefined social outcomes (OECD, 2015; Social Finance, 2011). More precisely, a bond-issuing organization raises funds from private-sector investors, charities, or foundations. These funds are distributed to service providers to cover their operating costs. If the measurable outcomes agreed up front are achieved, the government or the commissioner proceeds with payments to the bond-issuing organization or the investors. In reality, the term "bond" is more of a misnomer. In financial terms, SIBs are not real bonds but rather future contracts on social outcomes. (Galitopoulou & Noya, 2016: 4).

So we want to develop a mechanism to promote that. . .to give [these] people a pathway for taking their ideas through the clinical phase.

Applied to rare diseases, the SIB model involves three stakeholders: private investors, government (the National Health Service [NHS] for the United Kingdom), and Findacure. Investors invest in the SIB. Findacure uses the money to support generic drug applications for rare diseases involving high costs currently borne by the government. Successful ideas receive government approval for off-label prescriptions, and the government pays part of the savings back to the SIB. Findacure then uses part of the savings to fund additional clinical trials for other diseases while paying the rest back to investors. Colin explains:

There will be novel economic models for drug development. There are a [few] UK-based organizations...providing new concepts that rely on...therapies [being] too costly. If you can lower the economic burden of healthcare in these indications by, say, 20 percent, this will define the strategy for drug development. . .. These guys are setting up novel concepts of shares..., putting health shares on the market that contribute to drug development and lower the burden of health care costs. A regular person can buy them and get some returns. . .. It's extremely appealing.... You are not obliged to be a pharma company to develop a drug. The three of us can do it. You have to have some prerequisites for responsibilities, some know-how, and some reputation, and that's it. This is what smart patient organization groups do.

To show that the SIB is a viable financial tool for rare diseases, Findacure and CWR developed three proof-of-concept studies. They first developed patient

focus group reports in which they explored current and potential treatment options, the economic and financial burden of the diseases on their patients and patients' families, and patient perspectives. Findacure and CWR then developed health economic models, including cost of illness and budget impact calculations, to estimate the SIB's projected returns (see Table A1). Thus, to propose this novel social financing model, Findacure and CWR exploited a social financing practice from other fields and applied it to the publicly available formulas of generic drugs. The findings reveal that by using their rare disease patient and expert networks and knowledge to develop and fund proof-of-concept studies, Findacure and CWR circumvent a key driver of the rare disease market and government failures.

THE MUTUAL CONSTITUTION OF ORGANIZATIONAL ARRANGEMENTS AND PRACTICES IN GRAND SOCIETAL CHALLENGES

Our study details a theoretical mechanism involving the mutual constitution of the practices contributing to sustainable solutions to a societal challenge and the organizational arrangements that host these practices in the context of simultaneous market and government failures. We now summarize our discoveries and discuss their implications for the practice theory and the literature on organizational arrangements tackling societal challenges.

The process we reveal involves four stages: First, a practice (generic drug repurposing), whose standard of excellence (use state-of-the-art knowledge and resources to cure diseases) is currently embedded in a specific organizational arrangement and strategic intent (pharmaceutical drug discovery in for-profit organizations). Second, the current organizational arrangement engenders market and government failures, limiting innovation for a societal challenge. Field actors perceive that the current organizational arrangement constrains them from achieving the standard of excellence of the practice, thus, from tackling the societal challenge effectively. Third, one or more field actors manifest a strategic intent to reinforce the practice (generic drug repurposing), necessitating new organizational arrangements that can host the practice and enable practitioners to reinforce it according to their standard of excellence. Practitioners and other stakeholders collaborate in new arrangements (researchers, clinicians, patients, entrepreneurs, and philanthropists join from universities, for-profit organizations, and other parts of society). Four, the new organizational arrangements allow novel practices (mobilizing collaboration, leveraging the knowledge creation potential of patients and relatives, and catalyzing funding opportunities) that reinforce the repositioned practice and enable actors to circumvent market and government failures of innovation and sustain the new arrangements.

Although the first and second stages can be deduced from prior work on the relationship between organizational arrangement and practices (von Krogh et al., 2012), they are underexplored in relation to societal challenges, and the third suggests the need for a strategic intent that goes beyond the standards of excellence in practice, but that has sufficient motivational impetus to mobilize other field actors to join new organizational arrangements (Santos, 2012). The fourth stage is novel, suggesting that the act of building new organizational arrangements to liberate a practice leads to new within-field practices seeking to resolve market and government failures of innovation. These new practices then become necessary conditions for sustaining the organizational arrangements.

Implications of Discoveries

Our discoveries provide a unique view into the practices of private nonprofit actors as they attempt to resolve a societal problem perpetuated by market and government failures of innovation. First, our discovery that field actors adhere to the standards of excellence underlying the practice of drug discovery (Erden, Schneider, & von Krogh, 2014; MacIntyre, 1981; Moore, 2002; Moore & Beadle, 2006) to construe market and government failures in the rare disease domain extends scholarly understanding of field actors' responses to simultaneous market and government failures of innovation pertaining to a societal challenge. Curing diseases is the *raison d'etre* for practices in the pharmaceutical and medical sciences. Shaping their standards of excellence accordingly, scientists and physicians strive to advance their practices to understand more about diseases and how to cure them (e.g., Blumenthal, Campbell, Causino, & Louis, 1996). The notion that existing for-profit organizational arrangements were not living up to the standard of excellence—i.e., applying all available means to potentially curing all diseases, including those that lack commercial viability—drove some field actors to seek sustainable solutions rooted in a promising yet less commercially appealing practice of generic drug repurposing. This discovery places social practices and their standards of excellence at the center of field actors' responses to market and government failures of innovation.

In a MacIntyrean perspective, standards of excellence are often motivated by the virtue ethics (or the virtues) of field actors (MacIntyre, 1981). A

fundamental feature of MacIntyre's practice theory is thus that it invokes social norms or a set of collective standards of excellence that guide how practitioners act, solve problems, make decisions, create knowledge, and learn. Disruption and upheaval within organizational contexts—resulting from an inability to perform practices in accordance with such standards in resolving emerging challenges—may lead actors to break away in search of more appropriate, suitable, and compatible organizational arrangements.

In revealing this notion, we add to the literature on the comparative efficacy of organizational/governance arrangements in addressing societal issues (e.g., Luo & Kaul, 2019; Santos, 2012). For example, scholars have posited that the organizational arrangement of social entrepreneurship arises when social entrepreneurs place societal gains over commercial gains to pursue sustainable solutions to neglected problems with positive externalities (Mair & Marti, 2006; Santos, 2012). In line with this theorizing, our findings show that field actors institute or move to novel organizational arrangements that are largely independent from market and government mechanisms (e.g., social enterprise and nonprofit), where they can seek to achieve the standards of excellence of their social practices. Thus, understanding what standards of excellence mean in practices may shed light on the impetus for nonprofits and social entrepreneurship and offer new insights into how to tackle simultaneous market and government failures of innovation.

Our findings show that to reinforce a social practice whose standards of excellence relates to a societal challenge, field actors may seek to orchestrate a set of reinforcing practices within a new organizational arrangement. In our setting, the organizations we studied created a novel context to reinforce the existing practice of generic drug repurposing that would potentially help create treatments for rare diseases by mobilizing collaboration among key stakeholders, leveraging the knowledge creation potential of end users, and catalyzing funding for repurposing opportunities. Importantly, our discovery emphasizes the simultaneous orchestration of these complementary practices in achieving the strategic intent of realizing positive externalities for societal gain and sustaining novel organizational arrangements. Although there might be other reinforcing practices in other settings, the reinforcing practices that we uncovered have several implications.

Seminal work rooted in a community of practice view of knowledge has argued that firms possess an advantage over markets in coordinating diverse knowledge of stakeholders deeply embedded within various communities (Brown & Duguid, 1991, 2001). Knowledge creation in drug discovery and development is a highly complex, costly, uncertain activity spanning the boundaries of many specialized scientific communities, and is thus one area where the need for such community coordination is expected to be optimally addressed through firms. Our discovery demonstrates, by contrast, that some organizational arrangements—other than traditional for-profit firms—may have an advantage for coordinating knowledge creation among diverse stakeholders around a common practice when there exist sufficiently powerful collective virtues and priorities (i.e., strategic intent) to resolve a societal challenge (Nonaka & von Krogh, 2009). Indeed, existing literature on collective action (e.g., Doh et al., 2019; Jones, York, Vedula, Conger, & Lenox, 2019; Lumpkin & Bacq, 2019; Sarasvathy & Ramesh, 2018) highlighted the importance and effectiveness of including relevant stakeholders to tackle societal challenges. We suggest that studying practices and standards of excellence underlying practices of such contemporary "lightweight" organizational arrangements in addition to their governance mechanisms represents an important and intriguing area for future research on knowledge creation in organization studies.

Our discovery of the practice of leveraging patients and relatives as key sources of knowledge creation provides new insights into user innovation theory (von Hippel, 2009; von Hippel et al., 2014). The practice we reveal shows how field actors in generic drug repurposing for rare diseases can organize patients and relatives (users) to migrate into a new arrangement that empowers them to help resolve their own problems. In this way, patients and their relatives stop being on the receiving end of health care and instead become active user "innovators" who can help create societally beneficial knowledge. Whereas user innovation theory (von Hippel, 1986, 2005) explains how users share and organize their own communities, our discovery shows that a MacIntyrean liberation of practices (i.e., dissatisfaction of users that their practices cannot improve sufficiently within the context they are in) is a precondition for the occurrence of user innovation in the context of drug repurposing.

Finally, our discoveries highlight the importance of engaging with supporting/reinforcing practices of catalyzing financial means to sustain a practice which is potentially beneficial for tackling societal challenges. As we show in the case of generic drug repurposing, although the practice itself might be very promising, field actors who are willing to engage in the practice are bounded with conditions of the context they are embedded in. Although field actors might move to novel organizational arrangements, the conditions of the context necessitate field actors to seek financial resources and even develop new means to cultivate financial resources. In line with the research on social finance (e.g., Hangl, 2014;

Lehner & Nicholls, 2014), we suggest that reinforcing practices of developing resources for organizational arrangements that intent on tackling societal challenges continues to represent an important area for future research.

Limitations and Boundary Conditions

The previous contributions need interpretation in the light of several boundary conditions and limitations of our research. One important boundary condition concerns the nature of the positive externality that our informants attempt to capture in their search for a sustainable solution to the lack of rare disease treatments. Opportunities for repurposing generic drugs—products that were initially developed with a strong commercial interest—toward applications in rare diseases arise from (1) the scientific principle that pharmaceutical drugs can have multiple physiological effects and (2) a regulatory context that offers temporary market exclusivity to producers of new drug entities so as to incentivize investments in innovation.

Therefore, the dynamic we observe in the migration of the practice toward the nonprofit arrangement we studied is imbued with the institutional and regulatory characteristics of drug discovery and development. Our data thus limit the conclusions we can draw about the construal of market and government failures by nonprofit actors working on other societal issues. Future research in other empirical settings can deepen scholarly understanding of how actors' construal of market and government failures underlying societal challenges induces these actors to create new organizational arrangements enabling the standard of excellence within a practice. By directing attention to the nature of the positive externality, and the knowledge and resources that underlie it, such studies may provide additional insights.

A second limitation of this study is that we focused our in-depth analysis of the practices surrounding drug repurposing in two nonprofit rare disease organizations. This focus allowed us to deeply investigate practices spanning a wide array of rare diseases—a unique objective in the field of drug repurposing for rare diseases. Yet, other organizational arrangements applying drug repurposing to specific rare diseases, including for-profit social entrepreneurship organizations, also exist. We expect that the practices that we observed and the process through which they emerged are contingent on the nonprofit form that our focal organizations adopted. In particular, the ability to mobilize the efforts of a broad range of external stakeholders (e.g., academic researchers, clinicians, and philanthropists) may be markedly different for social entrepreneurs with a for-profit component. Extending our findings to such related, yet different, organizational arrangements would be an important elaboration of our discovery.

Moreover, the organizational arrangement of the nonprofits we studied was in a state of transformation, i.e., still developing financial models for sustaining their activities (e.g., social impact bonds). Whether these nonprofits will remain so, and whether this arrangement constitutes a more or less congenial environment for drug repurposing as a sustainable solution for rare disease treatments, remains to be seen. Future research may need to focus on whether and, if so, how nonprofits can sustain the standard of excellence in specific practices and combinations of practices.

Third, our data limit the conclusions we can draw about the potential of nonprofit generic drug repurposing for rare diseases to offer a scalable solution to the simultaneous market and government failure. Despite examples of successful repurposing efforts by the nonprofits we analyzed, to what extent the organizational arrangement we studied can offer a structural solution remains unclear. Moreover, our informants generally agreed that whereas generic drugs for rare diseases offer great potential for the many untreated rare diseases, basic R&D investments into new molecular entities will remain necessary as opportunities for repurposing are gradually depleted. Future longitudinal research will need to develop insights into the comparative long-term performance of nonprofits and for-profit social entrepreneurship vis-à-vis more traditional commercial organizational arrangements and novel regulatory frameworks in resolving the societal challenge of untreated rare diseases.

Finally, although our data cover informants from a wide range of organizations and roles involved in drug repurposing, our data and findings on repurposing practices derive from a small number of nonprofit organizations with a small core of employees. Whereas our efforts to triangulate our informants' reports with observational and secondary data provide confidence in the strength of our discoveries, future research will have to corroborate the mechanisms we reveal.

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APPENDIX A

TABLE A1
Results of the Cost of Illness, Budget Impact Modeling, and SIB Projected Returns (Findacure, 2017)

Disease Case	Cost of Illness (Per Annum)	Budget Impact Modeling (Per 5 Years)	SIB Projected Returns (after Repaying Costs)
Wolfram's syndrome	£990,588.45	£672,772.00	£61,782
Friedreich's ataxia	£7,560,471.81	£1,148,493.99	£300,000
Congenital hyperinsulinism	£4,561,827.58	£477,693.12	£840,800

WHEN TO HALT OR CONTINUE? AN ANALYSIS OF PROJECT TERMINATION FACTORS IN THE POSTMENOPAUSAL OSTEOPOROSIS DRUG MARKET

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While the pre-approval cost of developing a drug increased by 166% to $2.6 billion between 2003 and 2013, the success rate of developing a drug decreased by 10%[1]. Recent studies have emphasized that the high attrition rates at Phase II/Phase III clinical trials are the main contributing factor to the decreasing productivity in the pharmaceutical industry[2]. Given the high cost of Phase II/Phase III clinical trials, decreasing late-stage attrition probabilities thus constitutes a key potential solution to the problem of declining R&D productivity.

It is commonly accepted in the drug discovery and development literature that due to organizational, cultural, and behavioral issues decision makers in the pharmaceutical industry tend to push for the continuation of projects even under strong evidence for termination decisions[2–5]. Thus, one strategy for reducing late-stage attrition rates in pharmaceutical R&D is to prevent unnecessary delays during the drug development process by encouraging a "fail early" approach or implementing "quick kill strategies"[3–5]. Cognitive biases of managers and researchers, the language of failure, and insufficient numbers of alternative projects are some of the critical factors that prevent decision makers from opting for termination[5].

While prior research provides critical insights on the dimensions of project success[6] and the implementation of quick kill strategies[5,7], including reframing false positives in terms of opportunity costs[7] and fostering a stopping culture[5], there is still a need for a systematic effort to analyze factors that could further enhance the continuation decisions (i.e., progression-seeking behavior) during the drug development process. A detailed analysis of factors that

contribute to progression-seeking behavior, that we refer to as factors catalyzing progression-seeking behavior, can help decision makers to develop actionable strategies to reduce delays. In our analysis, we aim to identify critical factors that lead to faulty, missing, or biased decisions during the drug development process and eventually cause delays in the termination of drug development projects. We argue that factors such as incentive systems and the sunk-cost fallacy have contributed to a "push-norm" in the pharmaceutical companies that manifests itself in progression-seeking behavior. While it is difficult to change the push-norm and disentangle its exact underlying reasons, decision makers could at least have an influence on the catalyzing factors of progression-seeking behavior and try to tackle delays in termination decisions by addressing issues behind the catalyzing factors.

Toward an understanding of why drug projects are terminated.

By analyzing 11 closed projects in the postmenopausal osteoporosis therapeutic area and assessing why they were terminated (Table 1), we identified factors catalyzing progression-seeking behavior in the drug development process. There are two reasons why we chose the postmenopausal osteoporosis therapeutic area. First, there is little research left in the postmenopausal osteoporosis therapeutic area, and most of the drugs are already generic. This situation provided an opportunity to analyze the field retrospectively and access the relevant data irrespective of confidentiality concerns. Second, prior experience of two co-authors in the corresponding therapeutic area provided the necessary expertise and overview of the field as well as better access to data[8].

We conducted 21 semi-structured interviews with researchers and managers who participated in drug discovery projects of the drugs in our sample and scientific experts in the postmenopausal osteoporosis disease area[8]. In addition to the interviews, we collected publicly available data to develop timelines of drug development projects. The Adis Insight database (Springer, 2017) was used to collect the start of clinical phases, side effects,

approvals, and terminations. The data are complemented by the clinical trials registry of the US National Library of Medicine and reports from the FDA. In our analysis, we covered the period from pre-clinical discovery until the end of human clinical development.

Drug name	Molecular target group	Company	Trajectory
Alendronate	FPPS[3]	Merck	Launched
Risedronate	FPPS	Sanofi	Launched
Ibandronate	FPPS	Roche	Launched
Zoledronate	FPPS	Novartis	Launched
Denosumab	RANKL	Amgen	Launched
Balicatib	Cathepsin K	Novartis	Stopped in Phase II
Relacatib	Cathepsin K	GSK	Stopped in Phase I
Odanacatib	Cathepsin K	Merck	Stopped in Phase III
Romosozumab	Sclerostin	Amgen	Launched
Blosozumab	Sclerostin	Lilly	Stopped in Phase II
BPS 804	Sclerostin	Novartis	Stopped in Phase II

Table 1: Drug candidates in postmenopausal osteoporosis

To prevent retrospective bias, the bias stemming from cases when interviewees retrieve their memories about past events in an incomplete or flawed way[9], we implemented four measures. We specifically asked interviewees to provide information, not opinions. Whenever interviewees were not certain about the information they provided, we asked them to provide the source of information (e.g. reports). We cross-checked the information gathered from diverse sources and used secondary data to confirm the information obtained from the interviews[10–12].

Based on our analysis of 11 drugs, we identified that market-related factors, an abundance of resources, empty pipelines, and individual attachment to drug projects enhance the progression-seeking behavior in the drug development process and may result in delays in termination decisions (Figure 1). We argue that the awareness about factors catalyzing the

[3] FPPS: Farnesyl Pyrophosphate Synthase

progression-seeking behavior can help decision-makers to minimize delays in termination decisions. In addition to demonstrating the factors catalyzing progression-seeking behavior, we also provide five instances in postmenopausal osteoporosis projects where actions of decision makers resulted in delays. Here, while we do not claim to provide an exhaustive list of all possible scenarios, we aim to show that factors catalyzing progression-seeking behavior are manifested in the actions of organizational actors. A close monitoring of these actions by the leadership team, and decision makers in particular, can help prevent delays in drug discovery processes.

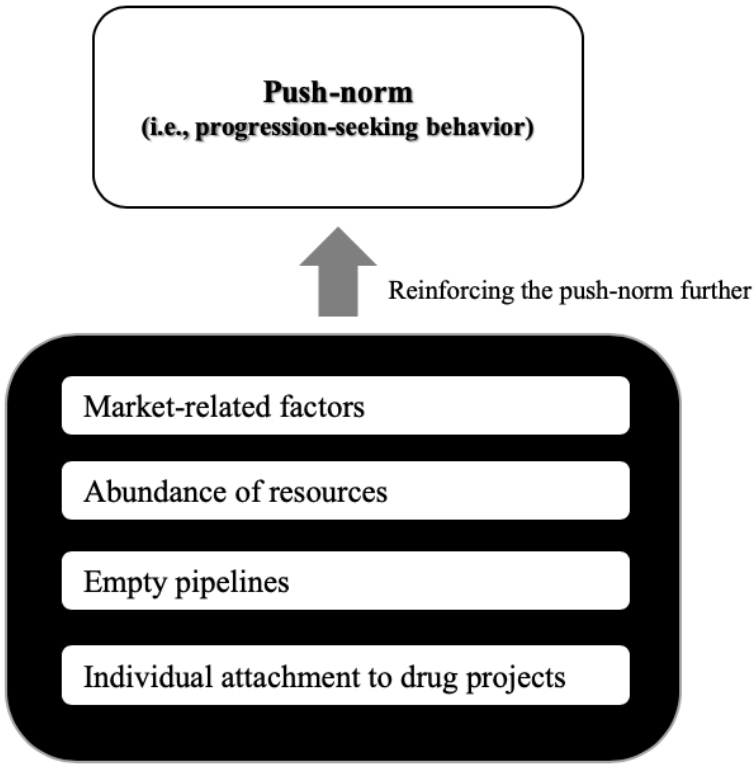

Figure 1: Four factors that enhances the push-norm

Factors catalyzing progression-seeking behavior.

Market-related factors. Our interviewees highlighted that the signals they receive from clinical findings are inherently uncertain due to the nature of the drug development process, and hence, ambiguous. Cases of ambiguous findings are when factors catalyzing the progression-seeking behavior start to weigh in and strongly influence decision making. In this

section, we explore potential biases and ambiguities arising from market-related factors, namely competition and market size.

The competitive landscape is one of the primary factors driving decisions about whether to continue with a drug project. When project teams start evaluating the competitive landscape, they might face two scenarios: a competitor already exists (late-mover) or competition is non-existent (first-mover). Companies primarily want to enjoy the benefits of being the first-mover (first in class), which are market exclusivity and access to health care practitioners and key opinion leaders. Hence, when a drug candidate could potentially be the first in class, our interviewees noted that there is often a cognitive bias toward pushing the projects, although scientific evidence might be ambiguous about its potential success. Indeed, some of our interviewees recalled situations in which one of their competitors terminated their drug project and the potential of being the first-mover encouraged them to continue with their own project.

In the second case, if a drug in a given therapeutic area already exists in the marketplace, pharmaceutical company leaders might be tempted to continue their projects for two reasons. First, knowing that there is already a company that passed through the regulatory hurdle acts as a driver to continue. Second, knowing that there are other companies in the area creates a peer pressure. As one of our interviewees described, having other companies in the same area signals that “there is something to win.” Thus, competitive dynamics might act as a continuation driver, although scientific evidence might not necessarily be supportive.

Market size in a particular therapeutic area is a critical factor that drives a company’s interest. Since drug discovery and development is a costly process, potential market size should justify the amount of investment made to bring a drug to the market. Thus, big markets attract companies not only to initiate a drug project but also to continue it. Indeed, our interviewees highlighted that market size was initially the strong driver for why

companies entered the osteoporosis market in the first place.

Abundance of resources. The amount of available tangible (e.g., financial resources and machinery) and intangible (e.g., expertise and footprint) resources constitutes an important factor catalyzing progression-seeking behavior in drug projects. Financial resources acted as an economic basis for deciding whether to continue. The amount of financial resources and machinery is a tricky concept. While the unavailability of sufficient resources is clearly a stopping criterion, the availability of too many resources acts as a go-driver that might lead to delays. Interviewees repeatedly emphasized that when companies are "loaded with money" after a successful project (e.g., a launch of a blockbuster), they can afford resourcing many development projects, and this perception may motivate decision makers to continue projects that are unlikely to be successful. For example, one of our interviewees recalled a case where there was only marginal benefit compared to the standard of care, but the company still decided to continue with the project because financial resources were available.

When companies focus on certain therapeutic areas for a long time, they establish a footprint in the area, which not only provides them with high-level expertise in terms of the development process, science, technology, regulatory hurdles, sales force and the launch process, but also the necessary set of lab equipment and machinery. Our interviewees emphasized that a footprint in a given area acts as a push-driver to continue drug projects. The interviewees described this situation as a "keep the ball rolling" approach to the decision making. The availability of human resources, machinery, sales force, and so on drove the continuation of a drug project. In one case, an interviewee said that they had a good machine to run clinical trials in osteoporosis as well as the people working in the clinical operation and the sales force. Oftentimes, a challenge that the leadership faces is "what are you going to do with all those people waiting for the next big molecule?" The interviewee emphasized

that “these are not valid arguments that can drive success—although having an established sales force may prevent investments [after launch], . . . if the drug does not add value, what’s the point?” Thus, the path-dependency in a given area might create a tendency toward pushing projects. Furthermore, since companies with a footprint in a therapeutic area had a positive experience in the past, they might be overly optimistic about “fixing the ends” in a follow-up project.

Empty pipelines. An insufficient number of projects in a company’s pipeline is an important factor in whether to continue with a drug project, in the case of small companies in particular[5]. There might be tendencies to push projects just because the company pipeline is empty. It is a risky criterion since the decision is not entirely based on whether the project is worthwhile, but rather the perception of a need to continue due to the lack of alternatives. Interviewees highlighted that in the case of empty pipelines, decision makers push the project without carefully evaluating its promise. As our interviewees emphasized, this is not the right motivation to continue a project since it is not based on facts and probabilities of success. In one of the cases, the company indeed continued with a project that eventually failed. The interviewee interpreted this situation as “there was a hole in the pipeline at that point. Is that the right thing to do? Probably no! The drug failed.” We observed that empty pipelines especially acted as a push-driver when there is an abundance of company resources.

Individual attachment to drug projects. While the desire for achieving successful outcomes is clearly one reason behind why it is so difficult to stop, another factor we discovered is the internal motivations of researchers and preferences of individuals in leadership positions also cause delays in termination decisions. Researchers have typically very high attachment to the drugs that they are working on, and their intrinsic motivation and curiosity to push for the success of the project because they have devoted significant amounts of “blood, sweat, and tears” in their work. Researchers are also often very much convinced

about the potential value of their work and encouraged by their companies to believe in their work. Thus, it is often challenging for researchers to provide evidence for the termination of their drug projects as it feels for them "as if giving up their baby."

Especially when researchers are highly specialized, and the continuation of a drug project strongly relates to their careers and jobs, their dependency on a particular drug project increases and hence, they may show a greater tendency to push for project continuation. The attachment of researchers to their drug projects lead to biases in the way they interpret data and information. One interviewee reflects on his experiences and notes that he often observed cases where researchers attribute a very high value to a little piece of data to justify continuation of their drug projects due to emotional reasoning (often called confirmation bias). Similarly, researchers might have tendencies to present or interpret the data in a biased way.

Our interviews showed that not only researchers' attachment to drug projects but also top managers' personal preferences influence the decision-making process about a drug project. Prior experience and academic backgrounds of managers shape their personal beliefs as well as interests, which in turn lead to biases. One interviewee recalled a case when the project leader's prior specialization was cancer, and he was convinced that the drug candidate causes cancer despite opposing evidence from pre-clinical studies and safety assessment tests. Interviewees repeatedly emphasize that although many formal procedures for decision making are in place, the final decision about continuation or termination depends on a few key opinion leaders or project champions, members of the senior leadership team who have sound knowledge and a strong interest in a decision area. Thus, depending on the opinion of a few people from the leadership team makes the process itself susceptible to personal biases.

Instances of progression-seeking behavior in post-menopausal osteoporosis disease area.

In our analysis of the post-menopausal osteoporosis drug market, we observed

instances when decision makers acted in a way to justify their continuation decisions by presenting arguments that subsequently resulted in delays. While we argue that such actions might be taken because of the inherent uncertainty of the drug development process, we invite the leadership to bring more attention to such arguments because they are intermingled with the push-norm in pharmaceutical companies.

Hope to mitigate side effects. Project teams might delay the decision to critically evaluate safety concerns ("side effects") during later phases of the drug development process. In addition to progression-seeking behavior stemming from organizational factors including pipeline considerations, resource availability, and decision-maker preferences, project teams' hope to mitigate side effects in the next phases of clinical trials is often used as an argument to justify continuation. However, our findings revealed that most projects with early safety concerns were terminated at later stages. Hence the hope to mitigate side effects resulted in delays to terminate.

Delay in integrating information that does not support the continuation decision. We observed that project teams may have tendencies to delay immediate decision making when new safety information becomes available. For example, interviewees highlighted that when it was found Balicatib (a cathepsin K inhibitor) could cause morphea and associated skin lesions, new information about morphea was not immediately incorporated into the decision-making process for other cathepsin K inhibitors. This example is one among many in which project teams have positive biases toward project continuity, and they were not reactive enough to new information that may be an important signal to terminate drug projects.

Selection of risky compounds. We also found that decision makers could be biased toward choosing drug candidates with higher potency since these are often considered to be more promising. However, in certain cases, the choice of a lower-potency candidate can

prevent unexpected side effects in the later stages of clinical trials, and hence reduces late-stage attrition rates. Indeed, one of our interviewees recalled an instance in which their competitor argued that a less potent compound is the better choice because there is lower risk of the rare side effects of jaw osteonecrosis based on their experience with a high-potency candidate. Thus, project teams may be committed to a high-potency candidate, and thus ignore its potential safety concerns.

Hope to find a way around existing patents. The patent landscape is one of the primary decision drivers in the pharmaceutical research process. Not being able to argue for having the freedom to operate and the right to exclude their competitors is a major criterion for halting development. However, legal experts in the pharmaceutical industry typically seek ways to circumvent existing patents. Our interviewees revealed that a cognitive bias might stem from the possibility of eluding patents. For example, a common practice in the pharmaceutical industry is to move development activities into countries where patent protection does not exist or is not enforced. Similarly, when the right to exclude is not provided, companies might try to reformulate the drug candidate to push for project continuation. Thus, having the possibility of eluding patents through expanding to new geographical locations or drug reformulation may cause delays in terminating a project.

Exaggeration of market size. Since market size estimates at earlier stages are inherently uncertain, there is a risk that market sizes are overestimated in a way that it leads to an argument to continue the project. Drug project managers who want to continue with the project might use market size estimates as a supporting argument. A potentially large market size can also lead to bias for continuing high-risk projects. Company leaders are loathe to miss the chance of accessing big markets and thus may push projects forward even in instances of weak scientific evidence. While uncertainty in market size estimates cannot be

entirely eliminated, large market size potential should not outweigh scientific indications of little or no effectiveness.

Lessons learned from the case of postmenopausal osteoporosis drug development

Based on our analysis of 11 drug candidates in the postmenopausal therapeutic area, we identified factors that catalyze the push-norm, progression-seeking behavior in companies, which leads to delays in project termination in drug development processes. Although challenges remain about reducing uncertainties and ambiguities in decision-making processes, pharmaceutical company leaders can nonetheless identify guidelines to minimize biases and integrate decision parameters to reinforce early termination. Based on this research, the following may apply:

- First-mover advantages should not outweigh the decision-making process in favor of drug project continuity. “Peer pressure” should not be the primary motive for entry into or continuation of drug development projects.
- Market size estimates must be involved in decision making early in the drug development process, but a large market potential should not serve as the sole driver for project continuation.
- Early safety signals should be taken as a clear termination reason unless there is clear scientific evidence on how they can be mitigated.
- Sufficient financial resources must not be a continuation driver. Similarly, resources such as expert knowledge about the regulatory pathway and launch processes or an in-place sales force are contraindicated as primary drivers of continuation decisions. Our data show that projects given the green light to continue due to resource-related arguments failed at a later stage and therefore created time lags.
- Decision makers can be made accountable for potential long-term implications of their actions through incentive mechanisms. Long-term accuracy of market estimates,

sales forecasting, or predicted technical probabilities of success should have a direct impact on bonuses.

- Leaders must be aware of interpretation biases that may derive from researchers' individual biases. Hence, triangulation activities, such as collecting and comparing interpretations from multiple sources, is suggested to reduce or eliminate bias in decision making.
- While eliminating biases may be challenging and require a significant time investment, leadership must also ensure that other delay-prevention mechanisms are in place. Examples include, inter alia, early consideration of clinical endpoint availability and whether additional endpoints are needed, the potential threat of entrants to the same market, and patient convenience as well as billing habits of physicians.

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10. CV

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ACADEMIC POSITIONS

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PUBLICATIONS

[1] Kucukkeles, B., Ben-Menahem, S., & von Krogh, G. (Forthcoming). Small Numbers, Big Concerns: Practices and Organizational Arrangements in Rare Disease Drug Repurposing. ***Academy of Management Discoveries.***

WORKING PAPERS

[2] Kucukkeles, B., Ben-Menahem, S., & von Krogh, G. Concurrent and Retrospective Resourcing Practices: Evidence from Pharmaceutical Industry. **Manuscript in preparation for submission to Administrative Science Quarterly.**

[3] Kucukkeles, B., Anthamatten, T., Ben-Menahem, S., von Krogh, G., Goldhahn, J. When to Halt or Continue? An Analysis of Project Termination Factors in the Postmenopausal Osteoporosis Drug Market. **Manuscript in preparation for submission to Nature Reviews Drug Discovery.**

ACADEMIC PRESENTATIONS

Kucukkeles, B., Ben-Menahem, S. & von Krogh, G. New Uses for Existing Resources: A Case of Drug Repurposing. **11th International Symposium on Process Organization Studies**. Crete, Greece, June, 2019.

Kucukkeles, B., Ben-Menahem, S. & von Krogh, G. Role of Reuse in Grand Challenges: A Case of Rare Disease Drug Development. **AOM Specialized Conference: From Start-up to Scale-up**. Tel-Aviv, Israel, December, 2018.

Kucukkeles, B., Ben-Menahem, S. & von Krogh, G. Understanding the Role of Reuse in Grand Challenges: The Case of Rare Diseases, **Strategic Management Society Conference**, Paris, September, 2018.

Kucukkeles, B., Ben-Menahem, S. & von Krogh, G. Systematizing Serendipity: Constructing Need- and Solution Spaces for Facilitating Serendipitous Opportunities. **Israel Strategy Conference**, Haifa, Israel, December, 2017.

Kucukkeles, B., Ben-Menahem, S. & von Krogh, G. The Emergence of Resourcing Practices in Epistemic Communities: The Case of Drug Repurposing. **Academy of Management Annual Meeting**, Atlanta, August, 2017.

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Kucukkeles, B., Ben-Menahem, S., von Krogh, G., Innovating Through Problem-solving Without Problem Formulation: Evidence from Drug Repositioning. **Strategic Management Society Conference**, Denver, US, October, 2015.

Kucukkeles, B., Ben-Menahem, S. & von Krogh, G. The Division of Labor Between Human and Computerized Technologies: A Problem-Solving Perspective. **OUI** (Open and User Innovation Society Meeting), Lisbon, July, 2015.

Kucukkeles B., Ben-Menahem S, von Krogh G. Dominant logics of problem solving for innovation: Lessons from drug discovery. Paper presented at the 31st **EGOS** Colloquium, Athens, Greece, July, 2015.

INVITED TALKS & SEMINARS

Kucukkeles, B., Academic Drug Discovery in Rare Diseases Symposium, poster presentation, Rare Disease Initiative Zurich, University Hospital Zurich, November, 2018.

Kucukkeles, B., Ben-Menahem, S. & von Krogh, G., Field Level Origins of Resourcing Practices, Brownbag Seminar, Department of Business Administration, University of Zurich, March, 2018.

Kucukkeles, B., Comprehensive Survey Analysis of Drug Repurposing Sector, 5th Annual Drug Repositioning, Repurposing, and Rescue Conference, Chicago, USA, May, 2016.

Kucukkeles, B. Seminar on Need-Solution Problem Solving, Faculty of Economics, and Management, Strasbourg University, May, 2016.

PROFESSIONAL SERVICES

Ad-hoc Reviewer	European Management Journal, AOM Annual Conferences (Awarded with the **ABCD Best Reviewer Award** – OMT division, 2017), SMS Annual Conferences, ISC (Israel Strategy Conference)
Part of the Editorial Team	Information Systems Journal (ISR)
	Between 2014-2015, I assisted the editorial team running the ISR Special Issue on Collaboration and Value Creation in Online Communities (Senior Editors: Samer Faraj, Karim Lakhani, Eric Monteiro, Georg von Krogh).

TEACHING

Management Research – Research Design and Qualitative Methods Module, Department of Management, Technology, and Economics, ETH Zurich, Master level (Semesterly between Fall 2014- Fall 2019)

Industry and Competitive Analysis – Resources and Resourcefulness in Organizations Module, Department of Management, Technology, and Economics, ETH Zurich, Master level (Fall 2018, Fall 2019)

Open and User Innovation, Lead User Innovation Module, Department of Management, Technology, and Economics, ETH Zurich, Master level (Fall 2019)

Translational Science and Health, Department of Health Sciences and Technology, ETH Zurich, Master level (Fall 2017, 2018)

SUPERVISION

Master Thesis

Claudia Carina Andrade Aramayo, Transformation of Development Projects to Independent Organizations, Fall 2018.

Stefan Odermatt, Global Market Entry Strategy and Technology Acceptance Perspective of an AI Startup targeting the Healthcare Market, Spring 2018.

Adrian Widmer, Building-up competitive advantage in the US custom software market as software service provider, Fall 2018.

Tino Anthamatten, Drivers of Go and No-Go decisions in drug development, Fall 2017. ***Awarded with the ETH Medal***, the best master thesis in the Department of Management, Technology, and Economics, ETH Zurich in 2017.

Valerie Chardonnens, Companies Operating in Small Markets with High Innovation-Cost Environment: Conditions that lead to a potentially good Business Model for Pharmaceutical Companies in Rare Disease Drug Development, Spring 2016.

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Arnaud Pincet, What Factors Drive the Collaboration between SMEs and Universities? A Comparative Case Study between Massachusetts and the DACH Region, a Motivational Approach to Knowledge Management, Spring, 2015.

Manveer Bahadur, Prospects of Synergy: A Business Performance Strategy, Fall 2014.

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Semester Projects

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PEDAGOGICAL TRAINING

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Using Rubrics to Grade, Assess and Improve Student Learning, ETH Zurich, Educational Development and Technology Center training, November, 2018.

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MISCELLANEOUS

Languages	English (fluent), Turkish (mother tongue), Spanish (intermediate), Italian (intermediate), German (beginner).
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