Stage-gate process for life sciences and medical innovation investment

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A R T I C L E   I N F O

A B S T R A C T

Life science innovation has led to significant improvements in clinical outcomes and has been a source of financial growth for individuals and institutions capable of performing appropriate investments in this sector. Several groups have developed methodologies to assist medical technology innovators in the design and development activities. Unfortunately, these tools have not aided the general investment community to profit from these enterprises. This situation has contributed to a general reduction in risk capital directed towards life sciences compared to other industries. We review the current investment practices in the life science sector and present a comprehensive stage-gate model that aims to captures this investment process. An analysis of best practices and in-depth interviews with 68 life sciences investors and entrepreneurs worldwide are used to support such model. A single case-control study comparing life science investment execution within two similar investment firms was conducted to evaluate feasibility in the implementation of these practices. The stage-gate model includes (I) General vision and investment strategy definition; (II) Venture search, screening and rapid pre-evaluation; (III) Due diligence and negotiation of terms; (IV) Portfolio management, evaluation, and exit. The difference in execution of investment and results from a post-performance Root Cause Analysis were consistent with a reduction in perceived risk from the case company trained with the proposed model compared to the control. This suggests that our developed model and process may be useful in encouraging life sciences investment via evidence-based evaluations.

1. Introduction

Over the past two centuries, medical innovation has dramatically changed the way we manage, treat and perceive disease (Brodsky, 2010). Consequently, it has been through appropriate technology development that clinicians, engineers, and scientists have enabled millions to live longer and, to a certain extent, healthier lives (Fuchs and Sox, 2001; Grimes, 1993). Hundreds of biomedical advancements have since taken the form of new procedures, compounds, tools, policies or guidelines, many of which have even become standards of care in the last decades (Bauchner et al., 2016; Howell, 1996). Consequently, medical innovation has proven to be not only necessary for society, but also an increasingly valuable economic activity (Cutler, 2007; Porter, 2010; Webster, 2002), capable of becoming an attractive basis for ambitious businesses (Drucker, 2014).

In general, life science products such as medical devices, pharmaceuticals, biologicals and biotechnological systems are commercialized within a highly regulated and multidisciplinary environment (Maak and Wylie, 2016). This situation has certainly defined a range of product development processes unique to this industry (Curfman and Redberg, 2011) fields. Among these models, the so-called Biodesign process (Zenios et al., 2015) has become a hallmark in medical devices and life science entrepreneurship. This process has become increasingly relevant for development teams as it presents useful strategies to guide technical activities and milestones in the pathway to commercialization of life-science technology, from ideation to market deployment. Consequently, Biodesign-like courses in academic and research settings are now offered more frequently than before, which has also encouraged public and private sponsors to embrace the idea of enabling social impact by supporting student-generated life science ventures (Asch and Rosin, 2015; Sinha and Barry, 2011).

Despite the many positive consequences that the development of the Biodesign process has brought to the life science innovation community, its value to inform prospective investors regarding best practices in the selection of promising ventures is questionable. This gap is especially apparent during evaluation of early-stage investments, where substantial additional resources are required to complete product development, clinical testing, regulatory approval, and commercializa-

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tion, all of which are necessary milestones to confirm market potential. Indeed, previous stage-gate models in life-sciences pertain primarily to product development activities and do not provide enough guidance to prospective investors on how to conduct other critical activities such as the filtering, selection, negotiation, and management of life-science ventures. Furthermore, convenient tools to formally evaluate promising life science investment prospects are virtually absent, and specific guidelines to perform other important tasks such as early-stage valuations in this sector remain largely unaddressed (Girling et al., 2010). Consequently, the process of executing private investments in the life science sector continues to be tedious, complex and particularly heuristic (Ioannidis, 2015a). This situation emphasizes the need for intuitive models capable of mitigating investment risk, through the dissemination of the general principles that define a successful life science investment cycle.

The lack of representative models and efficient risk mitigation strategies for life science investors is a critical gap capable of negatively impacting capital investment in this industry. For example, a recent study evaluating US investment trends from 2010 to 2015 observed a 15.8% decline in all-stage life sciences risk capital as a percentage of total investments, with the most significant reduction in capital injection being attributable to early-stage healthcare projects (Fleming, 2015). This decrease in life sciences investment has occurred despite a 95% increase in the total amount of venture capital injected across all other US industries totaling $39.6 Billion in 2015. Indeed, investment decline is usually a consequence of changes in risk perception. Several national and international metrics in medical research confirm the existence of significant gaps that limits the translation of scientific discovery into clinical and economic value (Moses et al., 2015). These observations are consistent with a perception of higher investment risk.

Considering that the investment community is currently shifting away from life sciences to other sectors, as well as within life sciences from early stage to late-stage investments, it is critical to understand the root causes of these changes to implement reforms capable of reversing it. The typical hypothesis explaining life science investment shifts proposes that medical technology investment has just become riskier over the years due to increased regulatory scrutiny and other market constraints (Bergsland et al., 2014; National Venture Capital Association, 2013). Ironically, it appears that innovation in life sciences happens much more frequently and within a much more informed framework than ever before (Collins, 2015; Holmes, 2016). This situation should reduce the risk for stakeholders, suggesting that current investment shifts are not only attributable to lack of promising projects or stringent market hurdles, but also to a mismatch in risk perception among investors and entrepreneurs.

The presence of numerous life-science products reaching commercial success every year shows that it is at least possible for informed investors to profit from entrepreneurship in this sector (Fernald et al., 2015). Therefore, it is desirable to understand how these groups can identify medical innovation with enough potential to be translated into successful ventures. Elucidating this process is paramount to revert declining life-science investment trends, enhancing the ability of these companies to create value. Providing clarity in this investment process will also help innovators account for the investor's risk while navigating through the regulatory, reimbursement, and clinical hurdles while keeping reasonable timelines and budgets. Here we aim to investigate the general process of life science investment, and to propose a simplified model to inform potential investors regarding best practices and an effective toolkit to democratize these opportunities.

2. Methods

The purpose of this study is to present a comprehensive stage-gate model of life science investment developed through in-depth interviews with 68 life sciences investors and entrepreneurs conducted between April 2014 and April 2016. Selected interviewees (ages 46.6 ± 10.8 years) had at least seven years of prior experience in life science investment activities and comprised senior professional staff from angel investment groups, venture capitalist firms and technology incubators based in the United States, Europe, Latin America, South East Asia and the Middle East. The interview process was conducted in agreement with a previously reported methodology (Pietzsch et al., 2009) used to inform medical device design and development processes, but adapted to generate a framework useful for investors. Unstructured interviews were the primary source of information used throughout this investigation. Despite its qualitative nature, this particular interview process was selected to add flexibility in the questioning of interviewees during the discovery and definition of our investment model. Furthermore, an unstructured interview format is a standard approach in the investigation of many unknown processes, which can lead to more comprehensive process descriptions than those potentially generated from structured interviews, which do not allow for clarification and additional interrogation of interviewees. All interviews were conducted remotely (via telecommunication) by two interviewers based in Boston MA, USA, and Mexico City, Mexico respectively, and comments were captured continuously during each interview session.

Apart from the previously described interview process, other experts and key opinion leaders from relevant stakeholder groups were also consulted during the drafting, evaluation, and refinement of the proposed investment model after interviews were already conducted. These experts were independent of the investors and entrepreneurs interviewed for this study and included executive personnel from early- and late-stage life science ventures that were involved in at least one capital investment event within the year preceding the study. Other consulted experts included hospital administrators, physicians, regulatory strategists, reimbursement advisers, insurance representatives, as well as managers in charge of product development, engineering, clinical testing, manufacturing, marketing, and sales of medical devices, pharmaceuticals, biologicals and in-vitro diagnostics. The role of these informal consultations was to provide clarification of terms, conditions and activities reported during interviews.

After interview responses, had been collected, all available information was analyzed to generate hypotheses regarding the underlying activities involved in successful life sciences investment. These activities were included in our model definition and included specific evaluation events leading to risk reduction, as well as stage gates acting as milestones leading to investment execution. The draft model was presented to interviewees to be revised and improved iteratively. This methodology followed a well-established research technique known as grounded theory building (Corbin and Strauss, 2014) that can be used to describe complex phenomena such as investment processes from a combination of empirical assessments (e.g. structured or unstructured interviews) and previously available information from literature (Pietzsch et al., 2009). A schematic showing the sequence used in the conduction of these interviews, as well as the structure of the initial and secondary phases of assessment is presented in Fig. 1. Columns in Fig. 1 denote the type of interviewed investor, while rows denote the different rounds of interviews. Boxes and parallelograms indicate specific activities in the interview process. Convergence in the model was measured by a reduction in requests for change between assessment rounds.

The sequence of tasks performed to construct, revise and refine our proposed life science investment model comprised the following activities:

a) Initial evaluation of life sciences investment practices and available standard operating procedures (SOPs) from eight interviewees actively involved with angel, venture, and corporate investment groups.

b) Identification of functional groups of experts, advisors, and consultants involved in the evaluation of prospective investments.